UNIVERSIDADE ESTADUAL DE CAMPINAS

FACULDADE DE CIÊNCIAS MÉDICAS

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FROUXIDÃO VAGINAL – DA INVISIBILIDADE AO DIAGNÓSTICO E TRATAMENTO

VAGINAL LAXITY – FROM INVISIBILITY TO DIAGNOSIS AND TREATMENT

CAMPINAS

2023

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Tese apresentada ao Programa de Pós-Graduação em Tocoginecologia da Faculdade de Ciências Médicas da Universidade Estadual de Campinas como parte dos requisitos exigidos para a obtenção do título de doutora em Ciência da Saúde, área de concentração em Fisiopatologia Ginecológica.

Thesis presented to the Post-Graduate Program of Obstetrics and Gynaecology from the School of Medical Sciences of the University of Campinas as part of the requirements needed for obtaining the PhD degree in Health Sciences, with a concentration area of Gynaecological Physiopathology.

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ESTE TRABALHO CORRESPONDE À PRIMEIRA VERSÃO DA TESE DEFENDIDA PELA ALUNA GLÁUCIA MIRANDA VARELLA PEREIRA, E ORIENTADA PELO PROF. DR. LUIZ GUSTAVO OLIVEIRA BRITO.

CAMPINAS

2023

Ficha catalográfica
Universidade Estadual de Campinas
Biblioteca da Faculdade de Ciências Médicas
Maristella Soares dos Santos - CRB 8/8402

P414f

Pereira, Gláucia Miranda Varella, 1981-
Frouxidão vaginal - Da invisibilidade ao diagnóstico e tratamento / Gláucia Miranda Varella Pereira. – Campinas, SP : [s.n.], 2023.

Orientador: Luiz Gustavo Oliveira Brito.
Coorientador: Cássia Raquel Teatin Juliato.
Tese (doutorado) – Universidade Estadual de Campinas, Faculdade de Ciências Médicas.

1. Disfunção do assoalho pélvico. 2. Frouxidão vaginal. 3. Disfunção sexual feminina. 4. Sintomas vaginais. 5. Ultrassom. I. Brito, Luiz Gustavo Oliveira, 1980-. II. Juliato, Cássia Raquel Teatin, 1975-. III. Universidade Estadual de Campinas. Faculdade de Ciências Médicas. IV. Título.

Informações Complementares

Título em outro idioma: Vaginal laxity - From invisibility to diagnosis and tratment
Palavras-chave em inglês:
Pelvic floor dysfunction
Vaginal laxity
Female sexual dysfunction
Vaginal symptoms
Ultrasound
Área de concentração: Fisiopatologia Ginecológica
Titulação: Doutora em Ciências da Saúde
Banca examinadora:
Luiz Gustavo Oliveira Brito [Orientador]
Zilma Silveira Nogueira Reis
Elizabeth Alves Gonçalves Ferreira
Maria Laura Costa do Nascimento
Rodolfo de Carvalho Pacagnella
Data de defesa: 25-08-2023
Programa de Pós-Graduação: Tocoginecologia

Identificação e informações acadêmicas do(a) aluno(a)
- ORCID do autor: https://orcid.org/0000-0003-4697-5295
- Currículo Lattes do autor: http://lattes.cnpq.br/8072128386816527

COMISSÃO EXAMINADORA DA DEFESA DE MESTRADO/DOUTORADO

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Data de Defesa: 25/08/2023

DEDICATÓRIA

Às mulheres com frouxidão vaginal ...

AGRADECIMENTOS

“ Você conhece todas as teorias, domina todas as técnicas, mas para tocar uma alma humana, seja simplesmente outra alma humana. ” Carl Gustav Jung

Essa tese foi construída por muitas mãos. Ao longo de sua escrita relembro com profunda gratidão de cada ideia nascendo, de cada aula na pós-graduação, de cada parceria firmada, da colaboração de colegas e funcionários, do comprometimento das pacientes, das horas dedicadas à escrita ... e toda essa jornada foi guiada pelos meus queridos orientadores, apoiada pela minha família e inspirada por Deus.

Agradeço a Deus por me guiar em mais essa caminhada. Gratidão pela proteção e bênçãos diárias.

Agradeço a Fundação de Amparo à Pesquisa do Estado de São Paulo, FAPESP, pelo apoio a todos os projetos desenvolvidos para a presente tese de doutorado e pelo indispensável suporte durante o estágio de pesquisa realizado em parceria com a Imperial College London e Chelsea and Westminster Hospital em Londres – Reino Unido no período de julho a dezembro de 2022 por meio dos processos nº 2019/26723-5 e nº 2021/13700-7, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).

Ao meu querido orientador, Professor Luiz Gustavo Oliveira Brito, que esteve ao meu lado a cada passo, incentivando e fazendo acontecer cada ideia, abrindo portas e inúmeras oportunidades. Você acreditou em mim e me impulsionou a enfrentar cada desafio que aparecia em nosso caminho. Você é um realizador de sonhos! Quão privilegiada eu sou de ter sido sua orientanda. Quanta gratidão e admiração eu tenho por você! Obrigada por tudo e por tanto!

Não posso deixar de enaltecer o papel da minha querida co-orientadora, Professora Cássia Raquel Teatin Juliato, ao longo desses quatro anos de aprendizado. Gratidão imensa por todo incentivo e suporte ao nosso projeto, desde o recrutamento no ambulatório, passando pela coleta de dados, até a escrita e organização da tese. Agradeço também as inúmeras oportunidades a mim ofertadas. Obrigada por ser exemplo de excelência!

À Dra Cristiane Martins Almeida e ao Dr Kleber Cursino de Andrade, que tomaram o projeto de pesquisa como seus, dedicando não só as suas expertises na coleta de dados ultrassonográficos, mas também um tempo precioso em suas agendas para atender com excelência, paciência e com muito carinho cada participante da pesquisa. Agradeço o precioso aprendizado, acompanhado de carinho e cuidado, aliados a uma parceria impecável. Gratidão imensa!

Ao setor de Ecografia do Caism, com destaque para o Dr Rodrigo Jales e Dra Renata Belluomini, que me receberam com muita atenção e delicadeza, disponibilizando os aparelhos e espaço para a coleta de dados. Agradeço ainda a Dra Isabella Valente, que contribuiu enormemente com a sua expertise e que esteve sempre disposta a ajudar no que fosse necessário. Esse projeto também é seu! Agradeço também a Dra Maira Mazzer, que também abraçou o projeto, dando todo o apoio durante a coleta de dados. A minha gratidão às queridas enfermeiras Dona Jandira, Maria Aparecida, Geneci e Genilda pela doação de seus esforços com entusiasmo e alegria!

Ao Setor de Fisioterapia do CAISM, e principalmente à querida Dra Marcela Ponzio Pinto e Silva, que abriu as portas do setor e de seu coração para acolher o Projeto de Pesquisa, disponibilizando o espaço e os materiais que foram necessários para o conforto e bem-estar das participantes. Agradeço ainda todas as oportunidades de aulas e aprendizado constante com toda equipe da Fisio! Gratidão às queridas Dra Mariana Maia, Dra Andrea Marques, Dra Marcela Bardin, Dra Ticiana Mira, e Dra Camila Araújo. Gratidão ainda à querida Denilsa que recebeu com carinho cada participante durante a coleta de dados. Muito grata também às queridas colegas fisioterapeutas Júlia Fante e Taís Beltramini pelo empenho, dedicação e paciência na aplicação dos questionários. Sem vocês, a coleta não seria possível! Gratidão!

À Natália Martinho, que empregou os seus talentos na análise do ultrassom 4D e que com muita paciência me ensinou um pouco do universo da ultrassonografia funcional do assoalho pélvico. Muito obrigada pela parceria!

Ao Ambulatório de Uroginecologia, onde aprendi tanto e pude realizar a coleta de dados com toda a estrutura necessária. Agradeço às tardes de quartas e quintas, aprendendo com cada discussão de caso e podendo contribuir também durante o Programa de Estágio Docente. Gratidão às Professoras Dra Cássia Juliato, Dra Daniela Yela, Dra Lúcia Paiva, ao Professor Dr Luiz Gustavo Brito, aos Dr. Edilson Castro e Dr João Paulo Pinto e aos amigos Rodrigo e Sara!

Ao Departamento de Tocoginecologia, por nos proporcionar um universo de excelência em conhecimento e em pesquisa! Gratidão imensa aos professores com quem tive a honra de ter aula durante às disciplinas de doutorado. Gratidão aos queridos Dr Luiz Gustavo Brito, Dra Maria Laura Nascimento, Dr Rodolfo Pacagnella, Dr Luiz Francisco Baccaro, e Dra Diama do Vale. Gratidão também à Melissa, que nos atende com tanta atenção e solicitude! Gratidão ao Helymar Machado, nosso estatístico por emprestar gentilmente sua competência e dedicação ao realizar nossas análises de dados.

Gratidão ao Hospital da Mulher Prof. Dr. José Aristodemo Pinotti – Caism, onde os projetos de pesquisa tomam vida, acolhendo todos os alunos de doutorado em um ambiente maravilhoso de cuidado e respeito às mulheres. Agradeço ao setor de Informática e em especial aos queridos Lúcio, Rita, Alexandre, André e Wagner. Gratidão!

Gratidão aos amigos que o Departamento de Tocoginecologia me proporcionou: Charles, Odette, Guta, Samantha, Marcela, Maria Cecília, Claudinha, Anna Lygia, Camila, André e Euller! Que alegria comemorar com vocês as nossas conquistas e porque não, os perrengues! A gente acabava dando um jeito de ficar tudo bem no final! Gratidão imensa!

To my dear supervisor, Dr Rufus Cartwright, for all your support and guidance during my six months of research at Imperial College London and Chelsea and Westminster Hospital. You opened many paths and provided me with unique moments in Urogynecology. Gratitude to the entire Urogynecology team at Chelsea and Westminster Hospital and especially to Dr Claudine Domoney, for believing in and embracing the research project. It was an honour to accompany her in the sexual dysfunction consultations. Gratitude to the entire Physiotherapy team at Chelsea and Westminster Hospital and especially to Dr Miti Rach, who welcomed me into her sector with so much affection and where I could participate in training and acquire so much knowledge. To Professor Mark Johnson, Director of Research and Development at Chelsea and Westminster Hospital - Imperial College London, for the unique opportunity to be a Visiting Research in his department until 2025. To Dr Stelios Myriknas for the warm welcome and discussions about perineal trauma.

À minha querida família! Agradeço todo o apoio e amor que me sustentaram ao longo desses quatro anos de doutorado. À minha querida mãe e ao meu pai (sempre presente) que me fizeram acreditar que tudo é possível com esforço, dedicação e amor. À Ju, que esteve ao meu lado nos momentos mais desafiadores desse doutorado. À minha querida irmã e sobrinhas por vibrarem comigo por mais essa conquista. Ao Max pelo companheirismo. Aos queridos Tia Maria José, Cris, Sérgio, Bruno, Brenda e Flávio, que me acolheram em Campinas com tanto amor e cuidado. Gratidão eterna a cada um de vocês!

Aos queridos componentes das Bancas de Qualificação e Defesa, que aceitaram lapidar esse trabalho que foi feito com tanto carinho. Vocês são a minha referência e o meu espelho profissional. Muito obrigada!

RESUMO

Introdução: A frouxidão vaginal (FV) é definida como queixa de excesso de flacidez vaginal. **Objetivo:** Identificar os fatores clínicos, diagnósticos e terapêuticos para a FV. **Métodos**: Uma revisão sistemática sobre o tratamento para a FV; uma adaptação transcultural e validação para a língua portuguesa do questionário *Female Sexual Distress Scale – Revised* (FSDS-R); um estudo transversal avaliando as medidas da espessura vaginal por ultrassom transvaginal (USTV) e transabdominal (USTA); um estudo qualitativo sobre a compreensão dos significados que as mulheres atribuem à sensação de FV e o seu impacto na percepção de si mesmas, no relacionamento afetivo íntimo e na sexualidade; um estudo transversal realizado no Reino Unido avaliando os fatores associados à FV e à disfunção sexual em uma população multiétnica; um Ensaio Clínico Randomizado (ECR) e o seu protocolo sobre o efeito da Radiofrequência (RF) e do Treinamento dos Músculos do Assoalho Pélvico (TMAP) no tratamento de mulheres com FV; e a partir do ECR, uma análise secundária dos achados ultrassonográficos das mulheres com FV submetidas à RF e ao TMAP. **Resultados:** Na revisão sistemática com 38 estudos, nenhuma diferença foi encontrada entre os grupos de intervenção e controle na função sexual e na sensação da FV nos tratamentos à base de energia. A satisfação das participantes nos tratamentos cirúrgicos foi alta. Na validação do FSDS-R, tanto o FSDS-R, quanto os questionários para função sexual e sintomas vaginais apresentaram validade discriminante entre mulheres com e sem FV e uma alta consistência interna em mulheres com e sem FV. No estudo transversal e na análise secundária, uma correlação significativa foi encontrada entre a espessura vaginal e os USTA e USTV em mulheres com FV. No estudo qualitativo, as 16 participantes entrevistadas enfrentaram dificuldades para identificarem os sintomas de FV e

apontaram estratégias para lidarem com a FV. No estudo transversal no Reino Unido, das 300 participantes incluídas, 69 apresentaram FV. As participantes com FV apresentaram piores resultados nos sintomas vaginais e na angústia sexual. Por fim, no ECR, tanto a RF quanto o TMAP apresentaram melhoras nos sintomas de prolapso genital e força muscular. As medidas da vagina proximal pelo USTA aumentaram no grupo TMAP após 6 meses. As medidas da vagina distal pelos USTA/USTV foram reduzidas após 6 meses de RF. Outras medidas do ultrassom translabial não apresentaram diferenças de acordo com a intervenção e/ou análise. O protocolo de estudo apresentou as etapas para a realização do ECR. **Conclusão**: A melhor compreensão da percepção do sintoma de FV se faz através da escuta atenta das pacientes. Multiparidade, idade, parto instrumental, laceração perineal, estado menopausal, e o parto vaginal e cesariana foram mais frequentemente associados às queixas de FV. A FV impacta negativamente a relação da mulher com a sua genitália, a sua autoestima, o seu bem-estar sexual, além de dificultar o vínculo afetivo com a parceria. O FSDS-R mostrou-se um instrumento valioso para avaliar a angústia sexual em mulheres com FV uma vez que estas apresentam piores scores na avaliação da angústia sexual. O USTA e o USTV são capazes de medir a espessura da parede vaginal em mulheres com FV. Os tratamentos à base de energias não se mostraram estatisticamente diferentes no reestabelecimento da função sexual e na sensação de FV quando comparados ao sham ou placebo na meta-análise, no entanto, melhora significativa foi observada em um ECR em mulheres tratadas com RF e TMAP após 30 dias e seis meses de follow-up.

Palavras-chave: disfunção do assoalho pélvico; frouxidão vaginal; disfunção sexual feminina; sintomas vaginais; ultrassom;

ABSTRACT

Introduction: Vaginal laxity (VL) is defined as a complaint of excessive vaginal laxity. **Objective**: To identify the clinical, diagnostic and therapeutic factors for VL. **Methods:** A systematic review of treatment for VL; a cross-cultural adaptation and validation for the Portuguese language of the Female Sexual Distress Scale–Revised (FSDS-R); a cross-sectional study evaluating vaginal thickness measurements by transvaginal (TVUS) and transabdominal (TAUS) ultrasound; a qualitative study on understanding the meanings that women attribute to the feeling of VL and its impact on self-perception, intimate affective relationships and sexuality; a cross-sectional study conducted in the United Kingdom evaluating associated factors of VL and sexual dysfunction in a multi-ethnic population; a Randomized Clinical Trial (RCT) and its protocol on the effect of Radiofrequency (RF) and Pelvic Floor Muscle Training (PFMT) in the treatment of women with VL; and from the RCT, a secondary analysis of the sonographic findings of women with VL who underwent RF and PFMT. **Results**: In the systematic review of 38 studies, no differences were found between intervention and control groups in sexual function and VL sensation in energy-based treatments. Participants' satisfaction with surgical treatments was high. In the validation of the FSDS-R, both the FSDS-R and the questionnaires for sexual function and vaginal symptoms showed discriminant validity between women with and without VL and high internal consistency in women with and without VL. In the cross-sectional study and secondary analysis, a significant correlation was found between vaginal thickness and TAUS and TVUS in women with VL. In the qualitative study, the 16 participants interviewed faced difficulties identifying VL symptoms and pointed out strategies to deal with VL. In the UK cross-sectional study, of the 300 participants included, 69 had VL. Participants with VL had worse results regarding

vaginal symptoms and sexual distress. Finally, in the RCT, both RF and PFMT showed improvements in genital prolapse symptoms and muscle strength. TAUS measurements of the proximal vagina increased in the PFMT group after 6 months. TAUS/TVUS measurements of the distal vagina were reduced after 6 months of RF. Other translabial ultrasound measurements did not differ according to the intervention and/or analysis. The study protocol presented the steps for performing the RCT. **Conclusion**: A better understanding of the perception of the VL symptom is achieved through attentive listening to the patients. Multiparity, age, instrumental delivery, perineal laceration, menopausal status, and vaginal delivery and caesarean section were most frequently associated with VL complaints. VL negatively impacts the woman's relationship with her genitalia, her self-esteem, and her sexual well-being, in addition to hindering the affective bond with the partner. The FSDS-R proved to be a valuable instrument to assess sexual distress in women with VL, as these have worse scores in the assessment of sexual distress. USTA and TVUS are able to measure vaginal wall thickness in women with VL. Energy-based treatments were not statistically different in restoring sexual function and VL sensation compared to sham or placebo in a meta-analysis, however, significant improvement was seen in an RCT in women treated with RF and PFMT after 30 days and six months of follow-up.

Keywords: pelvic floor dysfunction; vaginal laxity; female sexual dysfunction; vaginal symptoms; ultrasound;

SUMÁRIO

1.INTRODUÇÃO

1.1. Definição

A frouxidão vaginal (FV) é definida pela *International Urogynecological Association* (IUGA) e pela *International Continence Society* (ICS) como uma queixa de excessiva flacidez vaginal[1]. Mesmo não existindo um consenso a respeito de uma definição padrão para esta condição clínica, tem ocorrido um aumento na procura de tratamento para a FV, principalmente na área relacionada à estética genital[2,3].

Esta condição é raramente discutida entre os médicos e suas pacientes, possivelmente devido à escassez de tratamentos baseados em evidências[4]. Por parte das mulheres, o constrangimento dificulta o diálogo sobre a FV. Na opinião de uroginecologistas, a FV apresenta-se ainda como uma condição subnotificada e com relatos de incômodos que podem afetar a função sexual e os relacionamentos[5,6].

A prevalência de FV varia de 24% a 38% e parece estar associada à idade jovem, partos vaginais, sintomas de prolapso e prolapso objetivo[7]. Outros fatores de risco são macrossomia fetal, história de parto instrumental (fórcipe), multiparidade e alterações de tecidos conectivos[8].

1.2. Hipóteses sobre a Frouxidão Vaginal

Em uma entrevista com mais de quatrocentos médicos membros da IUGA, a maioria indicou o introito vaginal como sendo o local indicado para a ocorrência da flacidez vaginal e que tanto a musculatura como os tecidos eram responsáveis por esse sintoma[5].

Especula-se que a gravidez e o parto desempenham um papel na FV[5]. Apesar de não haver uma ligação comprovada entre FV e o parto, pesquisas apontam que o parto vaginal pode resultar em lesão do assoalho pélvico[7,9]. O trauma do assoalho pélvico e da vagina durante a gravidez e durante o parto vaginal podem acarretar no alongamento do introito vaginal, levando a mudanças permanentes na sensibilidade sexual durante o intercurso. Essas

alterações resultam em importante mudança da qualidade de vida da mulher [10,11].

Potenciais consequências associadas ao parto vaginal e que se estendem além do período pós-parto são: incontinência urinária, prolapso de órgão pélvico (POP), dor pélvica crônica e disfunção sexual[12–15]. Nem todas as mulheres se adaptam às mudanças psicológicas e físicas do pós-parto[16]. Dois terços das mulheres experimentaram piora significativa da função sexual seis meses após o parto vaginal[17]. Mulheres sem trauma perineal parecem apresentar uma maior chance de retornarem às atividades sexuais em seis semanas pós-parto em comparação com as mulheres com trauma perineal[18]. Além disso, a dispareunia é relatada por 41 a 67% das mulheres entre dois e três meses após o parto[12,19–21].

Tanto o parto vaginal como o trauma do músculo levantador do ânus estão associados ao aumento do diâmetro do hiato genital[22]. A avulsão do músculo levantador do ânus, principalmente se for comprovada bilateralmente, teria algum efeito sobre a função sexual feminina[23]. O grau de alongamento muscular parece variar de 25 a 250%[24]. Estudos de fisiologia muscular mostraram que, uma lesão substancial, macro e microscópica pode ocorrer se a fibra muscular esquelética for esticada para mais de 1,5 vezes em relação à extensão original[25]. Não se surpreende, portanto, que 10-35% das mulheres apresentem lesão traumática do músculo puborretal na sua inserção óssea[26–28]. Isso resulta em um aumento do hiato de 20-30%,[29] e um músculo do assoalho pélvico mais distensível e menos contrátil[22]. Em um estudo sobre a mudança periparto em dimensões hiatais, mais de 28% das primíparas foram diagnosticadas com hiperdistensão hiatal irreversível ou "microtraumas do levantador" aos 4 meses pós-parto, independente de avulsão,[29]e sem evidência de cura após dois anos de acompanhamento[30].

Outro estudo que avaliou mais de 300 mulheres com FV, foram encontradas associações entre a área hiatal, o hiato genital e o corpo perineal durante a manobra de Valsalva, sugerindo que a FV parece ser uma manifestação da hiperdistensibilidade do levantador do ânus e não da vagina[7]. As medidas do hiato do levantador do ânus estão fortemente associadas ao hiato genital e ao corpo perineal medidos pelo instrumento POP-Q e, portanto,

não é de surpreender que este último parâmetro também estivesse fortemente associado ao sintoma da FV[7]. Mulheres com flacidez vaginal podem ser representativas de um estágio inicial no desenvolvimento de prolapso de órgão pélvico; no entanto, isso não foi avaliado anteriormente[5]. Instrumentos padronizados para consultar mulheres em relação a tais sintomas ainda não existem[5].

A anatomia desempenha um papel importante na compreensão das diferentes estruturas envolvidas no suporte pélvico[31]. A cintura pélvica é composta por várias camadas de músculos e fáscias de suporte que se interligam e se sobrepõem, contribuindo para o suporte global e o funcionamento normal da vagina e de suas estruturas adjacentes[32,33]. A história e o exame físico determinarão se a mulher é uma candidata a procedimentos vaginais ou a uma abordagem de reconstrução vaginal mais complexa[34]. Antes que se possa manejar adequadamente essas mulheres, é importante entender a complexa mecânica estrutural da falência posterior da parede vaginal[35]. A falha da parede posterior pode envolver falha do suporte do corpo perineal e dos músculos levantadores do ânus, o que pode resultar em um hiato genital alargado[35]. Os músculos levantadores fornecem uma ação tônica e cefálica que mantém o hiato genital fechado a uma dimensão normal em resposta à pressão. Se os músculos levantadores estiverem enfraquecidos ou lesionados, ou se os anexos fasciais da parede vaginal posterior estiverem acometidos (compartimento posterior), ocorre a descida do corpo perineal e o hiato se abre[35]. O enfraquecimento da fáscia endopélvica em compartimento anterior poderia ser mais estudado para associar a hipermobilidade uretral e consequente incontinência urinária de esforço com a FV[36].

Os níveis séricos de estradiol na mulher em idade reprodutiva variam de 30 a 300 pg / mL, dependendo da fase do ciclo menstrual. Mulheres na pós-menopausa têm esse nível reduzido em mais de 90% para uma média de 6,5 pg / mL [37]. Mudanças profundas ocorrem na mucosa vulvovaginal e urogenital com a perda da estimulação estrogênica [38]. O hipoestrogenismo também resulta em alterações do tecido conectivo, mudanças na estrutura pélvica e declínio da qualidade do colágeno[39]. A idade e alterações hormonais geram uma deterioração e relaxamento do tecido conectivo e das fibras colágenas,

diminuindo o suporte dos órgãos pélvicos devido ao decréscimo do diâmetro e do número de fibras musculares estriadas periuretrais e do assoalho pélvico[40]. Essa fisiopatologia é importante para o entendimento de alguns tipos de tratamento como a radiofrequência e treinamento dos músculos do assoalho pélvico.

1.3. Diagnóstico

A redução da sensação vaginal durante a relação sexual pode estar relacionada a danos anatômicos no corpo perineal, prolapso no estágio 1, frouxidão do canal vaginal ou introito, dano subjacente aos nervos e tecido conjuntivo durante a gravidez e o parto ou, potencialmente, uma combinação desses fatores[41].

Até o momento, o diagnóstico da FV é baseado no auto relato das mulheres. Uma história médica abrangente, um exame físico e uma avaliação psicossexual são os passos iniciais para a identificação apropriada de mulheres com FV[42].

Somente dois instrumentos de avaliação da percepção da FV estão disponíveis na literatura científica. O questionário *International Consultation on Incontinence Questionnaire Vaginal Symptoms* (ICIQ-VS)[43], desenvolvido em 2006 e validado para a língua portuguesa em 2008[44], apresenta nove perguntas sobre os sintomas vaginais. Dentre elas, a quarta pergunta (letra A) refere-se à percepção de flacidez ou FV que pode ser graduada entre “um pouco” e “muito” e ao incômodo gerado pelo sintoma (letra B). O segundo instrumento que vem sendo usado em pesquisas clínicas para auxiliar na identificação e no grau da frouxidão é o *Vaginal Laxity Questionnaire* (VLQ). Este instrumento de avaliação autorreferido da FV, não validado para a Língua Portuguesa do Brasil, usa uma escala de sete pontos associada às perguntas: Como você avaliaria seu nível atual de frouxidão vaginal? ou frouxidão durante a relação sexual?[45]. Medidas objetivas para a avaliação da FV estão sendo pesquisadas[46].

A partir de achados de um estudo retrospectivo sobre a FV estar associada ao prolapso genital[7], a quantificação do prolapso por meio do sistema POP-Q, pode auxiliar no diagnóstico na FV.

O exame físico através da inspeção e do toque vaginal tem sido usado, principalmente, como critério de inclusão em estudos de tratamento cirúrgico da FV. São principalmente avaliados: o hiato genital e o relaxamento das paredes vaginais anteriores e posteriores[6,47]. O conhecimento da fisiopatologia da FV se torna essencial para uma melhor compreensão desse sintoma e consequente elaboração de métodos diagnósticos mais específicos para essa queixa.

1.4. Opções de Tratamento para a Frouxidão Vaginal

Procedimentos cirúrgicos para FV com reparo posterior/perineoplastia são mais comumente recomendados, todavia, 83% dos uroginecologistas entrevistados reportaram preocupação potencialmente importante com casos de dispareunia[5]. Nos últimos anos houve um número crescente de tipos de cirurgias vulvovaginais comercializadas como forma de melhorar aparência ou gratificação sexual. Entre elas destacam-se a chamada cirurgia cosmética gentinal feminina, a vaginoplastia designer, a revirginização e a amplificação do ponto G[48]. Alguns procedimentos, como a cirurgia cosmética gentinal feminina, parecem ser modificações dos procedimentos cirúrgicos vaginais tradicionais. Outros procedimentos são realizados para alterar o tamanho ou a forma do lábio maior ou lábio menor. A revirginização envolve reparo himenal em uma tentativa de aproximar o estado virginal. Apesar de serem realizados, a segurança e a eficácia destes procedimentos a longo prazo ainda não foram documentados [48].

Opções não cirúrgicas para o tratamento da FV incluem o laser, a radiofrequência, o tratamento tópico e o treinamento dos músculos do assoalho pélvico (TMAP). A função do músculo do assoalho pélvico parece ter um papel importante na função sexual feminina, e a contração do músculo elevador do ânus parece aumentar a resposta sexual [49]. A contração dos músculos do

assoalho pélvico também desempenha um papel importante na resposta orgástica feminina. Mulheres com músculos fracos que recebem reabilitação do assoalho pélvico percebem um efeito positivo em sua vida sexual [50]. Geralmente, o TMAP é recomendado como tratamento de primeira linha para a incontinência urinária, já que tem sido associado a mínimos efeitos adversos e ao baixo custo[51]. A força dos músculos do assoalho pélvico em mulheres com queixa de frouxidão vaginal foi avaliada em um ensaio clínico randomizado. O TMAP somado ao uso do laser (Erbium:YAG) melhorou significativamente a força muscular e a satisfação sexual nas participantes[52].

Na última década, houve um crescente número de estudos avaliando o efeito do laser de Erbium e o de CO_2 no tratamento da FV. A satisfação sexual e a percepção do estreitamento do canal vaginal foram observadas em mais de 70% dos casos[53,54]. Um estudo revelou ainda que 58% das participantes reportaram alta satisfação e 83% repetiriam a laser terapia caso fosse necessário[55].

Outra possibilidade terapêutica não cirúrgica para tratar a FV é a radiofrequência. De acordo com os princípios físicos, a faixa de radiofrequência do espectro eletromagnético atinge o tecido por meio de uma corrente elétrica alternada[56]. A radiofrequência é gerada pelo campo elétrico resultante da oscilação da corrente elétrica que, por sua vez, induz o movimento translacional de átomos e moléculas carregadas[57]. Na presença de um campo elétrico, as moléculas orientam-se ao longo da direção do campo, mas devido à viscosidade da água, é necessária energia para girar os dipolos resultando em transferência de energia para o tecido. A resistência ou impedância converte a corrente elétrica em energia térmica gerando calor em relação à quantidade de tempo de exposição[57], ou seja, na mucosa vaginal, a energia eletromagnética é convertida em energia cinética, à medida que os íons das células da mucosa vaginal se agitam. Com o atrito gerado entre os íons celulares, a energia cinética é convertida em energia térmica, tendo como resultado, um aumento da temperatura dentro da célula da mucosa vaginal[56].

A radiofrequência tem uma longa história de uso no tecido mucoso da vagina e na pele [58–60]. Através da criação de calor via impedância, à medida

que a corrente elétrica é conduzida através do tecido vaginal, a estimulação de fibroblastos ocorre e o resultado terapêutico é alcançado[61]. A efetividade da radiofrequência na umidade natural foi demonstrada em um estudo histológico de radiofrequência no tecido vaginal de ovelhas[62]. A radiofrequência também foi eficaz para o rejuvenescimento vulvovaginal[4]. Um estudo utilizando a radiofrequência de baixa energia para FV introital em mulheres na pré-menopausa apontou melhorias tanto na frouxidão quanto na função sexual. Os efeitos foram mantidos por 12 meses e nenhum evento adverso foi relatado[10]. Um estudo piloto para o uso da radiofrequência para o tratamento da frouxidão vaginal mostrou que o tratamento foi bem tolerado pelas participantes e apresentou melhora subjetiva do estreitamento vaginal, função sexual e diminuição do desconforto sexual [4].

1.5. Considerações Finais

Até o momento, evidências científicas foram incapazes de identificar a fisiopatologia da FV. Uma única escala para identificar a percepção das mulheres com FV foi publicada, no entanto não passou por nenhum processo de validação. Instrumentos diagnósticos e avaliativos específicos para a FV ainda não existem. Mesmo tendo sido definida pela ICS/IUGA em 2010, a FV é um sintoma ainda muito pouco compreendido. Portanto, é desafiador e necessário o estudo aprofundado desse sintoma.

2.OBJETIVOS

2.1. Objetivo Geral

Identificar os fatores clínicos, diagnósticos e terapêuticos para a frouxidão vaginal.

2.2. Objetivos Específicos

2.2.1. Revisar sistematicamente as evidências contemporâneas da eficácia e da segurança das intervenções para a FV.

2.2.2. Realizar a adaptação transcultural, tradução e validação da *Female Sexual Distress Scale-Revised* (FSDS-R) em português do Brasil para mulheres com FV.

2.2.3. Determinar se a espessura da parede vaginal medida por ultrassom pode diferir de acordo com as técnicas abdominal ou vaginal e avaliar se as variáveis clínicas estão associadas às medidas vaginais de mulheres com FV.

2.2.4. Compreender os significados que as mulheres atribuem à sensação de FV e seu impacto na percepção de si mesmas, na relação afetiva íntima e na sexualidade.

2.2.5. Investigar os fatores associados à FV e à disfunção sexual e suas relações com as desordens do assoalho pélvico em uma população feminina multiétnica.

2.2.6. Comparar o efeito da RF e do TMAP no tratamento de mulheres com FV.

2.2.6.1. Apresentar o protocolo do ensaio clínico randomizado que compara o efeito de RF e TMAP em mulheres com sintomas de FV.

2.2.6.2. Colaborar com o entendimento da avaliação objetiva de mulheres com FV comparando a espessura da parede vaginal medida pela ultrassonografia bidimensional (2D) transabdominal e transvaginal;

e a morfometria e função dos músculos do assoalho pélvico medidos pelo ultrassom quadridimensional (4D) nos grupos de RF e TMAP após 30 dias e 6 meses de acompanhamento.

3.METODOLOGIA

Para identificar de forma abrangente os fatores clínicos e diagnósticos que poderiam contribuir para o estudo da frouxidão vaginal, foram desenvolvidos projetos de pesquisa que seguissem uma ordem lógica a partir da concepção de um protocolo de estudo, e do desenvolvimento do ensaio clínico randomizado que foi o objeto de pesquisa principal da presente tese de doutorado. No decorrer da elaboração do projeto de pesquisa principal, foi identificada uma escassez de evidências em torno do tema. A partir daí, percebemos a necessidade da adaptação transcultural e validação de um dos instrumentos indispensáveis para a avaliação da angústia sexual em mulheres com FV, o FSDS-R. Ainda no processo de desenvolvimento do projeto de pesquisa principal, observamos que a literatura científica disponível, naquele momento, apresentava basicamente duas opções de tratamentos para a FV: o tratamento cirúrgico e o tratamento baseado em energias, como por exemplo, a radiofrequência e o laser. Uma revisão sistemática foi então planejada como parte da tese. No início da coleta de dados do projeto principal, foi verificada a importância de entender se a espessura vaginal diferia entre as mulheres com FV e se essas medidas eram capazes de serem captadas pelas duas abordagens ultrassonográficas mais utilizadas na ginecologia – o ultrassom transabdominal (USTA) e o ultrassom transvaginal (USTV). Dessa forma, um estudo transversal foi planejado para a presente tese e com a possibilidade de desenvolver uma análise secundária utilizando a ultrassonografia transperineal em pacientes com FV. Durante o período de recrutamento das participantes do ensaio clínico randomizado (projeto principal), foi observada a dificuldade das participantes em descreverem as suas queixas e se essas queixas estavam relacionadas à FV. Assim, foi incluído no planejamento, um estudo qualitativo que pudesse auxiliar na compreensão dos significados que as mulheres atribuíam à sensação de FV e que pudessem também avaliar o impacto da FV na percepção de si mesmas, na relação afetiva íntima e na sexualidade. Por fim, a FV e a disfunção sexual feminina foram estudadas em uma população multiétnica e associadas às desordens do assoalho pélvico, no doutorado sanduíche, a partir de uma oportunidade financiada e apoiada pela FAPESP e

em parceria com a universidade Imperial College London e com o Chelsea and Westminster Hospital, Londres – Reino Unido.

3.1. Revisão Sistemática – Tratamento de Mulheres com FV

Esta revisão sistemática foi realizada de acordo com a deretriz *Preferred Reporting Items for Systematic Review and Meta-Analyses* (PRISMA)[63] e o seu protocolo foi registrado no PROSPERO (número registrado: CRD42021252686). Cinco bases de dados foram utilizadas para a busca dos seguintes termos: ("vaginal laxity" OR "vaginal frouxidão" OR "vaginal relax" OR "wide vagina" OR "vaginal flaccidity"). Estudos em língua inglesa investigando qualquer tipo de tratamento para FV (estudos observacionais e ensaios controlados randomizados comparando tratamentos com placebo/sham ou com outro tipo de tratamento em mulheres com frouxidão/relaxamento/flacidez vaginal ou vagina larga diagnosticada por autorrelato, questionários, e/ou exame físico) foram incluídos. Consideramos também estudos que apresentaram como tema principal o tratamento da FV, mas que avaliaram outras queixas sexuais ou do assoalho pélvico. Nesse caso, os estudos tiveram dados avaliados apenas para flacidez vaginal. Excluímos estudos não relacionados ao tratamento da frouxidão/relaxamento/flacidez vaginal ou vagina larga; relatos de casos; estudos que a frouxidão/relaxamento/flacidez vaginal ou definição ampla da vagina não foi claramente identificada ou associada como um problema secundário do tópico principal do estudo. Em casos de estudos duplicados ou subanálises, consideramos o estudo com a maior população e com o seguimento de maior duração. Análise qualitativa e quantitativa dos estudos incluídos foi realizada utilizando os seus respectivos instrumentos de avaliação.

3.2. Adaptação Transcultural e Validação do FSDS-R

O presente estudo transversal incluiu mulheres com idade ≥ 18 anos, com FV (n=82) e sem FV (n=53) e seguiu a diretriz *Guidelines for the Process of Cross-Cultural Adaptation of Self-Report Measures*[64]. O Female Sexual

Distress Scale – Revised (FSDS-R)[65] é um questionário autoaplicável composto por 13 perguntas em inglês que podem ser respondidas como 0-nunca, 1-raramente, 2-ocasionalmente, 3-frequentemente e 4-sempre. A pontuação total do FSDS-R varia de 0 a 52 e fornece a medição da angústia sexual (quanto maior a pontuação, maior o sofrimento sexual). O estudo seguiu seis estágios de adaptação transcultural e validação. Dados clínicos e sociodemográficos e outros dois questionários (*International Consultation on Incontinence Questionnaire-Vaginal Symptoms – ICIQ-VS*[44] *e Female Sexual Function Index – FSFI*[66]) validados para o português juntaram-se ao processo de adaptação transcultural e validação do FSDS-R.

3.3. Estudo transversal – Medida da Espessura Vaginal pelo ultrassom transabdominal - USTA e ultrassom transvaginal - USTV em Mulheres com FV

Este estudo transversal incluiu 82 mulheres com idade ≥ 18 anos com queixas de FV avaliadas pelo *Vaginal Laxity Quesionnaire* (VLQ)[4]. Mulheres que relataram comorbidades graves ou distúrbios vulvovaginais, tratamento prévio para FV e uso de estrogênio vaginal nos últimos 6 meses foram excluídas. As participantes que relataram FV foram submetidas ao USTA, ao USTV, a exame físico (quantificação do prolapso genital e avaliação da força dos músculos do assoalho pélvico) e responderam aos questionários validados (*Female Sexual Function Index – FSFI*[66] *e International Consultation on Incontinence Questionnaire-Vaginal Symptoms – ICIQ-VS*[44]*, International Consultation on Incontinence Questionnaire Urinary Incontinence – Short-Form – ICIQ-SF*[67]*)*. O desfecho primário foi a medida da espessura da parede vaginal pelos ultrassons USTA e USTV. Os desfechos secundários foram as características sociodemográficas e clínicas das mulheres com queixa de FV.

3.4. Estudo Qualitativo sobre a Percepção das Mulheres com FV

Um estudo qualitativo por meio de entrevistas em profundidade e análise temática foi realizado seguindo as diretrizes do *Consolidated criteria for reporting qualitative research* – COREQ[68]. As participantes foram selecionadas

intencionalmente no período de fevereiro de 2020 a novembro de 2021 e consideramos o conceito de saturação teórica proposto por Glaser e Strauss[69]. Cada participante foi entrevistada em sala reservada por uma pesquisadora que garantiu o estabelecimento do rapport. Duas pesquisadoras independentes realizaram a transcrição completa de cada entrevista imediatamente após seu término. A coleta de dados foi interrompida quando os critérios de saturação teórica foram atingidos. Por fim, a análise temática proposta por Braun e Clarke foi realizada[70].

3.5. Estudo Transversal – Fatores Associados à FV e à Disfunção Sexual e os seus Relacionamentos com as Desordens do Assoalho Pélvico em uma População Multiétnica.

Um estudo transversal foi realizado de julho a dezembro de 2022 no Chelsea and Westminster Hospital. Todas as mulheres encaminhadas para atendimento clínico no Departamento de Uroginecologia foram incluídas. Excluímos gestantes, mulheres submetidas a cirurgia pélvica e mulheres incapazes de ler e compreender a língua inglesa. Avaliamos o prolapso de órgãos pélvicos (POP) por meio do sistema de quantificação de POP (POP-Q)[71]; a função sexual (*Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IUGA-Revised* – PISQ-IR)[72]; a percepção da FV (*Vaginal Laxity Questionnaire* – VLQ)[4]; a angústia sexual (*Female Sexual Distress Scale-Revised* – FSDS-R)[65]; as atitudes sexuais (*Brief Sexual Attitudes Scale* – BSAS)[73]; a qualidade de vida sexual (*Sexual Quality of Life-Female* – SQOL-F)[74] e sintomas vaginais (*International Consultation on Incontinence Questionnaire-Vaginal Symptoms – ICIQ-VS)*[43]. Os desfechos foram a identificação dos fatores associados à FV e à disfunção sexual pelas variáveis clínicas e questionários. Também avaliamos a associação entre FV e POP com os escores dos questionários.

3.6. Protocolo de Estudo e Ensaio Clínico Randomizado (Projeto Principal)

O protocolo de estudo e um ensaio clínico randomizado prospectivo, paralelo, de não-inferioridade, com dois braços (Registro: RBR-2zdvfp– REBEC) tiveram como objetivo comparar o efeito da radiofrequência e do treinamento dos músculos do assoalho pélvico – TMAP no tratamento de mulheres com FV. Ao considerar um poder de estudo de 80%, um alfa de 0,05 com um teste bicaudal, verificou-se que um número mínimo de participantes exigido em cada grupo, adicionado a um percentual de 30% de perda na amostra, totalizaria 68 mulheres, 34 em cada grupo. As participantes foram selecionadas aleatoriamente para um dos dois grupos de intervenção: radiofrequência (três sessões de radiofrequência com intervalo de 4 semanas entre as aplicações) ou TMAP (12 sessões individuais de TMAP supervisionadas por fisioterapeuta). O estudo foi realizado no setor de ecografia, no ambulatório de uroginecologia e no ambulatório de fisioterapia da Universidade Estadual de Campinas–UNICAMP e incluiu mulheres com idade ≥ 18 anos e com queixa auto referida de FV. As participantes foram avaliadas na linha de base (período pré-intervenção), foram submetidas a doze semanas de tratamento e acompanhadas em dois períodos: primeiro acompanhamento (30 dias após a intervenção) e segundo seguimento (seis meses após a intervenção).

3.6.1 Análise Secundária do Ensaio Clínico Randomizado (Projeto Principal): Avaliação ultrassonográfica em mulheres com frouxidão vaginal tratadas por treinamento dos músculos do assoalho pélvico ou radiofrequência: uma análise secundária de um ensaio clínico randomizado

A análise secundária do Ensaio Clínico Randomizado (projeto principal) tem como objetivo colaborar com a compreensão da avaliação objetiva de mulheres com FV comparando a espessura da parede vaginal medida pela ultrassonografia bidimensional transabdominal (USTA) e transvaginal (USTV);

e a morfometria e a função dos músculos do assoalho pélvico medidos pela ultrassonografia translabial quadridimensional (USTL-4D) nos grupos de RF e TMAP após 30 dias e 6 meses de acompanhamento. As participantes foram avaliadas pela USTA em posição supina com enchimento vesical moderado (300 ml de volume aproximado) e transdutor abdominal posicionado em região supra-púbica. As imagens foram capturadas no terço-proximal (fórnix vaginal), terço médio e terço-distal (próximo ao introito vaginal) da vagina. Subsequentemente, as participantes esvaziaram a bexiga e foram avaliadas pela USTV, em posição supina, com a pelve elevada. Quarenta mililitros de gel vaginal à base de água foram cuidadosamente introduzidos no canal vaginal por meio de duas seringas de 20 ml para afastarem as paredes vaginais, permitindo medidas independentes das paredes vaginais. Medidas das paredes anterior e posterior foram feitas nos terços proximal (fórnix vaginal), médio (na transição da uretra proximal e reto) e distal (uretra distal/introito vaginal e junção anorretal) da vagina. Durante as análises, as medidas anterior e posterior do USTV foram somadas e comparadas com as medidas do USTA. As medidas da morfometria e função dos músculos do assoalho pélvico foram realizadas em posição supina, após o esvaziamento vesical pela USTL – 4D. As medidas dos músculos do assoalho pélvico foram feitas em repouso e durante a contração. Todas as medidas foram feitas na linha de base, e 30 dias e 6 meses pós RF e TMAP, por pesquisadoras experientes e cegadas quanto ao grupo de intervenção. As medidas também foram comparadas com variáveis clínicas e escores de questionários validados.

4. RESULTADOS

4.1. Artigo 1. *Treatment of Women with Vaginal Laxity - Systematic Review with Metanalysis*

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THE JOURNAL OF SEXUAL MEDICINE
An Official Journal of The International Society for Sexual Medicine

Treatment of Women with Vaginal Laxity: Systematic Review with Metanalysis

Journal:	*Journal of Sexual Medicine*
Manuscript ID	Draft
Manuscript type:	Review Article
Subject:	Pelvic Floor Disorders and Therapy, Female Medical, Psychosexual Health (Female)
Keywords:	vaginal laxity, sexual function, systematic review, metanalysis, pelvic floor muscles

Abstract:

Background: Several treatments have been used for women reporting vaginal laxity (VL), however, little evidence is available to recommend which treatments are better indicated for these patients.
Aim: To summarize the best available evidence about the efficacy and safety of the interventions treating VL, whether conservative or surgical, by a systematic review and metanalysis.
Methods: A comprehensive search strategy was performed in Medline, Embase, Scopus, Web of Science, Cochrane Library, and Clinical Trials from inception to September 2022. Studies in the English language investigating any type of treatment for VL with or without a comparator, whether randomized controlled studies (RCT) or non-randomized. Case reports and studies without a clear definition for VL were excluded.
Outcomes: The outcomes were interventions (energy-based devices, surgery), adverse effects, sexual function, pelvic floor muscle (PFM) strength and improvement of VL by the VL questionnaire (VLQ).
Results: From 816 records, 38 studies remained in the final analysis. Laser and radiofrequency (RF) were the most frequently energy-based devices studied. Pooled data from eight observational studies have shown improved sexual function (MD=6.51[5.61-7.42;i2=85%, p<0.01) before and after intervention, whether by RF (MD=6.00[4.26-7.73];i2=80%;p<0.001) or laser (MD=6.83[5.01-8.65]i2=92%;p<0.01). However, this finding was not shown when only three RCTs were included, even when separated by the intervention (RF or laser). VLQ scores did not improve when RF was compared to sham controls (MD=1.01[-0.38,2.40];i2=94%;p<0.001). PFM strength improved after interventions were performed (MD=4.22[1.02,7.42];i2=77%;p<0.001). ROBBINS-I have classified all non-RCTs with serious remarks, except for one study; the RoB-1 analysis found a low and unclear risk of bias for all RCTs. GRADE certainty of the evidence was moderate for sexual function and the questionnaire VLQ and low for PFM strength.
Clinical Implications: Sexual function in women with VL who underwent RF and laser improved in observational studies but not in RCTs. Improvement in PFM strength was observed in women with VL after the intervention.
Strengths and Limitations: Crucial issues were raised for the

	understanding of VL, such as lack of standardization of the definition and for the development of future prospective studies. The limitation was that the heterogeneity of the interventions, and different follow-up periods did not make it possible to pool all available data. Conclusions: Vaginal tightening did not improve the sensation of women with VL after intervention. RF and laser improved sexual function in women with VL from observational studies, but not from RCTs. PFM strength was improved in women with VL after intervention.

Treatment of Women with Vaginal Laxity: Systematic Review with Metanalysis

Abstract

Background: Several treatments have been used for women reporting vaginal laxity (VL), however, little evidence is available to recommend which treatments are better indicated for these patients.

Aim: To summarize the best available evidence about the efficacy and safety of the interventions treating VL, whether conservative or surgical, by a systematic review and metanalysis.

Methods: A comprehensive search strategy was performed in Medline, Embase, Scopus, Web of Science, Cochrane Library, and Clinical Trials from inception to September 2022. Studies in the English language investigating any type of treatment for VL with or without a comparator, whether randomized controlled studies (RCT) or non-randomized. Case reports and studies without a clear definition for VL were excluded.

Outcomes: The outcomes were interventions (energy-based devices, surgery), adverse effects, sexual function, pelvic floor muscle (PFM) strength and improvement of VL by the VL questionnaire (VLQ).

Results: From 816 records, 38 studies remained in the final analysis. Laser and radiofrequency (RF) were the most frequently energy-based devices studied. Pooled data from eight observational studies have shown improved sexual function (MD=6.51[5.61-7.42;i2=85%, p<0.01) before and after intervention, whether by RF (MD=6.00[4.26-7.73];i2=80%;p<0.001) or laser (MD=6.83[5.01-8.65]i2=92%;p<0.01). However, this

finding was not shown when only three RCTs were included, even when separated by the intervention (RF or laser). VLQ scores did not improve when RF was compared to sham controls (MD=1.01[-0.38,2.40];i2=94%;p<0.001). PFM strength improved after interventions were performed (MD=4.22[1.02,7.42];i2=77%;p<0.001). ROBBINS-I have classified all non-RCTs with serious remarks, except for one study; the RoB-1 analysis found a low and unclear risk of bias for all RCTs. GRADE certainty of the evidence was moderate for sexual function and the questionnaire VLQ and low for PFM strength.

Clinical Implications: Sexual function in women with VL who underwent RF and laser improved in observational studies but not in RCTs. Improvement in PFM strength was observed in women with VL after the intervention.

Strengths and Limitations: Crucial issues were raised for the understanding of VL, such as lack of standardization of the definition and for the development of future prospective studies. The limitation was that the heterogeneity of the interventions, and different follow-up periods did not make it possible to pool all available data.

Conclusions: Vaginal tightening did not improve the sensation of women with VL after intervention. RF and laser improved sexual function in women with VL from observational studies, but not from RCTs. PFM strength was improved in women with VL after intervention.

Keywords: vaginal laxity; sexual function; systematic review; metanalysis; pelvic floor muscles

Introduction

Vaginal laxity (VL) has been given a number of denominations over the past few years. About a decade ago, vaginal laxity was described as a symptom of sexual dysfunction and defined as a complaint of excessive vaginal laxity[1]. Years later, it received the description of the sexual symptom that women with pelvic organ prolapse most commonly describe[2] and more recently as a vaginal symptom[3]. The term 'wide vagina' is characterized by a sensation of the overall increased size of the vagina causing decreased sexual function; feeling of an empty hole; decreased feeling of penile penetration during coitus, among others[4]. According to Greenhill, relaxation is known as decreased tension or diminution in the functional activity of a part. With regard to vulvar vaginal relaxation, it will be attributed to a lack of complete satisfaction during coitus to the looseness of the vagina[5].

Although surveys have shown that VL is the most frequently discussed physical condition after vaginal delivery among obstetricians and gynaecologists and that about 50% of women aged 25-45 years (with at least one vaginal delivery) reported some concern about this topic, it is still rarely discussed amongst patients and health professionals and/or underreported[6–8].

Surgical and conservative treatments for VL are gaining in popularity in recent years, which has caught the attention of influential scientific communities and the Food and Drug Administration (FDA)[9]. Although an increasing number of women are undergoing vaginoplasty, labiaplasty, and other genital procedures, few reports of vaginoplasty repairs for the treatment of VL have indicated improvement in post-surgical sexual symptoms[6,10–13]. Similarly, studies have investigated non-surgical options for the treatment of VL including energy-based equipment such as radiofrequency (RF) and

laser, but evidence from randomized clinical trials is still scarce[14,15]. Recent studies that aimed to report subjective improvements in sexual function for VL showed contradictory results[9,16]. Thus, it is important to produce evidence-based data to be incorporated by healthcare providers, and we aimed to review conservative and surgical treatments for women with VL.

Materials and Methods

This systematic review was carried out according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement[17] and its protocol was registered on PROSPERO (registered number: CRD42021252686).

After the development of the research question in accordance with the PICOS framework, a literature search was performed with no restriction using MEDLINE (via Pubmed), Embase, Scopus, Web of Science, Cochrane Library, and Clinical Trials electronic databases from inception to September 2022. The following terms were used and adapted according to each electronic database: ("vaginal laxity" OR "vaginal looseness" OR "vaginal relaxation" OR "wide vagina" OR "vaginal flaccidity"). The complete search strategy, including all terms used in this study, can be accessed in the supplementary material.

Eligibility Criteria

Studies in English language investigating any type of treatment for vaginal laxity (observational studies and randomized controlled trials comparing treatments with placebo/sham or with another type of treatment in women with vaginal laxity/relaxation/flaccidity or wide vagina diagnosed by self-report, questionnaires,

and/or physical examination) were included. We also considered studies that presented the treatment for vaginal laxity as a main topic but that evaluated other sexual or pelvic floor complaints. In this case, the studies had data evaluated only for VL. Our exclusion criteria were: studies unrelated to the treatment for vaginal laxity/relaxation/flaccidity or wide vagina; case reports; studies that vaginal laxity/relaxation/flaccidity or wide vagina definition was not clearly identified or associated as a secondary problem of the main study topic. In cases of duplicate studies or subanalysis, we considered the study with the largest population and the longest follow-up.

Data extraction

Two researchers (GMVP and LGOB) independently evaluated titles and abstracts. If the abstracts did not provide enough information to be evaluated regarding the eligibility criteria, they had their full texts analysed. Subsequently, the same investigators independently assessed the full texts of previously selected studies and determined study eligibility. A third researcher (CRTJ) assisted in any disagreements regarding the eligibility criteria of the studies and the decision was taken by consensus. Data were organized in spreadsheets and double-checked by the researchers. In case of questions or concerns regarding data presentation, the authors were contacted by email. A manual search of references was also performed by the research team.

The following variables were extracted: authorship, year of publication, country, study design, number and age of participants, type of intervention (radiofrequency, laser, surgical treatment and/or others), the definition of VL, study objectives, type of energy-based device, procedure details, reported adverse effects, follow-up period, used instruments to measure outcomes (eg. validated or non-validated questionnaires) and main results. Sexual function was measured by instruments such as the Female Sexual

Function Index (FSFI)[18], the Female Sexual Distress Scale-Revised (FSDS-R)[19] and the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12)[20]. The most common measurement for VL was the Vaginal Laxity Questionnaire (VLQ)[21].

Risk of bias and Quality assessment

Two independent investigators were responsible for the quality analysis of included studies for both clinical trials and observational studies, using the Cochrane Handbook for Systematic Reviews of Intervention[22] and the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I)[23], respectively. According to the instrument the Cochrane Handbook for Systematic Reviews of Intervention[22], based on the responses to the signalling questions, the risk of bias may be classified as "Low" or "High" risk of bias, or may be classified as "Some concerns". With regard to non-randomized studies, the ROBINS-I systematically organizes and presents evidence related to the risk of bias in non-randomized studies of interventions. This tool assesses the risk of bias within specified domains, enabling review authors to document the information on which judgments are based[23]. Lastly, the quality of evidence and the strength of recommendations of the included randomized clinical trials were assessed using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) criteria[24].

Data analysis

Data was meta-analysed in the RevMan version 5.4 for metanalysis (May 2020, Copenhagen, DK). We used the inverse variance method and mean difference plus 95% confidence intervals (CIs) were calculated for each study. Statistical heterogeneity was calculated by the i^2 test [25], where: 0-40% low heterogeneity; 30-60% moderate; over 50% substantial. As the number of pooled studies was less than 10, no funnel plots were

prepared to analyse publication bias. Furthermore, no metaregression or sensitivity analyses was possible due to the low number of studies and different interventions.

Sexual function was represented by continuous variables such as the total FSFI score and the VLQ score. Pelvic floor muscle (PFM) strength was measured by a perineometer. Forest plots were divided into randomized controlled studies and non-randomized studies; interventions were divided into subgroups for each graphic (radiofrequency, laser, and surgery) in order to reduce heterogeneity. However, we noticed a clinical heterogeneity in the definition of VL while reviewing the studies, and a random-effects model was applied to all graphics. Follow-ups were different according to the number of pooled studies: RCTs – 3 months for FSFI and VLQ, and 1 month for PFM strength; observational – energy-based devices (3 months) and surgery (6 months).

Results

Through the search of six databases (Supplementary Table 1), 816 records were identified. After removing duplicates, 125 articles were selected for full-text reading (Figure 1). Of these, 38 studies were included in the final analysis[12,15,33–42,21,43–52,26,53–60,27–32].According to the general characteristics of the included studies, most were carried out in the Asian continent (Table 1). Regarding the inclusion criteria, seven randomized controlled trials and 31 non-randomized trials constituted the assessed studies. The definition or classification of vaginal laxity varied greatly between studies. The terms "vaginal relaxation syndrome", "decreased sexual sensation during intercourse" and "subjective perception of laxity" most frequently appeared in studies. The investigated treatments were RF, laser, topical treatment, and surgical treatment; details from all procedures were written in Supplementary Tables 2 and 3.

With regard to laser treatment, eight studies investigated the effect of Erbium Yag Laser[26,27,50–53,57,58] and six studies the effect of Carbon Dioxide Laser[49,54–56,59,60]. The main pre-laser care was the disinfection of the vaginal canal and the use of topical anaesthesia (mainly lidocaine). Participants were informed to avoid sexual intercourse from two days to 14 days after laser treatment. Laser adverse events were mostly mild.

Fourteen studies investigated RF. Of these, nine with monopolar technology[15,21,28,41–43,45,46,48], one study with bipolar technology[47], two described their equipment as quadripolar[39,40] and two others as multipolar[38,44]. RF protocols ranged from three to six sessions. Most studies used gel during procedures. RF side effects were milder than those observed with laser.

In surgical procedures, types of anaesthesia range from general anaesthesia to local anaesthesia. Unlike energy-based treatments, participants took four to six weeks to return to sexual activity. In surgical treatments, adverse events were also more severe (wound dehiscence, implant extrusion, infection, etc.) when compared to energy-based treatments. Finally, only one study investigated the effect of topical treatment (Extract of Oak Gall) in women with vaginal relaxation[29]. Quercus inner layer extract, used at different concentrations (10 - 15 and 20 grams in 1.5%, 2% and 2.5% jells) revealed that sexual satisfaction, orgasm, lubrication, and vaginal tightness during intercourse were higher in the 2.5% oak extract jell, with no side effects.

Table 2 shows the main instruments, outcomes and follow-up periods of the analysed studies. Sexual function and satisfaction were the most frequently evaluated variables. Follow-up periods ranged from "after treatment" to 50.2 months. Some studies, in addition to questionnaires, performed ultrasound evaluation, quantification of genital prolapse, measurements of pelvic floor muscle strength and biopsies.

Sexual Function

Sexual function was assessed using the FSFI and PISQ-12 questionnaires in 22 of the 38 articles included. With regard to the type of treatment, six and 10 studies evaluated sexual function treated by laser[49,54–56,59,60] and radiofrequency[15,21,38–42,44–46], respectively. Improvement in sexual function was most often observed at 3-6-month follow-up periods in patients treated with laser and radiofrequency. Similar to the laser, six studies evaluated sexual function in surgical treatment[30,32–34,36,60]. The description of improvements in sexual function varied between studies ranging from non-significant improvement after surgery to progressive improvement up to 12- and 18-months post-surgery.

Vaginal tightness

The participants' perception of vaginal tightness was assessed by the four types of treatment. A moderate improvement[50,58] (42% - 76.2%) was observed in the studies that evaluated the laser between 1-3 months[51]. Improvement in vaginal tightness was most often seen between 1-3 months[38,40,45,48], but studies have also observed improvements reaching up to six[15,21,42] and 12 months[39,41] in radiofrequency. More expressive improvements were found in the surgical treatment[32,35] (89.1% - 92.8%) and in the topical treatment[29] using Jell 2.5% (93%).

Sexual Satisfaction

Sexual satisfaction was more frequently assessed by studies that investigated the laser. The percentage of improvement with laser treatment ranged between 58% and 92.7%[27,49,52,53,55,57,60] with improvements seen between 1-2 months[61] and 3-6 months[54] post-treatment. Smaller percentages of improvement were found in RF, ranging from 48% to 76.5%[41,43]. The other studies that evaluated sexual satisfaction in the treatment

with RF observed significant improvements[21,39,48]. Similar to laser treatment, the percentage of improvement in surgical treatment ranged from 66% to 90.9%[12,31,60], however, one study found no significant improvement[37]. Finally, topical treatment also reported significant improvement in sexual satisfaction[29].

Figure 3 shows the results of the randomized clinical trials related to sexual function, perception of vaginal laxity and pelvic floor muscle strength. Unlike what was shown in Table 2, no difference was observed between the intervention and control groups (MD = 2.38 [-0.50, 5.27], i^2 = 98%, p = 0.11, n = 401) in the mean difference between baseline and 3-month treatment using RF and laser in relation to sexual function assessed by FSFI. Similarly, the perception of vaginal laxity assessed by the VLQ did not differ between the intervention and control groups (MD = 1.01 [-0.38, 2.40], i^2 = 94%, p = 0.16, n = 282) in the mean difference between the baseline and 3-Months of treatment using radiofrequency. When considering the strength of the pelvic floor muscles in participants treated with laser+PFMT and RF, a significant difference was observed between the intervention and control groups (MD = 4.22 [1.02, 7.42], i^2 = 77%, p = 0.010, n =126).

Sexual function assessed by FSFI in participants treated with RF and laser in non-randomized studies is depicted in Figure 4. Sexual function differed significantly between groups (MD = 6.51 [5.61, 7.42], i2 = 85%, p < 0.00001, n = 524) on the difference between means between baseline and 3-4 months post-treatment. It was not possible to meta-analyse sexual function in participants treated by surgery.

The risk of bias assessment of randomized clinical trials is presented in Figure 2. Random sequence generation was unclear in one study and low risk in six studies. Allocation concealment was unclear in four studies and three studies had low risk.

Blinding of participants and staff was unclear in four studies and considered low risk in three studies. Outcome assessment blindness was low risk in only three studies. Selective reporting was unclear in all studies. Other biases were low risk in five studies. When assessing the risk of bias for non-randomized studies, the overall risk was serious in most of the investigated studies (Table 3). GRADE assessment for sexual function and vaginal laxity questionnaire showed a moderate level of evidence. A low level of evidence was found when assessing the pelvic floor muscle strength (Supplementary Table 4).

Discussion

Main Findings

Four treatment options for VL were investigated by the studies included in this review. The definition of VL varied among the studies, but it was possible to categorize them, and self-report followed by the VLQ instrument were the most tools to define it. Sexual function showed more frequent improvement during periods of 3 and 6 months for RF and laser. This trend was confirmed in the meta-analysis of observational studies, two for RF and one for laser compared with their sham controls. However, we did not find the same results when three RCTs were selected for metanalysis. The number of studies was lower than the pooled data from observational studies, and this might impact with different results. Perception of the VLQ did not change between intervention and control groups from RCTs. Surgical and topical treatments seem to be more effective in the perception of vaginal tightness, but the certainty of evidence is low and only from observational studies. PFM strength differed significantly between the intervention (one study using PFMT+laser and another using RF) and control groups in the energy-based treatments. Finally, almost all observational studies presented a low-quality score at the

I-ROBBINS classification, although the RCTs did not present a low risk of bias in the domains that were analysed in the retrieved studies.

Strengths and Limitations

To our knowledge, this is the first systematic review that performed a metanalysis for all published treatment options for women with VL. Furthermore, the present study raised crucial issues for the understanding of VL, such as the lack of standardization of the definition, and for the development of future prospective, randomized studies. As weaknesses, the low number of studies, the heterogeneity of the interventions, and different follow-up periods did not make it possible to pool all available data. Most of the studies were observational, with no control group. We used random-effects models for the forest plots and separated studies according to the intervention and follow-up periods, but this did not reduce the statistical heterogeneity.

Interpretation

Recent systematic reviews using energy-based treatments for genitourinary syndrome have found evidence suggesting that laser is effective in promoting improvements in vaginal health and symptoms of urinary incontinence[62], and RF significantly improves aesthetic appearance, sexual satisfaction, and vulvovaginal atrophy[63]. RF for VL was investigated by two RCTs included in the latest systematic review[63]. The low number of RCTs precluded a definitive conclusion, and more studies are needed for this complaint. The study with the largest number of participants was published in 2017 and compared RF with sham control, with no statistically significant difference with regard to FSFI and VLQ score improvement between the groups after treatment [15].

283 Considering the surgical treatment, all included procedures for tightening the
284 vaginal canal in the present systematic review. Procedures ranged from colporrhaphy +
285 perineoplasty to the use of gold thread implants. Even with moderate adverse effects,
286 surgical treatments showed a high level of sexual satisfaction among the participants.
287 Even with the advent of energy-based therapies and the trend of recent years in the
288 adoption of non-surgical procedures for vaginal rejuvenation, surgical treatment is still
289 the option of choice when conservative treatment fails. Another observation is the variety
290 of definitions for the surgical treatment of VL. Recently, two terminologies were
291 published; one regarding surgical procedures for the posterior compartment of women
292 with pelvic organ prolapse, and the other regarding cosmetic gynecology[64,65]. It is
293 important that future studies on surgical treatment should be aware of these documents
294 and aim to standardize the details of the procedure; one example is to avoid suffixes such
295 as "plasty".

296 Interestingly, vaginal tightness also showed a high level of satisfaction in a
297 randomized clinical trial that used an extract of oak gall as a topical treatment. Due to its
298 antimicrobial and anti-inflammatory effects, this extract has been used in the treatment of
299 bacterial vaginosis, vaginitis, and urolithiasis[66,67]. The study showed that not only the
300 vaginal tightening effect was observed, but also antioxidant effects on the vaginal wall.
301 Unlike the other treatments, the gel containing the extract of oak gall was applied five
302 minutes before sexual intercourse and its effect was evaluated on the same day. More
303 studies are needed to understand the effects of the extract of oak gall on VL.

304 Recently, a systematic review evaluated general cosmetic gynaecological
305 procedures[68]. Similar to our findings, both studies included surgical vaginal calibre
306 reduction and energy-based therapy for VL. In the studies that we included, the
307 researchers used the self-report or subjective perception of the participants through the

VLQ, the gynaecological vaginal examination, the participants' desire for vaginal rejuvenation procedures or increased vaginal tightening, and finally, the use of the definition of "vaginal relaxation syndrome" to define it. In addition to the difficulty of standardizing the definition of VL, the lack of a specific objective assessment for the symptom still challenges the planning of future studies.

Conclusion

We conclude that RF and laser improved sexual function in women with VL from observational studies, but not from RCTs. Vaginal tightening according to the VLQ did not improve the sensation of women with VL after intervention. PFM strength was improved in women with VL after intervention. The findings are different from the results of observational studies, and it is paramount the development of future, prospective studies on this topic, with a definition for VL implemented in guidelines, using appropriate terminologies in cosmetic gynaecology and surgical treatment so that clinical and methodological heterogeneity may reduce among the studies a better certainty of evidence can be produced.

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553

554 **Table legends**

555 Table 1. General characteristics of the selected studies of women treated for vaginal laxity
556 (VL).

557 Table 2. Main goals, follow-up period, and main results according to the studies of women
558 treated for vaginal laxity (VL).

559 Table 3. ROBBINS-I classification for the selected non-randomized controlled studies.

560 Supplementary Table 1 – Search Strategy

561 Supplementary Table 2 – Characteristics of the included studies regarding energy-based
562 treatment for vaginal laxity (VL)

563 Supplementary Table 3 - Characteristics of the included studies that assessed surgical
564 treatment for vaginal laxity (VL).

565 Supplementary Table 4. GRADE – Summary of Findings

566

567 **Figure legends**

568 Figure 1. PRISMA flowchart for selection of the studies

569 Figure 2. Risk of Bias (ROB-1) for selected randomized controlled studies

570 Figure 3. Forest plot for sexual function questionnaires (FSFI and VLQ scores) and pelvic
571 floor muscle (PFM) strength after VL treatment from randomized controlled studies

572 Figure 4. Forest plot for FSFI scores after radiofrequency, laser, and surgical treatment
573 of VL from non-randomized controlled studies

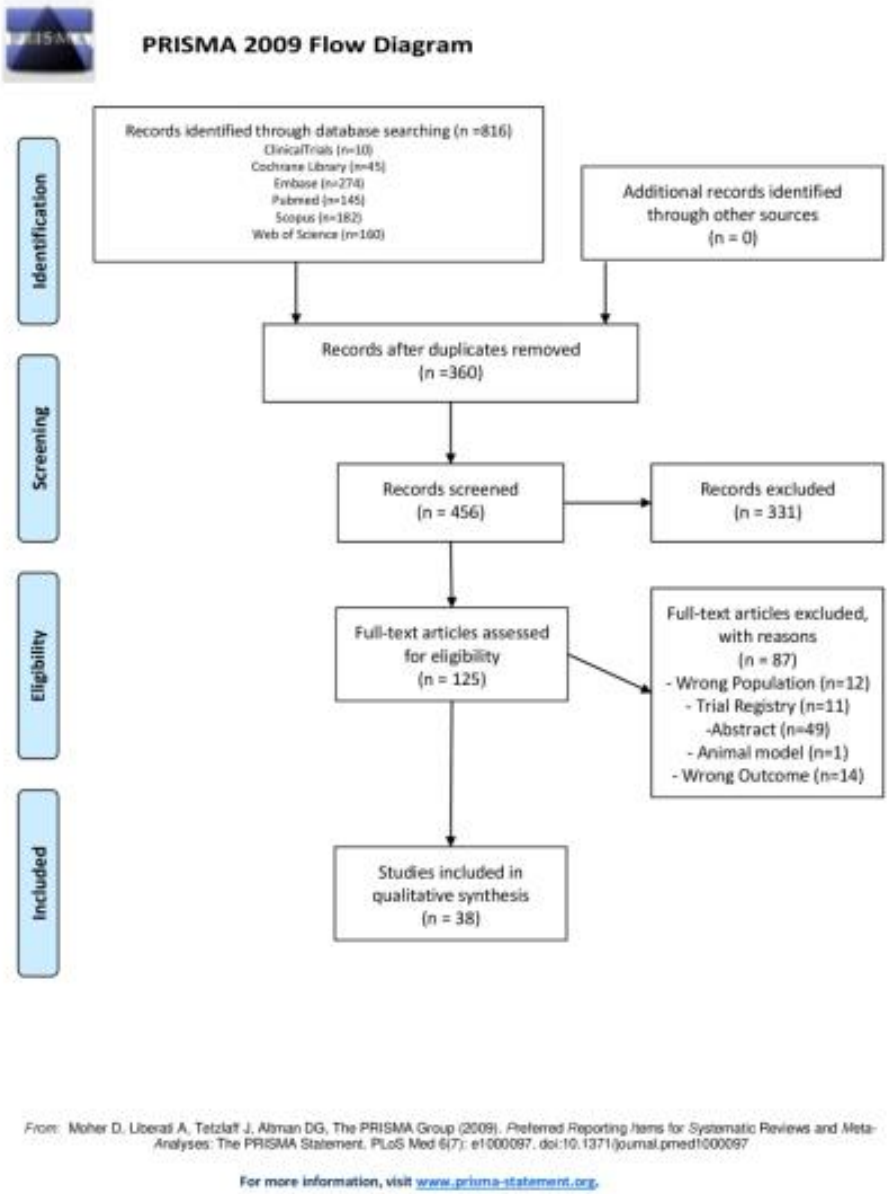

Figure 1. PRISMA flowchart for selection of the studies

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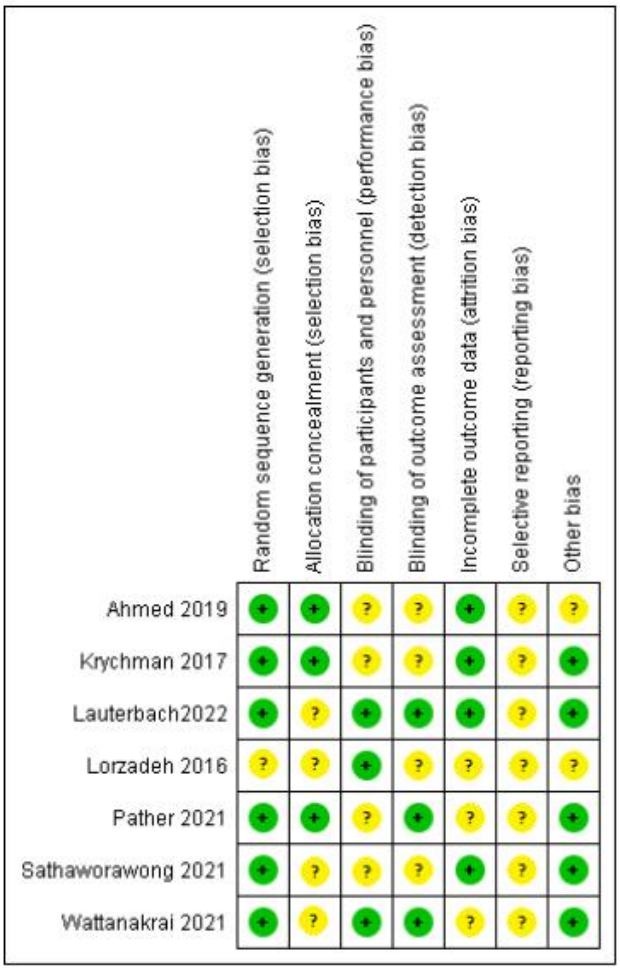

Figure 2. Risk of Bias (ROB-1) for selected randomized controlled studies

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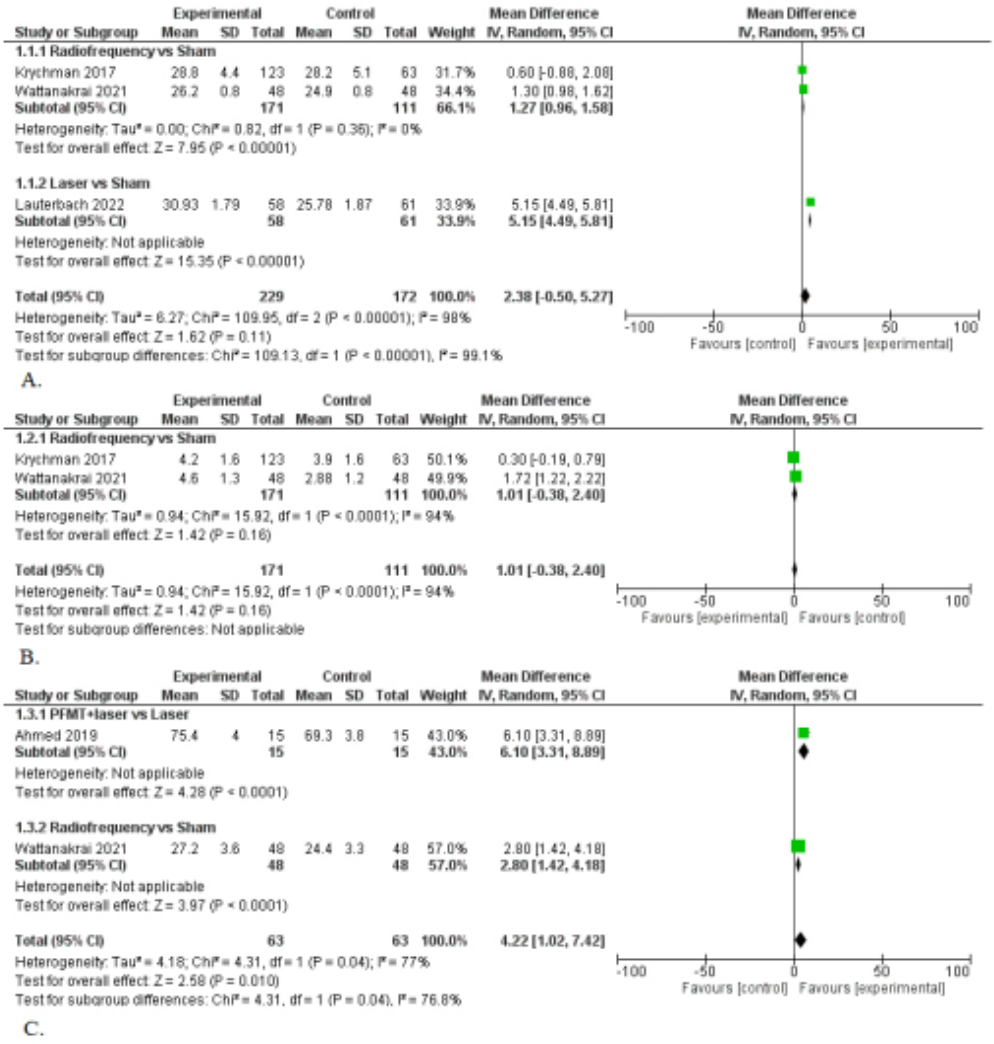

Figure 3. Forest plot for sexual function questionnaires (FSFI and VLQ scores) and pelvic floor muscle (PFM) strength after VL treatment from randomized controlled studies

564x591mm (38 x 38 DPI)

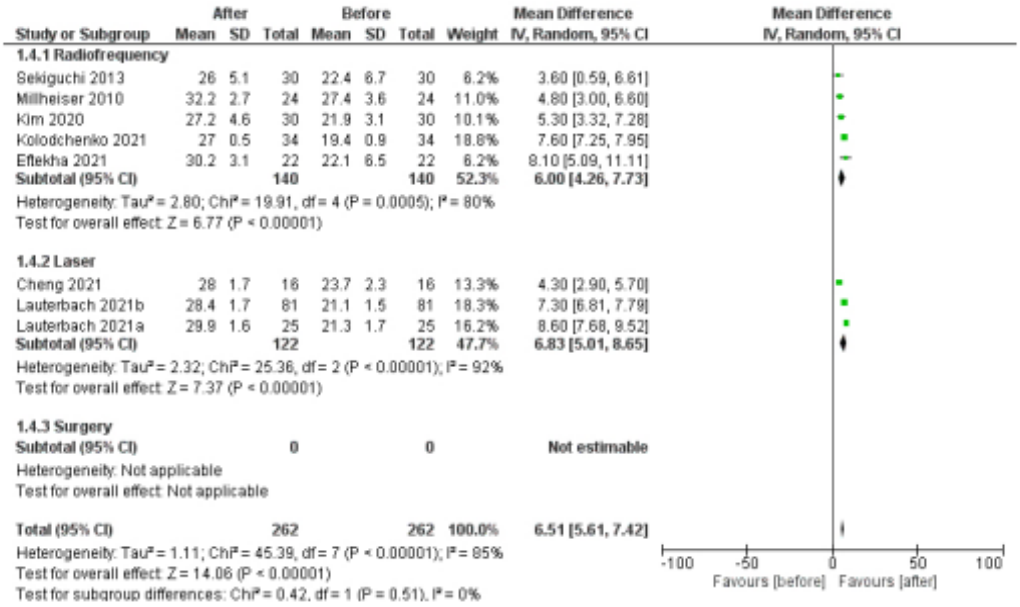

Figure 4. Forest plot for FSFI scores after radiofrequency, laser, and surgical treatment of VL from non-randomized controlled studies

279x163mm (72 x 72 DPI)

Table 1 – General characteristics of the selected studies of women treated for vaginal laxity (VL).

Author, year	Country	Study Design	Sample size (n)	Age (years)	Intervention	Definition/Classification of VL
Gaviria, 2012	Venezuela	Pilot	21	37.7 ± 9.75[α]	Laser	Vaginal relaxation syndrome; "loose vagina"; diminished sexual gratification; desire to improve vaginal tightness.
Lee, 2014	South Korea	Pilot	30	41.7 ± 5.75[α]	Laser	Vaginal relaxation syndrome.
Gaviria, 2016	Venezuela	Retrospective	60	39.0 ± 13.5[α]	Laser	Vaginal relaxation syndrome; "loose vagina"; desire to improve vaginal tightness.
Jomah, 2019	SA	Observational	39	39.0 ± 5.0[α]	Laser	Vaginal relaxation syndrome.
Ahmed, 2019	Egypt	RCT	30	PFMT (42.6 ± 81.91) PFMT+ER:YAG (39 ± 2.2)	Laser	Decreased sexual sensation; desire to increase the vaginal tightness.
Mitsuyuki, 2020	Japan/ Slovenia	Retrospective	364	42.8 ± 0.35[α]	Laser	Symptoms of vaginal looseness.
Toplu, 2021	Turkey	OS***	30	48.3 ± 7.0	Laser	Self-reported VL graded during pelvic examination
Lauterbach,2021	Israel	Prospective Cohort	81	47.7 ± 4.0[α]	Laser	Decrease in sexual sensation during intercourse; self-reported VL.
Lauterbach,2021	Israel	Prospective Cohort	25	45.2 ± 2.75[α]	Laser	Vaginal looseness; decrease vaginal sensation during sexual intercourse.
Lauterbach,2022	Israel	RCT	119	Laser 45.6±2.2 Control 44.8±3.1	Laser	Decreased sexual sensation during intercourse and self-reported vaginal looseness.
Cheng, 2021*	China	Retrospective	16	25 – 40 (range)	Laser	Complaint about VL confirmed by VE.
Sathaworawong, 2021	Thailand	RCT	42	38.14 ± 7.05	Laser	Decreased sexual sensation during sexual intercourse; VL diagnosed by a gynecologist.
Gao, 2022	China	Observational	29	37.2 ± 7.8	Laser	Subjects with VL.
Setyaningrum, 2022	Indonesia	Retrospective	14	29 – 63 (range)	Laser	Symptoms of VL.
Vicariotto, 2016	Italy	Prospective	11	41.7 ± 5.5	RF	Subjective perception of laxity of vaginal introitus (VLQ).
Vicariotto, 2017	Italy	Observational	25	41.4±5.8	RF	Subjective perception of laxity of vaginal introitus (VLQ).
Lalji, 2017	USA, Bulgaria	Prospective, multicentric	27	44.78 ±10.04	RF	Subjective perception of VL (VLQ).
Caruth, 2018	USA	Prospective	25	48.6±5.0[α]	RF	Symptoms of pelvic relaxation and VL; desire for VR.
Dobrokhotova, 2019	Russia	Observational	30	31.69 ± 4.97	RF	Vaginal relaxation syndrome in the postpartum period.

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Sekiguchi, 2013	Japan, USA	Prospective	30	42.9 ± 5.5 [α]	RF	Self-reported perception of VL (VLQ).
Kolodchenko, 2021	Ukraine	Prospective	34	38.2 ±7.6	RF	Self-reported VL.
Millheiser, 2010	USA	Pilot	24	37 ± 5.1	RF	Self-reported perception of VL (VLQ).
Krychman, 2017	USA, Canada	RCT	186	RF (40.8± 6.0); Sham (40.8 ± 5.7)	RF	Self-reported VL.
Kim, 2020	SK	Prospective	30	49.0 ± 7.0 [α]	RF	Self-reported perceptions of VL (VLQ).
Alinsod, 2015	USA	Prospective	23	43.6±8.2 [α]	RF	Self-reported vulvovaginal laxity (VLQ).
Wattanakrai, 2021	Thailand	RCT	32	RF (37.19±5.33); Sham (35.5±4.97)	RF	Self-assessment of VL (VLQ)
Eftekhar, 2021	Iran	Prospective	22	40.30 ± 8.01	RF	Sexual dissatisfaction suffering from VL.
Pather, 2021	Australia, India	RCT	63	RF (37.0 ± 4.75 [α]); Sham (36.0 ± 3.25 [α])	RF	Symptoms of VL (vaginal flatus or sexual concerns relating to vaginal laxity)
Pardo, 2006	Chile	Observational	53	45.0 ± 9.0 [α]	Colporrhaphy + PP	Sensation of a wide vagina plus reduction or lack of ability to reach orgasm.
Al-Hamadani, 2019	Iraq	Prospective	20	No quantitative data – reproductive age	PC and/or shots of PRP injection.	Sensation of the wide vagina and sexual dysfunction.
Moore, 2014	USA	Retrospective	60	43.6 ± 7.9	Modified PC	Complaint of VL/looseness (clinically confirmed by VE); desire for VR.
Park, 2015	SK	Retrospective	180	39.4 ± 16	VR using EST	Persistent subjective feeling of a wide vagina.
Kim, 2020	SK	Retrospective	27	48.9 ± 6.49 [α]	GTI	VL defined by (VLQ).
Ulubay, 2016	Turkey	Retrospective	38	46.0±10.3	PP	Sensation of a wide vagina.
Jamali, 2014 **	Iran	Prospective	76	34.02 ± 5.3	CP	VL confirmed by a gynecologist.
Cheng, 2021*	China	Retrospective	28	25 to 40 (range)	VP	Complaint about VL confirmed by VE.
Yang, 2022	China	Observational	52	39 (21-52)	HADM + EP	Women with grade II-III vaginal relaxation by VE.
Li, 2022	China	Retrospective	80	44.6 (22-62)	VP(ADM) + PP	Women with VL.
Lorzadeh, 2016	Iran	RCT	78	36 ± 5.4	EOG	Married women with vaginal relaxation.

Notes: RF: Radiofrequency; VLQ: Vaginal Laxity Questionnaire; [α] Mean and Standard Deviation from median, range or interval interquartile; USA: United States of America; SA = Saudi Arabia; RCT: Randomized Clinical Trial; PFMT: Pelvic Floor Muscle Training; PRP: platelets rich plasma; EP = enriched platelets; PC = posterior colpoperineorrhaphy; PP = perineoplasty; VP = vaginoplasty; CP = colpoperineoplasty ; VR = vaginal rejuvenation; VE = vaginal examination; GTI = gold thread implantation ; EST = elastic silicone thread; EOG = extract of oak gall; HADM; human acellular dermal matrix; ADM = acellular dermal matrix; VL: Vaginal Laxity; SUI: Stress urinary incontinence; ER-YAG = erbium laser; OS = Observational; SK = South Korea

* Study was used for Laser and Surgery; ** Same population (6-months and 18-months); *** Observational studies were studies that no definitions were written at the methodology section of the manuscript.

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Table 2. Main goals, follow-up period, and main results according to the studies of women treated for vaginal laxity (VL).

Author/Intervention	Main Measurements	Follow-Up	Main Outcomes
Gaviria, 2012 [a]	VAS for Pain; POP-Q; Laser Vaginal Tightening (LVT) Questionnaire.	3-Months	VAS (0: n=10; 1-2: n=11); All participants presented POP improvement after Laser session. LVT 3-Months (Tightness improvement: 4.8% mild;76.2% moderate, 19% strong; Sexual partners' improved sensation: 15% mild;50% moderate, 35% strong; Patients' sexual gratification: 95.2% more friction; 57.1% better orgasm; 14.3% more orgasm; 4.8% no improvement).
Lee, 2014 [a]	Partner's assessment of vaginal tightening scale; Subjects' own sexual satisfaction scale; Biopsies. PFM Strength (mm/Hg)	2-Months	Partner's assessment of vaginal tightening (76.6%); Subjects' own sexual satisfaction (70.0%). Histological findings: a thicker and more cellular epithelium; compact lamina propria with a denser arrangement of connective tissue. PFM Strength (mm/Hg): improvements in maximum and average pressure at 2-Months post-treatment ($P<0.01$, $P<0.05$, respectively).
Gaviria, 2016 [a]	Duration of the Results; Satisfaction with the Results; Experiences from Interviews.	Up to 3 years	The average duration of effect: 16 months; Results persisted after 3 years: 87.5%; Correlation between risk factors and persistence of the results (age ($P = 0.975$), number of sessions ($P = 0.502$), POP and/or UI ($P = 0.071$), menopause ($P = 0.388$), constipation ($p = 0.341$), smoking ($P = 0.825$). High satisfaction (58%); Willing to repeat the therapy (83%); Recommend the treatment (90%). Average Pain (1).
Jomah, 2019 [a]	Patient Satisfaction Questionnaire; Sexual Satisfaction Scale	1-2-Months	Sexual Satisfaction (78%);17 participants (n=39) with low satisfaction (0 and 1) presented parity average of 3.7. Improvement in sexual satisfaction (78% premenopausal women).
Ahmed, 2019 [a]	Sexual Satisfaction Scale. PFM Strength (cm/H_2O)	4,8 weeks	Sexual Satisfaction improvement: both groups at 4 and 8 weeks compared with the pretreatment, and at 8 weeks compared with 4 weeks ($P = 0.0001$, $P<0.01$, respectively); both groups at 8 weeks and at 4 weeks, in favor of group (PFMT + Laser) ($P = 0.0001$). PFM Strength (cm/H_2O): improvements in both groups at 4 and 8 weeks ($P=0.0001$).
Mitsuyuki, 2020 [a]	Patient Satisfaction Questionnaire; Objective Visual evaluation; VAS pain.	3, 12-Months	Sexual gratification after Laser (3-Months): Overall 92.7% improvement; 7.3% no improvement; Vaginal Tightening after Laser (12-Months): 60% tight or very tight; no vaginal looseness after Laser. Visual evaluation of introitus laxity: 69% improved laxity. Average Pain (1).
Toplu, 2021 [a]	General Satisfaction; PISQ-12	6-Months	General Satisfaction: 86% high-moderate; Vaginal tightness improvement: 66%; Quality Sexual Activity: 63%; PISQ-12 score was statistically insignificant. Results at 6-Months after Laser.
Lauterbach,2021 [a]	Sexual Encounters, Sexual Satisfaction. FSFI; VHI.	3, 6-Months	The rate of sexual intercourse increased from four times to 10 times per month at 3-Months follow-up and decreased to five times at 6-Months. Sexual satisfaction (3,6-Months): 89% and 80%, respectively. FSFI and VHI: improvements only at 3-Months ($P = 0.012$; $P=0.013$; respectively).
Lauterbach,2021 [a]	Biomechanical Parameters; FSFI; VHI.	3-Months	Vaginal elasticity and tightening improved after Laser ($P = 0.0027$, $P = 0.0014$, respectively). PFM Strength and Reflex increased after Laser ($P = 0.0011$, $P = 0.0022$, respectively). FSFI total score and desire, arousal, orgasm and satisfaction were higher after Laser ($P = 0.036$; $P = 0.035$; $P = 0.044$; $P = 0.039$; $P = 0.042$, respectively). VHI total scores were higher after Laser ($P = 0.0032$).
Lauterbach, 2022	FSFI; VHI; Sexual Intercourse rate	3, 6-Months	Sexual intercourse rate: (baseline, $P = 0.79$; 3-Months, $P = 0.011$, significant increase in the study group; 6-Months, $P = 0.52$)

Cheng, 2021*[a]	Satisfaction Rate; FSFI	3, 12-Months	Satisfaction Rate (12-Months): 87.5%. FSFI: improvements at 3-Months (P<0.01) and one year (P<0.05) after treatment.
Sathaworawong, 2021[β]	Vaginal tightness satisfaction survey, PFM Strength (mm/Hg)	1,3,6-Months	Vaginal Tightness satisfaction survey: improvement of symptoms in laser group 1-Month (P=0.002), 3-Months (P=0.004). No significant difference at 6-Months. Patients' overall satisfaction was higher in the laser group, 1 and 3-Months (P=0.003 and P=0.001, respectively). PFM Strength increased in both groups at all follow-ups (P < 0.001).
Gao, 2022	FSFI, VHI, VTI, histology	1-Month, 10-12-Months	FSFI: (before/1-Month first treatment, P<0.01; before/1-Month second treatment, P<0.01); VHI: (before/1-Month first treatment, P<0.05; before/1-Month second treatment, P<0.05); VTI, 10-12-Months: (both the anterior and posterior vaginal walls after treatment were significantly higher than the pre-treatment baseline, P<0.002, P<0.001, respectively). Histology: a thicker stratified squamous epithelium layer, angiogenesis and a denser lamina propria were observed after laser treatment.
Setyaningrum, 2022	Improvement in VL complaints		Total of 14 patients: 1 no improvement, 4 mild, 6 moderate, 3 high stated satisfaction;
Caruth, 2018[β]	ICIQ-VS, PFIQ-7	2-Months	ICIQ-VS and PFIQ-7: a significant improvement at 2-Months compared to baseline (P<0.001).
Dobrokhotova, 2019[β]	Biopsies, dynamic assessment; PFM Strength (mm/Hg), length of introitus	1-Month	Subjective improvement (73.3%); Dynamic assessment: all symptoms regarding a relaxed vagina have improved after the RF procedures (from P=0.03 to P<0.001). Biopsies: mRNA expression of proteins involved in collagenogenesis showed a significant decrease in the expression of decorin, MMP-2, collagen, and type 3 mRNA (P <0.05). PFM Strength (mm/Hg): significant increase in the strength of muscle contraction (P<0.001). Reduction of the length of introitus (P=0.05).
Lalji, 2017	VLQ; sexual gratification	1-Month	VLQ: All participants reported vaginal sensation of slightly, moderately or very tight after 1 month. Sexual gratification after 1 month: 48% answered strongly agree and 45% agree.
Sekiguchi, 2013[β]	GRA, FSFI, FSDS-R, VLQ, SSQ	1,3,6, 12-Months	GRA improved moderately and markedly at 33% at 3-Months, 41% at 6-Months, and 32% at 12-Months. FSFI total: significant improvement was observed at all follow-up periods, but 12-Months. FSDS-R: significant improvement was observed at all follow-up periods. VLQ: improvements throughout 12 months (P<0.001). SSQ: significant improvement in 76.5% at each follow-up period.
Kolodchenko, 2021[β]	GRA, VHI, FSFI	1, 4-Months	GRA for sexual satisfaction and vaginal laxity improved in both follow-up 1-4-Months (P<0.001; P<0.001, P<0.01, and P<0.001, respectively). Significant improvement in FSFI and VHI at 1-4-Months.
Vicariotto, 2016	PISQ-12, VLQ	After treatment, 1-2 months	VLQ and PISQ-12 improved significantly after treatment and at 30 and 60 days follow-up when compared to pre-treatment assessment.
Vicariotto, 2017	PISQ-12, VLQ, SSQ	After treatment, 1,2,6,9,12-Months	VLQ, PISQ-12 and SSQ: significant improvement after treatment and all follow-up periods when compared to before treatment.
Millheiser, 2010[β]	GRA, FSFI, FSDS-R, VLQ, SSQ	1,3,6-Months	GRA: improved moderately and markedly at 48% at 3-Months, 61% at 6-Months. Improvements in FSFI, VLQ and FSDS-R (P<0.001) at 6-Months. SSQ improved at 6-Months (P=0.002).

Wattanakrai, 2021[β]	Treatment Satisfaction, Biopsies, VLQ; FSFI; PFM Strength (Perineometer);	1,3 months	Treatment Satisfaction: higher in the active group (P<0.001). Biopsies: increased mucosal epithelial thickness, compact lamina propria, denser connective tissue, increased number of blood vessels, and increased elastic tissue in the active group. VLQ: significant improvement in both groups at 4 and 12 weeks, with greater improvement in the active group. PFM Strength: significant improvement in the active group at both follow-up periods. FSFI total: significant improvement in the both groups at 12 weeks. The active group also improved significantly at 4 weeks.
Alinsod, 2015	VLQ, SSQ	1 month	VLQ: Pronounced improvement with the 1st treatment, some additional and minimal improvements with 2nd and 3rd treatments. Similar trend with SSQ.
Eftekhar, 2021[β]	POP-Q, FSFI	3-Months	POP-Q improvement (3-Months): point Ba (P=0.02) and total vaginal length (0.014). The perineal body also improved but not significantly (P=0.058). Other points are slightly improved. FSFI: Significant improvement in all domains after 3-Months follow-up.
Pather, 2021[β]	VFS, POP-Q, MOS, Genital Hiatus, VLQ (tight), FSFI	3,6-Months	VFS (3,6-Months): did not reach statistical significance between sham and the active group. MOS (6-Months): improvement in the active group but not statistically significant. Genital Hiatus (6-Months): no difference was noted between groups. VLQ: improvements were observed in both groups but only the active group presented a significant improvement after 6-Months (P=0.01). FSFI: Active group improved significantly at 3-Months (P=0.02), but not after 6-Months (P=0.07)
Krychman, 2017	VLQ, FSFI, FSDS-R	1,3,6-Months	VLQ: No vaginal laxity at 6-Months was 3.39 times (OR = 3.39; 95% CI =1.54-7.45) greater in the active group than in the Sham group. FSFI and FSDS-R: a greater improvement was observed in the active group for FSFI and a borderline significant finding of less distress for the Active on FSDS-R when compared with Sham at 6-Months.
Kim, 2020	VLQ, FSFI, FSDS, Vaginal Pressure (cmH_2O) resting	4, 12-Weeks	FSFI domains: improvements in FSFI in all domains at 4 and 12 weeks; VLQ and FSDS: improvements at 4 and 12 weeks; No significant improvement was observed in resting vaginal pressure at 12 weeks.
Pardo, 2006[α]	Patients' Satisfaction.	6-Months	Great improvement in Sexual Life: 66%; Significant improvement: 24%; Slight improvement: 6%; No improvement 4%; 94% of women reached orgasm; 96% of women felt adequate vaginal tightening. Two patients regretted surgery.
Al-Hamadani, 2019[α]	Sabbatsberg Sexual Self-rating Scale.	10 weeks	Sabbatsberg Sexual Self-Rating Scale Scoring (10 weeks): P = 0.001 in all domains in both groups. Rich plasma injection was significantly increased compared to perineorrhaphy in Sexual interest (3.2 versus 3.7, P= 0.024), Sexual activity (3.4 versus 3.9, P=0.018), and Sexual pleasure (3.2 versus 3.8, P=0.022 respectively). No statistical difference was found in Sexual life, Importance of sex, and Orgasm.
Moore, 2014[α]	PISQ-12.	6-Months	PISQ-12 total score (6-Months): P<0.001; no change was observed in questions (Q1-sexual desire, Q5-pain during intercourse, and Q11-partner having an issue with premature ejaculation). No difference was found in pain with intercourse pre- to postoperatively.
Park, 2015[α]	FSFI; Vaginal width.	2,6, 12-Months	Overall FSFI: progressively improvement up to 12-Months (FSFI orgasm domain improvement: P<0.05); Vaginal width satisfaction: 92.8%.
Kim, 2020[α]	VL score; Vaginal dryness score; Pain at intercourse; Partners' satisfaction;	1–3-Months	Vaginal laxity improvement (89.1%); Vaginal dryness improvement (87%); Improvement in pain at intercourse and partners' satisfaction (p<0.0001).

Ulubay, 2016[a]	POP-Q; Patients' Satisfaction Rate with Operation; Partners' Satisfaction; Operation recommendation; Dyspareunia.	6-Months	Genital hiatus and perineal length improvement (P<0.01); no statistical change in total vaginal length. Patients' Satisfaction Rate with Operation (87.9%); Partners' Satisfaction (92.6%); Operation recommendation (87.9%); Dyspareunia (10%).
Jamali, 2014[a]	FSFI	6, 18-Months	All FSFI domains improved at 6 and 18-Months (P<0.001), but pain and lubrication after 6-Months.
Cheng, 2021*[a]	FSFI, Satisfaction Rate.	3, 12-Months	Severe and Moderate VL: FSFI total score after the operation (3,12-Months): P<0.01 in both periods and degrees. Satisfaction Rate (12-Months): severe VL 88.2%; moderate VL 90.9%.
Yang, 2022	FSFI, VHI, VAS	After surgery, 7-days, 1,3,6-Months	FSFI total score: (before/after surgery, P<0.001); VHI total: (Before/1-Month, P<0.0001; 3-Months, P<0.0001, 6-Months, P<0.0001); VAS (good quality of patient satisfaction after surgery).
Li, 2022	3D-Trasvaginal Ultrasound, FSFI	13.2 (6.1-50.2) Months	Reduced introital diameter (from 4.1 to 2.3 cm, P<0.05) and reduced vaginal angulation (from 182° to 122°, P<0.05) on maximum Valsalva manoeuvre. Pelvic floor muscle function improvements. FSFI: No significant improvement in the total score, P>0.05.
Lorzadeh, 2016[a]	Sexual satisfaction; Vaginal tightness; Vaginal dryness; Sexual problems	After intervention	Sexual satisfaction and frequency of orgasm were significant in the group oak extract jell 2.5%; Sense of vaginal tightness (93% in group jell 2.5%, 33% in group jell 2%, and 6.7% in group jell 1.5%); Vaginal dryness improvement (86% in group jell 2.5%, 43% in group jell 2%, and 33% in group jell 1.5%); Sexual problems (air at intercourse, orgasm inability, coital incontinence, lack of relaxation, and sense of vaginal mass were significantly reduced in group jell 2.5% (P<0.0001).

[a] Laser; [b] Radiofrequency; [c] Surgery; [d] Topical treatment; VL: Vaginal Laxity; * Study was used for Laser and Surgery; ** Same population (6-months and 18-months); POP-Q: Pelvic Organ Prolapse Quantification; POP: Pelvic organ prolapse; FSFI: Female Sexual Function Index; VAS: Visual Analog Scale; VHI: Vaginal Health Index; PISQ-12: Pelvic Organ Prolapse Incontinence Sexual Questionnaire; VLQ: Vaginal Laxity Questionnaire; VLBS: Vaginal Laxity Bother Score; VFS: Vaginal Flatus Score; MOS: Modified Oxford Score; SSQ: Sexual Satisfaction Questionnaire; GRA: Global Response Assessment; MFSQ: McCoy Female Sexuality Questionnaire; VTI: Vaginal tactile imaging;

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Table 3. ROBBINS-I classification for the selected non-randomized controlled studies.

Study	Confounding	Selection of Participants	Classification of Interventions	Deviations from Intended Interventions	Missing Data	Measurement of Outcomes	Selection of the Reported Result	Overall
Gaviria 2012	Serious	Moderate	Moderate	Serious	No information	Serious	Moderate	Serious
Lee 2014	Low	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Gaviria 2016	Serious	Moderate	Moderate	Serious	Moderate	Moderate	Moderate	Serious
Jomah 2019	Serious	Moderate	Moderate	Serious	Moderate	Serious	Moderate	Serious
Mitsuyuki 2020	Serious	Moderate	Moderate	Moderate	Serious	Serious	Moderate	Serious
Toplu 2021	Serious	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Serious
Lauterbach 2021	Serious	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Serious
Lauterbach 2021	Serious	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Serious
Cheng 2021	Serious	Serious	Moderate	Serious	Moderate	Serious	Moderate	Serious
Alinsod 2015	Serious	Moderate	Serious	Serious	Moderate	Serious	Moderate	Serious
Dobrokhotova 2019	Serious	Serious	Serious	Moderate	Moderate	Moderate	Serious	Serious
Kolodchenko 2021	Serious	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Serious
Caruth 2018	Serious	Moderate	Serious	Serious	Moderate	Serious	Moderate	Serious
Lalji 2017	Serious	Moderate	Serious	Moderate	Moderate	Moderate	Moderate	Serious
Eftekhar 2021	Serious	Moderate	Serious	Moderate	Moderate	Serious	Moderate	Serious
Millheiser 2010	Serious	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Serious

Kim 2020	Serious	Moderate	Serious	Moderate	Moderate	Moderate	Moderate	Serious
Sekiguchi 2013	Serious	Moderate	Moderate	Moderate	Serious	Serious	Moderate	Serious
Vicariotto 2016	Serious	Moderate	Serious	Moderate	Serious	Moderate	Moderate	Serious
Vicariotto 2017	Serious	Moderate	Serious	Moderate	Serious	Moderate	Moderate	Serious
Al-Hamadani 2019	Serious	Serious	Serious	Moderate	Moderate	Moderate	Serious	Serious
Jamali 2014	Serious	Serious	Serious	Moderate	Moderate	Moderate	Serious	Serious
Kim 2020	Serious	Serious	Moderate	Serious	Moderate	Serious	Serious	Serious
Moore 2014	Serious	Serious	Moderate	Moderate	Moderate	Moderate	Moderate	Serious
Pardo 2006	Serious	Serious	Moderate	Moderate	Moderate	Serious	Moderate	Serious
Park 2015	Serious	Serious	Moderate	Serious	Moderate	Serious	Moderate	Serious
Ulubay 2016	Serious	Serious	Moderate	Moderate	Moderate	Serious	Moderate	Serious

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Supplementary Table 1 – Search Strategy

DATE: 7th of September 2022

Pubmed (07/09/2022) – All Fields - n=145

("vaginal laxity" OR "vaginal looseness" OR "vaginal relaxation" OR "wide vagina" OR "vaginal flaccidity")

Embase (07/09/2022) – All Fields - n= 274

'vaginal laxity' OR 'vaginal looseness' OR 'vaginal relaxation' OR 'wide vagina' OR 'vaginal flaccidity'

Scopus (07/09/2022) – Title/Abstract/Keynotes - n= 182

(TITLE-ABS-KEY ("vaginal laxity") OR TITLE-ABS-KEY ("vaginal looseness") OR TITLE-ABS-KEY ("vaginal relaxation") OR TITLE-ABS-KEY ("wide vagina") OR TITLE-ABS-KEY ("vaginal flaccidity"))

Web of Science (07/09/2022) - n = 160

TÓPICO: ("vaginal laxity") OR TÓPICO: ("vaginal looseness") OR TÓPICO: ("vaginal relaxation") OR TÓPICO: ("wide vagina") OR TÓPICO: ("vaginal flaccidity")

Cochrane Library (07/09/2022) - n=45

(("vaginal laxity" OR "vaginal looseness" OR "vaginal relaxation" OR "wide vagina" OR "vaginal flaccidity")):ti,ab,kw; Any MeSH descriptor in all MeSH products.

Clinical Trials (07/09/2022) - n=10

("vaginal laxity" OR "vaginal looseness" OR "vaginal relaxation" OR "wide vagina" OR "vaginal flaccidity")

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Supplementary Table 2 – Characteristics of the included studies regarding energy-based treatment for vaginal laxity (VL)

Author	Device	Procedure	Pre-session Care	Post-session care	Parameters	Adverse Events
Gaviria,	Er:YAG 2940 nm laser	2 sessions / 15-30 days interval	Topical anesthesia (Lidocaine 2% + Prilocain).Wash and disinfection solution.	Avoid sexual activities for 72 hours.	90J vaginal wall (360° belt-shaped patterns)/10J vestibule and introitus.	No adverse events.
Lee,	Er:YAG 2940 nm laser	4 sessions; 1-2 weeks apart	Not informed.	Not informed.	GA: Session 1 and 2, 360° scope 3 multishots and 1.7 J/shot; pulse energy at 15 mJ. Session 3 and 4, 90° scope 3 multishots and 1.7 J/shot; pulse energy at 15 mJ (vaginal canal). GB: Sessions 1-4 called for the 90° scope 3 multishots and 1.7 J/shot, sessions 3 and 4 an additional 2 passes per session with the 360° scope in long-pulsed mode, a pulse width of 1000 ms (1 s), 3.7 J/shot (vaginal canal).	Vaginal ecchymosis with a mild burning sensation.
Gaviria,	Er:YAG 2940 nm laser	1-4 treatment sessions/ 15-30 days interval	Wash and disinfection solution. To the vestibule (Lidocaine 2%) and to the introitus area (Lidocaine spray 10%).	Avoid sexual activities for 72 hours.	360° laser irradiation of the vaginal canal; 90 J is delivered to each irradiation location with reinforcement of the lower vaginal third/ 10J vestibule and introitus.	Mild and transient edema and a tolerable heating sensation.
Ahmed	Er:YAG 2940 nm laser	2 treatment sessions with an interval of 4 weeks.	Wash and disinfection solution. Topical anesthesia (Lidocaine 2%).	Avoid sexual intercourse for 3 days.	4 passes per session /750J vaginal mucosa. 4 passes per session vestibule and introitus with a PS03 hand piece.	Not informed.
Jomah	Er:YAG 2940 nm laser	4 sessions with 2–3-week interval	Routine antiseptic. Topical anesthesia (Lidocaine or Prilocaine 1%).	Avoid sexual intercourse for 2 days.	360° scope via automatic dual step. First step: three passes of multiple pulses ranging from 1.7 to 2.2 J per pulse. Second step: two passes of long-pulsed wave of 3.7 J and a pulse width of 1 s.	Heating in the vagina during treatment, vaginal ecchymosis with a mild burning sensation.
Mitsuyuki,	Er:YAG laser	2-3 sessions/ 30 days interval	Topical anesthesia (Lidocaine 10%). Wash with a physiological solution.	Avoid sexual intercourse for 3 days.	250 joules of energy were delivered per pass, corresponding to 3 J/cm2 of fluence per one SMOOTH pulse in the vaginal canal (360°). 10 J of laser energy vestibule and introitus.	Transient edema after the treatment; stronger

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						vaginal discharge 40%, transient urge incontinence 3%.
Sathaworawong,	Er:YAG 2940 nm laser	2 sessions/monthly	Cleaning of perineum area with normal saline.	Avoid sexual intercourse for 7 days.	8–10 J/cm2 (vaginal canal); 10 J/cm2 (vestibule and introitus)/ A 7-mm spot-size handpiece with a pulse duration of 250 ms and a repetition rate of 1.6 Hz was used for both areas.	Mild and transient leukorrhea, dryness, dysuria, vaginal itching, and spot bleeding.
Setyaningrum,	Er:YAG 2940 nm laser	1-3 treatment sessions. 1-Month interval	Vaginal canal and introitus disinfected with betadine. Topical anesthesia.	Avoid sexual intercourse for 7 days.	Vaginal canal: 3 J/cm2 fluence, 7 mm spot size, 1.6 Hz frequency Introitus: 10 J/cm2, 2 mm spot size, 1.6 Hz frequency	A mild, nonitching fluor albus in one patient.
Lauterbach	Carbon dioxide (CO2) laser.	Three treatments/ 4 weeks interval	No	Refrain from vaginal intercourse or tampon.	Laser density was set to 10% and laser energy ranged from 7.5 to 10 to 12.5 mJ delivered to the vaginal mucosal surface including the introitus and fornices.	Unpainful suction; stinging sensation; local sensitivity; lower abdominal cramping; urinary tract infection.
Lauterbach	Carbon dioxide (CO2) laser.	Not informed.	Not informed.	Not informed.	Treatment of the entire vaginal circumference.	Not informed.
Lauterbach	Carbon dioxide (CO2) laser.	Single treatment session for study group and sham.	Not informed.	Refrain from vaginal intercourse or tampon for 14 days.	Treatment of the entire vaginal circumference with energy and without energy (sham group).	Discomfort and sense of pressure lasting up to 5 minutes. Vaginal discharge for 2 days. One participant

						reported low back pain.
Cheng,	Carbon dioxide (CO2) laser.	Three treatments/ 1-month interval	Not informed.	Not informed.	DOT 30 W, a dwell time of 1,000 usec, and a DOT spacing of 1,000 µm.	Not informed.
Toplu	Carbon dioxide (CO2) laser.	1-3 sessions	Cleaning of vulvovaginal area.	Not informed.	30-45 mJ; 1-1.2 mm distance settings.	Pain and discomfort during the procedure reported.
Gao	Carbon dioxide (CO2) laser.	2 sessions/1-Month interval.	Not informed.	Not informed.	10 mJ and a spot density of 10–15%.	No.
Vicariotto	Dynamic quadripolar RF	5 sessions (vaginal laxity arm) every 14±1 days;	Not informed.	No.	Not informed.	No.
Vicariotto,	Low-energy dynamic quadripolar RF	4-6 sessions/every 14±2 days	Coupling gel.	No impediment to sexual intercourse.	Power settings were 14% to 20% of the device maximum power (55 W) to treat vaginal mucosa.	No.
Lalji	Monopolar RF device (Exilis Ultra 360, BTL Industries Inc., Boston, MA)	3 once-a-week treatment sessions	Not informed.	Not informed.	Intravaginal tip: 30 points and 80% duty factor. Extra-vaginal: 90 points and 100% duty factor.	No.
Caruth	Bipolar RF-based device (Votiva, InMode MD Ltd., Lake Forest, CA); FractoraV handpieces	Group I: treated 16-20 minutes internally in the vaginal canal and 8-10 minutes per labium, Group II: treated 10-12 minutes in the vaginal canal and 5-6 minutes per labium and Group III: treated for 6-8 minutes in the vaginal canal and 3 minutes per labium.	Not informed.	Not informed.	RF energy level of 25- 30 and a cut-off temperature of 43oC. FractoraV with a coated 24-pin tip was used with an RF energy level ranging from 15 to 30.	No.
Dobrokhotova,	Non-ablative RF Exilis apparatus using Ultra Femme 360°	3 procedures/7 days interval	Cooling gel	Not informed.	Focused radio wave radiation with a frequency of up to 3 MHz was directed to the target tissue (vulvar, perineal region and intravaginal).	No.

	technology (BTL, Czech Republic - Great Britain)					
Sekiguchi	RF device (Viveve Vaginal Laxity RF Therapy System, Viveve, Inc. Sunnyvale, California USA)	Single procedure. 5-times each area with 21 overlapping pulses or up to a maximum total of 105 pulses.	Non-alcohol-based cleanser. Coupling fluid.	Avoid sexual intercourse for 10 days	RF treatments were delivered at 90 J/cm2. The duration of each pulse is 7.5 seconds in the vaginal introitus avoiding the urethra.	Mild pain, vaginal leukorrhea, and low abdominal pain.
Kolodchenko,	Nonablative/ noncoagulative multipolar RF/Pulsed electromagnetic field (PEMF)-based device (Venus Fiore TM, Venus Concept, Weston, FL).	3 treatments/ 1-month intervals	Ultrasound gel for coupling and lubrication.	Keep the treated area clean and to refrain from mechanical or thermal injury.	Energy level at 50%–70% output for all 3 pairs of electrodes (vaginal canal). Target temperature (42°C at the proximal thermometer and 45°C for the mid and distal thermometers.	Mild pain.
Millheiser,	RF (Viveve, Inc, Palo Alto, CA, USA)	Single treatment.	Non-alcohol based cleanser Coupling fluid.	Not informed.	The first three subjects were treated at an energy level of 60 joules per cm2, and in the absence of adverse events, the next three subjects were progressed to 75 joules per cm2, followed by 90 joules per cm2 for the remaining 18 subjects (vaginal mucosa hymenal ring and entire area avoiding the urethra).	No.
Krychman,	Surface-cooled, monopolar RF	Single treatment of up to 110 pulses.	Coupling fluid.	Not informed.	Active treatment energy dose of 90 J/cm^2; the Sham treatment energy dose of 1 J/ cm^2 (vaginal mucosa avoiding the urethra).	Vaginal discharge; pain or discomfort.
Kim, 2020	RF with a resistive electric transfer equipment (Hera V, Elimtek Co. Ltd., Seongnam-	2 sessions/ 3 weeks apart.	Coupling gel.	Not informed.	The output frequency of the equipment is 460 kHz ± 20%, and the energy is 0.6 W± 20% when the set temperature is exceeded and 20.3 W ± 20% when the temperature is below the set temperature (Vaginal wall; ventral regions for 4 minutes and the dorsal regions for 6 minutes;).	Pain

	si, Gyeonggi-do, Republic of Korea)					
Alinsod,	ThermiVa Transcutaneous temperature controlled RF (ThermiGyn, SouthLake, TX)	3-treatments/4-6 weeks interval .	Lubricant gel.	No impediment to sexual intercourse.	3-5 minutes per zone (labia majora and vaginal wall). Target temperature 40°C to 45°C. Total treatment time (<30 minutes).	No.
Wattanakrai,	RF and pulsed electromagnetic felds-based device (Venus Fiore™, Venus Concept, San Jose, CA)	3-treatments/3-week intervals	Ultrasound gel.	Avoid sexual intercourse for at least 24 h.	The active group: RF energy level of 50–60% (of 80 watts, 1 MHz maximum) target therapeutic temperature level of 41–44 °C. The Sham group: nontherapeutic RF energy level, 1% with PEMF turned off. (vaginal canal).	Pain, burning sensation, pain and burning during sexual intercourse; itching.
Eftekhar,	Higgs RF device (Danesh Bonyan Maya Slim Company)	Package 1: 3 sessions weekly. After 15 days, package 2 started weekly).	Not informed.	Not informed.	Endothermy (15 minutes); Endogym (30 minutes).	Not informed.
Pather,	ThermiVa RF generator (K130689-Symphoni RF Generator - ThermiAesthetics, Southlakes, Texas)	4 vaginal quadrants, with each quadrant receiving treatment for 3 minutes.	Not informed.	Not informed.	Active group (therapeutic temperatures of 42−47 C, vagina canal). Sham probes were identical in appearance; (therapeutic temperatures 25−27 C, vaginal canal).	No.

α: XS Dynamis, Fotona, Slovenia; β: Lutronic, Goyang, South Korea; θ: SmartXide2, DEKA, Florence, Italy; μ: Ilooda, Gyeonggido, Korea; RF: Radiofrequency; * Study was also used for surgery.

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Supplementary Table 3 - Characteristics of the included studies that assessed surgical treatment for vaginal laxity (VL).

Author, Year	Surgery Type	Anesthesia	Procedure	Post-operative Care	Return to Sexual Activity	Adverse Events
Pardo, 2006	Colporrhaphy + Perineoplasty.	Spinal anesthesia (n=36); general anesthesia (n=17)	Site-specific anterior and posterior repair plus additional perineoplasty (n=52). The surgeon was able to insert two fingers in the vagina after procedure.	Patients were discharged on the following day and were seen 7 days and 6 weeks later.	Six weeks after surgery	Minimal surgical wound dehiscence (affecting the vagina and the perineum).
Moore, 2014	Posterior colpoperineoraphy/ vaginoplasty. Concurrent procedures were also performed.	Spinal or general anesthesia.	Standard colpoperineoraphy/vaginoplasty to repair the vaginal caliber and introitus to its pre-childbirth anatomic state.	Vaginal packing for a short period of time and removed prior to discharge home. No heavy lifting or vigorous exercise for 4 weeks.	Six weeks after surgery.	Pain: no different from preoperatively to postoperatively.
Park, 2015	Vaginal rejuvenation using elastic silicone thread.	Sedation.	After marking and two incisions at 3 and 9 o'clock (for inlet and outlet of thread), the retriever was in the vaginal submucosa at 3 o'clock and rotated to adequately reach the outlet incision at 9 o'clock.	Packing was removed on postoperative day 1. Patients were seen postoperatively at 2, 6, and 12 months for follow-up.	Four weeks after surgery.	Implant extrusion (9 (5%); Implant snapping (7 (3.9%); Capsular contracture (7 (3.9%); Infection (3 (1.7%)
Jamali, 2014	Colpoperineoplasty	General anesthesia	The rectovaginal area was cut until the inner section of the levator ani muscle was visible. The appropriate amount of tissue was removed from the vagina according to the degree of vaginal laxity. The perineal body was reconstructed. The size of the vagina was appropriate if two fingers of the surgeon were fitted after repair.	One week, one, two, three, six, and 18 months after surgery for a checkup.	Six weeks after surgery.	Not informed.
Ulubay, 2016	Perineoplasty	General or local anesthesia.	The perineal skin was dissected with scissors or a scalpel. The perineal body was strengthened, and the superficial transverse perineal muscle was approximated with transverse interrupted sutures in the midline of the two layers. The rectovaginal fascia was approximated to the perineal body using interrupted sutures. Bulbocavernosus muscle was approximated with sutures at the level of the posterior fourchette.	Discharged on postoperative day 1	Not informed.	4 (10%) experienced dyspareunia after treatment.

Al-Hamadani, 2019	Posterior colpoperineorrhaphy + two additional shots of platelets rich plasma injection	Not informed.	Perineoplasty was performed in three layers of interrupted vicryl sutures, after sufficient lateral incision in the perineal muscles to allow lengthening of the perineum. Two additional shots of platelets rich plasma injection, one intraoperative and the other four weeks later, were used in one of the groups.	Discharging home next day	Six weeks after surgery.	Not informed.
Kim, 2020	Gold thread implantation.	Sedation.	38 mm or 50 mm for the dermis and subcutaneous layer of the labia majora; and 13 mm for the surroundings of the clitoris and labia minora; 25 mm for the vaginal introitus and walls between the lamina propria and muscular layer at 3, 6, 9, and 12 o'clock of the vaginal wall.	Not informed.	Not informed.	No.
Cheng, 2021*	Vaginoplasty.	Local anesthesia	Vaginal mucosa is elevated to expose the levator ani muscles, and stitches are started from the upper triangle of the vagina to the edge of the hymen to tighten the muscles. The perineal gap was also repaired if needed. Success was considered if no more than two fingers could be tightly inserted into the vagina.	Not informed.	Not informed.	Not informed.
Yang, 2022	Human acellular dermal matrix (HADM)/ Enriched platelet treatment (EPT)	Intravenous anesthesia	0.5-cm-long incisions at 3-5 points and at 7-9 points were given inside and outside the hymen mark. The HADM strap was fixed and guided into the puncture tunnel to complete a U-shaped suture. The strap was pulled and tightened to narrow the vaginal cavity. EPT: EPT therapy was given twice post-surgery, at a speed of 3300 rpm for 4 minutes and 3 minutes. Concentration was injected into vaginal mucosa, clitoris, G-spot and A point.	Gauze compressing the vaginal area for 10 minutes to cease bleeding.	Not informed.	No.
Li, 2022	Vaginoplasty (Acellular dermal matrix)/ Perineoplasty		Vaginoplasty: two incisions at 3 and 9 o'clock on the mucocutaneous junction of the vaginal orifice for the U-shaped tunnel. 15 cm × 1 cm piece of ADM was introduced into the tunnel, entering and exiting through the 9 o'clock and 3 o'clock incisions 3 times. The bulbocavernosus muscle and levator ani muscle were also reinforced. A perineoplasty was subsequently performed to reinforce the superficial transverse perineal muscle.	Gauze in the vaginal canal for 24 hours. Three days antibiotics.	1-Month after surgery	Minor implant visibility (n=4)

* Study was also used for Laser; VL: Vaginal Laxity

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Supplementary Table 4. GRADE – Summary of Findings

Outcomes	Relative Effect (95% Confidence Interval)	Number of Participants: Active treatment/Other (studies)	Certainty of Evidence (GRADE)	Comments
Sexual Function	MD 2.38 higher (0.5 lower to 5.27 higher)	Active 229/ Other 172 (3 RCT)	⨁⨁⨁◯ Moderate	Risk of Bias [a]; Inconsistency[c]; Indirectness[c]; Imprecision[c]; Other considerations[d]
Pelvic Floor Muscle Strength	MD 4.22 higher (1.02 higher to 7.42 higher)	Active 63/ Other 63 (2 RCT)	⨁⨁◯◯ Low	Risk of Bias[a]; Inconsistency[c]; Indirectness[c]; Imprecision[b]; Other considerations[d]
Vaginal Laxity Questionnaire	MD 1.01 higher (0.38 lower to 2.4 higher)	Active 171/ Other 111 (2 RCT)	⨁⨁⨁◯ Moderate	Risk of Bias[a]; Inconsistency[c]; Indirectness[c]; Imprecision[c]; Other considerations[d]

[a]Selective Reporting; [b] Small sample size; [c] Not serious; [d] None

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PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3-4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 4-5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4-5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5-6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5-7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5-7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 5-7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6-7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 4-7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 4-7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 4-7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 4-7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 4-7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 4-7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6-7
Certainty	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 6-7

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
assessment			
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7-8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 7-8
Study characteristics	17	Cite each included study and present its characteristics.	Page 7-8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 10-11
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 8-10
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 8-10
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 8-10
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 8-10
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 8-10
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 8-10
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 8-10
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 12-14
	23b	Discuss any limitations of the evidence included in the review.	Page 12
	23c	Discuss any limitations of the review processes used.	Page 12
	23d	Discuss implications of the results for practice, policy, and future research.	Page 12-14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Title Page
Competing interests	26	Declare any competing interests of review authors.	Title Page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Supp.Material

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

4.2. Artigo 2. *Cross-cultural adaptation and validation of the Brazilian Portuguese version of the Female Sexual Distress Scale-Revised questionnaire for women with vaginal laxity*

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Type of Use	Thesis/Dissertation
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International Urogynecology Journal
https://doi.org/10.1007/s00192-022-05227-0

ORIGINAL ARTICLE

Cross-cultural adaptation and validation of the Brazilian Portuguese version of the Female Sexual Distress Scale-Revised questionnaire for women with vaginal laxity

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Received: 5 March 2022 / Accepted: 29 April 2022

Abstract

Introduction and hypothesis Vaginal laxity (VL) can impair women´s quality of life and there are not many tools aimed at quantitatively addressing this complaint. Sexual distress can be present within this group of patients. The aim of our study is to carry out the cross-cultural adaptation/translation and validation of the Female Sexual Distress Scale-Revised (FSDS-R) for Brazilian Portuguese women with VL.

Methods Women age ≥ 18 years, with VL (n=82), and without VL (n=53) were included. Continuous variables were described in the form of mean/standard deviation or median/range, and Student's t test was used. The Chi-squared test was used for dichotomous variables. Cronbach's alpha coefficient was used for internal consistency and Spearman's correlation was used to assess construct validity (FSDS-R, Female Sexual Function Index [FSFI], and Incontinence Questionnaire Vaginal Symptoms [ICIQ-VS]). A significance level of 5% was established using a two-tailed test.

Results Women with VL presented more anal/vaginal sexual intercourse than women without VL (p=0.030). All three instruments (FSDS-R, FSFI, and ICIQ-VS) presented discriminant validity between women with and without VL (p<0.001). A high internal consistency (Cronbach´s alpha =0.887) was found in women with VL and without VL (0.917). Regarding construct validity (n=82), there was a strong positive correlation between FSDS-R score and ICIQ-VS scales, except for a weaker correlation between the ICIQ-VS vaginal symptoms subscale (r: +0.2788; p=0.013). A moderate negative correlation was found between FSDS-R and all FSFI domains (p<0.001), except for pain (p<0.062).

Conclusions The Brazilian version of the FSDS-R showed adequate internal consistency and discriminant validity, and a correlation was found with other instruments such as FSFI and ICIQ-VS.

Keywords Vaginal laxity · Sexual dysfunction · Surveys and questionnaires · Validation study

Introduction

Vaginal laxity (VL) is defined as a complaint of excess vaginal flaccidity and is described as a vaginal symptom of sexual function specific to pelvic floor dysfunction by the latest International Urogynecological Association (IUGA)/International Continence Society (ICS) terminology [1, 2]. Women with VL may be representative of an early stage of development of pelvic organ prolapse [3]; however, a consensus on this matter has not yet been reached. According to another study, VL differs from pelvic organ prolapse, the former being related to symptoms concentrated in the vagina and the latter involving the descent of one or more pelvic organs [4]. The decreased vaginal sensation during intercourse may be related to anatomical damage to the perineal body, vaginal canal or introitus, underlying nerve and connective tissue damage during pregnancy and childbirth, or potentially a combination of these factors [5].

The diagnosis of VL is based on the patients' self-report [6]. A comprehensive medical history, physical examination,

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Published online: 19 May 2022

and psychosexual evaluation are the initial steps for the proper identification of patients with VL. The Vaginal Laxity Questionnaire is an instrument used in clinical research to assist in the identification and severity of VL [7]. However, this instrument does not fully understand the extent of the impact on the quality of life of women with VL.

The Female Sexual Distress Scale-Revised – FSDS-R assesses sexual distress with a composite score ≥ 11 [8]. Sexual distress is characterized by a set of feelings and emotions that individuals have about their sexuality. It differs from sexual dysfunction related to symptoms of sexual function, such as arousal, orgasm, and pain, separate from emotions [8]. Assessing sexual distress in women complaining of VL can help to understand its pathophysiology. Sexual distress in women with VL has already been investigated in previous studies in the English language [7, 9]; however, this questionnaire has not yet been translated into or validated in Brazilian Portuguese, making it difficult to investigate the Brazilian population. Therefore, the aim of this study is to carry out the cross-cultural adaptation, translation, and validation of the Female Sexual Distress Scale-Revised (FSDS-R) in Brazilian Portuguese for women with VL.

Materials and methods

This is a cross-sectional study conducted from November 2021 to January 2022 at Women's Hospital - Prof. Dr. José Aristodemo Pinotti, CAISM, at the University of Campinas – Brazil. The study was approved by the Institutional Review Board under the number CAAE: 53164221.3.0000.5404 and followed the Guidelines for the Process of Cross-Cultural Adaptation of Self-Report Measures [10].

Study population

Women aged ≥ 18 years, with VL and women without VL assessed by a single, dichotomous question (do you consider yourself to have vaginal laxity) and by the Vaginal Laxity Questionnaire (VLQ) [7] were included in the present study. We considered the answers (very loose, moderately loose, slightly loose) for VL and (neither loose nor tight) for women without VL. Women with VL were recruited through advertisements on the Hospital's official website and referred to the study through the urogynecology outpatient clinic. Participants without VL were recruited in their first appointment at the Family Planning outpatient clinic. These participants were referred for counseling for or to receive contraceptive methods, without any complaints of prior genital or sexual dysfunction. We excluded women with reading and language comprehension difficulties, who had undergone surgeries for pelvic floor disorders, who had undergone previous treatment for VL, and who had used vaginal estrogen in the past 6 months. The women who agreed to participate in the study signed the consent form.

Regarding the sample size, as we know from the literature that there is heterogeneity for calculating the minimum sample size from instrument validation studies, these data show a variation ranging from 100 to 300 cases [11]. As the complaint of VL is rarely discussed among women and health professionals, we expect to analyze at least 100 participants.

The female sexual distress scale – revised – FSDS-R

The FSDS-R is a self-administered questionnaire validated by Derogatis et al., consisting of 13 questions in English that can be answered as 0-never, 1-rarely, 2-occasionally, 3-frequently, and 4-always [8]. The FSDS-R total score ranges from 0 to 52 and provides sexual distress measurement (the higher the score, the higher the sexual distress).

Translation and cross-cultural adaptation

Our study followed the six stages of translation and the cross-cultural adaptation process proposed by Beaton et al. [10]. Permission for the translation and validation of the FSDS-R was granted by Derogatis Measurement Assessments, LLC, and by the company Mapi Research Trust. After receiving authorization, we started stage I - translation.

The initial translation of the original questionnaire was performed by two native speakers of the Brazilian Portuguese language who were fluent in advanced English. The first translator had experience in sexual dysfunction and was aware of the topic assessed by the questionnaire. Their translation (T1) was responsible for the clinical relevance. In contrast, the second translator had no knowledge of the issues related to the questionnaire's topic and their translation (T2) was responsible for the language relevance. A synthesis of the two initial translations produced a common version called T-12. The synthesis process of the two translations was carefully analyzed and documented.

Subsequently, the translation of the T-12 version from Brazilian Portuguese into English was performed by two translators (back translation 1 and back translation 2) who were not aware of the original version of the questionnaire.

An expert committee composed of the authors, two health professionals specializing in gynecology and urogynecology who work at the Women's Hospital - CAISM, and translators, were responsible for consolidating all translated versions and developing the pre-final version to test the questionnaire. The pre-final version was applied to 30 volunteers complaining of VL. The volunteers were asked about the difficulty in understanding the questionnaire items. The expert committee was also responsible for evaluating questionnaire questions that might be not understood and needed clarification.

Finally, the approved version of the FSDS-R (Brazilian Portuguese version) was added to a form containing sociodemographic and clinical questions, in addition to two other questionnaires validated for Brazilian Portuguese. We chose to apply the form to all participants, including the thirty volunteers who participated in the cross-cultural adaptation test phase. The study objectives were explained to all women who agreed to participate. A researcher was responsible for collecting the signature of the consent form from each participant, delivering the data collection form, answering all possible questions, and providing guidance on each question in the questionnaires when needed, thus, ensuring due privacy for each participant during the data collection process.

Analyzed variables

Sociodemographic and clinical data were as follows: age, marital status, ethnicity, years of education, body mass index, menopausal status, number of pregnancies, births, and abortions, types of delivery, type of affective and/or sexual relationship, and complaints of VL.

Two questionnaires validated for the Portuguese language were also applied: the Female Sexual Function Index (FSFI) and the International Consultation on Incontinence Questionnaire Vaginal Symptoms (ICIQ-VS). The FSFI is a brief and multidimensional questionnaire that assesses sexual function in women. This instrument was developed and validated by Rosen et al. and consisted of 19 items. It investigates sexual response over the last 4 weeks and performance in six domains: sexual desire, arousal, lubrication, orgasm, satisfaction, and pain[12]. Validation in Portuguese occurred in 2008 by Thiel et al. [13]. Last, the ICIQ-VS is a 14-question questionnaire that assesses the presence and intensity of vaginal symptoms, associated sexual issues, as well as their relationship with quality of life in research and clinical practice. Tamanini et al. validated the ICIQ-VS in Portuguese in 2008 [14].

Statistical analysis

Data collected from the interviewed women were organized in a spreadsheet and exported for analysis into Intercooled Stata 13.0 (Stata, College Station, TX, USA). The normality of sampling was assessed by the Shapiro–Francia test. Continuous variables were described in the form of mean/standard deviation or median/range, and for calculating discriminant validity, Student's *t* test and Chi-squared test were used for continuous and dichotomous variables respectively. Cronbach's coefficient alpha, item–test correlation, item–rest correlation were used to measure the internal consistency (homogeneity of items belonging to the same scale). Spearman's correlation was calculated by comparing the FSDS-R and FSFI and ICIQ-VS scores for construct validity. Floor and ceiling effects were considered if more than 15% of participants had the lowest and highest scores on the questionnaires respectively. A significance level of 5% was established using a two-tailed test. No imputation method was used owing to missing data.

Results

After careful analysis of the FSDS-R instrument, both the initial translated versions and the back-translated versions were, in general, similar. In the initial translation, only the first, the tenth, and the twelfth questions presented moderate, mild, and mild divergences respectively. In question one, for the term "distressed," we opted for the translation of "*angustiada* - distressed" instead of "*desconfortável* - uncomfortable", as the term "*desconfortável* - uncomfortable" is broader and could be interpreted differently within the Brazilian context. In questions ten and twelve, the translated terms were synonymous and would not cause problems of interpretation or understanding. Likewise, the back-translation process showed mild differences related only to synonymous terms.

Sociodemographic and clinical characteristics

Table 1 shows the distribution of both groups according to sociodemographic and clinical characteristics. The mean age was similar in the two groups. Education longer than 8 years was frequent in both groups, with women without VL more likely to present a higher level of education (98.12% vs 78.04%). Women with VL were more likely to be multiparous and to have a higher number of pregnancies when compared with the non-VL group. On the other hand, women in the non-VL group were more likely to undergo cesarean and to perform vaginal intercourse than women with VL.

Discriminant validity

Table 2 describes the discriminant validity according to the FSDS-R, FSFI, and ICIQ-VS scores and their domains between the groups. Sexual distress measured by the FSDS-R presented significantly higher scores in women with VL than in the non-VL group (26.88±14.39 vs 11.09±11.92). Although the floor effect was seen in FSDS-R (17.04%), no ceiling effect was observed (4.44%) in this questionnaire. Regarding the FSFI questionnaire, women without VL presented higher scores in all FSFI domains, except for desire and pain. Higher scores were seen in women with VL in all ICIQ-VS subscales ($p<0.001$).

Table 1 Sociodemographic and clinical characteristics of the interviewed women (n=135)

Variables	Vaginal laxity group (n=82)		Nonvaginal laxity Group (n=53)		p Value
	Mean ± SD/p (%)	Median (min–max)	Mean ± SD/n (%)	Median (min–max)	
Age (years)	41.19±9.45	41 (22–60)	40.20±8.64	41 (21–61)	0.533*
Marital status					0.988**
Single	19 (23.18)		12 (22.64)		
Married	50 (60.97)		33 (62.27)		
Divorced	13 (15.85)		8 (15.09)		
Ethnicity					0.135**
White	42 (51.22)		36 (67.93)		
Black	10 (12.20)		3 (5.66)		
Other	30 (36.58)		14 (26.41)		
Years of education					**0.001****
< 8 years	18 (21.96)		1 (1.88)		
> 8 years	64 (78.04)		52 (98.12)		
BMI					0.151**
< 25 kg/m^2	30 (36.58)		26 (49.05)		
> 25 kg/m^2	52 (63.42)		27 (50.95)		
Gravidity	2 (0–8)		2 (1–3)		**0.001***
Type of birth					**0.001****
Vaginal	47 (59.49)		14 (26.41)		
Cesarean	20 (25.32)		35 (66.05)		
Both	12 (15.19)		4 (7.54)		
Parity					**0.011*****
Primiparous	19 (24.05)		24 (45.28)		
Multiparous	60 (75.95)		29 (54.72)		
Instrumental delivery					0.090**
No	63 (79.74)		48 (90.56)		
Yes	16 (20.26)		5 (9.44)		
Menopause status					0.948**
Premenopause	69 (87.34)		46 (86.79)		
Postmenopause	10 (12.66)		7 (13.21)		
Sex orientation					0.408**
Hetero-affective	77 (98.71)		53 (100.00)		
Homo-affective	1 (1.29)		0		
Type of sexual intercourse					**0.030****
Vaginal	55 (70.51)		46 (86.79)		
Vaginal and anal	23 (29.49)		7 (13.21)		

SD standard deviation, *BMI* Body Mass Index

*Student's t test

**Chi-squared test

Bold p values considered statistically significant

Internal consistency

Internal consistency with item correlation and Cronbach's alpha for FSDS-R, FSFI, and ICIQ-VS questionnaires are found in Table 3. The FSDS-R has demonstrated a high ICC of 0.88 and 0.91 respectively, for women with and without VL. The remaining questionnaires also presented a higher Cronbach's alpha ranging from 0.88 to 0.89 in the VL group and from 0.91 to 0.92 in the non-VL group in the FSFI scores and domains; and from 0.88 to 0.89 in the VL group and 0.92 in the non-VL group in the ICIQ-VS subscales.

Construct validity

The construct validity among the FSDS-R, FSFI, and ICIQ-VS questionnaires is described in Table 4. Construct validity

Table 2 Discriminant validity between women with and those without vaginal laxity according to the Female Sexual Distress Scale-Revised (FSDS-R), Female Sexual Function Index (FSFI), and Incontinence Questionnaire Vaginal Symptoms (ICIQ-VS) questionnaires

Questionnaires	Vaginal laxity group (n=82)			Nonvaginal laxity group (n=53)			p Value
	Mean ± SD/n (%)	(95% CI)	(min–max)	Mean ± SD/n (%)	(95% CI)	(min–max)	
FSDS-R	26.88±14.39	(23.63–30.13)	(1–52)	11.09±11.92	(7.80–14.38)	(0–50)	**0.001***
Floor effect (17.04)	6 (7.32)			17 (32.08)			**0.001****
Ceiling effect (4.44)	5 (6.10)			1 (1.89)			0.246**
FSFI							
Desire	3.14±1.18	(2.87–3.40)	(1.2–6.0)	3.44±0.97	(3.17–3.71)	(1.2–6.0)	0.131*
Arousal	3.41±1.23	(3.13–3.69)	(1.2–5.7)	4.24±1.17	(3.92–4.56)	1.2–6.0	**0.001***
Lubrication	4.16±1.35	(3.85–4.46)	1.2–6.0	4.79±1.25	(4.44–5.14)	1.2–6.0	**0.008***
Orgasm	3.66±1.42	(3.33–3.98)	1.2–6.0	4.58±1.20	(4.25–4.92)	1.2–6.0	**0.001***
Satisfaction	4.03±1.41	(3.71–4.35)	1.2–6.0	4.86±1.22	(4.53–5.20)	1.2–6.0	**0.001***
Pain	4.43±1.55	(4.08–4.78)	(1.6–6.0)	4.82±1.39	(4.43–5.20)	(1.2–6.0)	0.147*
Total	22.85±6.28	(21.43–24.27)	(6.0–34.5)	26.76±5.76	(25.17–28.35)	(7.6–33.6)	**0.001***
ICIQ-VS							
Vaginal symptoms	16.29±7.77	(14.54–18.04)	(2–39)	6.09±5.53	(4.56–7.61)	(0–28)	**0.001***
Q4. Vagina is too loose or lax	2.29±0.79	(2.11–2.47)	(1–3)	0	0	0	**0.001***
Sexual matters	26.06±19.88	(21.58–30.54)	(0–58)	4.54±8.82	(2.11–6.97)	(0–37)	**0.001***
Quality of life	6.05±3.42	(5.27–6.82)	(0–10)	1.33±2.47	(0.65–2.02)	(0–10)	**0.001***

Floor effect (>15 %)

SD standard deviation

*Student *t* test, **Chi-squared test

Table 3 Internal consistency with item-rest correlation and Cronbach's alpha for the Female Sexual Distress Scale – Revised (FSDS-R), Female Sexual Function Index (FSFI), and International Consultation on Incontinence Questionnaire Vaginal Symptoms (ICIQ-VS)

Questionnaire	Vaginal laxity group (n=82)			Nonvaginal laxity group (n=53)		
	Item-test correlation	Item-rest correlation	Cronbach's alpha	Item-test correlation	Item-rest correlation	Cronbach's alpha
FSDS-R	0.7101	0.6462	0.8879	0.7738	0.7235	0.9170
FSFI						
Desire	0.5126	0.4212	0.8970	0.5298	0.4436	0.9268
Arousal	0.7341	0.6745	0.8861	0.7454	0.6900	0.9179
Lubrication	0.6997	0.6342	0.8880	0.8202	0.7789	0.9149
Orgasm	0.8255	0.7836	0.8815	0.8142	0.7717	0.9152
Satisfaction	0.7092	0.6453	0.8874	0.7275	0.6690	0.9187
Pain	0.5248	0.4348	0.8964	0.7694	0.7183	0.9172
Total	0.5388	−0.3036	0.8855	0.5937	−0.1435	0.9150
ICIQ-VS						
Vaginal symptoms	0.6254	0.5483	0.8921	0.6751	0.6082	0.9219
Q4. Vagina is too loose or lax	0.5564	0.4702	0.8956			
Sexual matters	0.6905	0.6234	0.8889	0.6343		0.9237
Quality of life	0.5932	0.5116	0.8938	0.6671		0.9220

was performed to assess the relationship between the FSDS-R score and those from the other questionnaires. There was a strong positive correlation between FSDS-R score and ICIQ-VS scales, except for a weaker correlation between the ICIQ-VS vaginal symptoms subscale (r: +0.2788; p=0.013). A moderate negative correlation was found between FSDS-R and all FSFI domains (p<0.001), except for the pain domain (p<0.062).

Table 4 Construct validity among the Female Sexual Distress Scale – Revised (FSDS-R), Female Sexual Function Index (FSFI), and International Consultation on Incontinence Questionnaire Vaginal Symptoms (ICIQ-VS) questionnaires in participants with vaginal laxity (n=82)

Questionnaires	FSDS-R	
	r	p value
FSFI		
Desire	−0.4036	0.001
Arousal	−0.4571	0.001
Lubrication	−0.4016	0.001
Orgasm	−0.5565	0.001
Satisfaction	−0.4906	0.001
Pain	−0.2117	0.062
Total	−0.5510	0.001
ICIQ-VS		
Vaginal symptoms	0.2788	0.013
Q4. Vagina is too loose or lax	0.3881	0.001
Sexual matters	0.6415	0.001
Quality of life	0.4726	0.001

r Spearman correlation coefficient; Dancey & Reidy interpretation

Discussion

This study presents the cross-cultural adaptation and validation of the FSDS-R instrument for the Brazilian Portuguese language for women with VL. Overall, we found slight divergences throughout the cross-cultural adaptation process, and we may suggest that the final Brazilian version of the FSDS-R can be considered similar to the original English version. Considering the questionnaire scores, sexual distress, sexual dysfunction, and vaginal symptoms were higher in women with VL. Our findings showed an acceptable and satisfactory internal consistency for all questionnaires (FSDS-R, FSFI, and ICIQ-VS). Regarding construct validity, a correlation was found between FSDS-R score and ICIQ-VS vaginal symptom subscales. Similarly, a moderate negative correlation was found between FSDS-R and all FSFI domains, except for the pain domain.

In our sample, women with VL had a higher frequency of vaginal delivery and multiparity than participants without VL. These findings corroborate those of other previously published studies that also found evidence for a connection between vaginal delivery/parity and symptoms of VL [5, 15, 16].

As we notice the growing development of instruments to assess sexual function, it is possible to transform subjective measures into objective data [17]. However, most of the questionnaires assessing sexual function were developed in the English language [18]. Thus, because Brazil is a country with continental extension and a known prevalence of sexual dysfunction of 67.7% [19], we believe that the translation of the FSDS-R will contribute immensely to the assessment of sexual distress in women, not only with symptoms of VL but also with other sexual dysfunctions. In our findings, sexual distress, as well as sexual dysfunction and vaginal symptoms, was higher in women complaining of VL. Sexual distress has also been assessed in women with VL in previous studies, but these studies had lower mean scores than our findings. The study by Millheiser et al. had a mean total FSDS-R score of 13.6 ± 8.7 in a group of 24 women in the pre-treatment period [7]. Likewise, Krychman et al., in a randomized clinical trial, observed a total score of 19.4 ± 12.0 in a group of 122 patients in the active group [9]. The mean total score found in our population was 26.88 ± 14.39. We reinforce the need to assess sexual distress in patients complaining of vaginal laxity.

As observed in the original article [8], high inter-item correlations were also observed in our study. We found few studies that performed validation, translation, and/or cross-cultural adaptation of the FSDS-R for their respective populations. The study by Berenguer et al. translated the FSDS-R into the Portuguese language of Portugal and showed an internal consistency similar to our findings [20]. The construct validity and the correlations between FSDS-R and FSFI were also similar in the two studies, only differing in the pain domain (FSFI) in our study (r -0.2117; p=062) [20]. The Turkish version was published in 2016 with a population of 248 women with complaints of sexual interest/arousal disorder and other female sexual dysfunctions and participants without complaints of sexual dysfunction [21]. The authors performed a similar data analysis, differing only in the test-retest, factor structure, and cut-off point analysis, which we did not perform. In addition, a correlation analysis of the FSDS-R and the FSFI questionnaires was performed, as in the present study; however, the results differed slightly between studies [21]. The Persian version of the FSDS-R was constructed by a group of Iranian researchers in 2014 and applied to 652 healthy participants [22]. In this study, only the internal consistency could be compared with our study, proving to be similar to our findings [22]. Finally, the Polish version of the FSDS-R was applied to a population of 75 women with hypoactive sexual desire disorder, 31 women with other dysfunctions, and 104 participants without sexual dysfunction complaints. Internal consistency was similar to ours with a coefficient $\alpha > 0.70$ [23].

The strength of our study can be related to recruited participants—women complaining of VL, a symptom that has been rarely investigated. Moreover, we were able to perform the analyses that comprise the process of translation, validation, and cross-cultural adaptation for a country with a population of 214.1 million and compare it with other translations, and also with other studies that have already

used the FSDS-R in the same target population as our study. However, we have some limitations: we were not able to perform test-retest analysis in our population owing to COVID-19 pandemic restrictions. We believe that this analysis would add value to our study. Likewise, our sample size was affected by the restrictions of the COVID-19 pandemic in that we only applied the questionnaires to patients who already had appointments scheduled at the outpatient clinic, and it was not possible to invite other patients to participate in the study. Also, we also did not carry out further qualitative measurement analyses of the Brazilian version of the FSDS-R.

Conclusions

The FSDS-R is a valuable instrument for assessing sexual distress in women with VL. Its Brazilian version showed satisfactory internal consistency and construct validity, and a correlation was found when compared with FSFI and ICIQ-VS.

Acknowledgement We thank Dr. DeRogatis and the research team for kindly allowing us to carry out this study. We also thank Mapi Research Trust, Lyon, France (https://eprovide.mapi-trust.org) for all their help during the translation and validation process. We thank the São Paulo Research Foundation (FAPESP) for the support given to our study.

Author contributions G.M.V. Pereira: protocol/project development; data collection or management; data analysis; manuscript writing/editing; C.R.T. Juliato: protocol/project development; data collection or management; data analysis; manuscript writing/editing; D.A.Y. Gomes: data collection or management; data analysis; manuscript writing/editing; T.S. Beltramini: data collection or management; data analysis; M.V.C. Monteiro: data collection or management; data analysis; L.G.O. Brito: protocol/project development; data collection or management; data analysis; manuscript writing/editing.

Funding First author: Scholarship Grant 2019/26723-5, São Paulo Research Foundation (FAPESP). The remaining authors reported no disclosures.

Declarations

Conflicts of interest None.

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4.3. Artigo 3. *Measurement of the vaginal wall thickness by transabdominal and transvaginal ultrasound of women with vaginal laxity: a cross-sectional study*

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International Urogynecology Journal
https://doi.org/10.1007/s00192-022-05184-8

ORIGINAL ARTICLE

Measurement of the vaginal wall thickness by transabdominal and transvaginal ultrasound of women with vaginal laxity: a cross-sectional study

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Received: 5 December 2021 / Accepted: 8 March 2022

Abstract

Introduction and hypothesis An objective diagnostic method to understand vaginal laxity (VL) is still missing. The aim of our study is to determine whether vaginal wall thickness (VWT) measured by ultrasound may differ according to the abdominal or vaginal techniques and to assess whether clinical variables are associated with vaginal measurements of women with VL.

Methods A cross-sectional study conducted at a tertiary hospital included 82 women aged ≥ 18 years with VL complaints assessed by the Vaginal Laxity Questionnaire. Women who reported severe comorbidities or vulvovaginal disorders, previous treatment for VL, and use of vaginal estrogen in the last 6 months were excluded. Participants reporting VL underwent transabdominal (TAUS) and transvaginal ultrasound (TVUS) and physical examination and answered validated questionnaires. Descriptive data were given as mean and standard deviation, median (range), and absolute and relative frequency. The significance level adopted for this study was 5%. Sample size calculation was not performed for the present study.

Results Mean age was 41.20 ± 8.64 years, and most participants were multiparous, with previous vaginal delivery and having vaginal intercourse. A statistically significant difference (up to 3 mm) between TAUS and TVUS measurements of the VWT was found in the proximal, middle-third, and distal compartments. A significant correlation was found between VWT and TAUS or TVUS in the mid-third and distal compartments.

Conclusion A significant correlation was found between the VWT measurements in TVUS and TAUS. Our findings might give the health professional more possibilities for investigating VWT according to patient characteristics.

Keywords Vaginal laxity · Sexual dysfunction · Vaginal wall thickness · Ultrasound

Introduction

Vaginal laxity (VL) is a symptom of sexual dysfunction still poorly investigated, with a prevalence of approximately 24% [1]. It is defined as a complaint of excessive vaginal looseness [2] and can be self -reported by women, their partners, or both. This complaint appears to be associated with younger age, vaginal delivery, prolapse symptoms, and changes in connective tissue due to the aging process [3]. However, there is no objective diagnostic method for VL.

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Published online: 06 April 2022

Vaginal wall thickness (VWT) is a variable that has not been standardized or deeply investigated in relation to VL complaints. In the last decade, few studies have evaluated the VWT in women with genitourinary menopause syndrome and genital prolapse using ultrasound [4–7]. These studies used 2D and 3D (high-frequency) ultrasound, and the VWT was measured according to the performed technique. Anatomically, the vaginal wall is composed of the epithelial, muscular, and adventitial layers. It is related anteriorly to the urethra (lower portion) and to the base of the bladder (in its middle and upper portion) and is posteriorly separated from the rectum by the rectouterine excavation (upper portion), through the rectovaginal fascia (middle portion), and from the anal canal through the perineal body [6, 8].

Comparisons using objective measurements between patients with and without VL are also lacking in the literature [9]. A histological analysis could be an option for investigating VL; however, a biopsy is an invasive and sometimes uncomfortable technique that requires specific indication in clinical practice. In this context, imaging techniques for the pelvic and perineal region have already demonstrated their effectiveness in the clinical investigation of patients with sexual complaints [10–12]. Pelvic ultrasound is a popular, cost-effective tool used in healthcare. Several techniques can be used to investigate the pelvic region (transabdominal, transvaginal, transperineal), but, as far as we know, there is no consensus on the best technique to assess VWT and whether they are correlated. Furthermore, the use of imaging exams to understand VL complaints is still scarce. Thus, the aim of our study is to determine whether VWT measured by ultrasound may differ according to the abdominal or vaginal techniques and to assess whether clinical variables are associated with vaginal measurements of women with VL.

Materials and methods

Study recruitment and inclusion/exclusion criteria

This is a cross-sectional study conducted in the Women's Hospital-Professor Doutor José Aristodemo Pinotti-CAISM-University of Campinas-UNICAMP, Campinas, Brazil, from November 2019 to May 2021. Participants were part of a randomized clinical trial [13] and were recruited from the hospital Urogynecology and Physiotherapy outpatient clinics and through advertisements and posters on the hospital social media. All patients were contacted by telephone to apply the eligibility criteria and subsequently to schedule the assessments. Participants interested in the study but who did not meet the eligibility criteria were referred to the urogynecology outpatient clinic for follow-up. Institutional Review Board of the State University of Campinas-UNICAMP-CAAE-12919119.9.0000.5404 (08/08/2019) approved this study.

We included women aged ≥ 18 years, complaining of VL assessed by self-reported question (yes/no) and by the Vaginal Laxity Questionnaire (VLQ) [14] responses. This is a questionnaire developed by Millheiser et al. that assesses vaginal looseness/tightness through seven responses ranked as very loose, moderately loose, slightly loose, neither loose nor tight, slightly tight, moderately tight, or very tight. For the present study, we selected participants who responded very loose, moderately loose, or slightly loose on this instrument [14]. The exclusion criteria were women with severe comorbidities (cognitive deficit or neurological disorders, previous or current malignant tumors, cervical dysplasia, or decompensated metabolic diseases), active infection (urinary or vaginal), vaginal estrogen use in the last 6 months, and previous pelvic surgery who were undergoing physiotherapy for pelvic floor disorders. Participants interested in the study were contacted by phone, and the eligibility criteria were applied. Data were collected at the Physiotherapy Service (physical examination and questionnaires) and at the Echography Service (ultrasounds exams).

The primary outcome was the measurement of the VWT by the TAUS and TVUS ultrasound. The secondary outcomes were the sociodemographic and clinical characteristics of women with VL complaints.

Vaginal wall thickness measurements (Fig. 1)

Our measurements were based on two previous studies [15, 16] and performed by the same experienced researcher (C.M.A). Before using the techniques in our study group, the sonographer-gynecologist performed various measurements to strengthen the technique and reduce intraobserver variability as these data were fit to our study purpose. Before initiating the measurements, the participants were instructed to completely empty their bladders. Then, women drank 800 ml of water during a 20-min period. Forty minutes after finishing the last glass of water, participants underwent transabdominal ultrasound (TAUS). Patients were placed in a supine position with their lower limbs extended and with moderate bladder repletion of around 300 ml volume. The probe was positioned on the suprapubic region. TAUS measurement was performed with an abdominal probe (1–5-MHz C5-1 abdominal probe, Affiniti 70G Philips), and VWT measurements (anterior and posterior) were acquired along the longitudinal axis, obtained in the sagittal plane. Measurements were taken in its proximal third (vaginal fornix), middle third, and distal third (close to the vaginal introitus) and were recorded from external to external echogenic lines [17].

After finishing the TAUS measurement, the participants were instructed to completely empty their

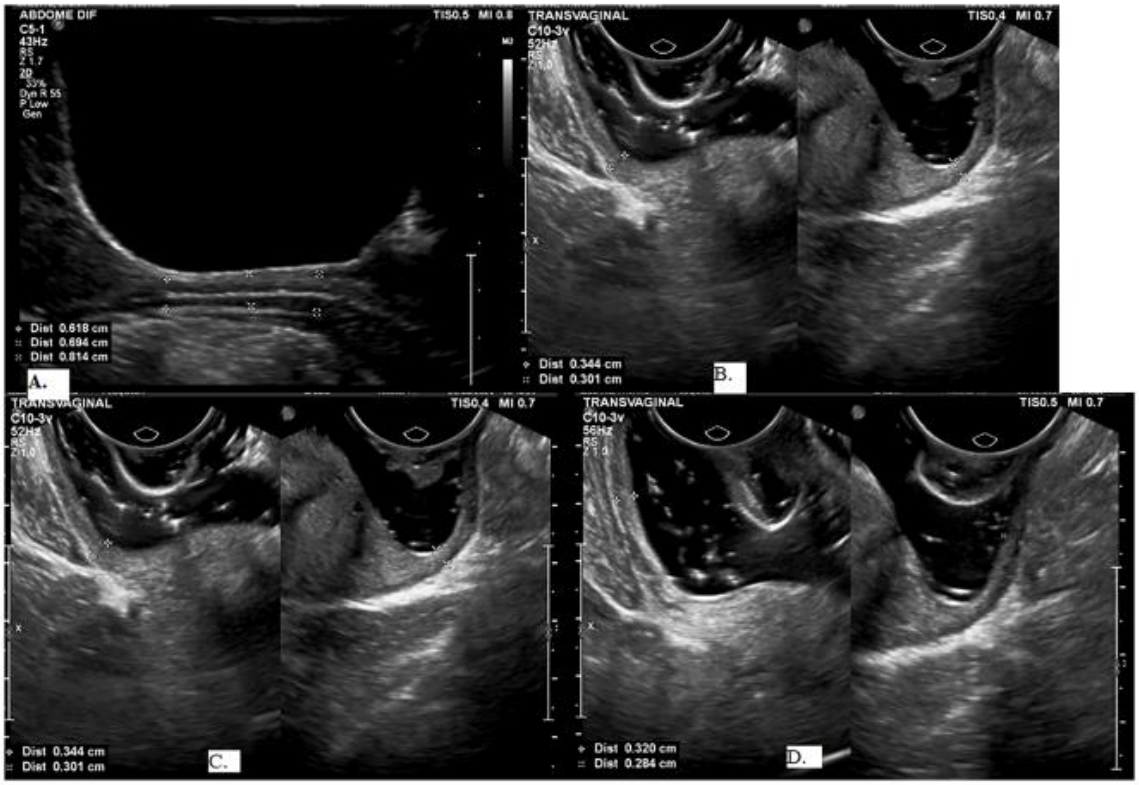

Fig. 1. Vaginal wall thickness measurements on transabdominal and transvaginal ultrasounds. A: transabdominal technique, with all portions of the vagina. B: transvaginal technique, proximal vagina; C: transvaginal technique, mid-third vagina; D: transvaginal technique, distal vagina

bladder and immediately return for transvaginal ultrasound (TVUS) measurement. The participants were placed in the supine position with their lower limbs flexed, feet supported, and pelvis elevated. Forty milliliters of water-based gel was carefully introduced into the vaginal canal through two 20-ml syringes to separate the vaginal walls, allowing the measurement of its walls independently without pressuring the probe against the vaginal wall. TVUS measurement was performed with a vaginal probe in the sagittal plane (3–10-MHz C10-3v vaginal probe, Affiniti 70G, Philips). The vaginal thickness of the anterior and posterior walls was measured in its proximal third (anterior and posterior vaginal fornix), middle third (at the transition from the proximal urethra and rectum), and distal third (at the distal urethra/vaginal introitus and anorectal junction). The measurements of the anterior and posterior vaginal walls obtained by TVUS were summed and their total values were compared with the TAUS measurements.

Data collection

We collected data regarding the medical history and sociodemographic characteristics of the participants. Subsequently, a physical examination was performed to assess pelvic organ prolapse using the Pelvic Organ Prolapse Quantification (POP-Q) and pelvic floor muscles using the Oxford Modified Scale [18, 19].

The following validated questionnaires were used for the present study. The Female Sexual Function Index (FSFI) assessed sexual function. The FSFI consists of 19 questions divided into 6 domains (desire, excitement, lubrication, orgasm, satisfaction, and pain) and presents a maximum score of 36 points. A cutoff point of 26.55 was proposed to differentiate women with and without risk for sexual dysfunction [20]. The vaginal symptoms (0–53 points), associated sexual matters (0–58 points), and impact on quality of life (0–10 points) were evaluated by the International Consultation on Incontinence Questionnaire-Vaginal Symptoms

(ICIQ-VS) [21]. We included question number 4 (vagina too loose/lax) from the ICIQ-VS in a separate analysis. Likewise, the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short form (ICIQ-UI SF) was used to assess the frequency, severity, and impact on quality of life of urinary incontinence (0–21) [22, 23]. Questionnaires with incomplete or blank responses were excluded from the analyses.

Statistical analysis

Statistical analysis was performed by SAS version 9.2 for Windows Statistical Analysis System (SAS Institute, 2002–2008, Cary, NC, USA). Data with descriptive values were displayed in mean and standard deviation, median (minimum–maximum), and absolute and relative frequency. Wilcoxon or Mann-Whitney tests were used for comparison between two groups and Kruskal-Wallis for comparison among three or more groups. Spearman's correlation coefficient was used to analyze the relationship between numerical variables and non-parametric distribution. An intraclass coefficient (ICC) was also calculated for these data. The significance level adopted for this study was 5%. So far, no study has been found comparing these ultrasound techniques; therefore, we did not perform the sample size calculation. Thus, no mean differences between the groups were described in the literature, and no definition of VWT was standardized.

Results

One hundred sixty-two participants were initially selected and answered the VLQ questionnaire. Three participants were excluded because of previous pelvic surgery, and 77 participants did not attend the appointment for physical examination, questionnaires, and ultrasound, leaving 82 participants. Table 1 displays the sociodemographic and obstetric data. Mean age of participants was 41.20 ± 8.64 years, and most women were married (60.97%), had premenopausal status (93.90%), were self-reported white (51.22%), had > 8 years of education (78.04%), and were overweight/obese (63.42%). About 57% of participants had a vaginal birth, and most participants were multiparous. Seventeen participants underwent instrumental delivery, with forceps being the most frequently used device. The other sociodemographic and obstetric characteristics of the participants complaining of VL are shown in Table 1.

The clinical characteristics of the participants complaining of VL are given in Table 2. The most frequent type of sexual intercourse was vaginal, and the mean duration of VL symptoms was 7.77 ± 6.74 months. Fecal and flatus incontinence was found in 6% and > 32%, respectively. Nocturia (69.5%), incomplete emptying (57.3%), and post-micturition dribble (63.4%) were the urinary complaints most frequently reported by the participants. POP-Q stage I was found in > 81% of the participants.

Table 3 describes the questionnaire scores and ultrasound measurements. Most women reported very to moderately loose VL (87.80%). Mean total FSFI score was 22.86 ± 6.22, suggesting risk for sexual dysfunction (cut-off point

Table 1. Sociodemographic and obstetric characteristics of participants with vaginal laxity ($n = 82$)

Variables	Vaginal laxity ($n = 82$)		
	Mean ± SD	n (%)	Median (min-max)
Age (years)	41.20 ± 8.64		41 (22–60)
Marital status			
Single		19 (23.18)	
Married		50 (60.97)	
Divorced		13 (15.85)	
Sexual orientation			
Hetero-affective		81 (98.78)	
Homo-affective		1 (1.22)	
Ethnicity			
White		42 (51.22)	
Black		10 (12.20)	
Other		30 (36.58)	
Years of education			
< 8 years		18 (21.96)	
> 8 years		64 (78.04)	
BMI			
< 25 kg/m^2		30 (36.58)	
> 25 kg/m^2		52 (63.42)	
Gravidity			2 (0–8)
Abortion (yes)		14 (17.07)	
Type of birth			
Vaginal		47 (57.32)	
Cesarean		20 (24.39)	
Both		12 (14.63)	
None		3 (3.66)	
Parity			
Primiparous		18 (21.95)	
Multiparous		61 (74.39)	
None		3 (3.66)	
Instrumental delivery			
No		65 (79.27)	
Forceps		16 (19.51)	
Vacuum-extractor		1 (1.22)	
Menopause status			
Premenopause		77 (93.90)	
Postmenopause		5 (6.10)	

SD: standard deviation; Min: minimum; Max: maximum; BMI: body mass index

Table 2. Clinical characteristics of participants with vaginal laxity ($n = 82$)

Variables		Mean ± SD	*n* (%)
Type of sexual intercourse			
	Vaginal		58 (70.73)
	Vaginal/anal		24 (29.27)
Source of vaginal laxity complaint			
	Self-report		66 (80.49)
	Partner		1 (1.22)
	Both		15 (18.29)
Duration of vaginal laxity complaint (years)		7.77 ± 6.74	
Intestinal habits			
	Regular		56 (68.29)
	Constipation		26 (31.71)
Flatus incontinence			27 (32.93)
Fecal incontinence			5 (6.10)
Urinary frequency		6.85 ± 3.24	
Dysuria			10 (12.20)
Nocturia			57 (69.51)
Pad use			24 (29.27)
Incomplete emptying			47 (57.32)
Straining			21 (25.61)
Post-micturition dribble			52 (63.41)
Hesitancy			12 (14.63)
Coital incontinence			
	No		57 (69.51)
	Orgasm		8 (9.76)
	Penetration		10 (12.20)
	Both		7 (8.54)
Modified Oxford Scale (0–5)		2.62 ± 0.81	
POP-Q			
Aa		-2.46 ± 0.40	
Ba		-2.45 ± 0.43	
Ap		-2.88 ± 0.24	
Bp		-2.88 ± 0.29	
C		-6.82 ± 1.30	
D		-8.30 ± 1.73	
TVL		9.71 ± 0.96	
GH		3.01 ± 0.60	
PB		3.32 ± 0.51	
POP-Q staging			
	Stage 0		15 (18.29)
	Stage I		67 (81.71)

SD: standard deviation; POP-Q: Pelvic Organ Prolapse Quantification; Points Aa, Ba: vaginal Anterior compartment; Points Ap, Bp: vaginal posterior compartment; Point C: cervix or vaginal vault; Point D: posterior fornix; TVL: total vaginal length; GH: genital hiatus, PB: perineal body

< 26.55). The lowest FSFI score domains were desire (3.11 ± 1.18), arousal (3.42 ± 1.23), and orgasm (3.64 ± 1.46). Sexual matters presented the highest mean scores (26.39 ± 20.26) in ICIQ-Vaginal Symptoms. The middle-third vaginal thickness mean in millimeters was smaller in both TAUS and TVUS compared to the other measurements. The comparative analysis between the VWT (measured by TAUS and TVUS) and the sociodemographic/clinical variables showed no significant difference (Supplementary Table 1).

Another comparative and agreement analysis between the TAUS and TVUS is shown in Table 4. There was a significant difference between the ultrasounds in the three

Table 3. Questionnaires scores and ultrasound measurements of women with vaginal laxity ($n = 82$)

Variables		Mean ± SD	*n* (%)
Vaginal Laxity Questionnaire			
	Very loose		31 (37.80)
	Moderately loose		41 (50.00)
	Slightly loose		10 (12.20)
FSFI			
	Desire (score range 1.2–6)	3.11 ± 1.18	
	Arousal (score range 0–6)	3.42 ± 1.23	
	Lubrication (score range 0–6)	4.21 ± 1.36	
	Orgasm (score range 0–6)	3.64 ± 1.46	
	Satisfaction (score range 0.8–6)	4.00 ± 1.34	
	Pain (score range 0–6)	4.48 ± 1.54	
	Total (min–max score 2–36)	22.86 ± 6.22	
ICIQ-VS			
	Vaginal symptoms (scoring 0–53)	16.05 ± 7.72	
	Sexual matters (scoring 0–58)	26.39 ± 20.26	
	Quality of life (scoring 0–10)	5.96 ± 3.46	
	Question 4-Vaginal Laxity (scoring 0–3)	2.30 ± 0.78	
ICIQ-UI-SF			
	ICIQ score (scoring 0–21)	9.33 ± 6.63	
Vaginal wall thickness (transabdominal ultrasound in mm)			
	Proximal	10.41 ± 3.51	
	Middle third	9.75 ± 3.45	
	Distal	11.07 ± 3.30	
Vaginal wall thickness (transvaginal ultrasound in mm)			
	Proximal	6.87 ± 1.48	
	Middle third	6.54 ± 1.60	
	Distal	7.81 ± 2.06	

SD: standard deviation; Min: minimum; Max: maximum; FSFI: Female Sexual Function Index; ICIQ-VS: International Consultation on Incontinence Questionnaire Vaginal Symptoms; ICIQ-UI-SF: International Consultation on Incontinence Questionnaire Urinary Incontinence Short Form

locations (proximal, middle third, and distal) of approximately 3 mm, with higher values for the TAUS compared to the TVUS. Nonetheless, there was low agreement among ultrasound measurements at the three locations. A significant correlation was found between the duration of vaginal laxity complaints and the TAUS distal vagina. A significant correlation was also found between TVUS proximal vagina and modified Oxford Scale and POP-Q points C, D, and total vaginal length. The other variables showed no significant correlation with ultrasound measurements (Supplementary Table 2). Finally, Fig. 2 shows that a significant correlation was found among the proximal, middle-third, and distal vagina measurements in TVUS (values in the vertical axis) and the proximal, middle-third, and distal vagina measurements in TAUS (values in the horizontal axis).

Discussion

Our study found a correlation between the measurements performed by TAUS and TVUS. These findings are in accordance with the results of previous studies [15, 16] and also show that both techniques are capable of measuring VWT in patients complaining of VL. Both measurement techniques can be easily performed and incorporated into patient care routines. We also observed a correlation among duration of vaginal laxity, pelvic floor muscle strength, and points assessed by the POP-Q and VWT measurements. These findings may help to understand the pathophysiology of vaginal laxity.

Both TVUS and TAUS techniques to measure VWT have already been described [15, 16]. It is not our objective

Table 4. Comparative and agreement analysis between the TAUS and TVUS ultrasounds

Measurements	Mean ± SD	*P**	ICC	(95% CI)	*P***
Proximal vagina		**0.001**	0.094	(– 0.064; 0.266)	0.057
TAUS	10.41 ± 3.51				
TVUS	6.87 ± 1.48				
Mean difference	3.54 ± 3.46				
Middle-third vagina		**0.001**	0.119	(– 0.060; 0.306)	**0.033**
TAUS	9.75 ± 3.45				
TVUS	6.54 ± 1.60				
Mean difference	3.21 ± 3.40				
Distal vagina		**0.001**	0.211	(–0.063; 0.453)	**0.001**
TAUS	11.07 ± 3.30				
TVUS	7.81 ± 2.06				
Mean difference	3.26 ± 3.12				

TAUS: Transabdominal ultrasound; TVUS: transvaginal ultrasound; SD: standard deviation; **P*-value referring to the Wilcoxon test for related samples for comparison between the TAUS and TVUS. ICC: intraclass correlation coefficient for agreement between measures; 95% CI ICC: 95% confidence interval of the ICC. ***P*-value of the ICC. Bold values considered statistically significant

to discuss the two techniques previously described with such properties by their respective research groups or to identify the best technique to measure the vaginal wall.

Prior to VWT assessment, a validated technique using a 2D ultrasound has been used to evaluate the bladder wall thickness [24, 25]. In the study by Panayi et al., unlike the transabdominal and transperineal techniques, transvaginal ultrasonography showed good interobserver repeatability for measuring the bladder wall thickness, being, therefore, considered the best approach to measure the bladder wall thickness [26]. Similarly, the transvaginal technique for measuring the VWT demonstrated good inter- and intraobserver reliability. Its measurements are closely related to histological measurements of VWT in cadavers [16]. Histologically, the vagina comprises four layers: the vaginal mucosa, vaginal submucosa, muscularis layer, and adventitia layer. The first is composed of stratified non-keratinized squamous epithelial tissue. The second layer is mainly made up of collagen and elastin. This layer is a vascularized connective tissue devoid of glands or mucosal muscularis. The two latter layers are formed by smooth muscle and loose connective tissue, respectively [27].

Regarding the transabdominal approach, Balica et al. defined two measures of the total mucosa thickness and total VWT; we base our measurements on the latter. VWT was described as the measurement between the outer layer of the anterior vaginal wall and the outer layer of the posterior vaginal wall at the level of the vesical trigone. According to the authors, the transabdominal approach is generally less uncomfortable and does not distort the vaginal canal.

Low agreement was found among ultrasound measurements at the three locations. This low agreement was expected, as measurements were performed using different ultrasound approaches with different preparations. In the transabdominal approach, measurements were performed with moderate bladder filling, and the anterior and posterior vaginal walls were measured at once using an abdominal probe. In the transvaginal approach, 40 ml water-based gel was introduced into the vaginal canal to separate the vaginal walls so that they could be measured separately using a vaginal probe. It is important to recognize that changes in TAUS and TVUS measurements are likely to be found. Furthermore, our study revealed a significant difference between the TAUS and TVUS measurements in the three locations of approximately 3 mm. Higher values were observed in the TAUS. So far, we have not found studies that compared both measures.

Considering TAUS measurement, the study by Balica et al. [17] reported that total VWT measurements averaged 14.5 mm ± 4.2 mm. In our study, we performed three

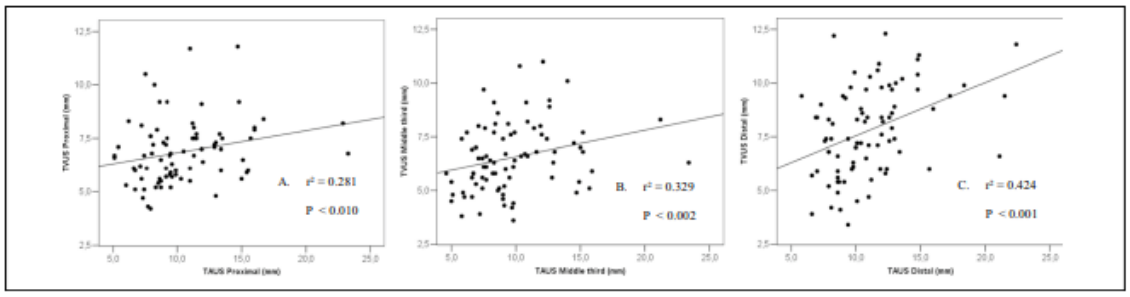

Fig. 2. Correlation between the vaginal thickness measurements in the transabdominal and transvaginal ultrasounds

measurements at three different locations (proximal, middle third, and distal vagina) using TAUS with a mean of 10.41 ± 3.51 mm (proximal), 9.75 ± 3.45 mm (middle third), and 11.07 ± 3.30 mm (distal). The slight measurement difference between the studies can be explained by the characteristics of the study population and by the differences in the measurement sites. The VWT of postmenopausal women with genitourinary syndrome of menopause was also assessed by TAUS in a cross-sectional study. The mean total vaginal thickness measurement was 10.73 ± 2.9 mm and 9.74 ± 2.9 mm in the symptomatic and asymptomatic groups, respectively, with no significant difference ($p = 0.35$) [5]. However, in a previous study, a significant difference was found between total vaginal thickness in pre- and postmenopausal women ($p = 0.0168$) [15]. TAUS was used for evaluating vaginal atrophy in postmenopausal women. The total vaginal thickness was also lower in post- than premenopausal women ($p = 0.005$) in a recent case-control study. Interestingly, they determined a cutoff value for the total vaginal thickness of 8.55 mm predicting vaginal atrophy [specificity of 99.72% (95% CI) and positive predictive value of 98.84% (95% CI); $p = 0.013$] [28].

Our measurements using the TVUS had a mean of 6.87 ± 1.48, 6.54 ± 1.60, and 7.81 ± 2.06 at the proximal, middle third, and distal locations, respectively. After performing the measurements separately, they were summed for the analysis. Our measurements are similar to those performed by Panayi et al. [16]. Another TVUS approach has recently been investigated. A study using 3D high-frequency TVUS showed that anterior and posterior vaginal wall thickness was significantly lower in women with genitourinary syndrome of menopause ($p = 0.007$ and $p = 0.049$, respectively) [7]. Ultrasound studies for sexual dysfunction were also performed using TVUS measurements. Gravina et al. measured the thickness of the urethrovaginal space in women with and without vaginal orgasm. They found that the urethrovaginal space and distal, middle, and proximal urethrovaginal segments were thinner in women without vaginal orgasm. Moreover, women with a thicker urethrovaginal space were more likely to experience vaginal orgasm ($r = 0.884$; $p = 0.015$) [29].

Regarding the analysis between clinical characteristics and ultrasound measurements, a significant correlation was found between the duration of VL complaints and the TAUS distal vagina and between TVUS proximal vagina and POP-Q points (C, D, and total vaginal length). VL has been identified as a symptom of sexual dysfunction related to pelvic organ prolapse [2, 18]. Interestingly, an association between VL and levator ani hyperdistensibility measures (genital hiatus and perineal body) and levator hiatal area has been demonstrated in previous studies using the four-dimensional translabial ultrasound [1, 30]. To date, we have not found studies investigating the relationship between points C and D or total vaginal length and VWT in women with VL complaints. The pathophysiology of VL is not well known, and more studies are needed to understand this symptom. In this context, some studies have investigated VWT in genital prolapse [4, 6, 31]. An observational study including women with symptoms of genital prolapse showed a relationship between VWT and the grade of vaginal prolapse. The authors observed that VWT decreases with increasing degree of prolapse (for prolapses that do not extend beyond the hymen) and VWT increases with increasing degree of prolapse for those that extend beyond the hymen [4]. Similarly, another study compared VWT in pre- and postmenopausal women with grade 1 or 2 prolapse and found significantly greater epithelial thickness in the proximal segment of the posterior wall than in the distal segment [6]. VWT tended to increase caudally in patients with and without prolapse assessed by MRI in another study [31].

The present study has strengths. To our knowledge, no previous study had compared the two ultrasound approaches (TAUS and TVUS). Both the TAUS and the TVUS were easily performed by the examiner to measure the VWT, and the presence of a correlation between them might suggest that the health professional will be able to choose the technique that best suits the investigative proposal. Furthermore, the study identified differences in execution between the techniques. The use of standardized vaginal gel in TVUS helped to visualize the vaginal walls independently, but TVUS can be uncomfortable. TAUS is less invasive and causes less embarrassment for patients, but difficulties in performing measurements in obese patients and in standardizing bladder filling may occur.

Limitations were found in this study. It was not possible to perform a sample calculation for the present study, which may generate a type II error regarding the association between clinical outcomes and vaginal thickness. In addition, we compromised the external validity of the study by excluding participants using vaginal estrogen and with previous pelvic surgery. Moreover, when comparing these two previously studied techniques, we judged that it was not necessary to use more than one examiner; thus, we did not calculate the inter-examiner reliability. Finally, we did not perform the reassessment of VWT measurements using the two techniques (TAUS and TVUS).

Conclusion

VWT measurements differed by 3 mm between TAUS and TVUS. A significant correlation was found between the VWT measurements in TVUS and the VWT measurements in TAUS. Both techniques were able to measure VWT in women complaining of VL.

A significant correlation was found between VWT measurement and duration of VL complaints, modified Oxford Scale, and POP-Q points C, D, and total vaginal length.

In our study, women complaining of VL were more likely to be at reproductive age, multiparous, and have undergone vaginal delivery, in addition to having pelvic floor muscle weakness, initial staging of genital prolapse, and associated sexual and urinary symptoms.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00192-022-05184-8.

Acknowledgements We are grateful to Dr. Rodrigo Menezes Jales for the administrative support, Dr. Helymar Machado, for the statistical analysis, and the São Paulo Research Foundation (FAPESP) for the support given to our study.

Author contributions GMVP: Protocol/project development; Data collection or management; Data analysis; Manuscript writing/editing

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CMA: Data collection or management; Data analysis; Manuscript writing/editing

ISV: Data collection or management; Data analysis

KCA: Data collection or management; Data analysis

LGOB: Protocol/project development; Data collection or management; Data analysis; Manuscript writing/editing

Funding First author: Scholarship Grant 2019/26723-5, São Paulo Research Foundation (FAPESP). The remaining authors reported no disclosures.

Declarations

Conflicts of interests None.

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4.4. Artigo 4. Experiences of women with symptoms of vaginal laxity – a qualitative study

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Experiences of women with symptoms of vaginal laxity – a qualitative study

--Manuscript Draft--

Manuscript Number:	
Article Type:	Original Research
Keywords:	Vaginal laxity; female sexual dysfunction, qualitative study; sexuality.
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Abstract:	Background: Vaginal laxity (VL) is rarely discussed among patients and their physicians possibly due to the lack of evidence-based treatments, embarrassment, and lack of knowledge in recognizing this condition. Aim: We aimed to understand the meanings that women attribute to the sensation of VL. Methods: This is a qualitative study using in-depth interviews and thematic analysis. Sixteen participants were intentionally selected from February 2020 to December 2021. One researcher interviewed each participant in a private room guaranteeing that rapport was established. Two independent researchers performed a complete transcript of each interview immediately after its end. Data collection was interrupted when theoretical saturation criteria were reached. We followed the thematic analysis proposed by Braun and Clarke. Findings: Of 16 patients, only one did not undergo delivery. Her complaint was not different from the rest of the group. Three major themes and ten subthemes were identified: the pathway towards the identification of symptoms of VL (from the invisibility of VL to the perception of symptoms; emotional reactions experienced when dealing with VL complaint and the help-seeking process), meanings associated with VL complaints ("I think the name itself weights", women´s perceptions, explanations and beliefs about causes of VL) and the impact of VL symptoms on women's´ relationships (with themselves, on sexual intercourse and their partner). Discussion: This qualitative study reveals how women deal with VL and the impact it causes on intrapersonal and interpersonal relationships. Conclusion: VL is a symptom that is still little understood by women, and little explored by health professionals, with repercussions on personal and marital life.

Cover Letter

August 6th 2023

To: The Editors-in-Chief
Professor Debra Bick
Midwifery

Dear Editor

We herewith send you the qualitative study "**Experiences of women with symptoms of vaginal laxity – a qualitative study**" for analysis in your respectful journal. To our knowledge, this is the first qualitative study about women with vaginal laxity. We expect that the study will contribute to the understanding of the pathophysiology of vaginal laxity in the future.

This study is an original work and has not received prior publication and is not under consideration for publication elsewhere. All authors have substantial contributions to this study: substantial contributions to conception and design, drafting and revising the article and consent to the final version that is presented here.

If you have any questions about the manuscript, Dr. Brito will be serving as the corresponding author. Thank you in advance for your consideration.

Sincerely yours,

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Experiences of women with symptoms of vaginal laxity – a qualitative study

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Glaucia Pereira: conception and design of the study, acquisition of data, analysis and interpretation of data, drafting and revising the article, final version approval.

Odette Sanchez: acquisition of data, analysis and interpretation of data, drafting and revising the article, final version approval.

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Lucia Lara: drafting and revising the article, final version approval.

Cássia Juliato: conception and design of the study, drafting and revising the article, final version approval.

Luiz Gustavo Brito: conception and design of the study, acquisition of data, analysis and interpretation of data, drafting and revising the article, final version approval.

Acknowledgements: We thank Sao Paulo Research Agency (FAPESP) for all the support for this study.

Funding: The first author received a scholarship grant from Sao Paulo Research Agency (FAPESP) number 2019/26723-5.

Declaration of Interest: The authors report there are no competing interests to declare.

Highlights (for review)

Problem or Issue: Vaginal laxity is defined as a complaint of excessive vaginal flaccidity.

What is Already Known: VL is a condition that is rarely discussed between women and health professionals.

What this Paper Adds: This is the first study that qualitatively assesses the perception of women with VL. Our findings will contribute to the development of new hypotheses for a better understanding of the pathophysiology of VL.

Experiences of women with symptoms of vaginal laxity – a qualitative study

ABSTRACT

Background: Vaginal laxity (VL) is rarely discussed among patients and their physicians possibly due to the lack of evidence-based treatments, embarrassment, and lack of knowledge in recognizing this condition.

Aim: We aimed to understand the meanings that women attribute to the sensation of VL.

Methods: This is a qualitative study using in-depth interviews and thematic analysis. Sixteen participants were intentionally selected from February 2020 to December 2021. One researcher interviewed each participant in a private room guaranteeing that rapport was established. Two independent researchers performed a complete transcript of each interview immediately after its end. Data collection was interrupted when theoretical saturation criteria were reached. We followed the thematic analysis proposed by Braun and Clarke.

Findings: Of 16 patients, only one did not undergo delivery. Her complaint was not different from the rest of the group. Three major themes and ten subthemes were identified: the pathway towards the identification of symptoms of VL (from the invisibility of VL to the perception of symptoms; emotional reactions experienced when dealing with VL complaint and the help-seeking process), meanings associated with VL complaints ("I think the name itself weights", women´s perceptions, explanations and beliefs about causes of VL) and the impact of VL symptoms on women's´ relationships (with themselves, on sexual intercourse and their partner).

Discussion: This qualitative study reveals how women deal with VL and the impact it causes on intrapersonal and interpersonal relationships.

Conclusion: VL is a symptom that is still little understood by women, and little explored by health professionals, with repercussions on personal and marital life.

Keywords: Vaginal laxity; female sexual dysfunction, qualitative study; sexuality.

INTRODUCTION

Vaginal laxity (VL) is defined as a complaint of excessive vaginal looseness and is most commonly described as a decreased sensation during sexual activity[1]. The prevalence of VL from 24% to 38% and appears to be associated with young age, vaginal deliveries, symptoms of pelvic organ prolapse, and is therefore also somatic dysfunction[2,3]. Other risk factors are foetal macrosomia, history of instrumental delivery (forceps), multiparity, and connective tissue changes[2].

VL is rarely discussed between women and health care professionals possibly due to the lack of evidence-based treatments, embarrassment reported by patients, and lack of knowledge to recognizing this condition by health care practitioners [4]. Despite this, there has been an increase in demand for the treatment of VL, especially in female genital cosmetic surgery [5,6].

The diagnosis of VL is based on patient self-report. Although numerous instruments have been used for psychosexual assessment, to the best of our knowledge, only two instruments assess perceptions specifically for VL, which is the Vaginal Laxity Questionnaire (VLQ) and the ICIQ Vaginal Symptoms Questionnaire [4,7]. Careful listening, a physical examination, and a psychosexual assessment are the initial steps in identifying patients with VL [8].

The fact that there is no consensus on a standard definition for VL, nor robust scientific evidence to explain the pathophysiology of this complaint, brings the need to search for other research tools that explore women's reports and perceptions. Another crucial point is to recognize the impact of VL on women's quality of life, how she

correlates this complaint to herself and her partner, as well as the need to reinforce woman-centred care approaches that enable a deeper understanding of this situation. Qualitative analysis can help to fill this gap, enabling the study of future diagnostic tools. Thus, the aim of this study is to understand the meanings that women attribute to the sensation of VL and its impact on their perception of themselves, of their intimate affective relationships, and their sexuality.

MATERIALS AND METHODS

We used a qualitative approach to understand the meanings that women attribute to the sensation of VL. The present study used in-depth interviews and followed the guidelines of the Consolidated criteria for reporting qualitative research – COREQ" as a support tool [9]. Local Institutional Review Board has approved the study (CAAE number 12919119.9.0000.5404).

Participants and Settings

Women were selected before the randomization/allocation procedure from a randomized clinical trial (February 2020 – December 2021) that offered treatment to women complaining of VL. [10]. Participants who agreed to participate in the study signed an informed consent form. We included women aged ≥ 18 years with a complaint of VL assessed by a direct question (yes/no) and the Vaginal Laxity Questionnaire (VLQ)[4] and excluded participants who did not consent to the conduction and recording of the interviews.

Data Collection

Data were collected between August and October 2021 after the clinical trial allocation period. A physiotherapist specializing in women's health with experience with patients complaining of VL (GMVP) contacted each participant via telephone and scheduled the interviews. Women were interviewed individually and answered open and semi-structured questions according to the interview script, with total security and privacy for the interview (Table S.1). The researcher (GMVP) took unstructured notes of the participants' behaviour during the interview, as well as non-verbal/facial expressions, and emotional responses to a given topic during the interview, and silences or pauses. The researcher could make adaptations whenever necessary, ensuring that the participants spoke freely about their life experiences and their perceptions about the sensation of VL. The researcher built a bond with the participants during the recruitment process of the clinical trial from which they were recruited; thus, we believe that rapport was established.

Two independent researchers (GMVP; ODRS, a psychologist with expertise in conducting qualitative studies) performed a complete transcript of each interview immediately after the interview ended to ensure that no observations were lost while maintaining their original form. Files (full audio transcription and digital files) were stored in a database. Data collection was interrupted when theoretical saturation criteria were reached[11]. No participant was excluded or withdrew their consent. Software to support the research of qualitative methods was used to assist organize the material, coding, and analysing the data (NVivo 11 - QSR International 2021).

Data Analysis

We followed the thematic analysis proposed by Braun and Clarke[12]. This method characterized by its flexibility allows for identifying, analysing, and reporting patterns

from a data set. Firstly, the transcript interviews were read several times to allow familiarization with the data. Subsequently, an initial code generation phase was carried out by two independent authors (GMVP and ODRS) after the identification of ideas and relevant information from the data set. The initial codes were revised through a systematic and exhaustive reading of the material to reflect on the participant's perceptions of the object of study. The NVivo 11 software was useful to organize, identify patterns through the data set and validate researchers' analysis. Through this software, a word cloud was created based on the frequency of words.

Next, we initiated the phase that allows searching for themes and sub-themes based on a process to group codes. These themes were supported by quotes to appropriately reflect the participants' meanings and perceptions. To ensure the validity of the data, all processes were discussed with two senior researchers (LGOB, FGS), which allows for reaching a consensus when divergences between analyses were identified.

Sociodemographic and clinical data were collected to better understand the characteristics of the participants. All interviews were conducted in Brazilian Portuguese language and the quotes supporting each theme and sub-theme were translated into English.

RESULTS

Sixteen women were interviewed for a total of seven hours and 25 minutes; table 1 shows their sociodemographic and clinical-related characteristics. The participants' age ranged from 31 to 50 years. Most of women were married and self-declared white ethnicity, premenopausal, multiparous, with previous vaginal delivery.

We presented the main themes and sub-themes that were defined during the thematic analysis (Table S.2 presents the transcript for each theme and subtheme). As a

result of this process, we constructed three major themes and their respective sub-themes represented in Figure 1. Figure 2 contains the words that most frequently emerged from the women´s transcripts.

Theme 1. The pathway taken in the identification of symptoms of VL

The pathway taken by women with VL symptoms until reaching the definition of the diagnosis and, consequently, access to treatments for the management of this condition, becomes a long and lonely process. VL symptoms are imbricated with the identification of a series of other pelvic floor symptoms that cause discomfort in women´s daily lives.

Subtheme 1.1: From the invisibility of VL to the perception of their symptoms

VL is an unknown and little-spoken topic, which demonstrates the low visibility and discussion of this topic either among patients or health professionals. In this sense, they highlight the importance of addressing this issue and the need for greater dissemination. Women reported that talking about VL with a person who does not complain about it is difficult and embarrassing. Moreover, the difficulty in naming the complaint also becomes a barrier to seeking specialized help. Thus, diagnosis of VL can be delayed, and consequently, access to treatment options. In this process, denial of the symptoms or thinking that "it's all in my head" is a mechanism that women use to deal with the symptoms. Interestingly, the identification of other pelvic floor symptoms connects the patients with VL such as stress urinary incontinence, flatus vaginalis, dyspareunia and anorgasmia.

Subtheme 1.2: Emotional reactions experienced when dealing with VL

Women experienced fear, fright, sadness, tension, shame, frustration, and concern when identifying VL symptoms. When these symptoms occur in a daily basis, the suffering seems to be enhanced. Fear and shame usually prevent women from seeking

immediate help. Moreover, it is possible to observe a certain guilt for having this complaint, as women believe that they may have had some responsibility in the past as they might have "damaged" their vagina during vaginal delivery, thus confronting its consequences today.

Subtheme 1.3: Help-seeking process

Some women reported seeking information about home treatments and exercises as alternatives to relieve symptoms. The possibility of performing surgeries as an alternative treatment was a recurring theme among the various interviewees. Another way used by the women was to seek friends with the same symptom, as of having the need to build a network support. The demand for specialized help intensifies when they observe that the symptoms worsen, especially those that interfere with sexual intercourse and the bond with the partner. However, the expectations around the cure and the gradual improvement of the symptoms were seen with a positive perspective, and a moment of personal overcoming.

Regarding the contact with health professionals, women reported that the first contact to address the topic was mediated by the gynaecologist; however, they recognize that this is a topic that is still little addressed in the consultations and feel that there is poor knowledge from physicians to deal with their complaints.

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Theme 2. "I think the name itself weighs" meanings associated with VL complaints

VL allows the surge of several meanings associated with the looseness of the vagina and weakness of the vaginal musculature. Thus, beliefs and explanations that women elaborate on the main causes of VL are reinforced, and these actions result in negative qualifiers that are linked to their own experiences.

Sub-theme 2.1: Women´s perceptions about VL

The term itself causes embarrassment in the interviewees. Participants identify it as a shocking term that generates shame and results in stigmas that emerge in interaction with others. Some of the qualifiers reveal VL as "weakness in the vagina muscles" ,"flabbiness or flaccid underneath", "open", “vacuum”, “withering”, “as if it were hollow inside” and “laxity”. The interviewees generally associate the complaint with the terms “loose thing”, “loose” or “wide”, “enlargement” of the vagina. Others describe having identified it as “something strange”, different or missing compared to other women, as well as changes in the appearance of the external genitalia.

Sub-theme 2.2: Women´s explains and beliefs about causes of VL

Women reported that VL could have been caused because their vagina had been excessively used or that they had badly behaved in the past that could have interfered with their current condition, blaming themselves for this. Others blamed health professionals and practices during childbirth with procedures such as episiotomy. They also reported that pregnancy and childbirth, genital prolapse, age and the ageing process would also be explanations.

Theme 3. VL symptoms and their impact on women's relationships

VL impacted relationships with their partners, sex-erotic relationships, and their perception of women´s body image (self-image and self-esteem).

Sub-theme 3.1: Self-relationship: “I don’t feel like a complete woman”.

Women reported difficulties looking at themselves and identifying the signs and symptoms associated with VL. Feeling uncomfortable or not liking their vaginas or vulvas, insecurity, incapability, powerlessness, guilt, or anger are the emotions women

reported during the interview. For some of them, self-care practices are not so frequent, and women may refer themselves as less feminine, with statements that denote the perception of feeling “less of a woman” or incomplete. Some of them reinforce the expectation of wanting to “be normal” and mention that these transformations make them feel that they are not the same person. Moreover, for another group of women, they feel the need to generate pleasure for their partners in sexual intercourse and VL impacted their self-esteem and their femininity.

Subtheme 3.2: Effect of VL on sexual intercourse

Decreased sexual desire, decreased lubrication and anorgasmia during sexual intercourse were recurrent reports, qualifying sexual intercourse as an "absence of sensation", "an empty thing" or "empty". One of the interviewees described the sensation during penetration as “a finger floating in space”.

Women reported that the duration and frequency of sexual penetration became shorter and with longer intervals between one and other. They have also mentioned the use of pillows and supports as an attempt to contract the vaginal musculature during penetration, as well as changes in the sexual position and simulation of orgasm to satisfy the partner. Sexual practice without penetration (foreplay activities to longer periods), reduction of the duration of sexual penetration and maintaining relations with the lights off in the bedroom were used as strategies to deal with uncomfortable situations VL would cause.

Women have the perception that narrowing the vagina is directly associated with pleasure. The feeling that it is not tight, the “lack of fit in the intercourse”, being “tight” or “loose” have a direct impact on sexual pleasure and satisfaction, especially with the partners, being the object of constant concern by them. More interestingly, some women

even think about having pain during sexual penetration as means of having achieved a narrower vagina as part of some expectations.

Subtheme 3.3: Relationship with the partner

Communicating about symptoms, especially those that interfere with sex-erotic relationships, is a reason for shame and embarrassment, which is why it is often an issue that is avoided. Evading this theme also intends to avoid any possibility of offending, hurting the partner or receiving any kind of questioning.

Women reported that they are recurrently concerned with the partner's pleasure during sexual intercourse, thus nullifying their own pleasure. Having sexual activities with the partner becomes an obligation even when some practices may cause discomfort, shame, and insecurities. Interestingly, they report situations where partners may avoid them and causes for that are elaborated such as possible betrayal, lack of affection or not feeling desired. All these points make their own sexual pleasure to not be their main priority.

DISCUSSION

Our study reveals how women deal with VL throughout their lives and the impact it causes on intrapersonal and interpersonal relationships, as well as the barriers they face in accessing early diagnosis and treatment. Obtaining a diagnosis of VL is a long and difficult process. Several factors collaborate to reinforce these barriers, among them: the delay in recognizing the problem; waiting for the condition to improve spontaneously; if the partner doesn't complain, it's not so bad; links to other nonspecific symptoms (for example, urinary leakage) believed to be related to VL. The lack of knowledge about the body and its physiology becomes evident, as well as the subordinate and passive women´s

position in the affective-sexual relationship. Feelings of shame and embarrassment by women reinforces the barriers for treatment and subsequent notification.

The invisibility of VL reinforces the need for discussion and research on the topic. A survey carried out among physicians of the International Urogynaecological Association (IUGA) revealed that 83% of respondents consider VL to be an underreported condition[13].

The scarcity of evidence on the pathophysiology of VL and the lack of objective diagnostic tools contribute to this underreported condition. Diagnosis of VL is based on women's self-report. The lack of clarity in the exposition of the theme by health professionals was some of the problems pointed out by the study participants. These findings support previous studies that identified that health professionals do not routinely address questions about sexuality with their patients; reasons would be lack of time, resources, health policies and training [14].

Given that, the Internet becomes one of the main alternatives for women to seek information. However, it does not guarantee reliable information. This source is used by them to build their opinions about VL and their expectations about treatment, bringing reflection about the role of social media on educating lay people. About treatment options for VL, for some participants, surgery appears as an alternative for immediate resolution of the symptom. Interestingly, surgical treatment of VL was perceived by IUGA member physicians as the most effective intervention when compared with Kegel exercises or physiotherapy[13].

As reasons for developing VL, blaming themselves for attitudes of the past, and attributing the aetiology of VL to it, are some of the behaviours observed in the interviewees. The ageing process, pregnancy and childbirth are understood as elements

that impact in the current condition. In this sense, although the aetiology of VL has not yet been clearly identified, studies point out to hypotheses that pregnancy and vaginal delivery affect the sensation of VL [2,15].

In the construction of the female identity, women identify the ability to give pleasure to their partner as a central condition, which affects their self-image. We noticed that, for women, the improvements in the symptoms associated with VL are understood as to recover their femininity. Studies suggest that negative changes in female sexual function are common, the main reasons for which are biological, psychological, interpersonal and sociocultural changes[16,17]. In this context, many women experience changes in their bodies[17,18], with potential changes in their sexual organs[19]. All these changes impact the way these women perceive themselves and, consequently, their body image. Body image is defined as the perception of the aesthetics or attractiveness of one's own body[20] and, thus, of sexual function and satisfaction[21]. Similar to our study, Thomas *et al.*[21] found that feeling attractive was an important aspect of women's sexual activity and the way in which they responded to perceived changes in their bodies also affected their sexual activities and sexual satisfaction.

A previous study revealed that couple communication was considered a priority for the women surveyed. The highest rates of emotional and partner relationship satisfaction were reported by women who rated their sexual relationships as active and satisfying[22]. In our study, symptoms such as decreased lubrication, anorgasmia, and the VL affect their perception of their partner's sexual satisfaction. Sexual relations are perceived as an obligation in their role as wives, and therefore, submitting to practices that they attribute as uncomfortable is a way of maintaining the bond with the partner. For Hinchliff *et al.,* placing the sexual needs of partners above their own needs implies the passivity of female sexuality. The feeling of duty, the uncertainty of not knowing what

else to do, the attempt to prevent the partners from seeking sex with another woman and the collapsed marriage were some of the reasons that made women engage in sexual relations when they had no desire[23].

Heterosexual women are less likely to endorse communication with their partners on topics other than sex as relevant to their sexual satisfaction than bisexual women[24]. According to the participants' reports, reporting VL interferes with intimacy with the partner, generating a distance between the couple. By avoiding contact and communication with the partner, the interviewees experience feelings of worthlessness and the need not to be exposed. Lack of communication is also seen as the possibility of extramarital sexual activities. When there is an attempt at communication, dissatisfaction with the dialogue with the partners is notorious when the interviewees reveal that the partners do not understand the complaint, stating to them that it is "things in your head".

VL symptoms are perceived as a barrier to having pleasurable penetrative sex. The study by Holt *et al.*[24], found that heterosexual women valued orgasm frequency more than other groups of women. Vaginal intercourse is avoided or postponed until the final moments of sexual activity. Frustrated attempts to keep the vagina tighter are revealed during the participants' speech. According to the interviewees, a tight vagina is considered ideal for both female and male orgasms. In this context, as they are unable to offer a tight vagina to their partners, anal intercourse is allowed to guarantee pleasure for the partner.

The present study has limitations that need to be elucidated. Our findings need to be interpreted considering that the study was carried out in a single centre, in a tertiary hospital, which reflects the perceptions of women who attend a specialized service. Future studies could include a population that comprehensively assesses aspects of VL from the LGBTQIAP+ group, such as homo and/or bisexual women. On the other hand, to the best of our knowledge, this is the first study that qualitatively assesses the perception of

women with VL. Based on our findings, new hypotheses can be developed for a better understanding of the pathophysiology of VL, as well as the need to develop specific assessment instruments for such complaints.

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TABLE LEGENDS

Table 1. Sociodemographic and clinical characteristics of the included women (n=16)

Table S.1. Interview Form

Table S.2. Participants' experiences assessed by themes and subthemes related to vaginal laxity

FIGURES CAPTIONS

Figure 1. The three major themes and their respective sub-themes

Figure 2. Word frequency based on NVivo (NVivo 11 – QSR International MA, USA) analysis.

Acknowledgments

Acknowledgements: We thank Sao Paulo Research Agency (FAPESP) for all the support for this study.

Table (Editable version)

Table 1. Sociodemographic and clinical characteristics of the included women (n=16)

Participant	Age	Marital Status	Ethnicity	BMI	Education	Gestation	Type of Birth	Parity	Instrumental Delivery	Menopause	Duration of the Interview (min.)
1	39	Married	White Background	> 25 Kg/m^2	> 9 years	1	Vaginal	Primiparous	No	No	18:26
2	37	Married	White Background	< 25 Kg/m^2	> 9 years	3	C-section	Multiparous	No	No	14:17
3	48	Married	Asian Background	< 25 Kg/m^2	> 9 years	2	Vaginal; C-section	Multiparous	No	No	22:46
4	31	Married	Black Background	> 25 Kg/m^2	> 9 years	2	Vaginal	Multiparous	No	No	24:13
5	45	Married	Black Background	> 25 Kg/m^2	> 9 years	4	Vaginal	Multiparous	No	No	26:29
6	43	Married	Black Background	< 25 Kg/m^2	> 9 years	4	Vaginal	Multiparous	No	No	18:56
7	43	Married	White Background	> 25 Kg/m^2	> 9 years	2	Vaginal	Multiparous	No	No	23:02
8	35	Divorced	White Background	> 25 Kg/m^2	> 9 years	3	Vaginal	Multiparous	Yes	No	56:16
9	47	Single	White Background	< 25 Kg/m^2	> 9 years	1	Vaginal	Primiparous	No	No	19:10
10	48	Divorced	Black Background	< 25 Kg/m^2	> 9 years	4	Vaginal	Multiparous	No	No	28:31
11	36	Divorced	Black Background	< 25 Kg/m^2	> 9 years	7	Vaginal; C-section	Multiparous	Yes	No	23:31
12	39	Married	Black Background	> 25 Kg/m^2	< 8 years	2	Vaginal; C-section	Multiparous	Yes	No	29:04
13	50	Divorced	Black Background	> 25 Kg/m^2	> 9 years	2	C-section	Multiparous	No	No	41:31
14	48	Single	White Background	> 25 Kg/m^2	> 9 years	0	No	Nulliparous	No	No	24:04
15	44	Married	Black Background	> 25 Kg/m^2	< 8 years	3	Vaginal	Multiparous	No	No	27:23
16	41	Married	White Background	< 25 Kg/m^2	> 9 years	2	C-section	Multiparous	No	No	15:59

Age: Years; BMI: Body Mass Index. Education: Years.

Figure

Click here to access/download;Figure;Figure 1 .png

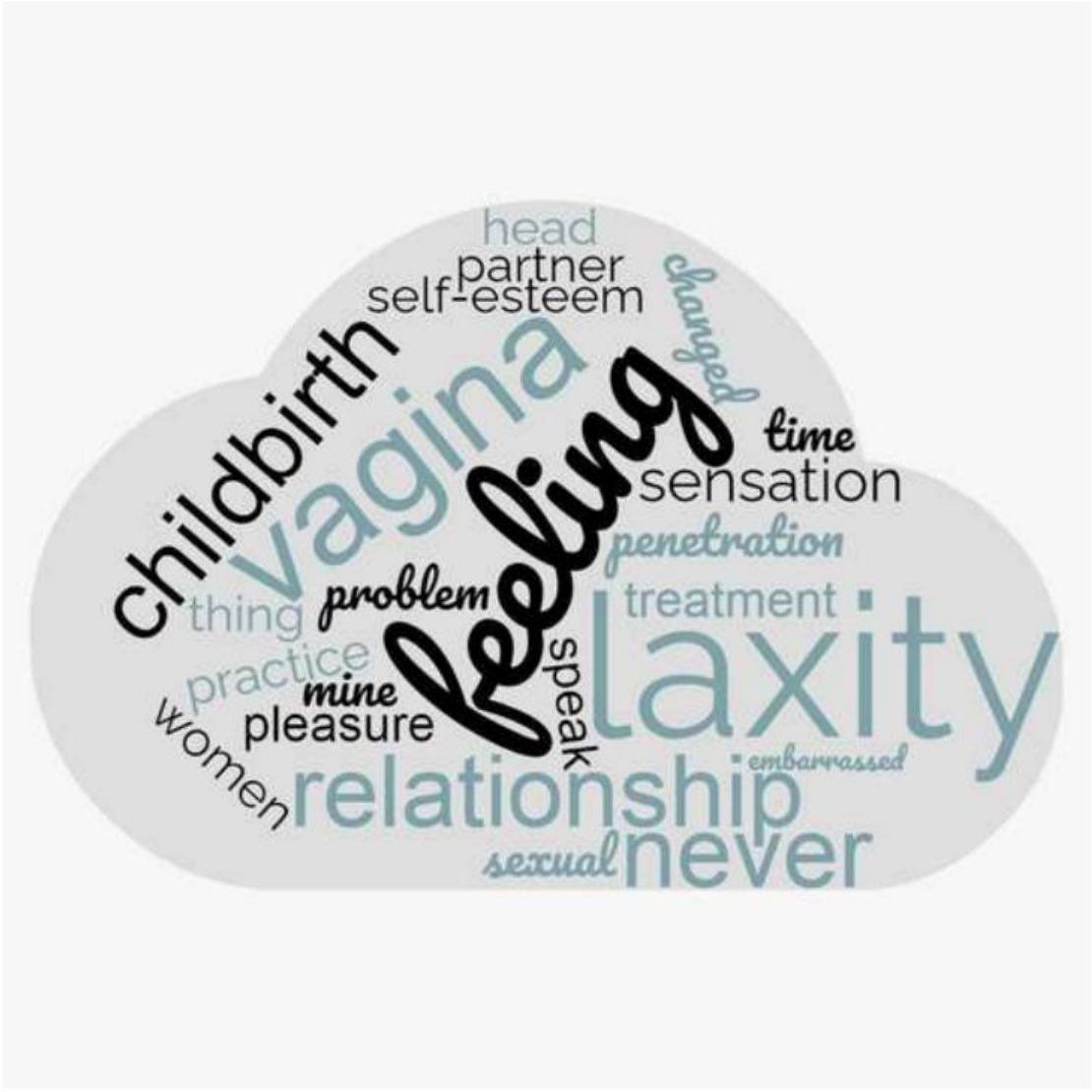
Theme 1. The pathway taken in the identification of symptoms of vaginal laxity		
From the invisibility of VL to the perception of their symptoms.	Emotional reactions experienced when dealing with the complaint	Help-seeking process
▪ VL is an unknown and little-spoken topic. ▪ Talking about the topic is difficult and embarrassing. ▪ Other symptoms are added to their perception of VL.	▪ Concern when identifying the symptoms. ▪ Fear and shame usually prevent seeking help. ▪ Guilt for behaviors in the past	▪ Home treatment and exercises on the Internet. ▪ Surgeries as an alternative treatment. ▪ The demand for specialized treatments.

Theme 2. "I think the name itself weighs" meanings associated with vaginal laxity complaints.	
Women´s perceptions about VL complaint	Women´s explains and beliefs about causes of VL
▪ The term causes embarrassment. ▪ Qualifiers describing vaginal laxity.	▪ Blame for vaginal use. ▪ Blaming the health. professional. ▪ Pregnancy and childbirth accentuated the symptoms.

Theme 3. Symptoms associated with vaginal laxity: their impacts on women's relationships		
Self-relationship: "I don't feel like a complete woman"	Effect of VL on sexual intercourse	Relationship with the partner
▪ Difficulties identifying the symptoms of VL. ▪ VL complaints impact the participants' self-image. ▪ Responsibility to generate pleasure in their partners.	▪ Lack of sensation during sexual intercourse. ▪ To adopt sexual practices to please the partner. ▪ Longer foreplay activities to reduce penetration duration.	▪ Avoid talking about VL with their partner. ▪ Concern with the partner's pleasure nullifying their own. ▪ The negative impact of VL on the affective bond with their partners.

Figure

Click here to access/download;Figure;Figure 2 .jpg



Supplementary Material

Table A.1. Interview Form	
Participant Initials:	Date:
Interview duration:	
1- How did you feel when a health professional told you that your symptoms could be called vaginal laxity? What does the expression "vaginal laxity" suggest to you? When you hear it, what comes to mind? What do you feel?	
	Researcher Notes:
2- How do you perceive the sensation of vaginal laxity? Describe this perception in your own words.	
	Researcher Notes:
3- When did you notice your sensation of vaginal laxity? How did you initially deal with that sensation?	
	Researcher Notes:
4- How did you seek help to understand this feeling? Can you describe in detail how this feeling has become more and more present in your life?	
	Researcher Notes:
5- How does your sensation of vaginal laxity interfere with your sexual intercourse? After the onset of your sense of vaginal laxity, how did you deal with your sexual intercourse? If there was a change during the moment of sexual practice, how did you notice it?	
	Researcher Notes:
6- How did your sensation of vaginal laxity interfere with your relationship with yourself? About your look at yourself? What about your self-esteem? What about your self-image? When you look at your genitalia, do you feel that your point of view has changed in relation to what you think of your body functioning?	
	Researcher Notes:
7- How did vaginal laxity influence the duration of penetration? In the foreplay of intercourse? In the form of initiation of sexual practice? In the frequency of sexual practice?	
	Researcher Notes:
8- How do you think vaginal laxity impacted your life with your partner?	
	Researcher Notes:
9- With regard to sexual relations, did you start to have any type of practice that you did not do before the onset of your sensation of vaginal laxity? Tell me a little more about it.	
	Researcher Notes:

10- How does the sensation of vaginal laxity interfere with your life?	
	Researcher Notes:
11- What motivated you to seek treatment? Have you tried other treatments previously? If so, talk about them and what went right or wrong. What do you think might be the best treatment?	
	Researcher Notes:
12- Describe your expectations about the possibility of treating your sensation of vaginal laxity. How do you see the future of your complaint?	
	Researcher Notes:
Would you like to add something?	

Table A.2. Participants' experiences assessed by themes and subthemes related to vaginal laxity

Theme and Subtheme	Participants' Experiences
Theme 1. The pathway taken in the identification of symptoms of vaginal laxity	
Subtheme 1.1: From the invisibility of vaginal laxity to the perception of their symptoms	*Is it a bit of a myth that is said? It's a little veiled ... it's a little talked about... it's unknown.* ***(Participant 1).*** *When I touched myself ... I knew there was something different with me, you know. I didn't know exactly what! But when I heard about the term vaginal laxity, I began to assimilate what I really perceived in myself.* ***(Participant 2).*** *It's hard for you to talk to people who have, you know ... one ... who don't have laxity and have a great life!* ***(Participant 3).*** *I was always kind of withdrawn in that sense... sexually, because I thought... oh, who am I going to talk to? ... Sometimes colleagues don't know much ... and there's the issue of prejudice too ... you can't go around saying that to others ... right? ... And so, gynaecologists, professionals ... did not have this knowledge ... I had no one to talk to ... and so I had the opportunity to meet C. (nurse).* ***(Participant 4).*** *Ah, I don't know... I think that, as always, we always let it go, ... saying, "no, ... it will pass!" ... this is something that will pass ... it's something in my head ... it's something that I have in my head because the other person is not complaining about anything, so ... then we leave it as it is, and it stays as it is... right? Because, sometimes you don't talk to the gynaecologist, you don't talk... and... you just let it go...right?* ***(Participant 5)*** *I noticed in these leaks (urine), in sexual relations in which I could not feel my partner ... my partner's penis ... (pause) ..., and in the vaginal area. It's like I... have nothing, doctor (emphatic)... like I'm a huge hole, and... (she thought)... and without any sensation!* **(Participant 6).** *Out of nowhere, I felt a drop of urine dripping ... on my underwear and there was a smell ... I said "it's not possible!" ... because I didn't pee! (emphatic) ... right? ... and sometimes I tried to hold it when I was bursting, then ... and it started to ooze and ... there was no way ... as soon as I realized ... in sexual intercourse, the impression of what happens is that ... can I say? ... that the penis did not fill my vagina! ... (pause) ... you know? ... so ... then it was wide! A wide vagina! (pause).* ***(Participant 3).*** *Yes... (she thought), when you clean yourself, you end up touching yourself, right? ... I feel the difference, and ... (she thought) ... with my underwear ... I feel that it enters the vagina a little, I have to wear daily pads so that it doesn't bother me much! (emphatic). That's it. It's also very bad during sex... that noise! I don't feel my partner, who is my husband in this case... that bothers me a lot.* ***(Participant 2).***
Subtheme 1.2: Emotional reactions experienced when dealing with the complaint	*I got frustrated! ... (pause) ... and the frustration has been coming for a long time! ... Because ... I have a 26-year-old son ... do the math ... more than 25 years with this frustration! ... like ... it's ... for me it's frustrating, because ... my husband, he enjoys it! Sure! (emphatic) ... any man has pleasure! ... but I ... I'm missing something!* ***(Participant 3).*** *It's impotence! (she smiled, embarrassed) ... like, totally sad! ... I am very sad! I am aimless, I am hurt!* ***(Participant 7).*** *At first, it scares (emphatic) ... and you think ... everything will fall out! (laughs) ... I don't know if that's it ... (pause) ... it scares me, but then ... with more information, you know ... like, knowing better ... I am calmer (pause).* ***(Participant 8).***

Subtheme 1.3: Help-seeking process	*I researched a lot on the internet... so the internet helped me a lot! ... it helped a lot ... with information ... and reading about ... more like that.* ***(Participant 9).***
	I looked on the internet... to do some exercises... I also asked gynaecologists for information... and we always came up with exercises. I do it at home... keep contracting and releasing it... so even then this one is not helping me at the moment... I don't know if I am doing it right. ***(Participant 10).***
	I talked to a friend who spoke... about vaginal looseness... because I didn't even know what it was... I imagined... I don't know... that I had to do some plastic surgery... surgery or something. ***(Participant 11).***
	No, because I didn't know what to do (laughs) ... Look ... before starting I thought I should have ... surgery! ... I said ... if I go there and he (surgeon) gives me some stitches, like ... that false virginity thing where you receive a stitch ... I thought that ... I said: "I have to find a doctor to operate on me... to give me some stitches... to close... I don't know! ... Something like that! ... if it's the bladder, he already makes the vagina tight! ***(Participant 3).***
	I came to participate in the research project. I also accompany T (a friend who introduced her to the research and also presents the same complaint). We exchange a lot of information... that's it. ***(Participant 1).***
	But I had no idea of looking for a treatment... I had no idea that there was a treatment for that... it was only after we talked (researcher)... that I got to know other people... who underwent the treatment... until then I thought that... I didn't have this notion of treatment ***(Participant 4).***
	A doctor even told me that this was a prolapsed bladder, she didn't tell me that I was wide! She said: "you can't lift weight because of your bladder"... but the bladder goes down, but not so much! ... I thought she was already here at the door! ... Each one said something, you know? ... One said that I wasn't wide... he treated the hormones and said that I needed surgery... so I was kind of lost! ... I only found myself here (at the university) when I was called to participate in the research ... Because then I knew exactly what I had. Because each one said the same thing! ***(Participant 7).***
	During sex, I realized, oddly enough, after I got to know the program (research project). Because then I started to pay more attention to it... if I was... I saw Vaginal Laxity on the internet, on the Research Program profile and... I said "wow! " It's about vaginal laxity then! And then I started to pay more attention to it and then I came up with this idea. I observed more like this... then I noticed this feeling of looseness during sex. It was just after signing up. ***(Participant 1).***
	I think the treatment that should be better is physio! (emphatic) ... you know, like that... from the bottom of my soul! ... because I'm going to learn to deal with my musculature ... because I like it... it's like we like our body! ... because when we want to take care of our bodies, we go to the gym! ... and that's the same thing! ***(Participant 6).***
	To seek help? ... the concern ... marriage ... concern ... it is to know what is happening to my body ... it is ... these differences that are happening ... the urinary loss ... the lack of pleasure... (pause)... the lack of feeling the (penis)... in sexual intercourse... all of that worries me a lot... I'm married, right... (pause). ***(Participant 12).***
	(...) I thought I was different... sometimes I would talk to a friend and say... wow! I already felt really bad. What was on your mind? ... (she thought) ... that it would be possible to do, in a way .... ah ... seeking professional guidance to see if it could solve it. ***(Participant 2).***

	My expectations are that I will get better... that everything will be perfect... and that from the treatment I will get to know myself much better... and that I will... ah that it will be 100%... wonderful! ***(Participant 9).***
	That I reach my goal... which is... I know I won't look like a young lady, but I know I will... feel a little more like a woman. ***(Participant 10).***
Theme 2. "I think the name itself weighs" meanings associated with vaginal laxity complaints.	
Sub-theme 2.1: Women´s perceptions about VL complaint	*Who wants to be recognized as a vaginal laxity? Imagine if this is diagnosed as a disease! And what is the name of your problem? ... It's vaginal laxity... it doesn't work!* ***(Participant 13).***
	... it's because we don't know how to deal with our own body ... so I think the name is kind of impactful ... even for you to say it to someone ... you feel ashamed ... because there are a lot of people who, if you say the name, will have a kind of apprehension. ***(Participant 6).***
	I always noticed something strange, like... you know? ... something was missing there ***(Participant 13).***
	You don't feel anything! ... a vacuum! ... and that's the impression! ... you feel like a vacuum!... and that's the feeling! ... then you don't want to ... then you don't feel like doing it! ... you want to do it but it's frustrating! ***(Participant 3).***
Sub-theme 2.2: Women´s explains and beliefs about causes of VL	*(...) maybe we don't know how to deal with it... we do everything wrong... we pick up a lot of weight since we were young... because I've already worked in the fields... I already held a big bag of coffee... I peed grabbing the coffee bags with effort ... when I was young ... I remember ... and sometimes I peed with so much effort to grab the bags ... I think that's what it was ... not because there was an oversight... it was because I really didn't know how to do things right... and it ended up damaging.* ***(Participant 16).***
	A wide thing! ... (pause) ... a wide thing that ... can't be filled ... you know ... it's been used! ... and ... it widened ... as if we had ... it's ... like, for example ... stuck something in there for a long time ... and it took that shape ... understand? ***(Participant 3).***
	... maybe, the professional who did it there... you know, after the birth... who makes that little cut... which I think is brutal against women (episiotomy)... but they say that if they don't do it, it can burst and make the case worse! ... but I think so... it's a very profound and very striking thing that they don't think about it! ***(Participant 13).***
	... I had that cut ... you know ... transversely in the vagina ... and it bothers me a lot and ... I have this feeling that it's not tight, you know? ... which is looser ***(Participant 15).***
	During sexual intercourse (emphatic) ... I felt it ... I felt it little by little ... it was right after my third delivery ... that I felt it more ... (pause). ***(Participant 8).***
	Ah... actually... after I had my second daughter, I already started to notice when I had sex... (pause)... that it really was loose... that it was wider, like that. ... ***(Participant 11).***
	I feel ... I think that ... this was caused by it ... or that, it's ... (she thought) ... maybe because I'm a little older, you know ... it starts appearing a lot of things in your head that (pause) ... that you end up getting ... putting you in trouble! ***(Participant 5).***

	It was uncomfortable... but I read some things and I thought it was normal! ... but later I found out that it wasn't (laughed, embarrassed) ... (pause). ***(Participant 8).***
	... until then ... I didn't know it was vaginal laxity ... I thought it was a bladder problem and so on ..., or something like that. ***(Participant 5).***
Theme 3. Symptoms associated with vaginal laxity: their impacts on women's relationships	
Sub-theme 3.1: Self-relationship: "I don't feel like a complete woman"	*So, I was pretty disconnected in that regard, right? I had a normal delivery, but the girl was born prematurely, very small, so I never had that concern... it just became more present later... and... I started to think about it... to observe it.* ***(Participant 1).***
	... my self-esteem is down there in that part ... I don't feel like a complete woman! (emphatic) ... right... I don't feel pleasure, right... it's like I'm hollow inside! (emphatic) ... that's not what I wanted to feel! ... I wish I could feel pleasure! ... I wanted to (emphatic) give pleasure, you know? ... and currently I'm not feeling anything anymore in this relationship between me and him ... I look in the mirror and say "it's not me! (emphatic) ... I feel less of a woman! ***(Participant 10).***
	Then... (she smiled) ... I am a woman... (pause) ... incapable of feeling pleasure... incapable of... (she thought)... of having satisfactory relations or of even sexually pleasing a man. I was thinking about it a lot... (pause)... my concern was this, right... that I was a woman... (pause)... like... (she thought)... a woman who cannot... (pause) ...in theory, manage their function... their life (...). I was feeling like rubbish... not having pleasure... thinking that I didn't have pleasure and I wasn't able to give pleasure to anyone either... (she thought)... right... but I still end up thinking that ... that I have to take care of the other's pleasure, and ... and forget my own. ***(Participant 16).***
	(...) it makes me feel incapable... that I can't, that I can't,... that I have a problem... and actually I didn't know what the problem would be... right, ... I thought it was a problem in my body ... but ... actually I think ... I think, I don't even know if it's more in the head or if it was really because of that. ***(Participant 5).***
	... I can't even look anymore... I can't even look at myself in front of the mirror... because then I cry! ***(Participant 7).***
	... I think I don't look at myself much anymore, you know ... (she became a little sadder) ... my self-esteem is very low ... (tears her eyes) ... (I asked if the vaginal laxity worsens her self-esteem) ... yes! ***(Participant 12).***
	I wasn't accepting myself that way... I wasn't conforming to that! ...I get so frustrated! ... I was already thinking I was ugly... I didn't feel like looking after myself anymore... I got fat because of the injections! ... you know? ... I got ugly! ... I felt horrible! ... very low self-esteem! ***(Participant 7).***
Subtheme 3.2: Effect of VL on sexual intercourse	*You have no desire to do it... and when you try it's horrible! (emphatic) ... because you feel lax, loose! It's the same thing as having nothing inside you!* ***(Participant 7).***
	I don't feel the penis... I don't feel like I have the strength to grab it... even when I try to force it to work the muscles... even when I try hard I can't! ***(Participant 13).***
	If I changed the practice? Yes (laughs), I try to squeeze more (laughs) and contract more (laughs). Benefit for me, no. It's just to make him feel... that it fills in more, right? He feels when I contract. In a way it is positive. ***(Participant 1).***

	Oh, it interferes a lot because I can't! ... I can't get along there in the intercourse! (emphatic) ... I get stuck... scared... try to change position... it's a wide thing! ***(Participant 14).***
	It changed because I didn't have sex for six months! ... I did other things, but in the vagina, I wouldn't let him ... touch me! ***(Participant 7).***
	Anal sex ... yes, I did ... (long pause) ... he wanted it ... not because I wanted it ... I don't know if he was looking for it for the laxity or for the pleasure of his head ... that I I don't know... I never asked. ***(Participant 12).***
	Yes, that's right, anal intercourse... which made me sad because I did it because I loved him so much... not because I wanted to! I did it to satisfy him, not because I felt good about it... I was very uncomfortable because sometimes it didn't work out very well and the pain was intense... you know? ***(Participant 15).***
	In reality (pause) ... the foreplay was the best part, because ... penetration was the worst part for me ... (pause) ... a lot of times I even avoided it ... I accepted the foreplay but the penetration, no! ... Uncomfortable. ***(Participant 2).***
	It shouldn't be as pleasurable as a narrower vagina... for both men and women. ***(Participant 1).***
	... I think they would like to have a woman who would be very tight. ***(Participant 5).***
	Now I don't want to have sex anymore... so I can have someone for me now... so that when I do... I feel like I'm the best in the world! (emphatic) ... as if I had a virgin! ... I want to feel pain so I can have the relationship! (emphatic) ... not the pain of evil ... the pain of good! ***(Participant 14).***
	Changed the frequency, right? It's... (she thought), wow, it's very interesting, isn't it? This week I'm 18 years married and I've never reached orgasm without penetration, (she thought) ... the way I'm reaching now (she smiled). Just playing there, (laughs) ... funny, right? We think we'll never find out, but... because we never had to go through that, right?... So we didn't... and now, when we need to, we discover different things (smiles). This enriches and tightens the bonds (smiles)... I think it's really cool... it's been really fun (laughs). ***(Participant 1).***
Subtheme 3.3: Relationship with the partner	*... man always complains! ... thinks the woman doesn't want to! ... that the woman has a headache ... because of this or that! ... and sometimes we don't talk ... the real thing ... and even if we tell them ... it always has to be the way they want it ... right? ... then ... it changed! (emphatic) ... it changed ... even if I didn't say it, even if I didn't talk ... it changed ... I didn't say it at all ... I kept it to myself ...* ***(Participant 5).***
	You have no pleasure, you are doing something there that is to be done! But it's not because you want to, or because you'd like to be at that moment, right... you love the person and everything, but... it's not what you'd like to be doing at that moment... so it's something that bothers me, yes! ***(Participant 15).***
	... I was already looking at it as an obligation! ... right ... it was embarrassing! ... (pause) ... it was one thing ... and ... just do it! ... because I don't feel anything! (...) Since I don't feel anything, it would last as long as he managed to ejaculate, because ... for me ... it wasn't making any difference! ... if he took too long, I would stay there ... and if he did it quickly ... too ... I couldn't wait to finish it soon! ***(Participant 3).***

	I didn't like that he didn't even come near me! ... I don't know if it's in my head or what it was ... I know it changed everything! I even thought about getting divorced! (...) I didn't want any more contact with my husband... I distanced myself from him... so, it affected a lot my relationship with my husband ... so, I cooled down! ***(Participant 7).***
	From the moment you stop having sexual intercourse with the person, the person starts to think ... she doesn't want me! ... she already has another one! ... right ... he will never understand the clinical problem of the thing! ... he thinks of cheating! ... he thinks of a lack of desire! ... because, as I say that I don't feel anything, then he doesn't understand either ... I say: "but you don't feel it lax?" ... he says: "no, it's normal for me" ... because for him ... he got used to the thing ... and he couldn't understand it ... neither do I! ... imagine him? ***(Participant 16).***
	It's because I think I end up pulling away... I think I'm not enough... that I'm not pleasing... and then he ends up pulling away... and there's no conversation, right... because you don't want to be exposed. Then when I expose myself, he says it's all in my head... that everything is normal for him. Then I think... "is it really true?" Is it okay for him? ... here come the doubts ... comes the questions. ***(Participant 11).***

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Number	Item	Guide questions/description	Page
Domain 1: Research team and reflexivity			
Personal Characteristics			
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group?	4-5
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD*	4-5
3.	Occupation	What was their occupation at the time of the study?	4-5
4.	Gender	Was the researcher male or female?	4-5
5.	Experience and training	What experience or training did the researcher have?	4-5
Relationship with participants			
6.	Relationship established	Was a relationship established prior to study commencement?	4-5
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. *personal goals, reasons for doing the research*	4-5
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. *Bias, assumptions, reasons and interests in the research topic*	4-5
Domain 2: study design			
Theoretical framework			
9.	Methodological orientation and Theory	What methodological orientation was stated to underpin the study? *e.g. grounded theory,*	5-6

		discourse analysis, ethnography, phenomenology, content analysis	
Participant selection			
10.	Sampling	How were participants selected? *e.g. purposive, convenience, consecutive, snowball*	4
11.	Method of approach	How were participants approached? e.g. *face-to-face, telephone, mail, email*	4-5
12.	Sample size	How many participants were in the study?	4
13.	Non-participation	How many people refused to participate or dropped out? Reasons?	4-5
Setting			
14.	Setting of data collection	Where was the data collected? e.g. *home, clinic, workplace*	4
15.	Presence of non-participants	Was anyone else present besides the participants and researchers?	4-5
16.	Description of sample	What are the important characteristics of the sample? *e.g. demographic data, date*	4-5
Data collection			
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	4-5
18.	Repeat interviews	Were repeat interviews carried out? If yes, how many?	N/A
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data?	5
20.	Field notes	Were field notes made during and/or after the interview or focus group?	4-5

21.	Duration	What was the duration of the interviews or focus group?	6
22.	Data saturation	Was data saturation discussed?	5
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction?	5-6
Domain 3: analysis and findings			
Data analysis			
24.	Number of data coders	How many data coders coded the data?	7-11
25.	Description of the coding tree	Did authors provide a description of the coding tree?	7-11
26.	Derivation of themes	Were themes identified in advance or derived from the data?	7-11
27.	Software	What software, if applicable, was used to manage the data?	6
28.	Participant checking	Did participants provide feedback on the findings?	7-11
Reporting			
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. *participant number*	7-11
30.	Data and findings consistent	Was there consistency between the data presented and the findings?	7-11
31.	Clarity of major themes	Were major themes clearly presented in the findings?	7-11
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	12-14

Allison Tong and others, Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups, *International Journal for Quality in Health Care*, Volume 19, Issue 6, December 2007, Pages 349–357, https://doi.org/10.1093/intqhc/mzm042

4.5. Artigo 5. *Associated factors of vaginal laxity and sexual function in a multi-ethnic population: a cross-sectional study*

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ARCH-D-23-01707 - Submission Confirmation

1 mensagem

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Dear Ms Pereira,

Thank you for submitting your manuscript,
"Associated factors of vaginal laxity and sexual function in a multiethnic population: a cross-sectional study", to Archives of Gynecology and Obstetrics

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Archives of Gynecology and Obstetrics

Associated factors of vaginal laxity and sexual function in a multiethnic population: a cross-sectional study

--Manuscript Draft--

Manuscript Number:	
Full Title:	Associated factors of vaginal laxity and sexual function in a multiethnic population: a cross-sectional study
Article Type:	Original Article
Section/Category:	Urogynecology
Keywords:	female sexual dysfunction; pelvic floor disorders; vaginal laxity; vaginal delivery; pelvic organ prolapse.
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Funding Information:	Fundação de Amparo à Pesquisa do Estado de São Paulo (2021/13700-7) — Ms Glaucia Miranda Varella Pereira
Abstract:	Purpose: Female sexual dysfunction (FSD), including vaginal laxity (VL), can lead to a decrease in quality of life and impact partner relationships. Little is known about ethnicity and variation in FSD. We aimed to investigate the associated factors of VL and FSD in a multi-ethnic population. Methods: This cross-sectional study was conducted at Chelsea and Westminster Hospital, from July to December 2022. All women referred to clinical care at the Urogynecology Clinic were included. Participants were assessed according to sociodemographic and clinical aspects, the pelvic organ prolapse quantification system (POP-Q), sexual function, VL, sexual attitudes, sexual distress, sexual quality of life, vaginal symptoms, and pelvic floor disorders. Unadjusted and adjusted associated factors of VL and FSD were analysed. Results: Among participants (n=300) vaginal delivery, multiparity, perineal laceration, menopause and gel hormone were significantly more frequent (all p<0.05) in those reporting VL. No differences were found in ethnicity. Compared to nulliparity, primiparity and multiparity increased by approximately four and twelve times the odds of VL, respectively (unadjusted OR 4.26; 95% CI 2.05 – 8.85 and OR 12.77; 95% CI 6.53 – 24.96). Menopause and perineal laceration increased by four and six times the odds of VL, respectively (unadjusted OR 4.65; 95% CI 2.73 – 7.93 and OR 6.13; 95% CI 3.58 – 10.49). In multivariate analysis, menopause, primiparity, multiparity, and POP

	remained associated with VL. Conclusion: Menopause, primiparity, multiparity and POP were highly associated with VL complaints in multivariate analysis. No differences were found in ethnicity.
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August 6th 2023

To: The Editors-in-Chief
K. O. Kagan
Archives of Gynecology and Obstetrics

Dear Editor

We herewith send you the study "**Associated factors of vaginal laxity and sexual function in a multi-ethnic population: a cross-sectional study**" for analysis in your respectful journal. This is a cross-sectional study conducted at Chelsea and Westminster Hospital, London, from July to December 2022 (reference number WCSLA1069). We expect that the present study will contribute to the understanding of the pathophysiology of vaginal laxity.

All authors have substantial contributions to this study: protocol/project development; data collection or management; data analysis; manuscript writing/editing, and consent to the final version that is presented here. Our study has not been published previously and it is not under consideration for publication elsewhere.

If you have any questions about the manuscript, Dr Cartwright will be serving as the corresponding author. Thank you in advance for your consideration.

Sincerely yours,

Glaucia Miranda Varella Pereira
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Title: Associated factors of vaginal laxity and sexual function in a multiethnic population: a cross-sectional study

What does this study adds to the clinical work: Obstetric factors parity, perineal laceration and types of delivery, and clinical factors age, menopause, POP, vaginal symptoms, and sexual distress were associated with vaginal laxity.

Introduction:

Women all over the world present pelvic floor disorders (PFD), but shame and social taboos still prevent open discussion on the subject[1]. Urinary incontinence (UI), faecal incontinence (FI), pelvic organ prolapse (POP) and sexual dysfunction (SD) are common and affect up to one-third of premenopausal women and 45% of postmenopausal women[2].

Sexual function is an important aspect of women's health. Female sexual dysfunction, in addition to being multifactorial and involving physical, social and psychological dimensions, can lead to a decrease in quality of life and affect the relationship with the partner[3]. In a UK survey, 50% of urogynecologists regularly investigate female sexual dysfunction during clinical visits and 49.5% after surgical procedures. According to the interviewees, the lack of time was the main barrier[4]. Female sexual dysfunction presents a high prevalence, ranging from 38 to 85% and can be influenced by cultural, physical, psychological and social aspects[5,6]. Little is known about ethnic diversities and variations in sexual complaints in peri- and postmenopausal women[7]. In a study with more than three thousand participants, ethnic differences were found in the variables arousal, pain, desire and frequency of sexual intercourse[8].

One of the vaginal symptoms of female sexual dysfunction - VL, has been identified in the terminology for female pelvic floor dysfunction and in the terminology for assessing the sexual health of women with pelvic floor dysfunction[9,10]. VL is defined as excess vaginal flaccidity and its prevalence ranged from 24% to 38%[11,12]. This symptom has been mainly studied with the advent of energy-based treatments and some aesthetical surgical procedures, and a negative impact on the quality of life of women and their relationships with their partners can already be perceived in some published studies[11,12].

Thus, we developed a study that could investigate the associated factors of VL and SD in the Urogynecological clinics that daily receive a multi-ethnic population of women. We also investigate the relationship between vaginal laxity/ sexual dysfunction and other pelvic floor disorders in this population.

Methods:

This cross-sectional study was conducted at Chelsea and Westminster Hospital, from July to December 2022 and followed the Strengthening the Reporting of Observational Studies in Epidemiology – STROBE checklist. The hospital audit department granted approval for the study (reference number WCSLA1069). All women referred to clinical care at the Urogynecology Clinic, during the period of the

study, were included. Pregnant women, women who have undergone pelvic surgery for PFD, women unable to read and understand the English language and the ones that did not provide consent for the purposes of the research were excluded from the study. As part of their clinical visit at the Urogynaecology Clinic and after signing the consent form, the participants underwent a vaginal exam to assess pelvic organ prolapse (POP) through Pelvic Organ Prolapse Quantification (POP-Q) system. Subsequently, the participants filled out questionnaires assessing sexual function, vaginal laxity, sexual attitudes, sexual quality of life, vaginal symptoms, as well as, urinary and anal incontinence, and POP. Sociodemographic and clinical data will be obtained from their medical records and/or before the vaginal examination.

Assessment Instruments

The evaluation of POP followed the recommendation of the International Continence Society (ICS) for the description and staging of genital prolapse using the POP-Q system[13,14]. Six anatomical points were evaluated with the aid of a disposable graduated ruler. Two on the anterior vaginal wall (Aa and Ba). Two on the posterior vaginal wall (Ap and Bp) and two points on the upper vagina (C and D). Genital hiatus, total vaginal length and perineal body were also measured. All points were measured in maximal Valsalva, except the total vaginal length[15]. The ICS clinically defined pelvic organ prolapse as significant at stage II or higher[14,15].

The sexual function of women with pelvic floor disorders was evaluated by the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IUGA-Revised (PISQ-IR)[16]. This instrument consists of 12 items (four domains: condition specific, partner related, global quality, and condition impact)for not sexually active (NSA) women (higher scores indicate a greater impact of the condition on sexual inactivity) and 21 items (six domains: arousal/orgasm, partner related, condition specific, global quality rating, condition impact, and desire) for sexually active (SA) women[16] (higher scores indicate better sexual function)[17].

The presence of complaints of vaginal laxity was assessed through the Vaginal Laxity Questionnaire (VLQ)[18], a self-reported assessment instrument that uses a seven-point scale associated with the questions "How would you rate your current level of vaginal laxity? or laxity during intercourse?". After collecting data using the 7-point scale, we summarized the scale to just 3 points (Loose, Not Loose, Not Tight (NLNT) and Tight) to present the data in our results. The vaginal symptoms of the included participants were also evaluated by the International Consultation on Incontinence Questionnaire Vaginal

Symptoms (ICIQ-VS) is a 14-item questionnaire that assesses the presence and intensity of vaginal symptoms, associated sexual issues, as well as their relationship with women's quality of life[19]. Higher scores indicate a worse scenario.

The Female Sexual Distress Scale-Revised (FSDS-R) was used to assess sexually related distress in our participants. This 13-item scale evaluates distress associated with inadequate or impaired sexual function and hypoactive sexual desire disorder[20]. Higher scores indicate worse distress[20]. The measurement of sexual attitudes in our participants was performed by a 23-item scale with four subscales (Permissiveness towards an open relationship, Responsibility in birth control, Communion (Attitude to towards the importance of melting together with sex partner), and Instrumentality (Attitude towards enjoying the physical sex) - the Brief Sexual Attitudes Scale (BSAS)[21]. A lower score on each subscale (attitude) indicates a greater amount of that respective attitude.

Lastly, the relationship between female sexual dysfunction and quality of life was measured by the Sexual Quality of Life-Female (SQOL-F)[22]. Each of the 18 items is rated on a six-option response (Strongly Agree to Strongly Disagree). Response categories can be scored from one to six, giving a total score of 18 to 108. Higher scores indicate better quality of female sexual life[22].

Outcomes

The primary outcome was the identification of the associated factors of VL and SD in a female multi-ethnic population as measured by the clinical variables, the VLQ, and sexual activity in the PISQ-IR questionnaire. The secondary outcomes included the association between VL and POP with the questionnaires' scores.

Sample size and Data Analysis

The sample size was determined using the previously reported normative data for the SQOL-F. It was estimated that 300 recruited participants provided 90% power to detect a one standard deviation difference in SQOL-F[22]. The analysis of the collected data was preceded by the creation of a computerized database where the variables were coded in a data dictionary and validated. A descriptive analysis of the data was performed to characterize the research participants, in the form of values of absolute frequency and percentage (relative) for categorical variables and values of mean and standard deviation for numerical variables. The chi-square or Fisher's exact tests were used to compare the categorical variables

between the groups and the Mann-Whitney test (2 groups) and the Kruskal-Wallis test (3 or more groups) were used for numerical variables between groups due to the absence of normal distribution of the variables. A linear, simple and multiple regression analysis was used (with a Stepwise criterion for selecting variables) to assess the relationship between the variables and the questionnaire scores, with variables without normal distribution transformed into ranks. For categorical dependent variables, simple and multiple logistic regression analysis was used (with Stepwise criterion for variable selection). Univariate and multivariate models of regression analysis were employed to estimate the associated factors of the VL. Statistical analyses will be performed using the statistical program SAS System for Windows (Statistical Analysis System, version 9.4.SAS Institute Inc, 2002-2012, Cary, NC, USA.), adopting a significance level of 5% ($p<0.05$).

Results:

The sociodemographic and clinical characteristics of the studied population are shown in Table 1. Of the 300 participants investigated, single, nulliparous, and premenopause women were more frequent. The mean age was 41.5 years. Our study identified four major ethnic groups: Asians (British Asians, other Asians; n=29), Whites (British Whites and other Whites; n=224), Blacks (British Blacks, Caribbean or African Blacks, other Blacks; n=30), and Other Ethnic Groups (Arabs, other ethnic groups; n=17). According to Office for National Statistics sources (2021 Census, https://www.ons.gov.uk/), in England, the percentage of major ethnic groups includes Asian (5.4 million), Black (2 .4 million), multiple ethnic groups (1.7 million), Whites (45.8 million) and other ethnic groups (1.2 million). Thirty-one per cent of participants rated their vagina as loose on the VLQ. The vast majority of participants (79.3%) were sexually active. Sixty-three participants presented POP, with stage 1 being the most frequent.

When comparing the perception of VL by the VLQ and sexual activity by the PISQ-IR with the clinical variables (Table 2), we found that the participants with a loose vagina had a significantly higher mean age (47.9 ± 10.8; P=0.008). Vaginal delivery (62.4%), multiparity (59.1%), perineal laceration (60.3%), menopause (52.6%), and gel hormone (16.1%), were significantly more frequent in participants with a loose vagina. Sexual activity is significantly more frequent among younger women (40.2 ± 12.2; P=0.001), nulliparous (51.3%) and no POP (82.8%). No differences were found in ethnicity (P=0.090).

Figure 1 shows the comparison between the perception of VL and the types of delivery (A) and parity (B). Women with a loose vagina have a higher frequency of vaginal delivery/both and multiparity than women with an NLNT or tight vagina.

Radar Charts in Figure 2 reveal the scoring of PISQ-IR for sexually active and non-sexually active women and BSAS questionnaires across different domains by VLQ and POP classification. Women sexually active with loose vaginas presented worse sexual function in all domains of PISQ-IR. Similarly, sexually active women with POP also presented worse sexual function in domains of PISQ-IR. Women non-sexually active with loose and NLNT vaginas and No/Yes POP were highly impacted by the Global Quality domain of PISQ-IR. Finally, birth control and communion were the sexual attitudes with the greater amount between VLQ and POP classification.

Table 3 compares the questionnaire scores with the perception of VL and POP. Participants with a loose vagina who were not sexually active and with POP had a significantly higher impact on sexual function in relation to the Condition Impact when compared to participants without a loose vagina and without POP (2.5 ± 1.0, $P=0.001$; 2.3 ± 0.9, $P=0.038$). Interestingly, sexually active participants with NLNT vagina had a better sexual function in the Partner Related (3.6 ± 0.5; $P<0.001$), Condition Specific (4.6 ± 0.6; $P=0.002$), Global Quality (3.7 ± 1.0; $P<0.001$), and Condition Impact (3.7 ± 0.5; $P<0.001$), domains. Better sexual function in Desire was found in women with tight vaginas (3.4 ± 0.7; $P=0.003$). Participants with a loose vagina and those with genital prolapse scored significantly worse across all domains on the ICIQ-VS, on SQoL-Female, and on FSDS-R scores. Participants with a loose vagina presented a significantly greater amount of the Communion (attitude towards the importance of merging with the sexual partner) attitude and the ones with no genital prolapse and a tight vagina had a greater amount of Permissiveness (permissiveness towards an open relationship).

Table 4 shows the analyses of clinical and obstetric factors in women with VL. Univariate analysis showed that age increased one time and primiparity and multiparity increased four times and approximately 12 times the chance of VL with OR 1.07; 95% CI 1.04-1.09; OR 4.26; 95% CI 2.05 – 8.85 and OR 12.77; 95% CI 6.53 – 24.96, respectively, remaining only primiparity and multiparity in the multivariate analysis. Menopause and perineal laceration increased approximately four-fold and six-fold the chance of VL with OR 4.65; 95% CI 2.73 – 7.93 and OR 6.13; 95% CI 3.58 – 10.49, respectively, remaining only menopause in the multivariate analysis. The odds of VL were increased in all types of birth (OR 9.06; 95% CI 4.78 – 17.19 vaginal delivery, OR 2.84; 95% CI 1.04 – 7.77 C-section, and OR 19.50; 95% CI 6.08 – 62.54 in

both). The POP-Q staging 1, 2 and 3 increased, approximately, threefold (OR 3.21), two-fold (OR 2.79), and 13-fold (OR 13.63) the chance of VL in the multivariate analysis, respectively. All subscales of ICIQ-VS, sexual distress (FSDS-R) and BSAS (Permissiveness) were associated with VL in univariate analysis. Interestingly, sexual quality of life (SQoL-F) and BSAS (Communion) appeared as protector factors for VL. The other clinical and obstetrical factors were not statistically significant when associated with VL in multivariate analysis. When stratifying the sexually active women with VL (n=69; Table S1), only multiparity, menopause and POP stage 2 remained as associated factors of VL in the multivariate analysis.

Discussion:

Main findings

This study showed that older age, vaginal delivery, multiparity, perineal laceration, and menopause were frequent in participants with VL. Sexually active women with VL and POP had worse scores on the PISQ-IR, ICIQ-VS, SQoL-F and FSDS-R. Age, menopause, POP staging, vaginal symptoms (ICIQ-VS), sexual distress (FSDS-R) and sexual attitude (Permissiveness) were clinical factors associated with VL. Obstetric factors associated with VL were parity, perineal laceration, and types of delivery (vaginal delivery, C-section, and both). Interestingly, no differences were found in ethnicity in any analysis.

Interpretation

Female sexual dysfunction has a multifactorial aetiology and encompasses four main domains: hypoactive sexual desire disorder, arousal disorder, orgasmic disorder, and sexual pain disorder[23]. Many women report complaints across a variety of symptoms. One of these symptoms, VL, still underreported, has a prevalence of 24% to 38%[11,12]. In our population, in line with previous studies[11,12], about 31% of the investigated women had symptoms of VL. Sexual function, vaginal symptoms, quality of sexual life and sexual distress were significantly worse in our VL participants. This highlights the need to assess sexual function in patients who visit urogynecology clinics.

Studies have shown associations between the hiatal area, the genital hiatus and the perineal body during the Valsalva manoeuvre, suggesting that VL appears to be a manifestation of hyperdistensibility of the levator ani[11,24]. In our findings, 45.2% of participants with VL had a POP. In addition, POP staging was an associated factor of VL in the multivariate analysis. Similar to our results, women with VL may be

representative of the early stage of POP[11,24]. Most studies investigating VL exclude participants with prolapse symptoms greater than grade II. Prolapse symptoms seem to negatively impact female sexual function[25,26]. In contrast with our findings, VL was not correlated with POP in one study[26].

Pregnancy and childbirth seem to play a role in VL. Even though there is no proven relationship between VL and childbirth, trauma to the pelvic floor and vagina during vaginal delivery can lead to enlargement of the vaginal introitus, resulting in changes in sexual sensitivity during intercourse[27,28]. Furthermore, the complaint of VL can be reported in the first delivery and worsen in subsequent deliveries[18]. In line with these findings, both parities, perineal lacerations and types of delivery were associated factors of VL in our participants. In the present study, not only was vaginal delivery an associated factor of VL, but also C-section delivery. Participants who submitted to both types of delivery had an even greater chance of developing VL. Studies investigating the effect of C-section on the pelvic floor have reported somewhat contradictory evidence. A systematic review showed that C-section was associated with a reduced risk for pelvic floor disorders[29]; however, another study revealed that even changes in the genital hiatus could occur, regardless of the type of delivery[30]. The protective effect of C-section on the pelvic floor remains under debate.

Age was significantly higher in participants with VL in our study. In addition to age, menopause was also an associated factor of VL. Age and hormonal changes generate deterioration and relaxation of the connective tissue and collagen fibres, reducing the support of pelvic organs due to the decrease in the diameter and number of periurethral and pelvic floor striated muscle fibres[31]. These changes seem to contribute to the symptoms of VL.

Strengths and Limitations

The strengths of the present study can be related to the assessment of VL and female sexual dysfunctions in four different ethnic groups. Although we did not find statistically significant differences between groups of women, we emphasize the importance of evaluating the role of ethnic diversity and its variations in sexual complaints in future studies. Another important factor was the investigation of associated factors for VL. These findings will contribute to understanding the pathophysiology of VL. Comprehensive analysis of female sexual aspects using validated instruments and POP staging added value to our study.

The limitations of our study include the study design that makes it impossible to carry out causal inference, the inclusion of a heterogeneous age group of women and the use of a questionnaire that has not yet been validated - the VLQ.

Conclusion:

Sexual function, vaginal symptoms, sexual quality of life and sexual distress were significantly affected in participants with VL. Obstetric factors for VL encompass parity, perineal laceration, and types of delivery, and the clinical factors were age, menopause, POP, vaginal symptoms, sexual distress, and sexual attitude (Permissiveness). No differences were found in ethnicity.

Statements & Declarations:

Conflict of interests: none

Funding: First author: Scholarship Grant 2021/13700-7, São Paulo Research Foundation (FAPESP). The remaining authors reported no disclosures.

Author Contribution:

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LGO Brito: Protocol/project development, Data analysis, Manuscript writing/editing

N Ledger: Data collection or management, Data analysis

CRT Juliato: Protocol/project development, Manuscript writing/editing

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Figure Legend:

Figure 1: Comparison between VLQ and Type Birth (A) and Parity (B) (n=300)

Figure 2: Radar Charts showing scoring of PISQ-IR and BSAS questionnaires across different domains by VLQ and POP classification (n=300).

Table Legend:

Table 1: Sociodemographic and Clinical Characteristics of the Studied Population n=300

Table 2: Comparison between Clinical Variables and Vaginal Laxity and Sexual Activity (n=300)

Table 3: Comparison between Questionnaire Scores, Vaginal Laxity Questionnaire and Pelvic Organ Prolapse (n=300)

Table 4: Univariate and Multivariate Analysis of Women with Vaginal Laxity (n=93)

Table S1. Univariate and Multivariate Analysis of Sexually Active Women with Vaginal Laxity (n=69)

black/white figure

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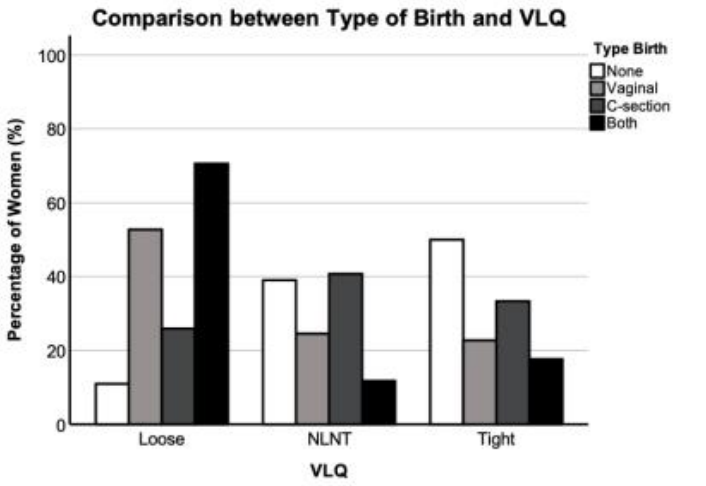

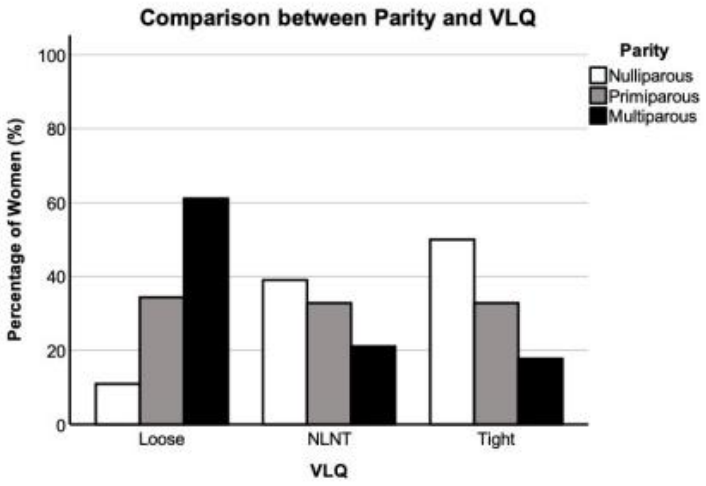

Figure 1: Comparison between VLQ and Type Birth (A) and Parity (B) (n=300)

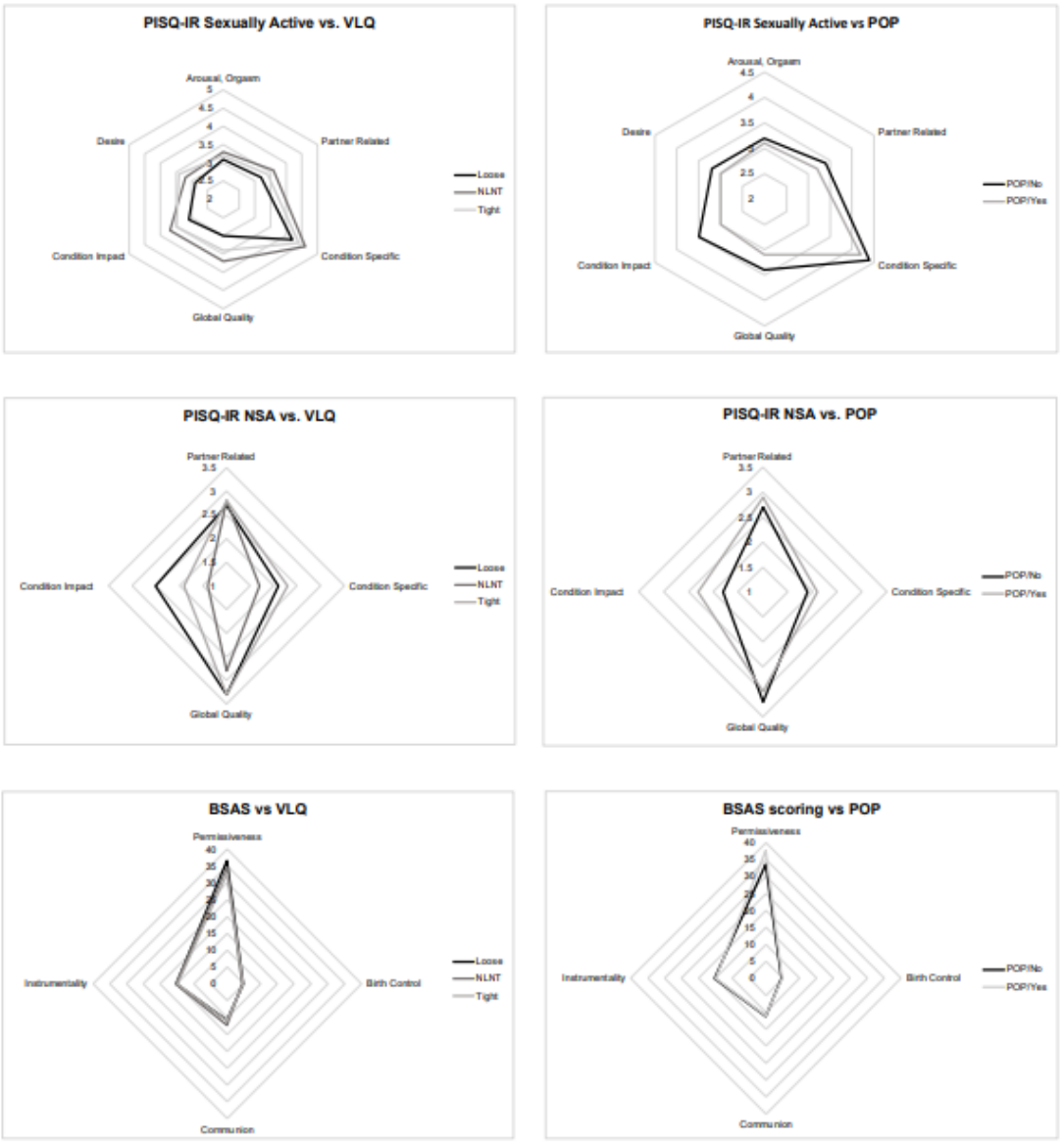

Figure 2: Radar Charts showing scoring of PISQ-IR and BSAS questionnaires across different domains by VLQ and POP classification (n=300).
*POP/No= Stage 0
**POP/Yes= Stages 1,2,3

Table 1. Sociodemographic and Clinical Characteristics of the Studied Population n=300	
Age (Years) [a]	41.5 ± 12.5
Marital Status [b]	
Single	145 (48.3)
Married	129 (43.0)
Divorced	23 (7.7)
Widowed	3 (1.0)
Ethnicity [b]	
White Background	224 (74.6)
Asian Background	29 (9.7)
Black Background	30 (10.0)
Other Background	17 (5.7)
Scholarity [b]	
< 8 Years	9 (3.0)
> 9 Years	291 (97.0)
Body Mass Index [b]	
< 25 Kg/m^2	186 (62.0)
≥ 25 Kg/m^2	114 (38.0)
Type of Birth [b]	
None	146 (48.7)
Vaginal	110 (36.7)
C-Section	27 (9.0)
Both	17 (5.7)
Parity [b]	
Nulliparous	146 (48.7)
Primiparous	64 (21.3)

Multiparous	90 (30.0)
Instrumental Delivery [b]	
Forceps delivery	25 (8.3)
Forceps/Vacuum Extractor Delivery	2 (0.7)
Vacuum Extractor Delivery	5 (1.7)
Perineal Laceration [b]	97 (32.3)
Menopause Status [b]	
Premenopausal	211 (70.3)
Menopausal	89 (29.7)
Hormone Use [b]	
Tablets	36 (12.0)
Patch	19 (6.3)
Gel	33 (11.0)
Implant	38 (12.7)
Antidepressant Use [b]	20 (6.7)
Vaginal Laxity Questionnaire [b]	
Loose	93 (31.0)
Neither Loose nor Tight	97 (32.3)
Tight	110 (36.7)
Pelvic Organ Prolapse [b]	
POP-Q Staging 0	237 (79.0)
POP-Q Staging 1	30 (10.0)
POP-Q Staging 2	28 (9.3)
POP-Q Staging 3	5 (1.7)
PISQ-IR [b]	
Not Sexually Active	62 (20.7)

Sexually Active	238 (79.3)

[a] Mean ± Standard Deviation ; [b] n (%);; PISQ-IR: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire, IUGA-Revised
POP-Q: Pelvic Organ Prolapse Quantification

Table 2. Comparison between Clinical Variables and Vaginal Laxity and Sexual Activity (n=300)

Variable	Loose	NLNT	Tight	P-Value	NSA	SA	P-Value
Age [a]	47.9 ± 10.8	40.0 ± 12.3	37.3 ± 11.9	**P=0.008**	46.2 ± 12.5	40.2 ± 12.2	**P=0.001**
Ethnicity [b]				P=0.597			P=0.090
White Background	75 (25.0)	70 (23.4)	79 (26.5)		39 (13.0)	185 (61.6)	
Asian Background	8 (2.6)	12 (4.0)	9 (3.0)		10 (3.3)	19 (6.3)	
Black Background	6 (2.0)	10 (3.3)	14 (4.6)		9 (3.0)	21 (7.0)	
Other Background	4 (1.3)	5 (1.7)	8 (2.6)		4 (1.3)	13 (4.3)	
Parity [b]				**P<0.001**			**P=0.009**
Nulliparous	16 (5.3)	57 (19.0)	73 (24.5)		24 (8.0)	122 (40.6)	
Primiparous	22 (7.3)	21 (7.0)	21 (7.0)		22 (7.3)	42 (14.0)	
Multiparous	55 (18.3)	19 (6.3)	16 (5.3)		16 (5.3)	74 (24.6)	
Type of Birth [b]				**P<0.001**			P=0.269
None	16 (5.3)	57 (19.0)	73 (24.5)		24 (8.0)	122 (40.6)	
Vaginal Delivery	58 (19.3)	27 (9.0)	25 (8.3)		29 (9.7)	81 (27.0)	
C-section	7 (2.3)	11 (3.6)	9 (3.0)		5 (1.7)	22 (7.3)	
Both	12 (4.0)	2 (0.7)	3 (1.0)		4 (1.3)	13 (4.3)	
Instrumental Delivery [b]				**P<0.001**			P=0.062
No	71 (23.6)	92 (30.6)	105 (35.0)		51 (17)	217 (72.3)	
Yes	22 (7.3)	5 (1.7)	5 (1.7)		11 (3.6)	21 (7.0)	

Perineal Laceration [b]				**P<0.001**			P=0.365
No	37 (12.3)	77 (25.6)	89 (29.7)		39 (13.0)	164 (54.6)	
Yes	56 (18.6)	20 (6.7)	21 (7.0)		23 (7.7)	74 (24.6)	
Menopausal Status [b]				**P<0.001**			P=0.087
Premenopausal	44 (14.6)	75 (25.0)	92 (83.6)		38 (61.2)	173 (57.6)	
Menopausal	49 (16.3)	22 (22.7)	18 (16.4)		24 (38.8)	65 (21.6)	
Antidepressant Medication Use [b]	8 (2.6)	4 (1.3)	8 (2.6)	P=0.442	6 (2.0)	14 (4.6)	P=0.266
Hormone Use [b]							
Tablets	11 (3.6)	13 (4.3)	12 (4.0)	P=0.858	6 (2.0)	30 (10.0)	P=0.663
Patch	8 (2.6)	3 (1.0)	8 (2.6)	P=0.261	5 (1.7)	14 (4.6)	P=0.559
Gel	15 (5.0)	12 (4.0)	6 (2.0)	**P=0.046**	9 (3.0)	24 (8.0)	P=0.361
Implant	12 (4.0)	12 (4.0)	14 (4.6)	P=0.994	6 (2.0)	32 (10.6)	P=0.524
Pelvic Organ Prolapse [b]				**P<0.001**			**P=0.007**
Stage 0	51 (17.0)	84 (28.0)	102 (34)		40 (13.3)	197 (65.8)	
Stage 1	20 (6.7)	6 (2.0)	4 (1.3)		9 (3.0)	21 (7.0)	
Stage 2	18 (6.0)	6 (2.0)	4 (1.3)		12 (4.0)	16 (5.3)	
Stage 3	4 (1.3)	1 (0.3)	0 (0.0)		1 (0.3)	4 (1.3)	

[a] Mean ± Standard Deviation ; [b] n (%); Chi-square test; Fisher's exact test; ; NLNT: Neither Loose nor Tight; NSA: Not sexually active; SA: Sexually active

Table 3. Comparison between Questionnaire Scores, Vaginal Laxity Questionnaire and Pelvic Organ Prolapse (n=300)

Variable	Loose	NLNT	Tight	P-Value	POP/No*	POP/Yes**	P-Value
PISQ-IR [a]				P=0.069			**P=0.002**
Not Sexually Active	24 (8.0)	23 (7.7)	15 (5.0)		40 (13.3)	22 (7.3)	
Sexually Active	69 (23.0)	74 (24.6)	95 (31.7)		197 (65.8)	41 (13.6)	
PISQ-IR NSA [b]							
Partner Related	2.7 ± 0.7	2.8 ± 0.5	2.8 ± 1.0	P=0.696	2.7 ± 0.7	2.9 ± 0.8	P=0.184
Condition Specific	2.1 ± 0.8	1.7 ± 0.8	2.3 ± 1.0	P=0.108	1.9 ± 0.9	2.1 ± 0.8	P=0.322
Global Quality	3.3 ± 0.9	2.8 ± 1.0	3.3 ± 1.0	P=0.191	3.2 ± 1.0	3.0 ± 0.8	P=0.473
Condition Impact	2.5 ± 1.0	1.4 ± 0.7	1.9 ± 0.9	**P=0.001**	1.8 ± 1.0	2.3 ± 0.9	**P=0.038**
PISQ-IR SA [b]							
Arousal, Orgasm	3.1 ± 0.6	3.3 ± 0.6	3.2 ± 0.6	P=0.087	3.2 ± 0.6	3.1 ± 0.7	P=0.239
Partner Related	3.2 ± 0.6	3.6 ± 0.5	3.4 ± 0.6	**P<0.001**	3.4 ± 0.6	3.2 ± 0.6	**P=0.011**
Condition Specific	4.2 ± 0.8	4.6 ± 0.6	4.4 ± 0.8	**P=0.002**	4.4 ± 0.7	4.2 ± 0.9	**P=0.042**
Global Quality	3.0 ± 1.1	3.7 ± 1.0	3.4 ± 1.1	**P<0.001**	3.4 ± 1.1	3.1 ± 0.9	P=0.056
Condition Impact	3.1 ± 0.8	3.7 ± 0.5	3.5 ± 0.8	**P<0.001**	3.5 ± 0.7	3.0 ± 0.8	**P<0.001**
Desire	2.9 ± 0.7	3.2 ± 0.6	3.4 ± 0.7	**P=0.003**	3.2 ± 0.7	3.0 ± 0.7	P=0.110
ICIQ-VS [b]							
Vaginal Symptoms	17.0 ± 10.7	6.8 ± 7.5	9.9 ± 8.2	**P<0.001**	9.1 ± 8.1	18.4 ± 11.7	**P<0.001**
Sexual Matters	23.1 ± 18.8	10.3 ± 15.4	19.8 ± 19.6	**P<0.001**	16.7 ± 19.2	21.8 ± 17.0	**P=0.008**

Quality of Life	4.9 ± 3.3	1.8 ± 2.7	3.2 ± 3.3	**P<0.001**	2.8 ± 3.2	5.2 ± 3.2	**P<0.001**
SQoL-F [b]	54.8 ± 25.3	72.5 ± 25.9	65.0 ± 27.7	**P<0.001**	66.7 ± 27.5	55.1 ± 224.6	**P=0.001**
FSDS-R [b]	19.5 ± 12.8	10.4 ± 12.5	16.4 ± 14.4	**P<0.001**	14.5 ± 13.7	19.0 ± 13.4	**P=0.014**
BSAS [b]							
Permissiveness	36.6 ± 8.3	34.6 ± 8.9	32.8 ± 8.5	**P=0.007**	33.7 ± 8.8	37.7 ± 7.6	**P=0.002**
Birth Control	4.8 ± 2.5	4.5 ± 2.0	4.7 ± 2.1	P=0.840	4.6 ± 2.2	4.8 ± 2.2	P=0.649
Communion	10.7 ± 3.2	12.2 ± 3.4	11.0 ± 3.9	**P=0.004**	11.3 ± 3.6	11.1 ± 3.4	P=0.755
Instrumentality	15.1 ± 4.4	15.3 ± 3.7	14.9 ± 3.7	P=0.802	15.2 ± 3.9	14.9 ± 3.8	P=0.550

[a] n (%); [b] Mean ± Standard Deviation; *= POP Stage 0; **= POP Stages 1,2,3; NLNT: Neither Loose nor Tight; POP: Pelvic Organ Prolapse; PISQ-IR: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire, IUGA-Revised; SA: Sexually Active; NSA: Not Sexually Active; ICIQ-VS: International Consultation on Incontinence Questionnaire Vaginal Symptoms; SQoL-F: Sexual Quality of Life Questionnaire – Female; FSDS-R: Female Sexual Distress Scale Revised; BSAS: Brief Sexual Attitudes Scale; Kruskal-Wallis Test; Mann-Whitney test.

Table 4. Univariate and Multivariate Analysis of Women with Vaginal Laxity (n=93)

Variables		Unadjusted OR (95% CI)	P-Value	Adjusted OR (95% CI)	P-Value
Age (Years)	47.9 ± 10.8	1.07 (1.04 – 1.09)	**<0.001**		
Ethnicity					
White Background	75 (80.6)	Ref.			
Asian Background	8 (8.6)	0.76 (0.32 – 1.79)	0.526		
Black Background	6 (6.4)	0.50 (0.20 – 1.27)	0.143		
Other Background	4 (4.3)	0.61 (0.19 – 1.94)	0.403		
Scholarity	93 (100)	3.70 (0.46- 30.01)	0.221		
Body Mass Index	93 (100)	1.05 (0.63 – 1.73)	0.865		
Parity					
Nulliparous	16 (17.2)	Ref.		Ref.	
Primiparous	22 (23.6)	4.26 (2.05 – 8.85)	**<0.001**	2.62 (1.16 – 5.91)	**0.020**
Multiparous	55 (59.1)	12.77 (6.53 – 24.96)	**<0.001**	7.14 (3.41 – 14.96)	**<0.001**
Menopause	49 (52.6)	4.65 (2.73 – 7.93)	**<0.001**	2.23 (1.19– 3.19)	**0.012**
Perineal Laceration	56 (60.2)	6.13 (3.58 – 10.49)	**<0.001**		
Type of Birth					
None	16 (17.2)	Ref.			
Vaginal Delivery	58 (62.3)	9.06 (4.78 – 17.19)	**<0.001**		
C-section	7 (7.5)	2.84 (1.04 – 7.77)	**0.042**		
Both	12 (12.9)	19.50 (6.08 – 62.54)	**<0.001**		
POP-Q					

POP-Q Staging 0	51 (54.8)	Ref.		Ref.	
POP-Q Staging 1	20 (21.5)	7.29 (3.21 – 16.56)	**<0.001**	3.21 (1.31 – 7.86)	**0.010**
POP-Q Staging 2	18 (19.3)	6.57 (2.86 – 15.10)	**<0.001**	2.79 (1.10 – 7.06)	**0.031**
POP-Q Staging 3	4 (4.3)	14.59 (1.56 – 133.40)	**0.018**	13.63 (1.09 – 170.58)	**0.043**
ICIQ-VS					
Vaginal Symptoms	17.0 ± 10.7	1.10 (1.07 – 1.13)	**<0.001**		
Sexual Matters	23.1 ± 18.8	1.02 (1.01 – 1.04)	**0.001**		
Quality of Life	4.9 ± 3.3	1.24 (1.15 – 1.34)	**<0.001**		
SQoL – Female	54.8 ± 25.3	0.98 (0.97 – 0.99)	**<0.001**		
FSDS-R	19.5 ± 12.8	1.03 (1.01 – 1.05)	**0.001**		
BSAS					
Permissiveness	36.6 ± 8.3	1.04 (1.01– 1.07)	**0.006**		
Birth Control	4.8 ± 2.5	1.05 (0.94 – 1.17)	0.427		
Communion	10.7 ± 3.2	0.93 (0.86 – 0.99)	**0.047**		
Instrumentality	15.1 ± 4.4	1.00 (0.94 – 1.07)	0.961		

Logistic Regression; OR: Odds Ratio; CI: Confidential Interval; n(%); mean ± standard deviation; POP: Pelvic Organ Prolapse; POP-Q: Pelvic Organ Prolapse Quantification; ICIQ-VS: International Consultation on Incontinence Questionnaire Vaginal Symptoms; SQoL-F: Sexual Quality of Life Questionnaire – Female; FSDS-R: Female Sexual Distress Scale Revised; BSAS: Brief Sexual Attitudes Scale; Adjusted for age, parity, menopause, staging of POP and perineal laceration;

Author Contribution

Author Contribution:

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LGO Brito: Protocol/project development, Data analysis, Manuscript writing/editing

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Conflict of interest statement

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Conflict of interest: The authors declare no conflicts of interest.

Supplementary Material

Table S1. Univariate and Multivariate Analysis of Sexually Active Women with Vaginal Laxity (n=69)

Variables		Unadjusted OR (95% CI)	P-Value	Adjusted OR (95% CI)	P=Value
Age (Years)	46.7±10.8	1.07 (1.04 – 1.10)	**<0.001**		
Ethnicity					
White Background	56 (81.3)	Ref.			
Asian Background	4 (5.7)	0.61 (0.20 – 1.93)	0.405		
Black Background	5 (7.2)	0.72 (0.25 – 2.06)	0.540		
Other Background	4 (5.7)	1.02 (0.30 – 3.46)	0.970		
Scholarity	69 (100)	2.94 (0.36-24.34)	0.318		
Body Mass Index		1.27 (0.72 – 2.26)	0.410		
Parity					
Nulliparous	13 (18.8)	Ref.		Ref.	
Primiparous	12 (17.4)	3.35 (1.39 – 8.11)	**0.007**		
Multiparous	44 (63.8)	12.30 (5.87 – 25.75)	**<0.001**	6.62 (2.87 – 15.24)	**<0.001**
Menopause	37 (53.6)	5.82 (3.12 – 10.86)	**<0.001**	2.93 (1.39– 6.19)	**0.005**
Perineal Laceration	41 (59.4)	6.04 (3.27 – 11.14)	**<0.001**		
Type of Birth					
None	13 (18.8)	Ref.			
Vaginal Delivery	42 (60.9)	9.03 (4.39 – 18.58)	**<0.001**		
C-section	6 (8.7)	3.14 (1.05 – 9.45)	**0.041**		
Both	8 (11.5)	13.415 (3.82 – 47.14)	**<0.001**		
POP-Q					

POP-Q Staging 0	40 (57.9)	Ref.		Ref.	
POP-Q Staging 1	13 (18.8)	6.38 (2.48 – 16.44)	**<0.001**		
POP-Q Staging 2	13 (18.8)	17.01 (4.62 – 62.56)	**<0.001**	8.94 (2.11 – 37.90)	**0.003**
POP-Q Staging 3	3 (4.5)	11.78 (1.19 – 116.24)	**0.035**		
ICIQ-VS					
Vaginal Symptoms	17.2±10.8	1.11 (1.07– 1.15)	**<0.001**		
Sexual Matters	22.2±18.2	1.02 (1.00 – 1.03)	**0.020**		
Quality of Life	4.6±3.2	1.21 (1.11 – 1.33)	**<0.001**		
SQoL-F	58.5±24.3	0.98 (0.97 – 0.99)	**0.001**		
FSDS-R	19.5±12.5	1.04 (1.01 – 1.06)	**0.001**		
BSAS					
Permissiveness	36.9±8.5	1.05 (1.01 – 1.09)	**0.007**		
Birth Control	4.9±2.6	1.06 (0.94 – 1.20)	0.343		
Communion	10.1±2.9	0.90 (0.83 – 0.99)	**0.021**		
Instrumentality	14.9±4.4	0.98 (0.91 – 1.05)	0.268		

Logistic Regression; OR: Odds Ratio; CI: Confidential Interval; n(%); mean ± standard deviation; POP: Pelvic Organ Prolapse; POP-Q: Pelvic Organ Prolapse Quantification; ICIQ-VS: International Consultation on Incontinence Questionnaire Vaginal Symptoms; SQoL-F: Sexual Quality of Life Questionnaire – Female; FSDS-R: Female Sexual Distress Scale Revised; BSAS: Brief Sexual Attitudes Scale; Adjusted for age, parity, menopause, staging of POP and perineal laceration;

4.6. Artigo 6. *Pelvic Floor Muscle Training Versus Radiofrequency for Women with Vaginal Laxity: Randomized Clinical Trial*

Obstetrics & Gynecology

Pelvic Floor Muscle Training Versus Radiofrequency for Women with Vaginal Laxity: Randomized Clinical Trial

--Manuscript Draft--

Manuscript Number:	
Full Title:	Pelvic Floor Muscle Training Versus Radiofrequency for Women with Vaginal Laxity: Randomized Clinical Trial
Article Type:	Original Research
Manuscript Classifications:	Gynecology, general; Surgery, general and specialties; Surgical specialties, plastic and reconstructive surgery; Surgical specialties, urology; Vaginal surgery
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Manuscript Region of Origin:	BRAZIL
Additional Information:	
Question	**Response**

Cover letter

August 12th 2023

The Editors-in-Chief
Jason D. Wright, MD
Obstetrics & Gynecology

Dear Dr. Wright

We herewith send you the manuscript **"Pelvic Floor Muscle Training Versus Radiofrequency for Women with Vaginal Laxity: Randomized Clinical Trial"** for analysis in your respectful journal.
We declare that none of the authors presents a conflict of interest. This study was IRB-approved, registered (Registro Brasileiro de Ensaios Clínicos–REBEC—RBR-2zdvfp, https://ensaiosclinicos.gov.br/rg/RBR-2zdvfp), and followed the CONSORT guidelines for RCTs. Moreover, this manuscript was not sent to any other journal for analysis. All data are deidentified and a spreadsheet containing the variables will be shared in a data repository website soon or it can be shared if requested.
All authors have substantial contributions to this study: substantial contributions to conception and design, writing and revising the article and consent to the final version that is presented here.
This study was approved for oral presentation at the meeting of the Society of Gynecological Surgeons (SGS) in Tucson, Arizona, 19-22 March 2023. After several suggestions from the panel, we have reanalyzed data, added the non-inferiority analysis and we are presenting its final format. Dr. Kate Meriwheter and Vivian Sung have suggested us to submit this paper to the journal.
If you have any questions about the manuscript, I will be serving as the corresponding author. Thank you in advance for your consideration.

Sincerely yours,

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Title Page

Pelvic Floor Muscle Training Versus Radiofrequency for Women with Vaginal Laxity: Randomized Clinical Trial

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Conflict of interests: The authors declare no conflict of interests.

Funding Source: This study received two grants from Sao Paulo Research Agency (FAPESP) numbers 19/26723-5 and 21/13700-7.

Short title: RF versus PFMT for women with vaginal laxity

Acknowledgments: We thank Sao Paulo Research Agency (FAPESP).

Clinical Trial Registration: Registro Brasileiro de Ensaios Clínicos–REBEC—RBR-2zdvfp as a clinical trial.

Manuscript word count: 3030

Abstract word count: 452

Manuscript

Pelvic Floor Muscle Training Versus Radiofrequency for Women with Vaginal Laxity: Randomized Clinical Trial

Keywords: randomized controlled trial; pelvic floor muscle training; radiofrequency; vaginal laxity

Short title: RF versus PFMT for women with vaginal laxity

Conflict of interests: The authors declare no conflict of interests.

Précis: Both radiofrequency and pelvic floor muscle treatment improved sexual, vaginal, and urinary symptoms 30 days and six months follow-ups of women with vaginal laxity.

Abstract

Objective: To compare the effect of radiofrequency (RF) and pelvic floor muscle training (PFMT) on the treatment of women with VL.

Methods: A prospective, parallel, non-inferiority, randomized clinical trial, including women aged ≥ 18 years, with a complaint of VL assessed by direct question (yes/no) and classified by questionnaire (Vaginal Laxity Questionnaire), from February 2020 to December 2021 in a tertiary hospital. Two groups (RF – Wavetronic 6000 Megapulse Fraxx and PFMT) were evaluated at baseline, 30 days, and six months follow-up (RF: 3 sessions 4 weeks apart; PFMT: 12 individual sessions for 12 weeks). The primary endpoint was the change of FSFI score after treatment. Secondary outcomes were improvement in symptoms of VL through the Global Response Assessment (GRA) and changes in questionnaire scores of sexual distress, vaginal symptoms, and urinary incontinence, in the modified Oxford Scale, and in the quantification of pelvic organ prolapse (POP-Q). A total of 42 participants per arm was sufficient to demonstrate a difference in sexual function on the FSFI at 90% power, one-sided type 1 error of 0.025 with a non-inferiority margin of 4 on the FSFI total score. Analysis was intention-to-treat and per protocol based.

Results: After recruiting 167 participants, 87 were included (RF n=42; PFMT n=45), with homogeneous clinical and sociodemographic characteristics. The type of sexual intercourse (p=0.486), duration of VL (p=0.941), perception of VL (p=0.681), and type of VL complaint (p=1.000) did not differ between groups and between follow-up periods. All questionnaires showed improvement ($p<0.05$) in their total scores and scales for both groups and follow-ups. After 30 days of treatment, RF was non-inferior to PFMT to improving FSFI total score (mean difference -0.08[-2.58 to 2.42] for RF and -1.95[-4.21 to 0.30] for PFMT) in PP (mean difference -0.46[-2.92 to 1.99] for RF

and -1.82[-4.10 to 0.45] for PFMT) and in the ITT analysis; however, this result was not maintained after six months of treatmentThe GRA was not statistically different between the groups and follow-ups in the PP analysis. On physical examination, POP-Q showed significant improvement in points Aa, Ba at 30 days follow-up and Aa, Ba, and Ap ($p<0.001$) at six months follow-up in the PFMT group and in points C ($p=0.004$) and D ($p=0.043$) at 30 days follow-up and at point C ($p=0.028$) at six months follow-up in the RF group. PFM strength significantly improved in the RF ($p=0.006$, 30 days; $p=0.049$, six months) and PFMT ($p<0.001$, both follow-ups) groups, with a significant gain in the PFMT group.

Conclusion: Both RF and PFMT improved sexual, vaginal, and urinary symptoms 30 days and six months follow-ups. After 30 days of treatment, RF was non-inferior to PFMT to improving FSFI total score; however, this result was not maintained after six months of treatment.

Introduction

Vaginal laxity (VL) is defined as a complaint of excessive vaginal looseness[1]. Its prevalence varies from 24% to 38% between studies[2,3]. This condition is related to reduced sensation in sexual intercourse and interferes with women's quality of life. It appears that pregnancy and childbirth play a role in VL[4,5]. Moreover, its pathophysiology is still not well defined [2,6].

In general, surgical treatment for women with VL is indicated when an anatomical defect has been identified; however, according to an Internet-based survey, most surgeons considered surgery as more effective than Kegel exercises or physical therapy. Moreover, North Americans were more likely to prefer and perform surgical treatment for this problem, even though they are aware that reports of dyspareunia may be present after procedure[7].

Conservative treatment should be considered as the preferred modality to start treatment for VL. For this purpose, very few clinical trials have been performed [8–10] and most of them uses energy-based devices, such as laser or radiofrequency (RF). RF acts by provoking local neocollagenesis and neoelastogenesis through fibroblastic stimulation[9]. On the other hand, pelvic floor muscle training (PFMT) is the primary option as conservative treatment for urinary incontinence (UI) and it is a low-cost option, with no side effects[11] Surprisingly, to this moment, there are no studies comparing whether PFMT could be as effective as energy-based devices, such as RF to treat VL. Given that, the aim of our study is to compare the effect of RF versus PFMT for women with VL.

Methods

Study design

Between February 2020 to December 2021 a prospective, parallel-group, two-arm, randomized clinical trial was carried out following the CONSORT recommendations[12]. It was approved by the Institutional Review Board (CAAE number 12919119.9.0000.5404) and registered in the Registro Brasileiro de Ensaios Clínicos–REBEC—RBR-2zdvfp as a clinical trial.

As there is no standardized diagnostic assessment for VL and its pathophysiological mechanism is not fully understood, we included women aged 18 and over, with self-reported VL complaints assessed by direct question (yes or no) and by the Vaginal Laxity Questionnaire (VLQ)[6] with the answers: very loose, moderately loose, slightly loose. VLQ presents one question (how would you rate your current level of vaginal laxity or looseness during intercourse?) with the possible answers: very loose, moderately loose, slightly loose, neither loose nor tight, slightly tight, moderately tight, or very tight[6].. Moreover, social media tools were used for informing about the study, as well as printed advertisements were distributed throughout the university.

We excluded participants with the following conditions: decompensated metabolic diseases or heart disease using a pacemaker; cognitive, peripheral, and/or central neurological disorders; the presence of any type of cancer or cervical dysplasia; active urinary or vaginal infection; participants undergoing physiotherapy for pelvic floor disorders or using vaginal estrogen in the last six months; participants undergoing pelvic floor disorder surgery; participants with greater than or equal to stage 2 prolapse; force of contraction of the pelvic floor muscles classified as zero according to the Modified Oxford scale[13].

During the visit for baseline assessment, women received a detailed presentation of the study and its assessments, interventions, and follow-up periods. After having all questions answered, the participants signed the consent form. Subsequently, the participants who gave their consent were submitted to a detailed medical history including questions related to sociodemographic and clinical data. Randomization occurred only after the baseline assessment in case of any conditions found during the first assessment.

Interventions

Women were divided into two groups: RF and PFMT. The detailed study protocol for each intervention was thoroughly described in a previous publication[14].

Participants allocated to the RF group received three RF sessions with an interval of four weeks between applications, totaling 12 weeks of intervention. The four-week interval between applications was chosen to allow adequate healing of the vaginal tissues. The applications were performed by a trained researcher[14]. We used the Wavetronic 6000 Touch device with the Megapulse HF FRAXX system monopolar radiofrequency (Loktal Medical Electronics, São Paulo, Brazil [15]. Participants were asked about pain during and after RF using a visual analogue scale (VAS) ranging from 0 to 10, with zero being no pain and 10 being severe pain.

Participants allocated to the PFMT group received 12 individual sessions of PFMT supervised by an experienced physiotherapist, lasting 40-60 minutes, once a week and continued home treatment with the aid of a printed and illustrated diary containing the complete PFMT treatment. In case of any questions about the treatment, the participants were able to contact the physiotherapist through video or audio calls or by messages through a telephone number made available exclusively for the study. Women received counseling to perform the proposed treatment, abstaining from any other training

for the PFM[14]. Since there is no gold standard treatment for VL, we based our PFMT program on the studies by Bo *et al.*[16] and Dumoulin *et al*[17]. The first PFMT session aimed to identify any muscle condition that interferes with the progress of the intervention; counseling on the correct contraction of the PFM with the help of vaginal palpation and educational material; presentation of the PFMT program; and finally, the first sequence of exercises[15].

Adherence to treatment was encouraged throughout the treatment and in case of any absence at RF sessions or if the attendance in PFMT sessions did not reach 80%; the participants were excluded from the study. Discontinuation of RF and PFMT and consequent referral for appropriate treatment would occur whether any complaint was present and attributed to these interventions.

Primary Outcome

The Female Sexual Function Index (FSFI) is a 19-question questionnaire that assessed the sexual response and performance of participants with VL over the past four weeks in six domains: sexual desire, arousal, lubrication, orgasm, satisfaction, and pain[18]. A cut-off score of 26.55 was used to differentiate women with or without risk for sexual dysfunction[19].

Secondary Outcomes

The presence and impact of vaginal symptoms, as well as their relationship to the quality of life of participants with VL, were assessed by the International Consultation on Incontinence Questionnaire—Vaginal Symptoms (ICIQ-VS); a validated instrument of 14 items[12]. We also assessed sexual distress in our study participants. Sexual distress is related to the feelings and emotions that individuals have about their sexuality and differs from sexual dysfunction[21]. We used the Female Sexual Distress Scale-Revised (FSDS-

164 R), a validated self-reported questionnaire with 13 questions scored from zero (never) to
165 four (always)[22]. Finally, the frequency, severity, and impact of urinary incontinence on
166 the participants' quality of life were assessed using the International Consultation on
167 Incontinence Questionnaire Short-Form (ICIQ-SF). It is a self-administered questionnaire
168 with four questions scored from zero to 21[23].

169 During the vaginal exam, we assessed the Pelvic Organ Prolapse Quantification
170 (POP-Q)[1] and the Modified Oxford Scale (MOS)[13]. Both exams were performed in the
171 supine position, with the lower limbs flexed and supported, and with the aid of disposable
172 gloves. POP-Q points were measured with a disposable ruler graduated in centimeters.
173 Subsequently, the POP staging was assessed (0-4)[1]. For MOS, PFM strength was graded
174 from zero to five by bi-digital vaginal palpation (0 = no contraction; 1= flicker; 2 = weak;
175 3 = moderate; 4 = good, and 5 = strong) [13].

176 Moreover, we investigated the improvement in the VL symptoms after RF and
177 PFMT through Global Response Assessment (GRA), a 7-level scale of response to the
178 question: "How are you now (levels of vaginal laxity/tightness and sexual satisfaction)
179 compared to before treatment" (markedly improved, moderately improved, slightly
180 improved, no change, slightly worse, moderately worse, markedly worse?)[6].

181 ***Sample size and Randomization***

182 We utilized the FSFI scores in the study by Krychman *et al*. since they found
183 significant improvement in sexual function in women with VL undergoing RF [9]. If there
184 is truly no difference between PFMT and RF, then 66 patients are required to be 90% sure
185 that the lower limit of a one-sided 95% confidence interval will be above the non-
186 inferiority limit of -4, and standard deviation of 5, data extracted from the FSFI total

score. Moreover, if we consider a percentage of 25% loss in the sample, was found a total of 84 participants, with 42 in each group (RF and PFMT).

In a 1:1 allocation ratio, a researcher not involved in the study using a computer program (https://www.randomizer.org/) performed the randomization sequence. The numbers corresponding to the study groups (1. RF and 2. PFMT) were organized in opaque sealed envelopes and grouped into two blocks, which were opened by the study participants after signing the consent form and the initial assessment. Both the researchers who supervised the completion of the questionnaires and who performed the vaginal examinations, and the data analysts were blinded to the treatment group of the participants. A specialized physiotherapist in women's health was responsible for the interventions and for the telephone follow-up of the participants. This investigator could not be blinded as we presented a restricted number of people at the research team within the hospital during the Covid-19 pandemic.

Statistical Analysis

We have used the SAS statistical package version 9.4 (SAS Institute, Cary, NC, USA) to analyze the data. For categorial variables, the chi-Square or fisher's exact tests were used between groups; for continuous variables, the Student t or Mann-Whitney test was considered. We determined noninferiority using a difference-in-means analysis with a 95% CI. Noninferiority was accepted if the lower limit of a 1-sided 95% CI did not cross the presupposed noninferiority limit. Analysis of variance for repeated measures (ANOVA) was used to compare scores between groups and evaluation periods, followed by Tukey's and contrast profile tests contrasts, with variables transformed into positions/ranks due to the non-distribution. McNemar's test (two categories) and Bowker's symmetry test (for three or more categories) were used to compare categorical variables and Wilcoxon's test (for related samples) for continuous variables between

212 baseline - 30 days -6 months after treatment. The significance level was 5% ($p<0.05$). For
213 ITT method, the last observation being carried forward (LOCF) in cases of missing
214 follow-up data was used.

215

216 **Results**

217 Figure 1 depicts the flowchart of the participants. One hundred sixty-seven
218 participants were initially selected. Of these, 80 participants who did not attend the initial
219 assessment and who underwent pelvic surgery were excluded. Finally, 87 participants
220 were randomized and allocated into radiofrequency (n=42), and PFMT (n=45)..

221 Both the per-protocol and the ITT analysis showed that baseline characteristics
222 were similar across groups (Table 1). Table 2 displays the pelvic floor symptoms in both
223 groups, and nocturia was the only symptom that significantly differed between the groups,
224 with a higher frequency in the RF group (per-protocol p=0.007, and ITT p=0.038). Self-
225 complaint of VL was the most frequent source of complaint. Most of these participants
226 responded 'moderately loose' on the VLQ questionnaire (Table 2). Tables 3 and 4 displays
227 the comparison of the questionnaires used in both groups between baseline and 30 days
228 or baseline and six months after treatment, all questionnaires but GRA were statistically
229 significant after treatment (Table 3).

230 Table 5 displays the non-inferiority analysis using a non-inferiority limit of 4.
231 After 30 days of treatment, RF was non-inferior to PFMT to improving FSFI total score
232 (mean difference -0.08[-2.58 to 2.42] for RF and -1.95[-4.21 to 0.30] for PFMT) in PP
233 (mean difference -0.46[-2.92 to 1.99] for RF and -1.82[-4.10 to 0.45] for PFMT) and in
234 the ITT analysis; however, this result was not maintained after six months of treatment.

235 Supplementary Tables 1 and 2 illustrate assessments of participants with vaginal
236 laxity through physical examinations in both groups and analyses during baseline, 30
237 days, and six-months after treatment. In the per-protocol and ITT analysis, the mean
238 strength of the pelvic floor muscles showed significant improvement in both groups and
239 periods according to the MOS. However, the improvement of the pelvic floor muscles in
240 the PFMT group was much higher when compared to the RF group in both periods.
241 Regarding the POP-Q system, points C and D were statistically significant in the RF
242 group in both analyses at 30 days follow-up. Points Aa, and Ba after 30 days of treatment
243 and points Aa, Ba and Ap after 6 months follow-up in the per-protocol and ITT analyses
244 were statistically significant in the PFMT group. Significant improvement was observed
245 in POP-Q staging and perineal body (six-months F/U) only in the PFMT group in both
246 analyses.

247 The PFMT group showed improvement in almost all assessments after 30 days of
248 treatment when compared to the RF group (Supplementary Table 3). Significant
249 improvements were observed in the MOS ($p<0.001$), POP-Q system for points Aa
250 ($p=0.017$), Ba ($p=0.038$), Ap ($p=0.049$) and POP-Q staging ($p= 0.025$). After 6-Months
251 of follow-up, only MOS and POP-Q point Ap remained significant.

252 Supplementary Table 4, Figures 2 and 3 display the significant comparisons
253 between questionnaires and continuous variables from physical examination between
254 groups (RF and PFMT) and among periods (baseline, 30 days, and six-months. There was
255 a significant difference for all FSFI domains with increased scores among baseline, 30
256 days, and six-months after treatment in both groups, with the pain domain showing higher
257 scores in the PFMT group 6-Months post-treatment. Considering the ICIQ-VS, FSDS-R
258 score, and ICIQ-SF total score questionnaires, there was a decrease in scores between
259 baseline and 30 days and baseline and 6-Months post-treatment in both groups. The MOS

displayed a significant interaction between assessments in the PFMT group. Perineal body decreased significantly in the PFMT group.

Adverse effects related to RF were mild vaginal discharge that disappeared on the fifth-day post-procedure. Two participants had redness and discomfort in the vaginal introitus and vulvar area. The participants were followed up and examined and it was noticed that these effects were not related to RF but to allergies to xylocaine or latex-made gloves. The participants chose to continue with the treatment and had the xylocaine removed from the routine of the procedure and the gloves replaced by nitrile gloves.

Discussion

This noninferiority randomized trial demonstrated that after 30 days of treatment, RF was non-inferior to PFMT to improving FSFI total score in PP and in the ITT analysis; however, RF was not considered non-inferior after six months of treatment when compared to PFMT. Moreover, all questionnaires improved in their total scores and scales for both groups and follow-ups. Interestingly, we have seen modifications in the POP-Q classification in the anterior compartment for the PFMT group and apical compartment (point C) for the RF group. Furthermore, PFM strength significantly improved in the RF and PFMT groups.

PFMT was compared with energy-based therapies in two other studies with women with urinary incontinence (UI). The study by Slongo *et al.* investigated RF and PFMT in the treatment of women with UI[14] and the study by Ahmed *et al.* compared PFMT and Er: YAG 2940 nm laser in the treatment of vaginal laxity[8]. The latter found improvement in PFM strength and sexual satisfaction in both groups[8]. However, PFMT was performed in both intervention groups and with a different therapy, which makes it

284 difficult to address further comparison with our findings. Despite investigating a different
285 population, the study by Slongo *et al.* showed that sexual function improved in RF and
286 PFMT[24].

287 Our analysis showed that the population presented homogeneous
288 sociodemographic and clinical data, except for complaints of nocturia. Despite not
289 showing a significant difference between the two groups regarding GRA, most
290 participants observed moderate improvement, followed by marked improvement after 30
291 days of treatment at GRA.

292 It is very interesting to emphasize that an energy-based device technique was
293 compared to a physical therapy protocol, and the results were similar after 30 days of
294 treatment, but data is not supported after six months. This is very important when we are
295 discussing the cost of a treatment in the current scenario. Use of energy-based devices
296 can increase expenses and may impair treatment for some patients, depending on the
297 health care scenario. Most of the studies using RF were sham-controlled, and the placebo
298 effect was the main treatment in these groups. We could demonstrate that a physical
299 therapy protocol could cause benefit for these women, and with no difference when
300 compared to the other group.

301 Interestingly, in this study, PFM strength showed significant improvement
302 between groups in both analyses. However, the PFMT showed improvement rates almost
303 twice as high as the RF group after 30 days of treatment. POP-Q showed improvement in
304 points Aa, Ba and Ap, in the per protocol analysis for the PFMT group. This trend was
305 not observed in the ITT analysis, which maintained the improvement only in points Aa
306 and Ba. Maybe PFMT could act in the biomechanics of the pelvic floor muscles and
307 modify the progression of POP-Q staging, and this hypothesis could explain these
308 alterations, however, this study was not planned for this, and longer follow-ups would be

necessary. A previous RCT performing PFMT to improve post operative anatomical results of POP surgery did not show any improvement on this regard [25]. However, a recent metanalysis demonstrated that women who received PFMT showed greater subjective improvement in prolapse symptoms and an objective improvement in POP severity [26].

Points C and D showed higher values after 30 days of treatment in the RF group in both analyses. This is another interesting point that needs further clarification. RF improves collagenesis and vaginal wall thickness, but apical improvement could be related to this, or other indirect effects and future studies are needed to explore this finding.

This is the first RCT comparing PFMT with an energy-based device for women with VL, using several validated questionnaires studying quality of life, pain during intercourse, sexual function, POP and urinary symptoms, and POP-Q classification aiming for anatomical changes. Plus, two follow-up periods were analyzed. Our weaknesses were the lack of a sham-controlled group (third arm), difficulty to blind researchers to assess treatments due to the COVID-19 pandemic that reduced the number of personnel involved in the study and limits generalizability. Although the adhesion was smaller in the PFMT group, the ITT analysis intended to reduce this limitation and we did not surpass the drop-out limit in both arms.

Conclusion

Within women with VL, we concluded that both RF and PFMT improved sexual, vaginal, and urinary symptoms 30 days and six months follow-ups. After 30 days of treatment, RF was non-inferior to PFMT to improving FSFI total score; however, this result was not maintained after six months of treatment.

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Figure legends

Figure 1 – CONSORT flowchart of the recruited women with vaginal laxity (VL) to undergo radiofrequency (RF) or pelvic floor muscle training (PFMT)

Figure 2 – Repeated measures ANOVA comparison of FSFI total score and domains between groups and among periods (baseline, 30 days, and 6 months).

Figure 3 - Repeated measures ANOVA comparison of FSDS-R, ICIQ, Modified Oxford Scale and POP-Q classification between groups and among periods (baseline, 30 days, and 6 months).

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Table 1. Sociodemographic and clinical characteristics of women with vaginal laxity (n=87)

Variables	Per Protocol Analysis					Intention-to-Treat Analysis				
	Radiofrequency (n=38)		PFMT (n=35)		p-Value	Radiofrequency (n=42)		PFMT (n=45)		p-Value
	Mean ± SD / n (%)	IQR	Mean ± SD / n (%)	IQR		Mean ± SD / n (%)	IQR	Mean ± SD / n (%)	IQR	
Age (years)	41.50 ± 8.70	(35.00 – 46.00)	41.40 ± 7.74	(35.00 – 47.00)	0.996 [α]	41.50 ± 9.01	(35.00 – 42.00)	41.20 ± 7.87	(35.00 – 47.00)	0.769 [β]
Marital Status					0.854 [ω]					0.675 [β]
Single	7 (18.42)		7 (20.00)			9 (23.42)		10 (22.22)		
Married	27 (71.05)		26 (74.29)			29 (69.05)		28 (62.22)		
Divorced	4 (10.53)		2 (5.71)			4 (9.52)		7 (15.56)		
Ethnicity					0.403 [ω]					0.244 [β]
White	18 (47.37)		22 (62.86)			18 (42.86)		27 (60.00)		
Black	5 (13.16)		4 (11.43)			5 (11.90)		5 (11.11)		
Other	15 (39.47)		9 (25.71)			19 (45.24)		13 (28.89)		
Years of Education					0.179 [ω]					0.317 [ω]
< 8 years	3 (7.89)		7 (20.00)			3 (7.14)		7 (15.56)		
> 8 years	35 (92.11)		28 (80.00)			39 (92.86)		38 (84.44)		
BMI					0.319 [ω]					0.184 [β]
< 25Kg/m^2	12 (31.58)		15 (42.86)			12 (28.57)		19 (42.22)		
> 25Kg/m^2	26 (68.42)		20 (57.14)			30 (71.43)		26 (57.78)		
Gravidity	2.82 ± 1.69	(2.00 – 4.00)	2.17 ± 1.25	(1.00 – 3.00)	0.100 [α]	2.79 ± 1.63	(2.00 – 3.00)	2.42 ± 1.48		0.242 [β]
Type of Birth					0.140 [ω]					0.570 [ω]

None	1 (2.63)		2 (5.71)			1 (2.38)		2 (4.44)	
Vaginal	24 (63.16)		16 (45.71)			26 (61.90)		23 (51.11)	
Cesarean	6 (15.79)		13 (37.14)			8 (19.05)		14 (31.11)	
Both	7 (18.42)		4 (11.43)			7 (16.67)		6 (13.33)	
Parity					0.478[ε]				0.370[ε]
Nulliparous	1 (2.63)		2 (5.71)			1 (2.38)		3 (6.67)	
Primiparous	6 (15.79)		9 (25.71)			7 (16.67)		11 (24.44)	
Multiparous	31 (81.58)		24 (68.57)			34 (80.95)		31 (68.89)	
Birth Weight (grams)	3122.70 ± 620.55	(2950 – 3250)	3409.20 ± 500.66	(3090 – 3662.5)	0.162[α]	3145.80 ± 616.19	(2895 – 3585)	3342.10 ± 521.98	0.405[#]
Instrumental Delivery	6 (15.79)		7 (20.00)		0.444[ε]	6 (14.29)		10 (22.22)	0.340[β]
Menopausal Status					1.000[ε]				0.841[β]
Premenopause	33 (86.84)		31 (88.57)			37 (88.10)		39 (86.67)	
Menopause	5 (13.16)		4 (11.43)			5 (11.90)		6 (13.33)	
Comorbidities					0.137[ε]				0.052[ε]
None	31 (81.58)		33 (94.29)			32 (76.19)		42 (93.33)	
Hypertension	6 (15.79)		1 (2.86)			8 (19.05)		2 (4.44)	
Diabetes	1 (2.63)		1 (2.86)			2 (4.76)		1 (2.22)	
Use of antidepressants	3 (7.89)		5 (14.29)		0.468[ε]	3 (7.14)		6 (13.33)	0.486[ε]

PFMT: Pelvic Floor Muscle Training; SD: Standard Deviation; IQR: Interquartile Range; BMI: Body Mass Index; [α] Student t test; [β] Chi-square test; [ε] Fisher test; [#] Mann-Whitney test

Table 2. Baseline pelvic floor symptoms of women with vaginal laxity (n=87).

Variables	Per Protocol Analysis			Intention-to-Treat Analysis		
	Radiofrequency (n=38) n (%)	PFMT (n=35) n (%)	p-Value	Radiofrequency (n=42) n (%)	PFMT (n=45) n (%)	p-Value
Nocturia	30 (78.95)	17 (48.57)	**0.007** [ω]	33 (78.57)	26 (57.78)	**0.038** [β]
Incomplete Emptying	19 (50.00)	18 (51.43)	0.903 [ω]	22 (52.38)	25 (55.56)	0.767 [β]
Post-micturition Dribble	26 (68.42)	21 (60.00)	0.453 [ω]	28 (66.67)	29 (64.44)	0.828 [β]
Coital Incontinence			0.130 [ω]			0.160 [ω]
During orgasm	2 (5.26)	3 (8.57)		3 (7.14)	7 (15.56)	
During penetration	3 (7.89)	9 (25.71)		3 (7.14)	9 (20.00)	
Both	4 (10.53)	1 (2.86)		4 (9.52)	3 (6.67)	
Type of sexual intercourse			0.806 [ω]			0.486 [β]
Vaginal	26 (68.42)	23 (65.71)		30 (71.43)	29 (64.44)	
Vaginal and Anal	12 (31.58)	12 (34.29)		12 (28.57)	16 (35.56)	
Vaginal Laxity Complaint			0.648 [ω]			1.000 [ω]
Self-complaint	32 (84.21)	27 (77.14)		35 (83.33)	36 (80.00)	
Partner-complaint	0	1 (2.86)		0	1 (2.22)	
Both	6 (15.79)	7 (20.00)		7 (16.67)	8 (17.78)	
Duration of VL Complaint			0.568 [ω]			0.941 [β]
< 5 years	17 (44.74)	18 (51.43)		19 (45.24)	20 (44.44)	
> 6 years	21 (55.26)	17 (48.57)		23 (54.76)	25 (55.56)	
Constipation	10 (26.32)	10 (28.57)	0.829 [ω]	11 (26.19)	13 (28.89)	0.778 [β]
Flatus Incontinence	11 (28.95)	14 (40.00)	0.320 [ω]	11 (26.19)	18 (40.00)	0.172 [β]
Fecal Incontinence	2 (5.26)	6 (17.14)	0.142 [ω]	2 (4.76)	6 (13.33)	0.268 [ω]

VL Questionnaire			0.697 [β]		0.681 [β]
Very Loose	15 (39.47)	12 (34.29)		16 (38.10)	17 (37.78)
Moderately Loose	19 (50.00)	17 (48.57)		22 (52.38)	21 (46.67)
Slightly Loose	4 (10.53)	6 (17.14)		4 (9.52)	7 (15.56)

PFMT: Pelvic Floor Muscle Training; PP: Per Protocol Analysis; ITT: Intention to Treat Analysis; [β] Chi-square test; *Fisher test; VL: Vaginal Laxity

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Table 3. Assessment of women with vaginal laxity using questionnaires by treatment group (per protocol analysis).

Questionnaire scores	Radiofrequency (n=35)			PFMT (n=35)			Radiofrequency (n=38)			PFMT (n=35)	
	Baseline	30 days Follow-up	p-Value	Baseline	30 days Follow-up	p-Value	Baseline	6-Months Follow-up	p-Value	6-Months Follow-up	p-Value
FSFI											
Desire	2.99 ± 1.14	3.90 ± 1.04	**0.001** *	3.30 ± 1.26	3.89 ± 1.10	**0.017** *	3.01 ± 1.14	3.88 ± 1.07	**0.001** *	4.11 ± 0.93	**0.001** *
Arousal	3.42 ± 1.21	4.43 ± 1.25	**0.001** *	3.69 ± 1.30	4.58 ± 1.01	**0.001** *	3.46 ± 1.23	4.14 ± 1.06	**0.001** *	4.66 ± 0.99	**0.001** *
Lubrication	4.05 ± 1.32	5.10 ± 1.16	**0.001** *	4.53 ± 1.41	5.15 ± 1.05	**0.016** *	4.10 ± 1.32	4.71 ± 1.12	**0.002** *	5.11 ± 0.98	**0.012** *
Orgasm	3.56 ± 1.42	4.68 ± 1.26	**0.001** *	3.90 ± 1.42	4.52 ± 1.43	**0.013** *	3.65 ± 1.44	4.64 ± 1.15	**0.001** *	4.77 ± 1.29	**0.001** *
Satisfaction	4.20 ± 1.35	5.01 ± 0.89	**0.001** *	3.94 ± 1.35	4.75 ± 1.15	**0.001** *	4.23 ± 1.33	4.84 ± 1.26	**0.031** *	5.05 ± 0.93	**0.001** *
Pain	4.33 ± 1.58	5.16 ± 0.98	**0.001** *	4.90 ± 1.27	5.48 ± 1.15	**0.009** *	4.32 ± 1.56	5.05 ± 1.02	**0.001** *	5.51 ± 0.88	**0.005** *
Total Score	22.56 ± 6.76	28.31 ± 5.15	**0.001** *	24.29 ± 5.84	28.39 ± 5.36	**0.001** *	22.76 ± 6.80	27.27 ± 4.96	**0.001** *	29.22 ± 4.70	**0.001** *
ICIQ – Vaginal Symptoms											
Vaginal Symptoms	16.34 ± 6.89	8.65 ± 6.05	**0.001** *	13.82 ± 7.89	7.22 ± 7.15	**0.001** *	16.18 ± 6.76	8.55 ± 6.53	**0.001** *	7.17 ± 7.27	**0.001** *
Sexual Matters	26.77 ± 19.76	14.77 ± 18.21	**0.001** *	26.68 ± 21.58	11.77 ± 17.27	**0.001** *	26.11 ± 20.06	14.68 ± 18.63	**0.001** *	10.89 ± 14.94	**0.001** *
Quality of Life	6.22 ± 3.62	2.42 ± 3.08	**0.001** *	5.28 ± 3.53	2.37 ± 3.37	**0.001** *	6.18 ± 3.52	3.32 ± 3.63	**0.001** *	3.20 ± 5.43	**0.002** *
Q.4 – Vaginal Laxity	2.37 ± 0.80	1.08 ± 0.74	**0.001** *	2.05 ± 0.83	1.05 ± 1.05	**0.001** *	2.39 ± 0.79	1.24 ± 0.97	**0.001** *	1.03 ± 0.98	**0.001** *
FSDS-R	25.17 ± 15.12	14.54 ± 12.70	**0.001** *	27.85 ± 15.38	13.71 ± 12.07	**0.001** *	24.82 ± 15.13	15.95 ± 14.04	**0.001** *	12.31 ± 12.00	**0.001** *
ICIQ-Short Form	9.11 ± 7.05	4.14 ± 5.00	**0.001** *	9.4 ± 6.44	3.6 ± 5.6	**0.001** *	9.18 ± 7.06	4.92 ± 5.73	**0.001** *	3.89 ± 5.42	**0.001** *

Global Response		0.654 [β]		0.138 [∝]
Assessment n (%)				
Markedly improved	9 (25.71)	13 (37.14)	12 (31.58)	15 (42.86)
Moderately improved	19 (54.29)	15 (42.86)	14 (36.84)	15 (42.86)
Slightly improved	5 (14.29)	6 (17.14)	7 (18.42)	5 (14.29)
No change	2 (5.71)	1 (2.86)	5 (13.16)	0 (0)

[α] Wilcoxon test; [∝] Fisher test; PFMT: Pelvic Floor Muscle Training; FSFI: Female Sexual Function Index; ICIQ: International Consultation on Incontinence Questionnaire; Q.4: Question number 4; FSDS-R: Female Sexual Distress Scale – Revised

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Table 4. Assessment of women complaining of vaginal laxity using questionnaires by treatment group (intention-to-treat analysis).

Questionnaire/ Scores	Radiofrequency (n=42)			PFMT (n=45)			Radiofrequency (n=42)		PFMT (n=45)	
	Baseline	30 days Follow-up	p-Value	Baseline	30 days Follow-up	p-Value	6-Months Follow-up	p-Value	6-Months Follow-up	p-Value
FSFI										
Desire	3.01 ± 1.16	3.77 ± 1.13	**0.001** *	3.41 ± 1.26	3.87 ± 1.12	**0.007** *	3.80 ± 1.13	**0.001** *	4.04 ± 1.00	**0.001** *
Arousal	3.39 ± 1.23	4.23 ± 1.34	**0.001** *	3.73 ± 1.26	4.43 ± 1.07	**0.001** *	4.00 ± 1.14	**0.001** *	4.49 ± 1.06	**0.001** *
Lubrication	4.06 ± 1.30	4.94 ± 1.23	**0.001** *	4.52 ± 1.34	5.00 ± 1.09	**0.011** *	4.61 ± 1.15	**0.002** *	4.97 ± 1.03	**0.012** *
Orgasm	3.56 ± 1.44	4.50 ± 1.38	**0.001** *	3.91 ± 1.44	4.39 ± 1.47	**0.005** *	4.46 ± 1.29	**0.001** *	4.58 ± 1.38	**0.001** *
Satisfaction	4.15 ± 1.36	4.83 ± 1.07	**0.001** *	4.04 ± 1.45	4.68 ± 1.31	**0.001** *	4.70 ± 1.34	**0.031** *	4.91 ± 1.18	**0.001** *
Pain	4.26 ± 1.58	4.95 ± 1.19	**0.001** *	4.86 ± 1.26	5.32 ± 1.20	**0.010** *	4.92 ± 1.16	**0.001** *	5.33 ± 1.02	**0.005** *
Total Score	22.42 ± 6.71	27.21 ± 5.93	**0.001** *	24.48 ± 5.80	27.68 ± 5.58	**0.001** *	26.50 ± 5.49	**0.001** *	28.32 ± 5.20	**0.001** *
ICIQ – Vaginal Symptoms										
Vaginal Symptoms	17.07 ± 7.19	10.67 ± 7.79	**0.001** *	13.83 ± 7.89	7.23 ± 7.15	**0.001** *	10.17 ± 8.17	**0.001** *	9.82 ± 8.91	**0.001** *
Sexual Matters	25.98 ± 20.31	15.98 ± 19.18	**0.001** *	26.69 ± 21.59	11.77 ± 17.28	**0.001** *	15.64 ± 19.27	**0.001** *	14.20 ± 16.62	**0.001** *
Quality of Life	6.24 ± 3.51	3.07 ± 3.39	**0.001** *	5.29 ± 3.54	2.37 ± 3.38	**0.001** *	3.67 ± 3.75	**0.001** *	4.16 ± 5.30	**0.002** *
Q.4 – Vaginal Laxity	2.38 ± 0.79	1.31 ± 0.90	**0.001** *	2.06 ± 0.84	1.06 ± 1.06	**0.001** *	1.33 ± 1.00	**0.001** *	1.36 ± 1.09	**0.001** *
FSDS-R	24.74 ± 15.13	15.88 ± 13.46	**0.001** *	28.42 ± 14.74	17.42 ± 13.97	**0.001** *	16.71 ± 14.34	**0.001** *	16.33 ± 14.23	**0.001** *

ICIQ-Short Form	8.45 ± 7.13	4.31 ± 5.32	**0.001** [a]	10.16 ± 6.36	5.64 ± 6.77	**0.001** [a]	4.60 ± 5.59	**0.001** [a]	5.87 ± 6.57	**0.001** [a]

ITT: Intention to treat; [a] Wilcoxon test; PFMT: Pelvic Floor Muscle Training; FSFI: Female Sexual Function Index; ICIQ: International Consultation on Incontinence Questionnaire; Q.4: Question number 4; FSDS-R: Female Sexual Distress Scale - Revised

Table 5. Non-inferiority analysis of patient FSFI total scores 30 days and six months after treatment with radiofrequency compared with pelvic floor muscle treatment using a non-inferiority limit of -4

Outcome	Mean± SD [95% CI]		Mean Difference [95% CI]	p value
FSFI Total Score (PP analysis)	***Radiofrequency (n=35)***	***PFMT (n=35)***		
30 days	28.31±5.15 [26.54 – 30.08]	28.39±5.36 [26.55-30.23]	-0.08 [-2.58 to 2.42]	0.474
6 Months	27.26±4.96[25.63-28.89]	29.22±4.69[27.60-30.83]	-1.95[-4.21 to 0.30]	0.045
FSFI Total Score (ITT analysis)	***Radiofrequency (n=42)***	***PFMT (n=45)***		
30 days	27.21±5.93 [25.36 – 29.06]	27.68±5.58[26.00-29.35]	-0.46 [-2.92 to 1.99]	0.354
6 Months	26.49±5.49[24.79-28.20]	28.31± 5.20[26.75-29.88]	-1.82 [-4.10 to 0.45]	0.058

PP: per protocol; ITT: intention-to-treat; FSFI: Female Sexual Function Index; PFMT: Pelvic Floor Muscle Training; SD: Standard Deviation; CI: Confidence Interval;

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Supplementary Table 1. Assessment of women with vaginal laxity through physical examination by treatment group (per protocol analysis).

Physical Examination	Radiofrequency (n=35)			PFMT (n=35)			Radiofrequency (n=38)			PFMT (n=35)	
	Baseline	30 days Follow-up	p-Value	Baseline	30 days Follow-up	p-Value	Baseline	6-Months Follow-up	p-Value	6-Months Follow-up	p-Value
Modified Oxford Scale	2.54 ± 0.61	2.82 ± 0.66	**0.002** [a]	2.77 ± 0.94	4.54 ± 0.61	**0.001** [a]	2.55 ± 0.60	2.79 ± 0.70	**0.049** [a]	4.49 ± 0.74	**0.001** [a]
POP-Q											
Aa	- 2.42 ± 0.45	- 2.50 ± 0.38	0.230 [a]	- 2.42 ± 0.34	- 2.71 ± 0.34	**0.001** [a]	- 2.42 ± 0.44	- 2.51 ± 0.41	0.161 [a]	- 2.69 ± 0.37	**0.001** [a]
Ba	- 2.42 ± 0.45	- 2.52 ± 0.43	0.089 [a]	- 2.37 ± 0.39	- 2.72 ± 0.35	**0.001** [a]	- 2.46 ± 0.46	- 2.55 ± 0.42	0.161 [a]	- 2.71 ± 0.33	**0.001** [a]
Ap	- 2.84 ± 0.26	- 2.85 ± 0.25	0.661 [a]	- 2.85 ± 0.28	- 2.95 ± 0.14	**0.032** [a]	- 2.86 ± 0.26	- 2.82 ± 0.32	0.563 [a]	- 2.99 ± 0.08	**0.031** [a]
Bp	- 2.81 ± 0.38	- 2.85 ± 0.28	0.324 [a]	- 2.88 ± 0.24	- 2.95 ± 0.15	0.133 [a]	- 2.83 ± 0.37	- 2.84 ± 0.29	0.973 [a]	- 2.99 ± 0.08	0.063 [a]
C	- 6.70 ± 1.24	- 7.05 ± 1.00	**0.006** [a]	- 7.01 ± 1.14	- 7.10 ± 2.88	0.863 [a]	- 6.59 ± 1.26	- 6.92 ± 1.04	**0.028** [a]	- 7.50 ± 0.75	0.053 [a]
D	- 8.04 ± 2.34	- 8.31 ± 2.35	**0.044** [a]	- 8.05 ± 3.25	- 8.38 ± 3.30	0.684 [a]	- 8.01 ± 2.25	- 8.18 ± 2.24	0.435 [a]	- 8.93 ± 0.81	0.087 [a]
TVL	9.81 ± 0.97	9.95 ± 0.95	0.208 [a]	9.82 ± 0.81	9.94 ± 0.88	0.449 [a]	9.72 ± 0.99	9.26 ± 3.48	0.828 [a]	8.77 ± 4.99	0.845 [a]
Genital Hiatus	3.12 ± 0.57	2.91 ± 1.13	0.299 [a]	2.94 ± 0.60	2.90 ± 0.45	0.597 [a]	3.13 ± 0.58	3.12 ± 0.46	0.946 [a]	2.81 ± 0.52	0.079 [a]
Perineal Body	3.24 ± 0.45	3.31 ± 0.45	0.303 [a]	3.31 ± 0.47	3.24 ± 0.45	0.281 [a]	3.25 ± 0.45	3.16 ± 0.40	0.140 [a]	3.19 ± 0.44	**0.047** [a]
POP-Q Staging			1.000 [c]			**0.001** [c]			0.180 [c]		**0.001** [c]
Stage 0	8 (22.86)	8 (22.86)		3 (8.57)	18 (51.43)		8 (21.05)	11 (28.95)		16 (45.71)	
Stage 1	27 (77.14)	27 (77.14)		32 (91.43)	17 (48.57)		30 (71.05)	27 (71.05)		19 (54.29)	

[a] Wilcoxon test; [c] Mcnemar test; PFMT: Pelvic Floor Muscle Training; POP-Q: Pelvic Organ Prolapse Quantification; TVL: Total Vaginal Length.

Supplementary Table 2. Assessment of women complaining of vaginal laxity through physical examination/ultrasound by treatment group (intention-to-treat analysis).

Physical Examination	Radiofrequency (n=42)			PFMT (n=45)			Radiofrequency (n=42)		PFMT (n=45)	
	Baseline	30 days Follow-up	p-Value	Baseline	30 days Follow-up	p-Value	6-Months Follow-up	p-Value	6-Months Follow-up	p-Value
Modified Oxford Scale	2.57 ± 0.63	2.81 ± 0.67	**0.006** [α]	2.73 ± 0.86	4.11 ± 1.01	**0.001** [α]	2.79 ± 0.72	**0.049** [α]	4.07 ± 1.05	**0.001** [α]
POP-Q										
Aa	- 2.44 ± 0.44	- 2.50 ± 0.38	0.270 [α]	- 2.47 ± 0.34	- 2.69 ± 0.34	**0.001** [α]	- 2.52 ± 0.41	0.161 [α]	- 2.67 ± 0.35	**0.001** [α]
Ba	- 2.48 ± 0.44	- 2.56 ± 0.42	0.145 [α]	- 2.41 ± 0.42	- 2.69 ± 0.39	**0.001** [α]	- 2.56 ± 0.40	0.161 [α]	- 2.68 ± 0.37	**0.001** [α]
Ap	- 2.87 ± 0.25	- 2.88 ± 0.24	1.000 [α]	- 2.86 ± 0.27	- 2.93 ± 0.17	0.063 [α]	- 2.83 ± 0.31	0.563 [α]	- 2.96 ± 0.14	**0.031** [α]
Bp	- 2.85 ± 0.36	- 2.88 ± 0.27	0.531 [α]	- 2.88 ± 0.24	- 2.93 ± 0.17	0.234 [α]	- 2.86 ± 0.28	0.973 [α]	- 2.96 ± 0.14	0.063 [α]
C	- 6.73 ± 1.30	- 7.02 ± 1.12	**0.004** [α]	- 6.90 ± 1.23	- 6.97 ± 2.64	0.054 [α]	- 7.02 ± 1.09	**0.028** [α]	- 7.28 ± 1.04	0.052 [α]
D	- 7.64 ± 3.65	- 7.87 ± 3.69	**0.043** [α]	- 8.07 ± 2.93	- 8.32 ± 2.98	0.367 [α]	- 7.80 ± 3.66	0.435 [α]	- 8.74 ± 1.00	0.087 [α]
TVL	9.87 ± 1.05	9.99 ± 1.04	0.301 [α]	9.67 ± 0.95	9.76 ± 1.01	0.652 [α]	9.45 ± 3.37	0.828 [α]	8.84 ± 4.43	0.845 [α]
Genital Hiatus	3.06 ± 0.61	2.88 ± 1.07	0.562 [α]	2.96 ± 0.61	2.92 ± 0.50	0.672 [α]	3.05 ± 0.50	0.946 [α]	2.86 ± 0.55	0.079 [α]
Perineal Body	3.25 ± 0.45	3.31 ± 0.44	0.414 [α]	3.39 ± 0.51	3.33 ± 0.51	0.371 [α]	3.17 ± 0.41	0.140 [α]	3.29 ± 0.51	**0.046** [α]
POP-Q Staging			1.000 [β]			**0.001** [β]		0.180 [β]		**0.001** [β]
Stage 0 – n (%)	9 (21.43)	9 (21.43)		6 (13.33)	21 (46.67)		12 (28.57)		19 (42.22)	
Stage 1 – n (%)	33 (78.57)	33 (78.57)		39 (86.67)	24 (53.33)		30 (71.43)		26 (57.78)	

ITT: Intention to treat; [α] Wilcoxon test; [β] Mcnemar test; PFMT: Pelvic Floor Muscle Training; POP-Q: Pelvic Organ Prolapse Quantification;

Supplementary Table 3. Comparative analysis between radiofrequency and PFMT groups after 30 days and 6-Months of follow-up (ITT).

Variables	Radiofrequency (n=42)	PFMT (n=45)	p-Value	Radiofrequency (n=42)	PFMT (n=45)	p-Value
	30 days Follow-up	30 days Follow-up		6-Months Follow-up	6-Months Follow-up	
FSFI Total Score	28.31 ± 5.15	28.39 ± 5.36	0.949[α]	26.50 ± 5.49	28.32 ± 5.20	0.083
ICIQ – Vaginal Symptoms						
Vaginal Symptoms	8.65 ± 6.05	7.22 ± 7.15	0.370[α]	10.17 ± 8.17	9.82 ± 8.91	0.695
Sexual Matters	14.77 ± 18.21	11.77 ± 17.27	0.482[α]	15.64 ± 19.27	14.20 ± 16.62	0.910
Quality of Life	2.42 ± 3.08	2.37 ± 3.37	0.941[α]	3.64 ± 3.75	4.16 ± 5.30	1.000
Q.4 – Vaginal Laxity	1.08 ± 0.74	1.05 ± 1.05	0.896[α]	1.33 ± 1.00	1.36 ± 1.09	0.950
FSDS-R	14.54 ± 12.70	13.71 ± 12.07	0.780[α]	16.71 ± 14.34	16.33 ± 14.23	0.855
ICIQ – Short Form	4.14 ± 5.00	3.6 ± 5.6	0.671[α]	4.60 ± 5.59	5.87 ± 6.57	0.411
Modified Oxford Scale	2.82 ± 0.66	4.54 ± 0.61	**0.001[α]**	2.79 ± 0.72	4.07 ± 1.05	**0.001**
POP-Q						
Aa	- 2.5 ± 0.38	- 2.71 ± 0.34	**0.017[α]**	- 2.52 ± 0.41	- 2.67 ± 0.35	0.107
Ba	- 2.52 ± 0.43	- 2.72 ± 0.35	**0.038[α]**	- 2.56 ± 0.40	- 2.68 ± 0.37	0.156
Ap	- 2.85 ± 0.25	- 2.95 ± 0.14	**0.049[α]**	- 2.83 ± 0.31	- 2.96 ± 0.14	**0.028**
Bp	- 2.85 ± 0.28	- 2.95 ± 0.15	0.068[α]	- 2.86 ± 0.28	- 2.96 ± 0.14	0.053
C	- 7.05 ± 1.00	- 7.10 ± 2.88	0.934[α]	- 7.02 ± 1.09	- 7.28 ± 1.04	0.079
D	- 8.31 ± 2.35	- 8.38 ± 3.30	0.917[α]	- 7.80 ± 3.66	- 8.74 ± 1.00	0.232
TVL	9.95 ± 0.95	9.94 ± 0.88	0.948[α]	9.45 ± 3.37	8.84 ± 4.43	0.443
Genital Hiatus	2.91 ± 1.13	2.90 ± 0.45	0.945[α]	3.05 ± 0.50	2.86 ± 0.55	0.106

Perineal Body	3.31 ± 0.45	3.24 ± 0.45	0.515[α]	3.17 ± 0.41	3.29 ± 0.51	0.265
POP-Q Stage			**0.025**[α]			0.184
Stage 0	8 (22.86)	18 (51.43)		12 (28.57)	19 (42.22)	
Stage 1	27 (77.14)	17 (48.57)		30 (71.43)	26 (57.78)	

PFMT: Pelvic Floor Muscle Training; [α] Two-sample t test with equal variances; [0] Chi-square test; FSFI: Female Sexual Function Index; ICIQ: International Consultation on Incontinence Questionnaire; Q4: Question number 4; POP-Q: Pelvic Organ Prolapse Quantification; TVL: Total Vaginal Length; FSDS-R: Female Sexual Distress Scale - Revised

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Supplementary Table 4. Repeated measures ANOVA (analysis of variance) for comparison of numerical variables between radiofrequency and pelvic floor muscle training among baseline, 30 days and 6-Months follow-up (n=87)

Variables* (n=87)					Comparison between RF and PFMT		Comparison between assessment periods		Interaction between groups and assessment periods	
		Baseline Mean ± SD	30 days Mean ± SD	6-Months Mean ± SD	p-value[1] B-F1 B-F2	Interpretation[a]	p-value[1] B-F1 B-F2	Interpretation[b]	p-value[1] B-F1 B-F2	Interpretation[c]
FSFI										
Desire	RF	3.01 ± 1.16	3.77 ± 1.13	3.80 ± 1.13	0.270	-	**0.001**	Increase between	0.092	-
	PFMT	3.41 ± 1.26	3.87 ± 1.12	4.04 ± 1.00	0.121			baseline and F1 and F2 in both groups.	0.481	
Arousal	RF	3.39 ± 1.23	4.23 ± 1.34	4.00 ± 1.14	0.283	-	**0.001**	Increase between	0.460	-
	PFMT	3.73 ± 1.26	4.43 ± 1.07	4.49 ± 1.06	0.055			baseline and F1 and F2 in both groups.	0.470	
Lubrication	RF	4.06 ± 1.30	4.94 ± 1.23	4.61 ± 1.15	0.223	-	**0.001**	Increase between	0.111	-
	PFMT	4.52 ± 1.34	5.00 ± 1.09	4.97 ± 1.03	0.062			baseline and F1 and F2 in both groups.	0.592	
Orgasm	RF	3.56 ± 1.44	4.50 ± 1.38	4.46 ± 1.29		-	**0.001**			-

	PFMT	3.91 ± 1.44	4.39 ± 1.47	4.58 ± 1.38	0.652 0.352			Increase between baseline and F1 and F2 in both groups.	0.100; 0.489	
Satisfaction	RF	4.15 ± 1.36	4.83 ± 1.07	4.70 ± 1.34	0.474	-	**0.001**	Increase between	0.962	-
	PFMT	4.04 ± 1.45	4.68 ± 1.31	4.91 ± 1.18	0.968			baseline and F1 and F2 in both groups.	0.159	
Pain	RF	4.26 ± 1.58	4.95 ± 1.19	4.92 ± 1.16	0.055	Greater values	**0.001**	Increase between	0.792	-
	PFMT	4.86 ± 1.26	5.32 ± 1.20	5.33 ± 1.02	**0.041**	in the PFMT group at F2.		baseline and F1 and F2 in both groups.	0.777	
Total Score	RF	22.42 ± 6.71	27.21 ± 5.93	26.50 ± 5.49	0.387	-	**0.001**	Increase between	0.266	-
	PFMT	24.48 ± 5.80	27.68 ± 5.58	28.32 ± 5.20	0.082			baseline and F1 and F2 in both groups.	0.667	
ICIQ-Vaginal Symptoms										
Vaginal	RF	17.07 ± 7.19	10.67 ± 7.79	10.17 ± 8.17	0.303	-	**0.001**	Decrease between	0.262	-
Symptoms	PFMT	13.83 ± 7.89	7.23 ± 7.15	9.82 ± 8.91	0.338			baseline and F1 and F2 in both groups.	0.231	
Sexual Matter	RF	25.98 ± 20.31	15.98 ± 19.18	15.64 ± 19.27	0.994	-	**0.001**	Decrease between	0.553	-
	PFMT	26.69 ± 21.59	11.77 ± 17.28	14.20 ± 16.62	0.996			baseline and F1 and F2 in both groups.	0.647	

Quality of Life	RF	6.24 ± 3.51	3.07 ± 3.39	3.67 ± 3.75	0.886	-	**0.001**	Decrease between	0.293	-
	PFMT	5.29 ± 3.54	2.37 ± 3.38	4.16 ± 5.30	0.769			baseline and F1 and	0.466	
								F2 in both groups.		
Question 4 -	RF	2.38 ± 0.79	1.31 ± 0.90	1.33 ± 1.00	0.692	-	**0.001**	Decrease between	0.100	-
Vaginal Laxity	PFMT	2.06 ± 0.84	1.06 ± 1.06	1.36 ± 1.09	0.556			baseline and F1 and	0.197	
								F2 in both groups.		
FSDS-R Total	RF	24.74 ± 15.13	15.88 ± 13.46	16.71 ± 14.34	0.326	-	**0.001**	Decrease between	0.451	-
	PFMT	28.42 ± 14.74	17.42 ± 13.97	16.33 ± 14.23	0.594			baseline and F1 and	0.207	
								F2 in both groups.		
ICIQ-SF Total	RF	8.45 ± 7.13	4.31 ± 5.32	4.60 ± 5.59	0.204	-	**0.001**	Decrease between	0.828	-
	PFMT	10.16 ± 6.36	5.64 ± 6.77	5.87 ± 6.57	0.238			baseline and F1 and	0.647	
								F2 in both groups.		
Modified	RF	2.57 ± 0.63	2.81 ± 0.67	2.79 ± 0.72	**0.001**	Higher values in	**0.001**	Increase between	**0.001**	Increase between
Oxford Scale	PFMT	2.73 ± 0.86	4.11 ± 1.01	4.07 ± 1.05		the PFMT group		baseline and F1 and		assessments in the
						at F1 and F2.		F2 in both groups.		PFMT group.
POP-Q										
Aa	RF	- 2.44 ± 0.44	- 2.50 ± 0.38	- 2.52 ± 0.41	0.201	-	**0.001**	Higher values in the	**0.001**	Decrease between
	PFMT	- 2.47 ± 0.34	- 2.69 ± 0.34	- 2.67 ± 0.35	0.360			RF group at F1.	0.067	baseline and F1 in the
								Decrease between		PFMT group, and
										decrease between

							baseline and F2 in the PFMT group.		assessments in the PFMT group.
Ba	RF	- 2.48 ± 0.44	- 2.56 ± 0.42	- 2.56 ± 0.40	0.699	-	**0.001**	Decrease between baseline and F1 and F2 in the PFMT group.	**0.002**	Decrease between assessments in the PFMT group.
	PFMT	- 2.41 ± 0.42	- 2.69 ± 0.39	- 2.68 ± 0.37	0.767		**0.021**			
Ap	RF	- 2.87 ± 0.25	- 2.88 ± 0.24	- 2.83 ± 0.31	0.647	-	0.052		0.191	Higher values in the RF group at F2; Decrease between baseline and F2 in the PFMT group, and decrease between evaluations in the PFMT group.
	PFMT	- 2.86 ± 0.27	- 2.93 ± 0.17	- 2.96 ± 0.14	0.251		0.165		**0.036**	
Bp	RF	- 2.85 ± 0.36	- 2.88 ± 0.27	- 2.86 ± 0.28	0.596	-	0.093		0.540	-
	PFMT	- 2.88 ± 0.24	- 2.93 ± 0.17	- 2.96 ± 0.14	0.238		0.155		0.132	
C	RF	- 6.73 ± 1.30	- 7.02 ± 1.12	- 7.02 ± 1.09	0.206	-	**0.001**	Decrease between baseline and F1 and F2 in both groups.	0.457	-
	PFMT	- 6.90 ± 1.23	- 6.97 ± 2.64	- 7.28 ± 1.04	0.184		**0.002**		0.473	
D	RF	- 7.64 ± 3.65	- 7.87 ± 3.69	- 7.80 ± 3.66		-				-

	PFMT	- 8.07 ± 2.93	- 8.32 ± 2.98	- 8.74 ± 1.00	0.464 0.305		**0.028** 0.051	Decrease between baseline and F1 in the RF group.	0.821 0.491	
TVL	RF	9.87 ± 1.05	9.99 ± 1.04	9.45 ± 3.37	0.385	-	0.162		0.742	-
	PFMT	9.67 ± 0.95	9.76 ± 1.01	8.84 ± 4.43	0.420		0.577		0.968	
Genital Hiatus	RF	3.06 ± 0.61	2.88 ± 1.07	3.05 ± 0.50	0.390	-	0.298		0.612	-
	PFMT	2.96 ± 0.61	2.92 ± 0.50	2.86 ± 0.55	0.186		0.311		0.443	
Perineal Body	RF	3.25 ± 0.45	3.31 ± 0.44	3.17 ± 0.41	0.461	-	0.948	Decrease between	0.382	-
	PFMT	3.39 ± 0.51	3.33 ± 0.51	3.29 ± 0.51	0.268		**0.005**	baseline and F2 in the PFMT group.	0.856	

* Variables transformed into ranks in the analyzes due to the absence of a Normal distribution; RF: Radiofrequency; PFMT: Pelvic Floor Muscle Training; FSFI: Female Sexual Function Index; ICIQ: International Consultation on Incontinence Questionnaire; VS: Vaginal Symptoms; Q.4: Question number 4; POP-Q: Pelvic Organ Prolapse Quantification; FSDS-R: Female Sexual Distress Scale – Revised; [a] Significant differences between groups (Tukey's test); [b] Significant differences between assessment periods (profile test by contrast); [c] Interaction effect: delta Radiofrequency, delta PFMT: Radiofrequency≠ PFMT.; SD: Standard deviation; B: Baseline assessment; F1: Follow-up 1 assessment (30 days post-intervention); F2: Follow-up 2 assessment (6 Months post-intervention); [1] ANOVA for repeated measures with variables transformed into ranks due to the absence of normal distribution;

Figure 1

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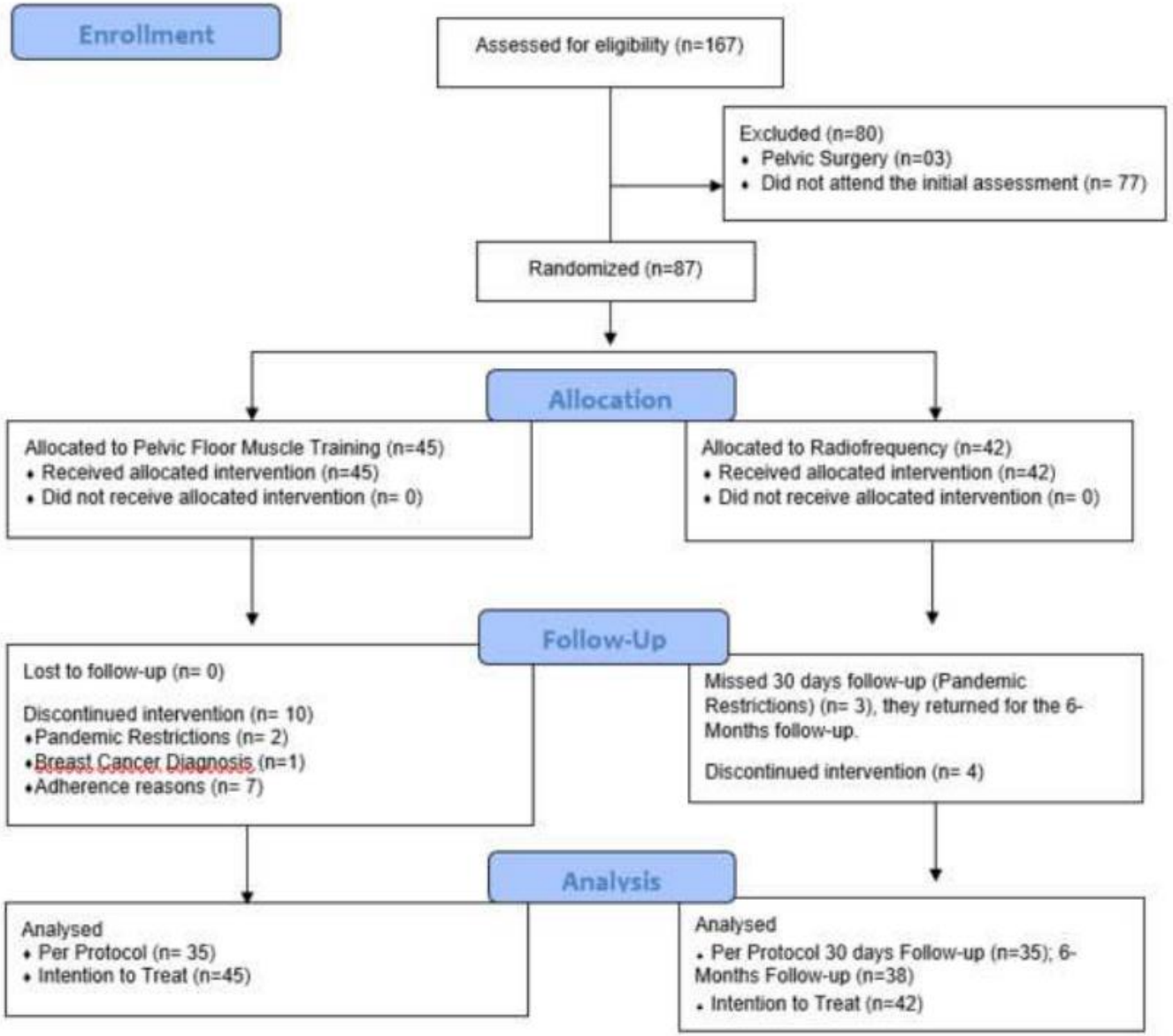

Figure 2

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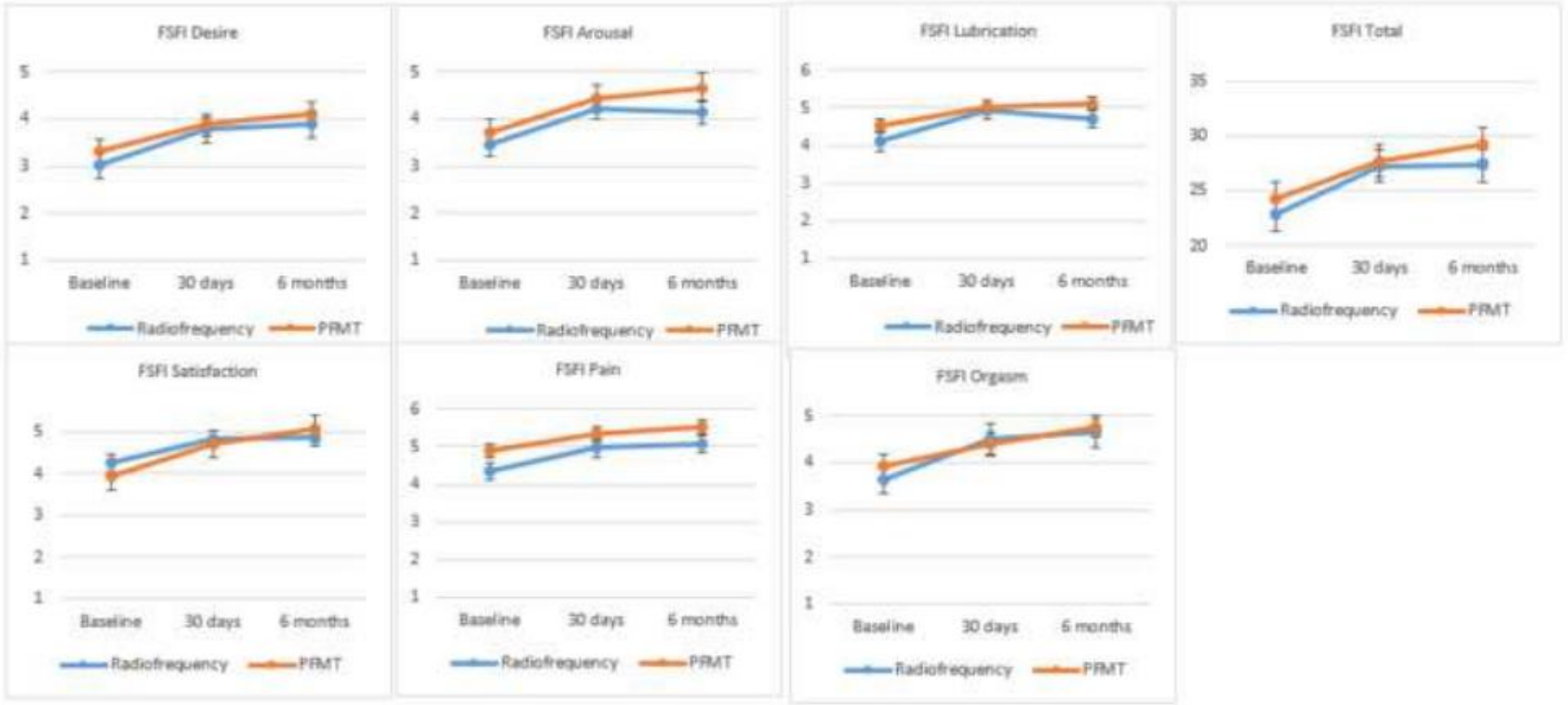

Figure 3

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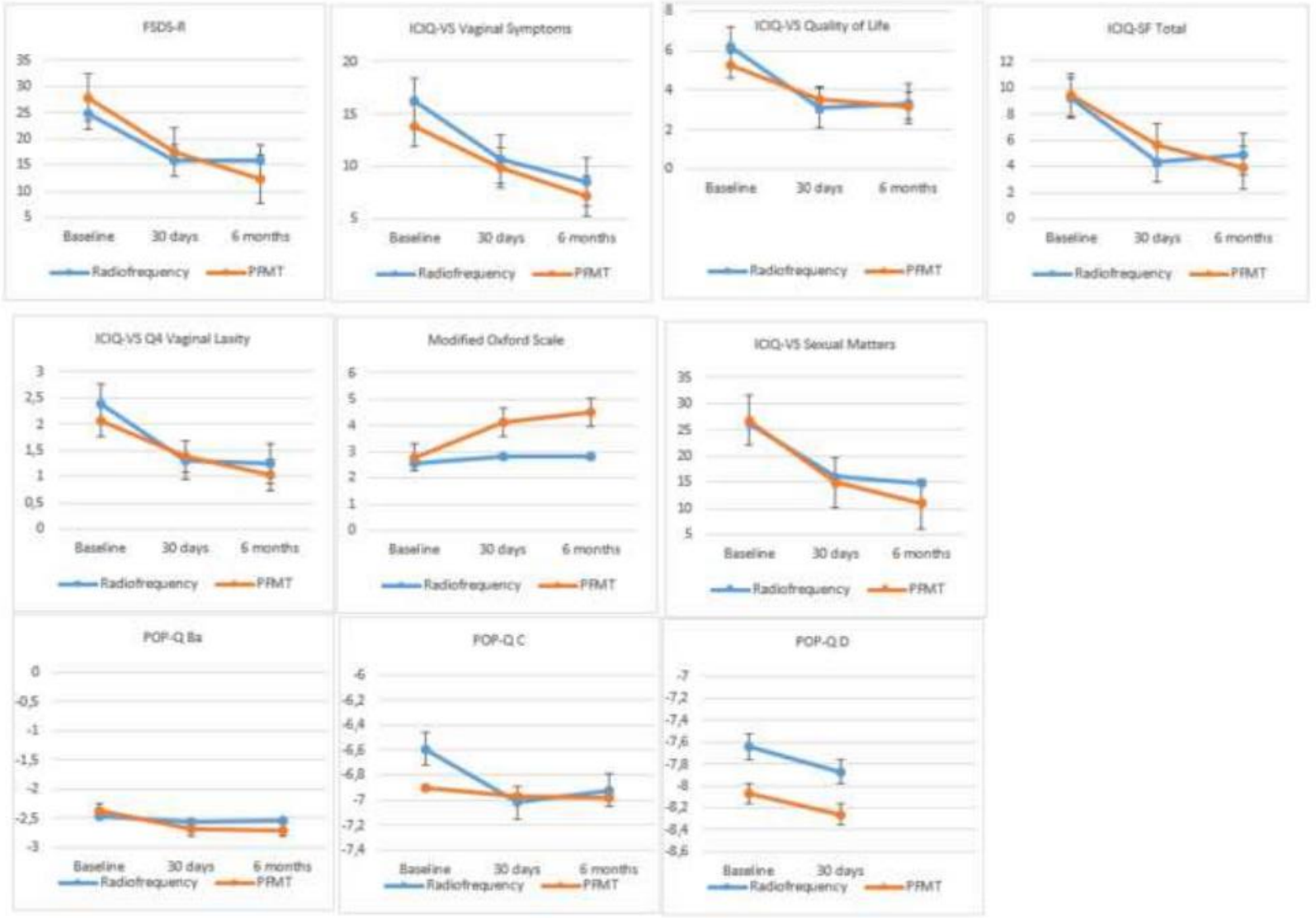

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	6
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6-7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	7-10
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	10-11
	6b	Any changes to trial outcomes after the trial commenced, with reasons	10-11
Sample size	7a	How sample size was determined	11-12
	7b	When applicable, explanation of any interim analyses and stopping guidelines	11-12
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	11-12
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	11-12
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	11-12
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	11-12
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	11-12

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	6
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6-7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	7-10
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	10-11
	6b	Any changes to trial outcomes after the trial commenced, with reasons	10-11
Sample size	7a	How sample size was determined	11-12
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Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	11-12
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4.6.1 Protocolo de Estudo: *Effect of radiofrequency and pelvic floor muscle training in the treatment of women with vaginal laxity: A study protocol*

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Glaucia Varella

--

Gláucia Varella, Physiotherapist
Masters in Women's Health - Dept Obstetrics and Gynecology - UFMG
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PLOS ONE

STUDY PROTOCOL

Effect of radiofrequency and pelvic floor muscle training in the treatment of women with vaginal laxity: A study protocol

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OPEN ACCESS

Citation: Pereira GMV, Juliato CRT, de Almeida CM, de Andrade KC, Fante JF, Martinho N, et al. (2021) Effect of radiofrequency and pelvic floor muscle training in the treatment of women with vaginal laxity: A study protocol. PLoS ONE 16(11): e0259650. https://doi.org/10.1371/journal.pone.0259650

Editor: Jose María Blasco, Universitat de Valencia, SPAIN

Received: March 17, 2021

Accepted: October 19, 2021

Published: November 9, 2021

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0259650

Funding: The first author GMVP receives Scholarship Grant from the São Paulo Research Foundation (FAPESP) - Grant 2019/26723-5.

Abstract

Background

Vaginal laxity is an underreported condition that negatively affects women's sexual function and their relationships. Evidence-based studies are needed to better understand this complaint and to discuss its treatment options. Thus, we present a study protocol to compare the effect of radiofrequency and pelvic floor muscle training in the treatment of women with complaints of vaginal laxity.

Methods/Design

This is a prospective, parallel-group, two-arm, randomized clinical trial (Registry: RBR-2zdvfp–REBEC). Participants will be randomly assigned to one of the two groups of intervention (Radiofrequency or Pelvic Floor Muscle Training). The study will be performed in the Urogynecology outpatient clinic and in the physiotherapy outpatient clinic at the State University of Campinas–UNICAMP and will include women aged $\geq$ 18 years and with self-reported complaints of vaginal laxity. Participants will be assessed at baseline (pre-intervention period) and will be followed up in two periods: first follow-up (30 days after intervention) and second follow-up (six months after intervention).

Expected results

The results of this randomized clinical trial will have a positive impact on the participants' quality of life, as well as add value to the development of treatment options for women with complaints of vaginal laxity.

Trial registration

Registry: RBR-2zdvfp–Registro Brasileiro de Ensaios Clínicos–REBEC (19/02/2020).

Competing interests: The authors declare no competing Interests.

Abbreviations: IUGA, International Urogynecological Association; ICS, International Continence Society; PFMT, Pelvic Floor Muscle Training; RF, Radiofrequency; CAISM, State University of Campinas–UNICAMP; VLQ, Vaginal Laxity Questionnaire; GRA, Global Response Assessment; FSFI, Female Sexual Function Index; FSDS-R, Female Sexual Distress Scale-Revised; ICIQ-VS, International Consultation on Incontinence Questionnaire—Vaginal Symptoms; ICIQ-SF, International Consultation on Incontinence Questionnaire Short-Form; POP-Q, Pelvic Organ Prolapse Quantification; PFMS, Pelvic Floor Muscle Strength; PFMM, Pelvic Floor Muscle Morphometry; VT, Vaginal Thickness.

Introduction

Vaginal laxity (VL) is defined by the International Urogynecological Association (IUGA) and the International Continence Society (ICS) as a complaint of excessive vaginal flaccidity [1]. This condition is rarely discussed between patients and their doctors, possibly due to the lack of evidence-based treatments, embarrassment and lack of knowledge in the assessment of this condition [2]. According to urogynecologists, VL still presents itself as an underreported condition with reports of discomfort that can affect sexual function and relationships [3, 4]. The way women perceive their genitalia has a strong and positive impact on their sexual function [5].

The prevalence of VL is 24% and appears to be associated with younger age, vaginal births, pelvic organ prolapse (POP) symptoms or physical exam findings. Therefore, it is a somatic, not psychogenic, dysfunction [6].

It is speculated that pregnancy and childbirth play a role in VL [3]. Although there is no proven link between VL and childbirth, research shows that vaginal delivery can result in pelvic floor injury [6, 7]. Pelvic floor and vagina trauma during pregnancy and vaginal delivery can lead to the lengthening of the vaginal opening leading to permanent changes in sexual and physical sensitivity during sexual intercourse. These changes promote an important reduction in the quality of life of women and their partnership [8, 9].

Potential consequences associated with vaginal delivery that extend beyond the postpartum period are urinary incontinence (UI), POP, chronic pelvic pain (CPP), and sexual dysfunction [10–13]. Not all women adapt to the psychological and physical changes in the postpartum period, which can lead to changes in the emotional relationship with their partner [14]. Both vaginal delivery and levator ani muscle trauma are associated with an increase in the diameter of the genital hiatus [15]. The genital hiatus is limited by the puborectalis muscle, a component of the levator ani muscle, and appears to play an important role in defining the high vaginal pressure zone [16]. Avulsion of the levator ani muscle, especially if proven bilaterally, would have some effect on female sexual function [17].

The diagnosis of VL has been based on patients' self-reporting. A comprehensive medical history, physical examination and psychosexual assessment are the initial steps to properly identify patients with VL [18].

The reduction in vaginal sensation during sexual intercourse may be related to anatomical damage to the perineal body, POP stage 1, laxity of the vaginal canal or introitus, damage to the nerves and connective tissue during pregnancy and childbirth or, potentially, a combination of these factors [19].

Surgical and non-surgical treatments for VL have been proposed. Surgical procedures for VL such as posterior colporrhaphy or perineorrhaphy are more commonly recommended. These procedures aim to reduce the size of the vaginal introitus, not necessarily treating the VL pathophysiology. Besides, 83% of the interviewed urogynecologists reported concerns with a potential risk for post-operative dyspareunia [3]. Post-surgical dyspareunia would further impair the quality of life of a woman who already complained of sexual dysfunction. Thus, it is necessary to develop non-surgical techniques that can assist in the treatment of other factors associated with VL, such as muscle hyperdistensibility and not just surgically reducing the size of the genital hiatus.

A non-surgical option for the treatment of VL includes pelvic floor muscle training (PFMT), which was initially recommended as a first-line treatment for UI [2, 20]. Pelvic floor muscle function appears to play an important role in female sexual function, and contraction of the levator ani muscle appears to increase the sexual response [21]. The contraction of the pelvic floor muscles also plays an important role in the female orgasmic response. Women

with weak muscles who receive pelvic floor rehabilitation and strengthen the muscles in that region perceive a positive effect on their sex life [22]. Pelvic floor muscle training could have an effect on the hypertensile muscles of women complaining of VL.

Another non-surgical therapeutic possibility to treat VL is radiofrequency (RF). Despite the scarcity of controlled clinical trials to evaluate the therapeutic advantages, safety and efficacy of radiofrequency [23], the studies carried out to date have shown good tolerance, as well as, subjective improvement of vaginal narrowing, sexual function and decreased sexual discomfort [2] with effects maintained by 12 months and without any adverse events [8]. RF seems to improve vaginal vascularization and collagen fiber reorganization, which may also contribute to a decrease in the sensation of VL [24].

To our knowledge, to date, no clinical trial has been developed to assess the role of pelvic floor muscle and radiofrequency training in VL. Thus, the general objective will be to compare the effect of RF and PFMT in women with VL symptoms. The specific objectives are related to the assessment of the sexual function, vaginal symptoms, and sexual distress, as well as, to assess the impact of UI on patients' quality of life. The POP staging, contractility, and pelvic floor muscle function will be also evaluated. Finally, we will assess the impression of improvement in VL complaints after the interventions.

Our hypothesis is that RF will be different from PFMT in treating women with VL symptoms.

Materials and methods

Trial design

This is a prospective, parallel-group, two-arm, randomized clinical trial. It involves three assessments in which primary and secondary outcomes will be evaluated: one pre-intervention visit, one 30-day post-intervention visit, and a six-month consultation after the intervention. Participants will be randomly assigned to one of the two groups of intervention (RF or PFMT). The study will follow the CONSORT recommendations [25] and the SPIRIT Statement (Standard Protocol Items: Recommendations for Interventional Trials) [26]. Fig 1 shows the detailed study steps.

The term VL was recently defined and little is known about this complaint. There is still no gold standard treatment for VL and further studies are needed to understand its pathophysiology. Although its pathophysiology is not completely known, there is a consensus on the association of VL with pregnancy and childbirth [2, 10, 27]. Some proposed mechanisms involve overstretching of the vaginal walls and introitus during vaginal birth and an increase in levator ani hiatal dimensions resulting from macro and microtrauma of the levator ani muscle [7, 17]. Although supervised PFMT is recommended as a first-line treatment for stress or mixed UI in women by most of the guidelines [28–30], more studies are needed to demonstrate the effect of PFMT on female sexual function. A randomized controlled trial concluded that women reporting improvement in sexual function demonstrated greatest increase in PFM strength and endurance [31].

Regarding RF, a recent randomized, multicenter, sham-controlled clinical trial found a statistically significant and clinically important improvement of VL with RF when compared with Sham treatment [32]. In our study, RF will be applied once every 4 weeks (a total of three applications) and will probably be less likely to face problems related to treatment adherence when compared to PFMT. Although the RF procedure has been shown to be well tolerated, adverse effects may occur [32, 33]. PFMT is generally free of adverse effects.

Study setting

Patient recruitment and assessment/treatment will be carried out in the Urogynecology outpatient clinic at the School of Medical Sciences and in the Physiotherapy outpatient clinic at the

	STUDY PERIOD							
	Enrolment	*Baseline*	Post-allocation: Allocation, Interventions, Follow-up					
TIMEPOINT**	*February 2020 to June 2021*	0	Allocation	*1-4 w*	*5-8 w*	*9-12 w*	*F1*	*F2*
ENROLMENT:								
Eligibility criteria	X							
Recruitment	X							
Initial Assessment	X							
Informed consent	X							
Allocation			X					
INTERVENTIONS:								
Radiofrequency				♦—	—	—♦		
PFMT				♦—	—	—♦		
ASSESSMENTS:								
Sociodemographic Data		X						
Medical History		X						
BMI		X						
Sexual life Data		X						
Obstetric History		X						
Urinary/Intestinal Habits		X						
Physical Examination		X					X	X
Female Sexual Function Index		X					X	X
Female Sexual Distress Scale-Revised		X					X	X
ICIQ-VS and ICIQ-SF		X					X	X
Ultrasound Examination		X					X	X
Global Response Assessment							X	X
Adverse Events				X	X	X	X	X

Fig 1. Description of the study steps. F1: Follow-up (30 days after intervention); F2: Follow-up (6-months after intervention); w: week; PFMT: Pelvic Floor Muscle Training; BMI: Body Mass Index; ICIQ-VS: International Consultation on Incontinence Questionnaire—Vaginal Symptoms; ICIQ-SF: International Consultation on Incontinence Questionnaire Short-Form.

https://doi.org/10.1371/journal.pone.0259650.g001

Centro de Atenção Integral à Saúde da Mulher (CAISM)—Hospital da Mulher Professor Dr. José Aristodemo Pinotti, both units affiliated to the State University of Campinas—UNICAMP.

Study population

Women with self-reported complaints of VL. There is no objective and standardized diagnostic evaluation for VL and its pathophysiological mechanism is not yet known [34].

Sample size

The sample calculation was based on the study by Krychman *et al.* [32], who demonstrated that RF therapy was associated with significant clinical and statistically significant improvement in sexual function in women with VL, when data analysis was performed in a group containing 73 patients. To calculate the sample of the present study, we used values of sexual function assessed using the FSFI questionnaire. There was an increase of 7 points in the FSFI score in the group treated with radiofrequency and an increase of 3 points in the control group. When considering a study power of 80%, an alpha of 0.05 with two-tailed test, it was found that the minimum number of participants required in each group will be added to a percentage of 30% loss in the sample, totaling 68 women, 34 in each group (isolated RF and isolated PFMT).

Eligibility criteria

We will include women aged $\geq$ 18 and $\leq$ 60 years, with VL complaints assessed by direct question (yes / no) and by the VLQ [2] (very loose, moderately loose, slightly loose), and willing to attend treatments on the scheduled date and places.

Participants who present the following conditions will be excluded from the study: use of a pacemaker; decompensated heart disease; cognitive deficit; peripheral or central neurological disorders; the presence of any type of cancer; the presence of cervical dysplasia; history of active urinary or vaginal infection; decompensated metabolic diseases; patients undergoing physical therapy for pelvic floor disorders; patients using vaginal estrogen in the last 6 months; patients already undergoing surgery for prolapse or urinary or anal incontinence; patients with stage 2 POP onwards; force of contraction of the pelvic floor muscles equal to zero according to the modified Oxford scale [35].

Recruitment

Women will be recruited from the Urogynecology outpatient clinic (CAISM / UNICAMP) and by social media advertisements, publicity posters, and printed ads from this study. All patients will be contacted by telephone by the researcher who applies the eligibility criteria and sends the VLQ via email or virtual communication platforms. The recruited participants will have their names, contact numbers, and VLQ responses recorded in a spreadsheet. A contact telephone with a virtual communication platform specific to this study is available for participants to contact the researchers whenever necessary. Participants will later be called by phone for the initial assessment. Participants interested in the study who did not pass the eligibility criteria are referred to the Urogynecology outpatient clinic for follow-up.

Allocation

The randomization sequence will be carried out through a computer program, in a 1:1 allocation ratio, in two blocks. The numbers corresponding to the study groups (1. Radiofrequency

and 2. Pelvic Floor Muscle Training) will be placed in opaque sealed envelopes that will be opened by the study participants after signing the consent form and undergoing initial assessment in the first clinical visit.

The researchers who will assist in completing the questionnaires and physical examination, the researchers responsible for ultrasound and the data analysts will be blinded for the treatment group to which the participants were randomized to.

Initial assessment (first clinical visit)

Patients registered on the recruitment spreadsheet will be contacted by phone and the initial evaluation will be scheduled. In the initial evaluation, the participants will go through a lecture given by the researcher (G.M.V.P) in order to present the study, the assessments, the interventions, and the follow-up periods. At this point, the participants will be able to have all questions answered about the study. Participants who agree to participate in the study will receive a consent form for reading and signing. Participants will have their personal details protected and a number will substitute their identities.

Interventions

The intervention period for both groups will be 12 weeks.

1- Radiofrequency. The RF group will receive three radio frequency applications at 4-week intervals, (an initial application, a second application after four weeks, and a third application also after four weeks) comprising 12 weeks of intervention. The four-week period between applications will allow adequate healing of the vaginal tissues submitted to the application of radiofrequency. The procedure will be performed by a trained researcher (G.M.V.P) with a supervision of an experienced urogynecologist (C.R.T.J/L.G.O.B).

The Wavetronic 6000 Touch device with the Megapulse HF FRAXX system (Loktal Medical Electronics, São Paulo, Brazil) will be used, equipped with an electronic energy fractionation circuit, connected to a vaginal electrode with 64 microneedles 200μ in diameter and 1mm in length, and divided into an array of eight columns, with eight needles each. When pressing the trigger pedal, these 64 needles are not energized simultaneously and the energy release is randomized in columns of eight needles in a predefined sequence, which does not allow two adjacent columns to fire in sequence, preventing the thermal sum of the columns (control fractional firing system (*Smart Shoot*). This allows for cooling between the points and the preservation of tissues adjacent to the vaporized points, so that neocolagenesis and neoelastogenesis can occur, through fibroblastic stimulation [24].

1.1-Procedure. Topical anesthesia in the posterior vestibule and vaginal opening (mucosa) with 2% lidocaine gel, 2 to 3 minutes before the procedure (Table 1). A patient in a lithotomy position, with the lower limbs flexed and supported, will be introduced a disposable (high-impact polystyrene) vaginal speculum. A careful vaginal examination will be performed for any changes in the vaginal wall. Whiff test will be performed using a swab to collect vaginal discharge. A drop of 10% potassium hydroxide will be added over the vaginal secretion [36]. If a characteristic fishy odor is felt, the patient will not undergo RF and will be referred for evaluation of possible vaginosis. If the vaginal wall is intact and the whiff test is negative, the procedure will be continued, starting with topical anesthesia of the vaginal walls with 10% lidocaine spray. After 2 minutes, vaginal antisepsis with 2% aqueous chlorhexidine and cleaning with sterile 0.9% saline will be performed. After cleaning, the entire liquid content of the serum will be wiped with sterile gauze before starting to apply the RF.

The device will be calibrated in FRAXX mode, 45 Watts, Low (initial application) and Medium (second and third application) Energy program (40 and 60 milliseconds,

Table 1. Pelvic floor muscle training and radiofrequency sessions according to the treatment duration.

Period	Interventions			
	Radiofrequency	**Pelvic Floor Muscle Training**		
1 to 4 weeks	1st application	1st phase	2nd phase	3rd phase
	• 2% Lidocaine Gel • Vaginal Examination with speculum • Whiff Test • 10% lidocaine spray • Cleaning: 2% aqueous chlorhexidine and sterile 0.9% saline • RF: 45Watts, Low Energy program (40 milliseconds) • Post-procedure orientation: 10-day sexual abstinence	• PFM maximum contraction (6 r / sustained 6 s/ 6 s rest: 1 time). Supine position. • PFM maximal contraction + transverse contraction (6 r / sustained 6 s/ 6 s rest: 1 time). Supine position. • PFM maximal contraction + hip elevation (6 r / sustained 6 s/ 6 s rest: 1 time). Supine position.	• PFM maximum contraction (1 cough / 3 r). Supine position. • PFM maximal contraction with the lower limbs extended and abducted (6 r / sustained 6 s/ 6 s rest: 2 times). Supine position. • PFM contraction in three stages—mild, moderate, maximum (6 r: 2 times). Sitting position. • PFM maximal contraction (6 r / sustained 6 s/ 6 s rest: 2 times). Standing position.	• Pelvic mobilization (anterior and posterior tilts, lateral tilts and rotation of the pelvis). Standing position. No PFM contraction in this phase. 10 repetitions each pelvic movement.
5 to 8 weeks	2nd application Same procedure (above)	• PFM maximum contraction (6 r / sustained 8 s/ 8 s rest: 1 time). Supine position. • PFM maximal contraction + transverse contraction (6 r / sustained 8 s/ 8 s rest: 1 time). Supine position. • PFM maximal contraction + hip elevation (6 r / sustained 8 s/ 8 s rest: 1 time). Supine position.	• PFM maximum contraction (2 cough / 3 r). Supine position. • Fast PFM maximal (8 r: 2 time). Supine position. • PFM contraction in six stages—mild, moderate, maximum–maximum, moderate, mild (8 r: 2 times). Sitting position. • PFM maximal contraction (8 r /sustained 8 s/ 8 s rest: 2 times). Standing position. • PFM maximal contraction (8 r /sustained 8 s/ 8 s rest: 2 times). Four supports (hands and knees).	• Same Intervention (above)
9 to 12 weeks	3rd application Same procedure (above)	• PFM maximum contraction (6 r / sustained 10 s: 1 time). Supine position. • PFM maximal contraction + transverse contraction (6 r / sustained 10 s/ 10 s rest: 1 time). Supine position. • PFM maximal contraction + hip elevation (6 r / sustained 10 s/10 s rest: 1 time). Supine position.	• PFM maximum contraction (3 cough / 3 r). Supine position. • Fast PFM maximal (10 r: 2 time). Sitting position. • PFM contraction in six stages—mild, moderate, maximum–maximum, moderate, mild (10 r: 2 times). Sitting position. • PFM maximal contraction (10 r /sustained 10 s/10 s rest: 2 times). Standing position. • PFM maximal contraction (10 r /sustained 10 s/10 s rest: 2 times). Four to two supports (right hand and left knee/ left hand and right knee).	• Same Intervention (above)

https://doi.org/10.1371/journal.pone.0259650.t001

respectively), and the fractional vaginal electrode will be used. Applications will be under direct view. The electrode will be lightly pressed against the mucosa, without pressing, so that all microneedles are in uniform contact with the tissue. The application will be carried out sequentially on the lateral vaginal walls, in rows, avoiding overlapping, starting from the proximal third of the vagina to the distal third in the vestibule exposed by the opening of the speculum. The speculum will be gently rotated to the anteroposterior position for the application of the anterior and posterior vaginal walls. At the end of the procedure, the speculum will be gently removed. Patients will be advised on post-treatment care and the use of 5% dexpanthenol cream in the vaginal opening is recommended two to three times daily if there is any discomfort in the region for 2 to 3 days and interrupt sexual intercourse for 10 days. Patients will

be instructed to contact the researchers if they experience any discomfort or notice any changes in vaginal discharge. These patients will be evaluated by an experienced gynecologist. There will be three vaginal applications at 4-week intervals, totaling 12 weeks of treatment.

2- Pelvic floor muscle training. The patients in the PFMT group will be assisted during the sessions by an experienced physiotherapist (G.M.V.P). The participants of this group will have 12 individual sessions of supervised PFMT, lasting 40–60 minutes, once a week, and totaling 12 weeks of treatment and continue their treatment with home PFMT program. To follow the treatment at home, patients will receive a printed diary containing the complete PFMT program, with figures illustrating the positions and orientations for each exercise for the pelvic floor muscles. Patients will have the possibility to contact the physiotherapist for questions regarding home treatment by video call, audio call or messages through a telephone number made available exclusively for the study. Patients will be instructed not to perform other exercises for the pelvic floor, different from the exercises proposed by the intervention program of the present study. Our intervention program for PFMT is based on the studies of Bo *et al.* [37] and Dumoulin *et al.* [38].

2.1- Procedure. The first PFMT session is longer and focused on the careful evaluation of the pelvic floor muscles in order to identify any muscle condition that interferes with the progress of the intervention; guidance on the correct performance of the pelvic floor muscle contraction with the aid of vaginal palpation and educational material; presentation of the PFMT program; and finally, the first sequence of exercises.

Patients will be instructed to perform three phases of exercise in each session, with at least two sessions of the PFMT program per day (Table 1). The exercises will undergo progression every 4 weeks of intervention, totaling three progressions (6 repetitions, sustained for 6 seconds, 6 seconds for rest, 8 repetitions, sustained for 8 seconds, 8 seconds for rest, and 10 repetitions, sustained for 10 seconds, 10 seconds for rest). The first phase comprises three exercises of maximum contraction of the pelvic floor muscles in the supine position, with the lower limbs semiflected and the feet supported, associated with contraction transverse exercise, and hip elevation. The second phase comprises pre-contraction of the pelvic floor muscles associated with cough; maximum sustained contraction in the supine position with the lower limbs extended and abducted; fast contractions in both supine and sitting positions, contraction in three stages (mild, moderate, maximum) in a sitting posture; maximum sustained contraction in standing posture and four supports (hands and knees). The third phase comprises the relaxation period with breathing exercises associated with pelvic mobilization in a standing posture. No pelvic floor muscles contraction in this phase. Patients will be instructed on the importance of adhering to the PFMT. In case of two absences, the patients will be contacted and their permanence in the study will be reassessed.

Primary outcomes

The primary outcome will be the indication of improvement in the VL symptoms after the proposed interventions assessed through a single question with seven possible answers. The Global Response Assessment (GRA) [2] is a 7-level scale with response to the question: "How are you now (levels of vaginal laxity/tightness and sexual satisfaction) compared to before treatment" (markedly improved, moderately improved, slightly improved, no change, slightly worse, moderately worse, markedly worse?). This scale item has been already used to evaluate improvement in vaginal laxity symptoms after treatment [2].

Secondary outcomes

The description of secondary outcomes is described below together with their measurement instruments.

Female Sexual Function Index (FSFI) [39]: a brief and multidimensional instrument to assess sexual function in women. The questionnaire was developed and validated by Rosen *et al.* and consists of 19 items that investigate sexual response over the past four weeks and performance in six domains: sexual desire, arousal, lubrication, orgasm, satisfaction, and pain [39]. The validation in Portuguese took place in 2008 by Thiel *et al.* [40]. The answers are scored according to the sum of the items that make up each domain (simple score) and multiplied by the domain factor generating the weighted score [40]. The maximum score is 36 points, adding up the total of each domain. Wiegel *et al.* proposed a cut-off score to differentiate women with or without sexual dysfunction in the amount of 26.55 [41].

Female Sexual Distress Scale-Revised (FSDS-R): a self-report questionnaire with 13 questions scored on a 5-point Likert scale from 0 (never) to 4 (always) to assess the sexual distress. Sexual distress is characterized by a set of feelings (for example, unhappiness, guilt, frustration, stress, worry) and emotions that individuals have about their sexuality. It differs from sexual dysfunction related to symptoms of sexual function, such as arousal, orgasm and pain, separate from emotions [42]. The Portuguese translation was developed by Berenguer *et al.* [43].

International Consultation on Incontinence Questionnaire—Vaginal Symptoms (ICIQ-VS): is a 14-item questionnaire validated for the Portuguese language by Tamanini *et al.* that assesses the presence and the impact of vaginal symptoms, as well as their relationship with quality of life [44, 45].

International Consultation on Incontinence Questionnaire Short-Form (ICIQ-SF): validated in Portuguese by Tamanini *et al.*, is a simple, brief, and self-administered questionnaire, capable of quickly and effectively assessing the impact of urinary incontinence on patients' quality of life. It consists of four questions that assess the frequency, severity, and impact of urinary incontinence. Your score can vary from 0 to 21, the greater the commitment, the higher the total value [46, 47].

Pelvic Organ Prolapse Quantification (POP-Q): the ICS recommends POP description and staging using this instrument [48, 49]. The staging classification is defined as [50] Stage 0: there is no demonstrated prolapse; Stage I: the most distal part of the prolapse is more than 1 cm above the level of the hymen; Stage II: the most distal portion of the prolapse is between 1 cm above the hymen and 1 cm below the hymen; Stage III: the most distal portion of the prolapse is more than 1 cm beyond the plane of the hymen, but everted at least 2 cm less than the total vaginal length; Stage IV: complete eversion or eversion of up to 2 cm from the total length of the lower genital tract. The hymen is the reference point used to describe the quantitative prolapse and represents the zero point. Six anatomical points will be evaluated with the aid of a disposable graduated ruler. Two on the anterior vaginal wall (Aa and Ba). Two on the posterior vaginal wall (Ap and Bp) and two points on the upper vagina (C and D). The genital hiatus, the total vaginal length and the perineal body will also be measured. All points will be measured in Valsalva maximum, except the total vaginal length [50]. The ICS clinically defined significant POP in stage II or higher [49, 50].

Pelvic Floor Muscle Strength (PFMS): the strength of the pelvic floor muscles will be graduated according to the modified Oxford scale (5-point) by means of bi-digital vaginal palpation with the patients in the supine position with the lower limbs supported [35].

Pelvic Floor Muscle Morphometry (PFMM) and Vaginal Thickness (VT): the morphometry of the pelvic floor muscles will be assessed during rest, during contraction of the pelvic floor muscles, and during the Valsalva maneuver [51]. The vaginal thickness will be assessed in its proximal, middle, and distal third using two approaches—transabdominal and transvaginal [52, 53]. The equipment used for transabdominal, transvaginal and transperineal ultrasound measurements will be the GE Voluson 730 Expert® (GE Medical System Kretz-Technik GmbH and Co OHG, Zipf, Austria). The 2 to 6 MHz convex RAB4-8L 3D / 4D probe will be

used to record the morphometry of the pelvic floor muscles. Measurements will be performed at rest, Valsalva maneuver, and pelvic floor muscle contraction with the patient in the supine position [51] for the angle of the levator plate, the anorectal angle, the thickness of the levator ani muscle, and the area of the levator hiatus in cm^2. For vaginal thickness, probes 4C-D 2 at 5 MHz transabdominal and 5 to 9 MHz transvaginal will be used to measure the vagina in its proximal, middle, and distal thirds [52, 53].

Baseline assessment

After signing the consent form, patients will be submitted to an anamnesis that includes questions related to the date of birth, marital status, ethnicity, education, body mass index, physical activity, surgeries, prior diseases, and medication. Questions related to sexual life such as sexual activity (yes / no), type of sexual behavior (homosexual, heterosexual, bisexual), type of sexual intercourse (vaginal, anal or both), origin of VL complaint (participant, partner or both), time of VL symptoms (months). In addition, patients will be asked about their perception of VL symptoms. Questions related to obstetric history and urinary / intestinal habits will also be included.

Subsequently, patients who sign the consent form will be referred for a physical examination consisting of the assessment of the strength of the pelvic floor muscles and POP quantification. The questionnaires will be self-completed by the participants and collected at the end of the baseline assessment. Patients will then be referred for ultrasound exams. These procedures will be performed in the initial assessment (first visit).

Follow-up period assessment

Patients will be followed up in two periods after the interventions: first follow-up (30 days after intervention) and second follow-up (six months after intervention). The assessment procedures in the follow-up period will be the same as those used in the baseline physical examination, questionnaires, and ultrasound exams. We will add the Global Response Assessment.

Data collection and management

Researchers with over 20 years of research experience will coordinate data collection. An assistant researcher will be responsible for checking all signatures of the consent form and the answers to each questionnaire to ensure that there is no blank answer. A researcher will perform a physical examination of all patients in the study. An experienced physiotherapist (over 10 years) and specialist in women's health, under the supervision of the main researchers, will carry out both the interventions and different researcher with experience and expertise in ultrasound will perform the ultrasound exams. Patients will be contacted and monitored by telephone.

The analysis of the collected data will be preceded by the elaboration of a computerized database where the variables will be coded in a data dictionary and validated. This database will often be filled in by an assistant researcher and supervised by the main researcher.

Harms

The suspension of the intervention will occur through the verification of significant levels of discomfort during the application of vaginal RF (Visual Analogue Scale), as well as the significant occurrence of events such as urinary tract infection, vulvovaginitis, irritation and vaginal injury after application of vaginal RF (telephone contact). In these cases, an appropriate

medical treatment will be offered. Women will be discontinued if they miss any radiofrequency sessions or if their presence in physiotherapy sessions does not reach 80%.

Data analysis

Initially, a descriptive analysis of the data will be performed to characterize the research participants, in the form of values of absolute frequency and percentage (relative) for categorical variables and values of mean and standard deviation for numerical variables.

Statistical analysis of comparison and correlation of the obtained data will be performed. The Kolmogorov-Smirnov test will be performed to analyze the sample's normality. Depending on the results obtained in the normality test, the Analysis of Variance (data with normal distribution) or Wilcoxon and Mann-Whitney Test (non-parametric data) will be used for comparative analyzes between the groups. Likewise, Pearson or Spearman tests will be used for correlational analyzes. Categorical variables will be analyzed using the chi-square test or Fisher's exact test. Statistical analyzes will be performed using the statistical program SAS System for Windows (Statistical Analysis System), version 9.4, adopting a significance level of 5% ($p < 0.05$). Study endpoints will be analyzed primarily for the per protocol population, and repeated, for sensitivity reasons, for intention-to-treat population [54].

Ethical considerations

The present study has been analyzed and approved by the Research Ethics Committee of the State University of Campinas–UNICAMP–CAAE—12919119.9.0000.5404 (08/08/2019)–and CEP 3.495.558 (08/0/8/2019). This study is also registered in the Registro Brasileiro de Ensaios Clínicos–REBEC—RBR-2zdvfp as a clinical trial (19/02/2020).

All participants who agree to participate in the study will receive a consent form for reading and signing. In addition, participants will have their personal data protected and a number will replace their identities within the study.

Trial status

This trial is currently recruiting participants for the study. The initial assessments have also been started. This study was initiated in 2019 and is planned to finish in 2023.

Discussion

Vaginal laxity is a complaint that is still little discussed among patients and their physicians and the lack of evidence-based treatment negatively impacts the management of this condition. There is a need to evaluate non-surgical options that offer minimal adverse effects at lower costs for women with VL complaints.

The present study aims to investigate two types of non-surgical treatment for VL and to compare the effect of both therapies. If therapies prove to be equally effective for VL complaints, our study will open a path for non-surgical options for VL management. In addition, while we await evidence on the VL pathophysiology, our study will contribute to developing knowledge of treatment options for this condition that negatively affects women's sexual lives and relationships.

Dissemination of study findings

The present study is a part of a Ph.D. thesis and its results will be presented to the scientific board of the State University of Campinas–UNICAMP and to national and international scientific conferences.

Study amendments

Any protocol amendments that are necessary will be effectively communicated and modified in the relevant parties (trial registry, Research Ethics Committee, funding agency, and journal). Any inquiries regarding the study will be properly answered by the researchers in the initial assessment period and during the period of the study.

Supporting information

S1 Checklist. SPIRIT 2013 checklist study protocol.
(DOC)

S1 File.
(DOCX)

S2 File.
(DOCX)

Acknowledgments

The authors would like to thank the Hospital da Mulher Prof. Dr. José Aristodemo Pinotti—CAISM for authorizing data collection and interventions. We would like to thank the CAISM Ultrasound Service and its team for the partnership and assistance in our study, in particular to Dr. Renata Telles Piva Belluomini, Dr. Isabella Salvetti Valente and Dr. Maira Furtado Greco Mazzer. We would also like to thank the Physiotherapy Service for embracing our study by offering us its facilities and all support for our data collection and interventions. We also thank the Urogynecology outpatient clinics at the Faculty of Medical Sciences of the State University of Campinas, where our patients will be referred, and evaluated during the period of recruitment and data collection. Special thanks to the Department of Obstetrics and Gynecology at the State University of Campinas and the São Paulo Research Foundation -FAPESP.

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4.6.2 Análise Secundária do Ensaio Clínico Ranzomizado: *Ultrasound assessment in women with vaginal laxity treated by pelvic floor muscle training or radiofrequency: a secondary analysis of a randomized clinical trial*

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Subject: Submission Confirmation
To: Luiz Gustavo Oliveira Brito <lgobrito@unicamp.br>

Ref.: Ms. No.

Ultrasound assessment in women with vaginal laxity treated by pelvic floor muscle training or radiofrequency: a secondary analysis of a randomized clinical trial
Ultrasound in Medicine & Biology

Dear Prof Brito,

Thank you very much for submitting your manuscript titled, "Ultrasound assessment in women with vaginal laxity treated by pelvic floor muscle training or radiofrequency: a secondary analysis of a randomized clinical trial." for publication in Ultrasound in Medicine & Biology.

Your manuscript will be given a reference number once an Editor or Associate Editor has been assigned.

With kind regards,

Ultrasound in Medicine & Biology

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Ultrasound in Medicine & Biology

Ultrasound assessment in women with vaginal laxity treated by pelvic floor muscle training or radiofrequency: a secondary analysis of a randomized clinical trial

--Manuscript Draft--

Manuscript Number:	
Article Type:	Original Contribution
Keywords:	vaginal laxity; ultrasound; radiofrequency; pelvic floor muscle treatment; clinical trial
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Abstract:	Objective: To compare the vaginal wall thickness (VWT) measurement by two (2D-US) and pelvic floor muscle morphometry/function by four-dimensional translabial ultrasound (4D-TLUS) in women with vaginal laxity (VL) who underwent treatment with radiofrequency (RF) or pelvic floor muscle training (PFMT) after 30 days and 6 months. Methods: A secondary analysis of a randomized clinical trial that occurred between February 2020 and December 2021 was performed. Women with VL were enrolled and treated with RF or PFMT for 12 weeks. Ultrasound examiners were blinded for the groups. Transabdominal (TAUS) and transvaginal (TVUS) ultrasound were performed with 2D-US analysis. The 4D-TLUS was used for PFM morphometry/function assessment. We performed per-protocol (PP) and intention-to-treat (ITT) analysis (5% significance). Results: There was a weak correlation between 2D TAUS and TVUS measurements and anterior-posterior diameter difference and VL perception, sexual function and vaginal symptoms. Women with ballooning presented significantly worse scoring in sexual function and vaginal symptoms; and higher TVL, Ba and Bp measurements (POP-Q classification) than women without ballooning. Measurements of the TAUS proximal vagina increased in the PFMT group after 6 months. TAUS/TVUS distal vagina measurements were reduced after 6 months of RF. Other 4D-TLUS measurements did not present differences according to the intervention and/or analysis. Conclusion: Among women with VL, 2D-US measurements, whether abdominal or vaginal, of the VWT present a weak correlation with clinical instruments. Women with ballooning on 4D-TLUS presented significantly worse scoring in sexual function and vaginal symptoms; and higher TVL, Ba and Bp measurements.
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Cover Letter

July 31st 2023

To: The Editors-in-Chief
Paul S. Sidhu
Ultrasound in Medicine and Biology

Dear Editor

We herewith send you the study "**Ultrasound assessment in women with vaginal laxity treated by pelvic floor muscle training or radiofrequency: a secondary analysis of a randomized clinical trial**" for analysis in your respectful journal. This is a secondary analysis from a randomized clinical trial registered at Registro Brasileiro de Ensaios Clínicos–REBEC—RBR-2zdvfp and approved by the Institutional Review Board of the University of Campinas–UNICAMP (CAAE number 12919119.9.0000.5404). We expect that the present study through the ultrasound assessment will contribute to the understanding of the pathophysiology of vaginal laxity in the future.

All authors have substantial contributions to this study: the conception and design of the study; the acquisition of data; analysis and interpretation of data; drafting the article/revising the content, and consent to the final version that is presented here. Our study has not been published previously and it is not under consideration for publication elsewhere.

If you have any questions about the manuscript, Dr Brito will be serving as the corresponding author. Thank you in advance for your consideration.

Sincerely yours,

Luiz Gustavo Oliveira Brito, MD PhD (on behalf of the authors)
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Title: Ultrasound assessment in women with vaginal laxity treated by pelvic floor muscle training or radiofrequency: a secondary analysis of a randomized clinical trial

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Funding Source: This study received two grants from Sao Paulo Research Agency (FAPESP) numbers 2019/26723-5 and 2021/13700-7.

Clinical Trial Registration: Registro Brasileiro de Ensaios Clínicos–REBEC—RBR-2zdvfp as a clinical trial.

Abstract word count: 246

Manuscript word count: 3464

41 **Abstract**

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43 and pelvic floor muscle morphometry/function by four-dimensional translabial
44 ultrasound (4D-TLUS) in women with vaginal laxity (VL) who underwent treatment
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53 significance).

54 **Results:** There was a weak correlation between 2D TAUS and TVUS measurements and
55 anterior-posterior diameter difference and VL perception, sexual function and vaginal
56 symptoms. Women with ballooning presented significantly worse scoring in sexual
57 function and vaginal symptoms; and higher TVL, Ba and Bp measurements (POP-Q
58 classification) than women without ballooning. Measurements of the TAUS proximal
59 vagina increased in the PFMT group after 6 months. TAUS/TVUS distal vagina
60 measurements were reduced after 6 months of RF. Other 4D-TLUS measurements did
61 not present differences according to the intervention and/or analysis.

62 **Conclusion:** Among women with VL, 2D-US measurements, whether abdominal or
63 vaginal, of the VWT present a weak correlation with clinical instruments. Women with

64 ballooning on 4D-TLUS presented significantly worse scoring in sexual function and
65 vaginal symptoms; and higher TVL, Ba and Bp measurements.

66 **Keywords:** vaginal laxity; ultrasound; radiofrequency; pelvic floor muscle treatment;
67 clinical trial

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Introduction

Vaginal laxity (VL) has gained visibility in the last decade with the advent of energy-based therapies. It is defined as a complaint of excessive vaginal flaccidity, with a prevalence that varies between 24-38%[1,2]. Although ultrasound has been used throughout the years to evaluate aspects of the pelvis and pelvic floor, few studies have investigated VL using this assessment technique field[1,3,4].

The technique of measuring the vaginal wall thickness (VWT) with two-dimensional ultrasound (2D-US) was validated against the gold standard of histological measurement, with the advantage of being highly reproducible and being able to be performed in real-time[5]. Studies have evaluated VWT both transvaginally and transabdominally in pre-and postmenopausal women; however, more studies are needed to assess the usefulness and sensitivity of these measurements in research and clinical practice[6,7].

The four-dimensional translabial ultrasound (4D-TLUS) has been widely used in the evaluation of pelvic organ prolapse and in conditions related to macrotrauma or hyperdistension of the levator ani muscle[8,9]. Recently, measurements of hiatal ballooning of the levator ani muscle have been associated with VL[10,11]. Thus, this secondary analysis aims to collaborate with the understanding of the objective assessment of women with VL treated by radiofrequency (RF) or pelvic floor muscle training (PFMT) by comparing the VWT measured by transabdominal/transvaginal 2D-US, and the pelvic floor muscle morphometry/function measured by 4D-TLUS after 30 days and 6 months of intervention.

Materials and Methods

This is a secondary analysis of a prospective, parallel-group, two-arm, randomized clinical trial, carried out between February 2020 and December 2021, approved by the Institutional Review Board of the University of Campinas–UNICAMP (CAAE number 12919119.9.0000.5404) and registered in the Registro Brasileiro de Ensaios Clínicos–REBEC—RBR-2zdvfp (February 19th, 2020). The main study aimed to compare the effect of RF and PFMT on the treatment of women with VL.

Women between 18 and 60 years old with a self-reported complaint of vaginal laxity and classified by the Vaginal Laxity Questionnaire (VLQ)[12] (very loose, moderately loose, slightly loose) were recruited from the Urogynecology and the Physiotherapy outpatient clinic of a tertiary hospital from the University of Campinas — UNICAMP. Exclusion criteria are detailed elsewhere[13].

All participants received a detailed presentation of all phases of the study and only after fully understanding the study, the consent form was signed. These participants underwent assessment at baseline and at 30 days and six months after interventions. At baseline, participants were assessed for sociodemographic and clinical data, answered validated questionnaires, and underwent physical and ultrasound examinations. For the questionnaires, we included the Female Sexual Function Index (FSFI) for sexual function[14], the Female Sexual Distress Scale-Revised (FSDS-R) for sexual distress[15], the International Consultation on Incontinence Questionnaire—Vaginal Symptoms (ICIQ-VS), for vaginal symptoms and quality of life[16], all validated for Brazilian Portuguese language. Regarding physical examination, participants underwent Pelvic Organ Prolapse Quantification (POP-Q)[17] and Pelvic Floor Muscle Strength graduated by the modified Oxford scale (5-point)[18]. The randomization process only occurred after the baseline assessment, if any exclusion criteria were identified in the evaluation. In the post-

intervention follow-ups, the participants were submitted to questionnaires, and physical and ultrasound examinations.

A researcher not involved in the study performed the randomization sequence (1:1 allocation ratio), using a computer program (https://www.randomizer.org/). The numbers 1- Radiofrequency (RF) and 2- Pelvic Floor Muscle Training (PFMT) corresponding to the study groups were organized in opaque envelopes and grouped into two blocks. The envelopes were opened by the participants after signing the consent form and undergoing the baseline assessment. Two blinded researchers (C.M.A.; K.C.A) were responsible for performing the ultrasound assessments. A third blinded researcher (N.M.) was responsible for ultrasound data analysis and another one for the questionnaire's application and physical examination. A detailed description of the clinical interventions can be found in the study protocol[13].

Vaginal Wall Thickness (VWT) assessment

Participants were instructed to completely empty their bladders and subsequently drank 800 mL of water over a period of 20 minutes. Transabdominal ultrasound (TAUS) (Figure 1) was performed 40 minutes after the last glass of water, in the supine position, with the lower limbs extended and with moderate bladder repletion, around 300 ml of volume. The probe was positioned in the suprapubic region. To measure the VWT (anterior and posterior), an abdominal probe (1–5-MHz C5-1 abdominal probe, Affiniti 70G Philips) was used and the images were acquired along the longitudinal axis, in the sagittal plane. Measurements were taken in the proximal third (vaginal fornix), middle third and distal third (near vaginal introitus) and recorded from external to external echogenic lines[19]. At the end of the TAUS measurement, participants were instructed to completely empty their bladder and immediately return for the transvaginal ultrasound (TVUS) measurement (Figure 2). Positioning was the same used in TAUS, plus the

158 elevation of the pelvis. Forty millilitres of water-based gel were carefully introduced into
159 the vaginal canal using two 20 ml syringes to separate the vaginal walls, allowing
160 independent measurement of the walls without pressing the probe against the vaginal
161 wall. To measure the TVUS, a vaginal probe was used in the sagittal plane (3–10-MHz
162 C10-3v vaginal probe, Affiniti 70G, Philips). The vaginal thickness of the anterior and
163 posterior walls was measured in its proximal third (anterior and posterior vaginal fornix),
164 middle third (at the transition of the proximal urethra and rectum), and distal third (at the
165 distal urethra/vaginal introitus and anorectal junction). During the analyses, the
166 measurements of the anterior and posterior vaginal walls obtained by the TVUS were
167 added and their total values were compared with the TAUS measurements. A single-
168 blinded experienced researcher (C.M.A.) performed all TAUS and TVUS measurements.
169 This protocol was previously published and we could confirm that there was a correlation
170 between TAUS and TVUS measurements[20].

171 ***Pelvic Floor Muscles Morphological and Functional assessment***

172 Four-dimensional translabial ultrasound was performed using a 2-8 MHz
173 wideband convex ultra-light volume transducer, with an acquisition angle of 85 degrees
174 (Voluson S10 Expert, GE Medical Systems). Participants were positioned in supine, with
175 the lower limbs flexed and after bladder empty. Ultrasound volume datasets analysis was
176 performed offline using the 4D View 10.0 software (GE Medical Ultrasound) by a second
177 researcher, blinded for data collection (N.M.). An inter-reliability test retest series,
178 performed prior to commencing the study's measurements, yielded an intraclass
179 correlation coefficient (ICC) above 0.7, showing strong agreement for all
180 measurements[21].

181 Levator avulsion (Figure 3) was assessed using the Tomographic Ultrasound
182 Imaging resource as previously described by Dietz and collaborators[22]. Hiatal ballooning

(Figure 4) was measured during maximal Valsalva and categorized in absence (<25 cm^2), mild (25-29.9 cm^2), moderate (30-34.9 cm^2), marked (35-39.9 cm^2) and severe (≥40 cm^2)[23].

Levator hiatus dimensions were measured from volumes obtained at rest and during PFM maximal voluntary contraction (Figure 4). Measurements of area, circumference and anteroposterior and side-to-side (right-left) diameters of the levator hiatus were performed on rendered images at the level of the minimum hiatal dimension. Hiatal area narrowing was calculated by subtracting the value measured at rest from its value measured during PFM contraction (Hiatal area narrowing = hiatal area rest – hiatal area contraction). Similarly, the difference between the levator hiatus diameters was calculated by subtracting the value measured at rest from the values measured during PFM contraction[24].

Finally, puborectalis muscle retraction was analyzed from the measurements of the hiatal circumference and the bone arch (the non-elastic arch of the hiatal circumference), as previously described[25]. The muscular arch (the part of the hiatal circumference that contracts and lengthens during contraction and the Valsalva maneuver, respectively) corresponds to the difference between the hiatal circumference and the bony arch. Thus, puborectalis muscle retraction (ε) was calculated in relation to the resting state during contraction: εcont = Ccont-Crest / Crest-lb, where εcont = deformation during contraction, Ccont = hiatal circumference during contraction, Crest = hiatal circumference at rest and lb = bone arch of the hiatal circumference.

Statistical Analysis

The chi-square or Fisher's exact tests were used to compare the categorical variables between the two groups. The Mann-Whitney test (two groups) and the Kruskal-

Wallis test (three or more groups) were used to compare numeric variables and to compare scores between groups and assessment periods, and analysis of variance for repeated measures (ANOVA) was used, followed by Tukey and contrast profile tests, with variables transformed into ranks due to the absence of normal distribution. The McNemar test (two categories) and the Bowker test (for three or more categories) were used to compare categorical variables and the Wilcoxon test for numerical variables, between the two assessment periods. Spearman's correlation coefficient was used for the analysis between numerical variables with Dancey & Reidy's interpretation (0.1-0.39: Weak; 0.4-0.69: Moderate; 0.7-0.9: Strong). The significance level adopted for the statistical tests was 5% ($p<0.05$). We considered for per-protocol analysis those participants who attended all PFMT visits and all RF sessions. For intention-to-treat (ITT) analysis, we considered those who did not complete the entire treatment protocol or who missed one of the follow-up periods due to pandemic restrictions or adherence-related issues. We used SAS statistical package (Cary, NC, USA) version 9.4 for analysis.

Results

A total of 87 patients were randomized into RF and PFMT groups. The clinical and sociodemographic characteristics of women with VL are shown in Table 1. No differences were observed between groups when PP and ITT analysis were performed.

Tables 2 describes the correlation between baseline questionnaire scores and VWT. Weak correlations were observed between TAUS proximal vagina and VLQ ($r=0.227$; $P=0.034$) and FSFI lubrication ($r=-0.233$; $P=0.029$); TVUS proximal vagina and VLQ ($r=0.239$; $P=0.025$) and ICIQ-VS question 4 ($r=-0.295$; $P=0.005$); TVUS middle-third vagina and FSFI desire ($r=0.224$; $P=0.037$) and FSFI satisfaction ($r=0.246$;

231 P=0.021) and ICIQ-VS QoL (r=-0.226; P=0.035); and finally, TVUS distal vagina and
232 FSFI desire (r= 0.240; P=0.024), FSFI orgasm (r= 0.211; P=0.049), FSFI satisfaction
233 (r=0.298; P=0.004) and FSFI total score (r=0.222; P=0.038).

234 Similarly, weak positive correlations were found between anterior-posterior
235 Diameter Difference (Contraction) and VLQ (r=0.280; P=0.025), and FSFI lubrication
236 (r=0.350; P=0.004); and a weak negative correlation with ICIQ-VS (r=-0.295; P=0.017).
237 There were weak negative correlations between Right-Left Diameter Difference
238 (Contraction) and FSFI arousal (r=-0.328; P=0.008), FSFI satisfaction (r=-0.279;
239 P=0.025), and FSFI Total Score (r=-0.293; P=0.018) (Table 3).

240 Women with ballooning presented significantly worse scoring in FSFI arousal,
241 satisfaction, and pain domains, FSFI Total Score, and all domains of ICIQ-VS. When
242 considering the POP-Q system, women with ballooning had significantly worse
243 measurements at points Ba, Ap, Bp and TVL when compared to women without
244 ballooning. Participants with right levator ani avulsion also presented significantly worse
245 points C and D when compared to participants without avulsion, but not on points Ap and
246 Bp (Table 4).

247 Tables 5 and 6 display the analysis of variance for repeated measures for
248 comparison among 2D-US and 4D-TLUS measurements, groups (RF and PFMT) and
249 assessment periods. Higher values in TAUS distal vagina and TVUS proximal vagina
250 were observed in the RF group at 30 days and in the PFMT group at 6 months,
251 respectively. TAUS proximal vagina measurements increased in the PFMT group after 6
252 months of treatment. A greater reduction in the measurements of TAUS and TVUS distal
253 vagina in the RF group was perceived after 6 months of treatment. Higher values were
254 found in Hiatal Area Narrowing and Anterior-Posterior Diameter Difference
255 (Contraction) in the PFMT group at 30 days follow-up.

On the other hand, higher values were observed in Puborectalis Retraction in the RF group at baseline, 30 days, and 6 months follow-up. Hiatal area narrowing increased between baseline and 30 days and between baseline and 6 months in both groups (PP analysis). At ITT analysis, hiatal area narrowing increased between baseline and 6 months follow-up in the RF group. Puborectalis retraction decreased values between baseline and 30 days and between baseline and 6 months in both groups in PP analysis (between baseline and 6 months in both groups in ITT). Anterior-posterior diameter difference (contraction) increased values between baseline and 6 months and between 30 days and 6 months in the RF group and increase between baseline and 30 days in the PFMT group in PP analysis and between baseline and 6 months in the PP/ITT analysis. Right-left diameter difference (contraction) significantly increased values in PFMT (baseline and 30 days) only in the PP analysis.

Discussion

To our knowledge, this is the first comparative study of US assessment of VWT and pelvic floor muscle morphometry and function in women with VL. This makes this section even harder to compare the literature with our findings, as there is scant data on this subject.

Preliminary data suggest that the measurement of VWT may be useful for assessing vaginal changes[7]. In our sample, VWT measurements were thinner in the middle third vagina and thicker in the distal vagina, in both the RF group and the PFMT group and ultrasound techniques (TAUS and TVUS) at baseline assessment. The vaginal wall is composed of three main layers: the vaginal mucosa (divided histologically into mucosa and submucosa), the muscular layer, and the adventitia layer[26]. The structure of

280 the vaginal epithelium changes throughout a woman's life and is influenced by hormonal
281 and environmental conditions. Hormonal influences have mild effects on the thickness of
282 the vaginal epithelium[27] but affect glycogen stores as glycogen synthesis is influenced by
283 estrogen levels[28]. In addition, the mucous layer measures between 2 and 5 mm in
284 thickness, also influenced by hormonal stimulus[29].

285 In line with our findings regarding the FSFI orgasm domain, a positive and
286 significant correlation was found between the thickness of the distal urethrovaginal
287 segment and vaginal orgasm, in a study that measured the urethrovaginal space via
288 TVUS[30]. However, our measures differ as we added the anterior and posterior
289 measurements of the vagina, without considering urethral measurements. Similar to
290 orgasm, we also found a weak correlation between VWT and the FSFI desire, satisfaction,
291 lubrication domains, and FSFI total score. As previously stated, the vaginal walls can
292 differ in thickness; however, a statistically significant correlation regarding
293 measurements of VWT cannot solely explain the female sexual function; there are also
294 other biological (neurological, hormonal), psychosexual, and contextual factors that
295 should be considered[31,32]. Thus, our findings should not be interpreted without
296 considering the multifactorial nature of sexual function.

297 The VLQ was positively correlated with the VWT measured in the proximal
298 vagina in both TVUS and TAUS approaches. Similarly, question 4 of ICIQ-VS regarding
299 the perception of VL was also correlated with VWT in the TVUS proximal vagina. One
300 study found that the vaginal innervation is uniform with nerves distributed throughout the
301 vagina, with no location consistently demonstrating the greatest innervation. However,
302 samples from the posterior proximal portion of the vagina had the highest number of
303 nerves in 35% of women[33]. This finding may explain the existing correlation between the
304 perception of VL and the proximal portion of the vagina found in our study. In our

population, mean VWT is smaller in the proximal vagina when compared to the distal vagina. This might suggest that the innervation of the proximal portion of the vagina appears to be lower in women with perceived VL. However, the pathophysiology of VL is still unclear and the role of vaginal structures for this condition is still unknown.

The relationship between levator diameter measurements and VLQ scores appears to have not yet been evaluated; however, we found a positive correlation between the A-P diameter difference during contraction and the VLQ score. The higher the VLQ score, the lower the perception of VL[12]. Thus, despite a weak correlation, our findings suggest that as the levator contractile capacity improves, the VLQ scores increase, indicating an improvement in the perception of symptoms of VL. Interestingly, a weak negative correlation between A-P diameter difference in contraction and vaginal symptoms was observed in our sample, also suggesting that alterations in levator structure and consequently its function may impact vaginal symptoms. In a previous study[34], even though the effect of problems with vaginal symptoms on women´s sexual life was low, larger defects in the levator ani showed that women who trained this muscle were 45% less likely to have VL symptoms.

A better muscle function was related to arousal, orgasm and improved sexual function[35]. Curiously, in our findings, the FSFI scores (arousal, satisfaction, and total score) were weakly (negative) correlated with the R-L diameter difference, and the FSFI lubrication weakly (positive) correlated with the A-P diameter difference. According to van Delft *et al*., the hiatal area and hiatal anteroposterior diameter are significantly smaller during contraction than at rest. The contractility of the pelvic floor muscles assessed by US seems to decrease significantly after delivery[36,37]. Changes in the levator muscle, secondary to pregnancy and childbirth can affect sexual functions[35]. Our findings on the inverse relationship between levator ani diameters and sexual function can be explained

330 by the shape of the levator hiatus. In a recent study that used the A-P/R-L diameter ratio
331 of the minimal levator hiatus, the larger the ratio, the more oval the pelvic hiatus[38]. This
332 measure was negatively correlated with compression pressures[38].

333 Different from what was previously found[11], ballooning was not found in the
334 majority of our population (approximately 72-73%). However, we found measurements
335 that suggest hyperdistension of the levator ani. Worse scores in the FSFI (Arousal,
336 satisfaction, pain, and Total score) and ICIQ-VS questionnaires were observed in
337 participants with ballooning. Similarly, the study by Aydın *et al.* revealed that a change
338 in the anteroposterior diameter of the levator hiatus during Valsalva was associated with
339 sexual dysfunction[39]. Retrospective studies have found an association between VL and
340 levator distensibility. However, the population characteristics of these studies differ from
341 ours, mainly in a higher mean age and in the significant symptoms of pelvic organ
342 prolapse found in these studies[1,11]. More studies are needed to understand the role of
343 levator distensibility in sexual dysfunction. Participants with ballooning also had worse
344 measures related to POP-Q points Ba, Ap and TVL. The levator ani avulsion seems to
345 compromise the measurements of the POP-Q posterior and superior compartments when
346 compared to participants without avulsion. In line with our findings, evidence shows that
347 levator ani defects and a larger hiatal biometry increase the risk of pelvic organ prolapse[40].
348 The levator avulsion injury is diagnosed by ultrasonography (minimum hiatal dimension
349 plane) when the discontinuity between the inferior pubic ramus and the puborectalis
350 muscle is observed[41]. Signs and symptoms of pelvic floor dysfunction are found in
351 women with partial elevator trauma or non-persistent injuries, however, in the case of
352 avulsion, the picture of dysfunction is particularly worse[42].

353 Differently from what we have found in the literature through histological
354 evaluation after treatment with RF[28], the increase in the VWT was observed only in the

355 middle third (30 days and 6 months follow-up) and distal vagina (30 days follow-up) on
356 TVUS. On the other hand, an increase in VWT was found in all measurement techniques
357 (TAUS and TVUS) and during follow-ups in participants treated with PFMT. The
358 anatomical interactions between the pelvic floor muscles and the vagina have been
359 described in detail in previous studies[43], however, to this moment, we did not find any
360 evidence of the effect of PFMT on vaginal thickness.

361 On the other hand, studies on the effect of PFMT on improving muscle function
362 and sexual function seem to be well-advanced[44]. Our findings showed the Hiatal Area
363 Narrowing and A-P Diameter Difference measurements were significantly higher in the
364 PFMT group 30 days post-treatment. A significant increase was also observed in these
365 two variables and in the R-L Diameter Difference, in the follow-up periods in the PFMT
366 group. The measures of puborectalis retraction decreased in the follow-up periods in the
367 PFMT group. These findings suggest that muscle function improved with pelvic floor
368 muscle training. The functional features of lifting the pelvic organs and compressing
369 closing the levator hiatus of the levator ani muscle have been previously studied[45,46]. In
370 addition to the supportive features of the pelvic organs, the levator plays an important
371 role in sexual function, as its contraction facilitates and enhances sexual responses[44,47].
372 PFMT improved muscle function measured by US in our population of women with VL.

373 The present study has limitations. In this study, we focused on the 4D-TLUS
374 evaluation of measurements at rest and contraction of the pelvic floor muscles.
375 Assessment of pelvic floor muscles in Valsalva would add value to our findings and could
376 be useful in a future study. Another issue that should be considered is the fact that we did
377 not use the histological evaluation of the participants to compare with the measurements
378 of VWT. However, we intended to use ultrasound because it is less invasive, causes little
379 discomfort and is part of the clinical practice of professionals who work in the care of

women with VL or other sexual complaints. Moreover, the use of ultrasound for the objective assessment of VWT and the morphometry and contractile function of the pelvic floor muscles has contributed to the understanding of VL and raised questions for future studies about the importance of studying VL and the cost-effectiveness of treatment options such as energy-based devices.

Acknowledgments: We thank Sao Paulo Research Agency (FAPESP).

Conflict of Interest Statement: The authors declare no conflict of interests.

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542 Figure Captions List

543 Figure 1. Transabdominal ultrasound measurement of the vaginal wall thickness
544 (proximal third, middle third and distal third).

545 Figure 2. Transvaginal ultrasound measurement of the vaginal wall thickness (proximal
546 third, middle third and distal third).

547 Figure 3. Tomographic ultrasound imaging of the pelvic floor showing a complete right-
548 sided levator avulsion with levator-urethra gap (LUG) > 2.5 cm.

549 Figure 4. Levator hiatus dimensions at rest (A) and during voluntary contraction (B) in a
550 participant with vaginal laxity. Hiatal ballooning (C) on Valsalva maneuver in another
551 participant with vaginal laxity (axial plane).

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Table 1. Baseline sociodemographic and clinical characteristics of women with vaginal laxity

Variables	Per Protocol			Intention to Treat		
	Radiofrequency (n=38) Mean ± SD / n (%)	PFMT (n=35) Mean ± SD / n (%)	p-Value	Radiofrequency (n=42) Mean ± SD / n (%)	PFMT (n=45) Mean ± SD / n (%)	p-Value
Age (years)	41.50 ± 8.70	41.40 ± 7.74	0.996 [a]	41.50 ± 9.01	41.20 ± 7.87	0.769 [a]
BMI			0.319 [β]			0.184 [β]
< 25Kg/m²	12 (31.58)	15 (42.86)		12 (28.57)	19 (42.22)	
> 25Kg/m²	26 (68.42)	20 (57.14)		30 (71.43)	26 (57.78)	
Gravidity	2.82 ± 1.69	2.17 ± 1.25	0.100 [a]	2.79 ± 1.63	2.42 ± 1.48	0.242 [a]
Type of Birth			0.140 [c]			0.570 [c]
None	1 (2.63)	2 (5.71)		1 (2.38)	2 (4.44)	
Vaginal	24 (63.16)	16 (45.71)		26 (61.90)	23 (51.11)	
Cesarean	6 (15.79)	13 (37.14)		8 (19.05)	14 (31.11)	
Both	7 (18.42)	4 (11.43)		7 (16.67)	6 (13.33)	
Parity			0.478 [c]			0.370 [c]
Nulliparous	1 (2.63)	2 (5.71)		1 (2.38)	3 (6.67)	
Primiparous	6 (15.79)	9 (25.71)		7 (16.67)	11 (24.44)	
Multiparous	31 (81.58)	24 (68.57)		34 (80.95)	31 (68.89)	
Birth Weight (grams)	3122.70 ± 620.55	3409.20 ± 500.66	0.162 [a]	3145.80 ± 616.19	3342.10 ± 521.98	0.405 [a]
Instrumental Delivery	6 (15.79)	7 (20.00)	0.444 [c]	6 (14.29)	10 (22.22)	0.340 [β]
POP-Q Staging			0.136 [β]			0.318 [β]
Stage 0 – n (%)	8 (21.05)	3 (8.57)		9 (21.43)	6 (13.33)	
Stage 1 – n (%)	30 (71.05)	32 (91.43)		33 (78.57)	39 (86.67)	
Menopause Status			1.000 [c]			0.841 [β]
Premenopause	33 (86.84)	31 (88.57)		37 (88.10)	39 (86.67)	

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Menopause	5 (13.16)	4 (11.43)		5 (11.90)	6 (13.33)	
4D Translabial Ultrasound						
Ballooning* n (%)			0.549[α]			0.549[α]
No (<25 cm^2)	27 (72.97)	25 (73.52)		27 (72.97)	25 (73.52)	
Mild (25-29.9 cm^2)	5 (13.51)	5 (15.15)		5 (13.51)	5 (15.15)	
Moderate (30-34.9 cm^2)	3 (8.11)	2 (6.06)		3 (8.11)	2 (6.06)	
Marked (35-39.9 cm^2)	0	2 (6.06)		0	2 (6.06)	
Severe (≥ 40 cm^2)	2 (5.41)	0		2 (5.41)	0	
Levator Ani Avulsion** (Right)	2 (5.26)	3 (8.57)	0.659[α]	2 (5.26)	3 (8.57)	0.659[α]
Levator Ani Avulsion** (Left)	1 (2.63)	1 (2.85)	1.000[α]	1 (2.63)	1 (2.85)	1.000[α]
2D Ultrasound (mm)						
TAUS Proximal	11.25 ± 4.04	10.00 ±3.08	0.191[μ]	11.23 ±3.90	9.90 ±3.14	0.092[μ]
TAUS Middle Third	10.68 ± 4.10	9.33 ± 2.69	0.272[μ]	10.65 ±3.96	9.31 ±2.73	0.158[μ]
TAUS Distal	11.86 ±3.77	10.35 ± 2.38	0.090[μ]	11.79 ±3.67	10.41 ±2.61	0.077[μ]
TVUS Proximal	6.83 ± 1.43	6.92 ±1.46	0.651[μ]	6.79 ±1.39	6.95 ±1.59	0.625[μ]
TVUS Middle Third	6.38 ± 1.36	6.38 ±1.50	0.838[μ]	6.44 ±1.54	6.57 ±1.59	0.555[μ]
TVUS Distal	7.94 ± 1.83	7.44 ±2.20	0.267[μ]	7.94 ±1.83	7.76 ±2.20	0.687[μ]

PFMT: Pelvic Floor Muscle Training; SD: Standard Deviation; BMI: Body Mass Index; 4D: Four-dimensional; 2D:Two-dimensional; A-P: Anteroposterior; L-L: Laterolateral; TAUS: Transabdominal Ultrasound; TVUS: Transvaginal Ultrasound; [β] Chi-square test; [α]Fisher test; [μ] Mann-Whitney test; *Ballooning (Radiofrequency n=37; PFMT n=34);** Levator Avulsion (Radiofrequency n=38; PFMT n=35).

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Table 2. Correlation between baseline questionnaire scores and measurements of the vaginal wall thickness (n=87)

Questionnaire	TAUS Proximal		TAUS Middle-third		TAUS Distal		TVUS Proximal		TVUS Middle-third		TVUS Distal	
Scores	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value
VLQ	**0.227**	**0.034**	0.194	0.071	0.188	0.081	**0.239**	**0.025**	0.057	0.598	0.113	0.293
FSFI												
Desire	0.149	0.168	0.061	0.570	0.187	0.082	0.119	0.270	**0.224**	**0.037**	**0.240**	**0.024**
Arousal	-0.128	0.233	-0.122	0.259	-0.080	0.459	0.127	0.237	0.082	0.446	0.180	0.093
Lubrication	**-0.233**	**0.029**	-0.188	0.081	-0.096	0.375	0.115	0.284	0.047	0.662	0.078	0.467
Orgasm	-0.141	0.190	-0.110	0.308	-0.038	0.721	0.174	0.106	0.194	0.071	**0.211**	**0.049**
Satisfaction	-0.062	0.563	-0.047	0.664	0.077	0.994	-0.092	0.394	**0.246**	**0.021**	**0.298**	**0.004**
Pain	-0.189	0.078	-0.089	0.408	-0.092	0.394	0.022	0.837	-0.005	0.958	0.001	0.986
Total Score	-0.125	0.247	-0.100	0.354	-0.022	0.835	0.120	0.268	0.170	0.113	**0.222**	**0.038**
ICIQ-VS												
Vaginal Symptoms	0.119	0.268	0.136	0.206	0.007	0.945	-0.154	0.153	-0.063	0.556	-0.165	0.124
Sexual Matters	-0.064	0.554	-0.024	0.818	-0.056	0.601	-0.200	0.062	-0.059	0.583	-0.022	0.839
QoL	-0.113	0.294	0.044	0.681	-0.107	0.320	-0.156	0.148	**-0.226**	**0.035**	-0.160	0.137
Question 4	-0.016	0.878	0.016	0.882	-0.120	0.264	**-0.295**	**0.005**	-0.076	0.479	-0.179	0.095
FSDS-R	0.011	0.914	0.086	0.424	-0.059	0.584	-0.189	0.079	-0.152	0.158	-0.161	0.134
ICIQ-SF	-0.087	0.422	0.054	0.614	-0.064	0.550	-0.125	0.248	-0.113	0.295	-0.102	0.346

TAUS: Transabdominal Ultrasound; TVUS: Transvaginal Ultrasound; VLQ: Vaginal Laxity Questionnaire; FSFI: Female Sexual Function Index; QoL: Quality of Life; FSDS-R: Female Sexual Distress Scale – Revised; ICIQ-VS: International Consultation on Incontinence Questionnaire – Short Form; ICIQ-SF: International Consultation on Incontinence Questionnaire – Vaginal Symptoms; r = Spearman correlation coefficient; Dancey & Reidy interpretation (0.1-0.39: Weak; 0.4-0.69: Moderate; 0.7-0.9: Strong);

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Table 3. Correlation between baseline questionnaire scores/POP-Q and measurements of the 4D translabial ultrasound (n=87)

Variables	Hiatal Area Narrowing (Delta)		Puborectalis Retraction		A-P Diameter Difference		R-L Diameter Difference	
	r	p-value	r	p-value	r	p-value	r	p-value
VLQ	0.135	0.286	-0.159	0.206	**0.280**	**0.025**	0.066	0.599
FSFI								
Desire	-0.032	0.795	0.010	0.932	0.095	0.450	-0.188	0.134
Arousal	-0.102	0.418	-0.022	0.859	0.130	0.305	**-0.328**	**0.008**
Lubrication	0.088	0.485	-0.174	0.168	**0.350**	**0.004**	-0.075	0.551
Orgasm	0.015	0.901	-0.073	0.563	0.217	0.084	-0.186	0.140
Satisfaction	-0.098	0.439	0.141	0.264	0.042	0.741	**-0.279**	**0.025**
Pain	-0.125	0.322	0.024	0.846	-0.011	0.930	-0.218	0.083
Total Score	-0.077	0.540	0.081	0.948	0.129	0.307	**-0.293**	**0.018**
ICIQ-VS								
Vaginal Symptoms	0.085	0.503	0.172	0.171	**-0.295**	**0.017**	0.062	0.960
Sexual Matters	-0.036	0.775	-0.048	0.704	-0.183	0.145	0.063	0.620
QoL	0.079	0.530	-0.059	0.642	-0.055	0.663	0.144	0.255
Question 4	0.090	0.943	0.023	0.853	-0.244	0.051	0.051	0.687
FSDS-R	0.130	0.302	-0.112	0.377	-0.029	0.819	0.245	0.050
ICIQ-SF	-0.014	0.909	0.103	0.417	-0.145	0.249	0.051	0.684
POP-Q								
Aa	0.092	0.461	-0.153	0.227	0.159	0.206	0.032	0.798
Ba	0.137	0.277	-0.177	0.161	0.162	0.200	0.197	0.117
Ap	-0.107	0.395	0.243	0.052	-0.122	0.333	-0.123	0.329
Bp	-0.139	0.270	0.230	0.066	-0.090	0.478	-0.193	0.125

C	0.038	0.765	0.095	0.454	-0.083	0.511	0.110	0.382
D	-0.013	0.913	0.092	0.468	-0.115	0.361	0.141	0.265
TVL	0.030	0.806	-0.100	0.429	0.076	0.547	0.030	0.981
Gh	-0.024	0.849	0.181	0.152	-0.031	0.803	-0.017	0.888
Pb	0.018	0.883	0.217	0.084	0.021	0.863	-0.078	0.539

4D: four-dimensional; POP-Q: Pelvic Organ Prolapse Quantification; A-P: Anterior-Posterior; R-L: Right-Left; PFM: Pelvic Floor Muscle; VLQ: Vaginal Laxity Questionnaire; FSFI: Female Sexual Function Index; QoL: Quality of Life; FSDS-R: Female Sexual Distress Scale – Revised; ICIQ-VS: International Consultation on Incontinence Questionnaire – Short Form; ICIQ-SF: International Consultation on Incontinence Questionnaire – Vaginal Symptoms; r = Spearman correlation coefficient; Dancey & Reidy interpretation (0.1-0.39: Weak; 0.4-0.69: Moderate; 0.7-0.9: Strong);

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Table 4. Baseline comparison between questionnaire scores/clinical variables and ballooning/ levator ani avulsion

Questionnaire Scores/Clinical Variables	Ballooning No	Ballooning Yes	p-value	Levator Ani Avulsion (Right) No	Levator Ani Avulsion (Right) Yes	p-value	Levator Ani Avulsion (Left) No	Levator Ani Avulsion (Left) Yes	p-value
	Mean±SD	Mean±SD		Mean±SD	Mean±SD		Mean±SD	Mean±SD	
VLQ	2.00±0.71	1.84±0.67	0.102	1.80±0.45	1.80±0.69	0.890	1.81±0.67	1.50±0.71	0.537
FSFI									
Desire	3.28±1.24	3.12±0.97	0.131	3.48±0.78	2.99±1.17	0.251	3.04±1.16	2.85±1.06	0.738
Arousal	3.77±1.23	3.15±0.93	**0.036**	3.72±0.34	3.44±1.26	0.735	3.47±1.22	3.15±1.48	0.801
Lubrication	4.47±1.34	4.08±1.18	0.160	4.74±0.93	4.19±1.41	0.539	4.21±1.39	4.95±1.06	0.523
Orgasm	3.99±1.39	3.12±1.51	0.210	3.76±0.92	3.70±1.47	0.900	3.72±1.44	3.40±1.41	0.727
Satisfaction	4.40±1.16	3.36±1.48	**0.035**	4.24±0.54	4.03±1.42	0.839	4.06±1.39	3.80±0.28	0.507
Pain	4.86±1.30	3.52±1.51	**0.049**	5.12±1.18	4.47±1.46	0.365	4.47±1.44	6.00±0.01	0.084
Total Score	24.77±5.91	20.35±5.44	**0.037**	25.06±2.94	22.82±6.34	0.476	22.96±6.23	24.15±4.74	0.908
ICIQ-VS									
Vaginal Symptoms	13.61±6.92	21.90±6.21	**0.007**	14.00±5.34	14.85±7.16	0.900	14.97±7.03	9.00±1.41	0.153
Sexual Matters	23.00±20.55	42.80±15.12	**0.018**	26.80±22.33	25.83±21.10	0.960	25.77±21.26	30.00±14.14	0.742
QoL	5.45±3.51	8.00±2.05	**0.005**	4.60±3.13	5.61±3.52	0.441	5.48±3.48	7.00±4.24	0.586
Question 4	2.16±0.82	2.70±0.67	0.117	2.40±0.89	2.20±0.83	0.589	2.19±0.83	3.00±0.01	0.157
FSDS-R	23.39±14.92	33.00±13.93	0.054	20.80±11.84	26.63±15.30	0.453	26.23±14.89	24.50±27.58	0.877
Modified Oxford Scale	2.78±0.76	2.40±0.70	0.298	2.20±0.84	2.69±0.79	0.187	2.66±0.81	2.50±0.71	0.687
POP-Q									

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Aa	-2.48±0.37	-2.45±0.16	0.130	-2.50±0.01	-2.45±0.41	0.887	-2.46±0.40	-2.25±0.35	0.325
Ba	-2.50±0.41	-2.35±0.24	**0.021**	-2.50±0.01	-2.43±0.45	0.836	-2.44±0.44	-2.25±0.35	0.371
Ap	-2.91±0.22	-2.80±0.26	**0.017**	-2.70±0.27	-2.89±0.31	**0.044**	-2.88±0.25	-2.75±0.35	0.362
Bp	-2.93±0.17	-2.80±0.26	**0.007**	-2.70±0.27	-2.89±0.31	**0.026**	-2.88±0.31	-2.75±0.35	0.307
C	-6.76±1.17	-7.20±1.23	0.470	-7.80±0.27	-6.75±1.27	**0.043**	-6.85±1.21	-6.00±2.83	0.662
D	-8.11±1.94	-9.00±1.05	0.167	-9.40±0.55	-7.85±3.01	**0.024**	-7.98±2.96	-7.50±2.12	0.510
TVL	9.64±0.85	10.50±0.85	**0.022**	10.30±0.67	9.71±0.84	0.101	9.77±0.84	9.25±0.35	0.380
Gh	2.94±0.56	3.10±0.66	0.099	2.80±0.57	3.05±0.61	0.425	3.05±0.60	2.50±0.71	0.242
Pb	3.24±0.42	3.10±0.46	0.075	3.50±0.50	3.27±0.46	0.300	3.30±0.47	3.00±0.01	0.293

SD: Standard Deviation; VLQ: Vaginal Laxity Questionnaire; FSFI: Female Sexual Function Index; QoL: Quality of Life; FSDS-R: Female Sexual Distress Scale – Revised; ICIQ-VS: International Consultation on Incontinence Questionnaire – Short Form; ICIQ-SF: International Consultation on Incontinence Questionnaire – Vaginal Symptoms; Ballooning Yes: >25 cm^2; Ballooning No (<25 cm^2). Mann-Whitney test; Kruskal-Wallis test;

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Table 5. Repeated measures ANOVA (analysis of variance) for comparison of 2D ultrasound measurements between radiofrequency and pelvic floor muscle training groups and assessment periods (per protocol and intention to treat).

2D Ultrasound Measurement (n=73)					**Comparison between** *RF **and** *PFMT		**Comparison** between assessment periods		**Interaction between** groups and assessment periods	
		Baseline Mean ± SD	**30 days** Mean ± SD	**6-Months** Mean ± SD	**p-value**[I] B-F1; B-F2	**Interpretation**	**p-value**[I] B-F1; B-F2	**Interpretation**	**p-value**[I] B-F1; B-F2	**Interpretation**
TAUS Proximal	RF	11.25 ± 4.04	11.18±2.95	9.88±2.80	0.071; 0.975	-	0.209; 0.585	-	0.959; **0.007**	Greater increase in the PFMT group at F2.
	PFMT	10.00 ±3.08	10.24 ± 2.78	10.82±2.43						
TAUS Middle Third	RF	10.68 ± 4.10	10.53±2.91	9.72±2.42	0.161; 0.509	-	0.194; 0.570	-	0.968; 0.237	-
	PFMT	9.33 ± 2.69	9.59 ± 2.32	9.86±2.37						
TAUS Distal	RF	11.86 ± 3.77	11.61±2.72	10.44±2.51	**0.023**; 0.665	Higher values in the RF group at F1.	0.584; 0.968	-	0.809; **0.018**	Greater decrease in the RF group at F2.
	PFMT	10.35 ± 2.38	10.41 ± 2.79	11.18±2.68						
TVUS Proximal	RF	6.83 ± 1.43	6.82±1.39	7.24±1.74	0.287; 0.450	-	0.170; **0.006**	Higher values in the PFMT group at F2.	0.356; 0.793	-
	PFMT	6.92 ±1.46	7.37 ± 1.45	7.49±1.36						
TVUS Middle	RF	6.44 ± 1.54	6.47±1.40	6.64±1.98	0.800; 0.439	-	0.542; 0.405	-	0.900; 0.562	-
	PFMT	6.38 ±1.50	6.58 ± 1.78	6.73±1.59						
TVUS Distal	RF	7.94 ± 1.83	7.97±2.13	7.26±2.12	0.292; 0.997	-	0.914; 0.212	-	0.668; **0.044**	Greater decrease in the RF group at F2.
	PFMT	7.44 ±2.20	7.61 ± 1.67	7.64±1.67						
2D Ultrasound Measurement (n=87)					**Comparison between **RF and **PFMT**		**Comparison between assessment periods**		**Interaction between groups and assessment periods**	
		Baseline Mean ± SD	**30 days** Mean ± SD	**6-Months** Mean ± SD	**p-value**[I] B-F1; B-F2	**Interpretation**	**p-value**[I] B-F1; B-F2	**Interpretation**	**p-value**[I] B-F1; B-F2	**Interpretation**
TAUS Proximal	RF	11.23 ± 3.90	11.10±2.91	9.99 ± 2.77	0.051; 0.625	-	0.281; 0.775	-	0.890; **0.006**	Greater increase in the PFMT group at F2.
	PFMT	9.90 ± 3.14	10.08±2.92	10.53 ± 2.71						
TAUS Middle Third	RF	10.65 ± 3.96	10.47±2.87	9.79 ± 2.42	0.093; 0.266	-	0.233; 0.632	-	0.984; 0.268	-
	PFMT	9.31 ± 2.73	9.51±2.46	9.72 ± 2.51						
TAUS Distal	RF	11.79 ± 3.67	11.60±2.69	10.51 ± 2.51	**0.018**; 0.532	Higher values in the RF group at F1.	0.522; 0.865	-	0.680; **0.018**	Greater reduction in the RF group at F2.
	PFMT	10.41 ± 2.61	10.45±2.90	11.05 ± 2.83						

TVUS Proximal	RF	6.79 ± 1.39	6.78±1.35	7.17 ± 1.69	0.316; 0.520	-	0.191; **0.006**	Higher values in the RF group at F2.	0.409; 0.970	-
	PFMT	6.95 ± 1.59	7.30±1.58	7.40 ± 1.53						
TVUS Middle	RF	6.44 ± 1.54	6.52±1.58	6.68 ± 2.05	0.520; 0.286	-	0.555; 0.420	-	0.862; 0.627	-
	PFMT	6.57 ± 1.59	6.72±1.79	6.84 ± 1.63						
TVUS Distal	RF	7.94 ± 1.83	7.96±2.10	7.32 ± 2.10	0.822; 0.454	-	0.908; 0.159	-	0.721; **0.037**	Greater reduction in the RF group at F2.
	PFMT	7.76 ± 2.20	7.88±1.79	7.91 ± 1.78						

2D: Two-dimensional ultrasound; SD: Standard deviation; *RF: Radiofrequency (n=38); *PFMT: Pelvic Floor Muscle Training (n=35); **RF: Radiofrequency (n=42); **PFMT: Pelvic Floor Muscle Training (n=45); TAUS: Transabdominal Ultrasound; TVUS: Transvaginal Ultrasound; B: Baseline assessment; F1: Follow-up 1 assessment (30 days post-intervention); F2: Follow-up 2 assessment (6 Months post-intervention); [1]ANOVA for repeated measures with variables transformed into ranks due to the absence of normal distribution, *per protocol and **intention to treat.

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Table 6. Repeated measures ANOVA (analysis of variance) for comparison of 4D translabial ultrasound measurements between radiofrequency and pelvic floor muscle training groups and assessment periods (per protocol and intention to treat).

	4D Ultrasound Measurement (n=73)					Comparison between *RF and *PFMT		Comparison between assessment periods		Interaction between groups and assessment periods	
			Baseline Mean ± SD	30 days Mean ± SD	6-Months Mean ± SD	p-value[1]	Interpretation	p-value[1]	Interpretation	p-value[1]	Interpretation
PFM Contraction	Hiatal Area Narrowing (Delta)	RF	1.61±2.63	2.54±1.70	3.36±2.32	**0.030**	Higher values in the PFMT group in F1.	**0.001**	Increase between baseline and F1 and between baseline and F2 in both groups.	0.522	-
		PFMT	2.84±2.63	4.07±3.17	4.73±4.03						
	Puborectalis Retraction	RF	-0.10±0.11	-0.14±0.07	-0.15±0.09	**0.001**	Higher values in the RF group at baseline, F1 and F2.	**0.001**	Decrease between baseline and F1 and between baseline and F2 in both groups.	0.578	-
		PFMT	-0.17±0.12	-0.21±0.09	-0.23±0.11						
	A-P Diameter Difference	RF	0.62±0.54	0.72±0.40	1.05±0.68	**0.014**	Higher values in the PFMT group in F1	**0.001**	Increase between baseline and F2 and between F1 and F2 in the RF group, and increase between baseline and F1 and between baseline and F2 in the PFMT group.	0.537	-
		PFMT	0.90±0.66	1.02±0.50	1.23±0.59						
	R-L Diameter Difference	RF	0.09±0.47	0.17±0.39	0.15±0.48	0.180	-	**0.019**	Increase between baseline and F1 in the PFMT group.	0.504	-
		PFMT	0.20±0.45	0.42±0.36	0.39±0.50						
	4D Ultrasound Measurement (n=87)					**Comparison between **RF and **PFMT**		**Comparison between assessment periods**		**Interaction between groups and assessment periods**	
			Baseline Mean ± SD	**30 days** Mean ± SD	**6-Months** Mean ± SD	**p-value[1]**	**Interpretation**	**p-value[1]**	**Interpretation**	**p-value[1]**	**Interpretation**
PFM Contraction	Hiatal Area Narrowing (Delta)	RF	1.58 ± 2.52	2.43 ±1.68	3.12 ±2.12	0.075	-	**0.001**	Increase between baseline and F2 in RF group.	0.376	-
		PFMT	2.79 ±2.51	3.67 ±2.90	3.91 ±3.29						
	Puborectalis Retraction	RF	-0.10 ±0.11	-0.13 ±0.08	-0.15 ±0.08	**0.001**	Higher values in the RF group at baseline, F1 and F2.	**0.004**	Decrease between baseline and F2 in both groups.	0.851	-
		PFMT	-0.17 ±0.11	-0.20±0.08	-0.21 ±0.10						
	A-P Diameter Difference	RF	0.63 ±0.52	0.73 ±0.43	1.01 ±0.61	**0.044**	Higher values in the PFMT group in F1.	**0.001**	Increase between baseline and F2 and between F1 and F2 in the RF group, and increase between baseline and F2 in the PFMT group.	0.349	-
		PFMT	0.90 ±0.64	0.98 ±0.48	1.09 ±0.51						

	R-L Diameter Difference	RF PFMT	0.04 ± 0.47 0.21 ±0.43	0.13 ±0.38 0.40 ±0.34	0.13 ±0.43 0.38 ±0.42	**0.005**	Higher values in the PFMT group in F1 and F2.	0.094	-	0.454	-

4D: four-dimensional; SD: Standard deviation; *RF: Radiofrequency (n=38); *PFMT: Pelvic Floor Muscle Training (n=35); **RF: Radiofrequency (n=42); **PFMT: Pelvic Floor Muscle Training (n=45); A-P: Anterior-Posterior; R-L: Right-Left; F1: Follow-up 1 assessment (30 days post-intervention); F2: Follow-up 2 assessment (6 Months post-intervention); [1]ANOVA for repeated measures with variables transformed into ranks due to the absence of normal distribution, *per protocol and **intention to treat.

Figure 1

Click here to access/download;Figure;Figure TAUS_Figure 1.png

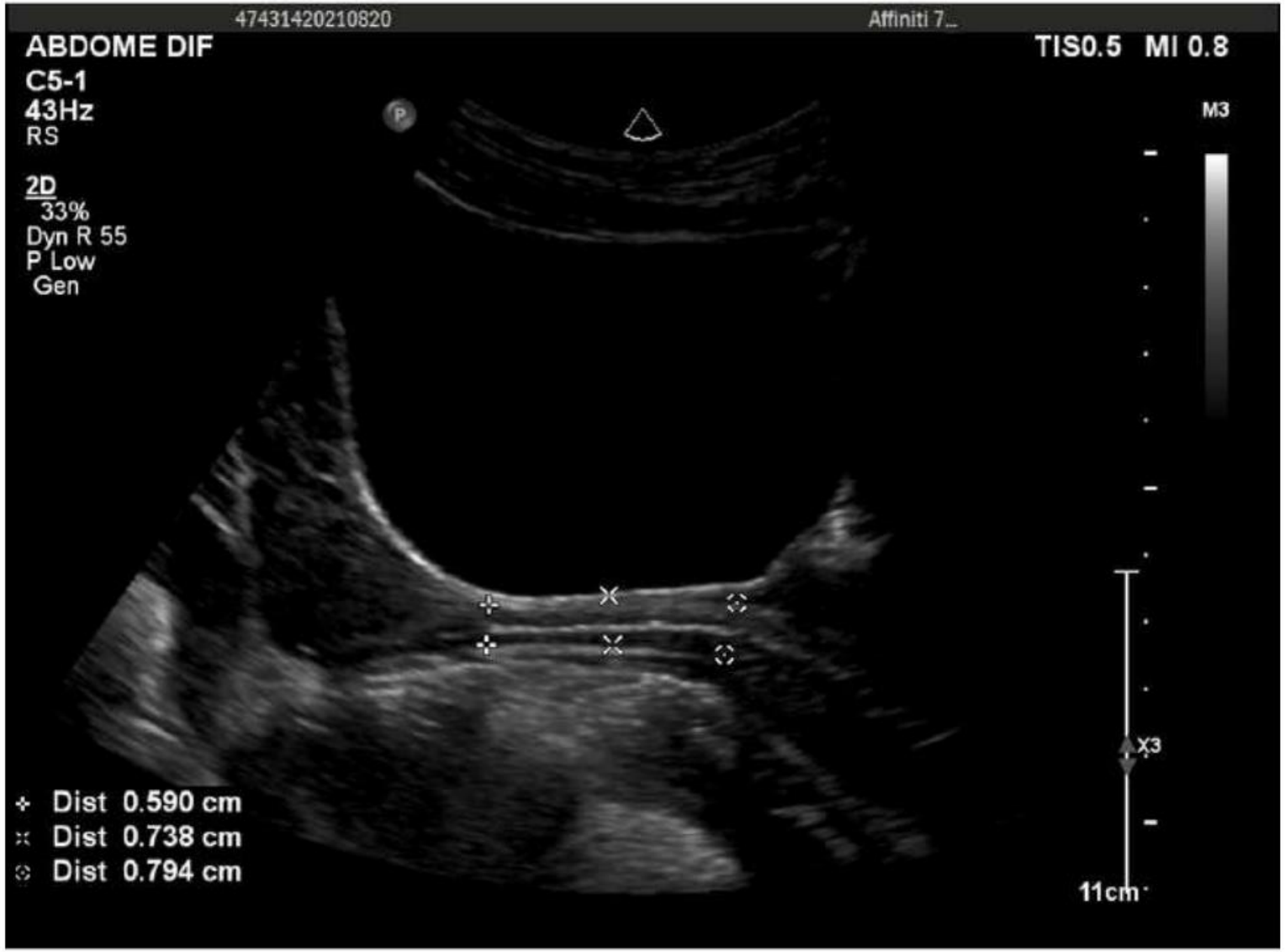


Figure 2

Click here to access/download;Figure;Figure TVUS_Figure 2.png

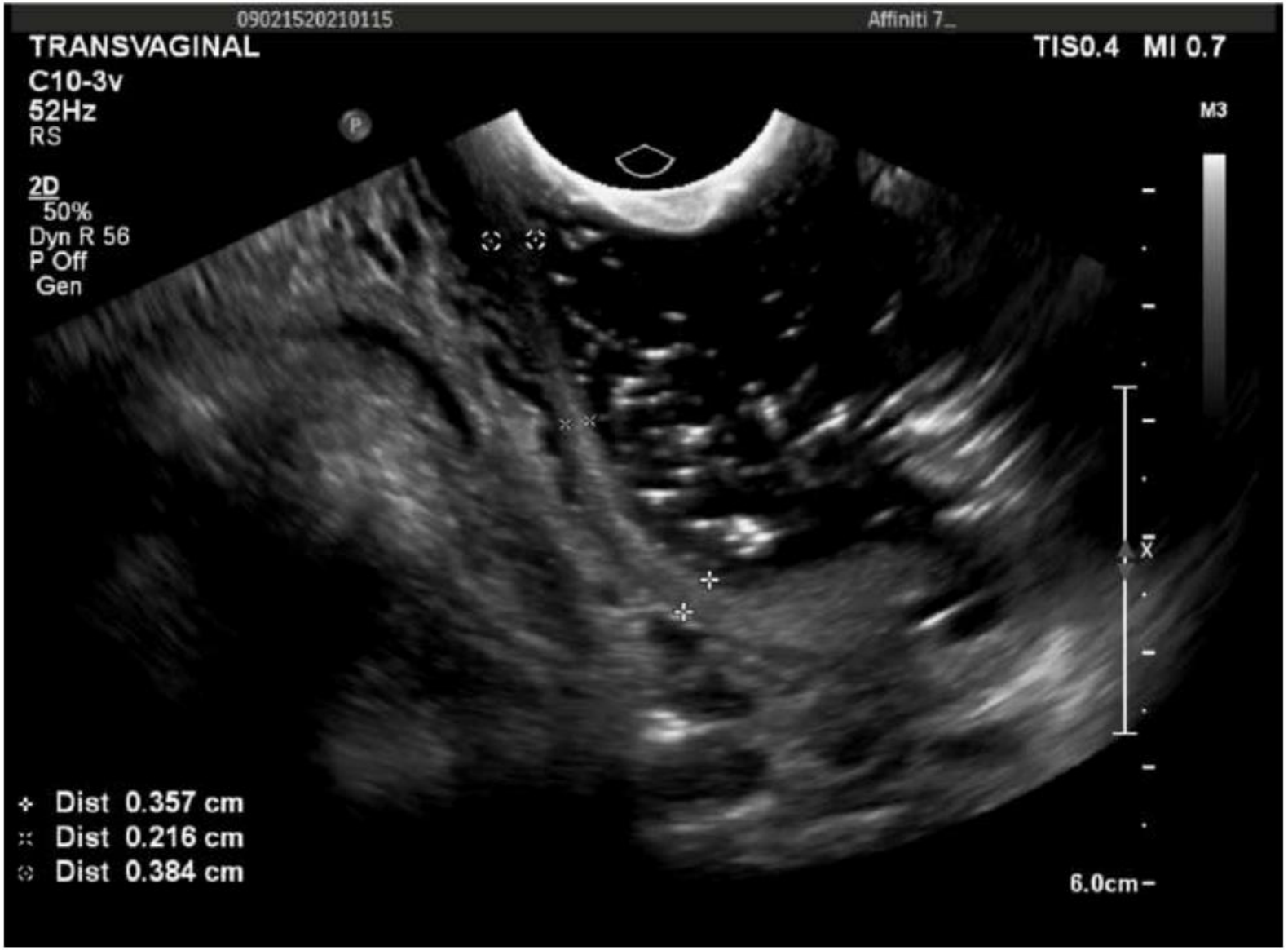


Figure 3

Click here to access/download;Figure;Avulsion_Figure 3.jpg

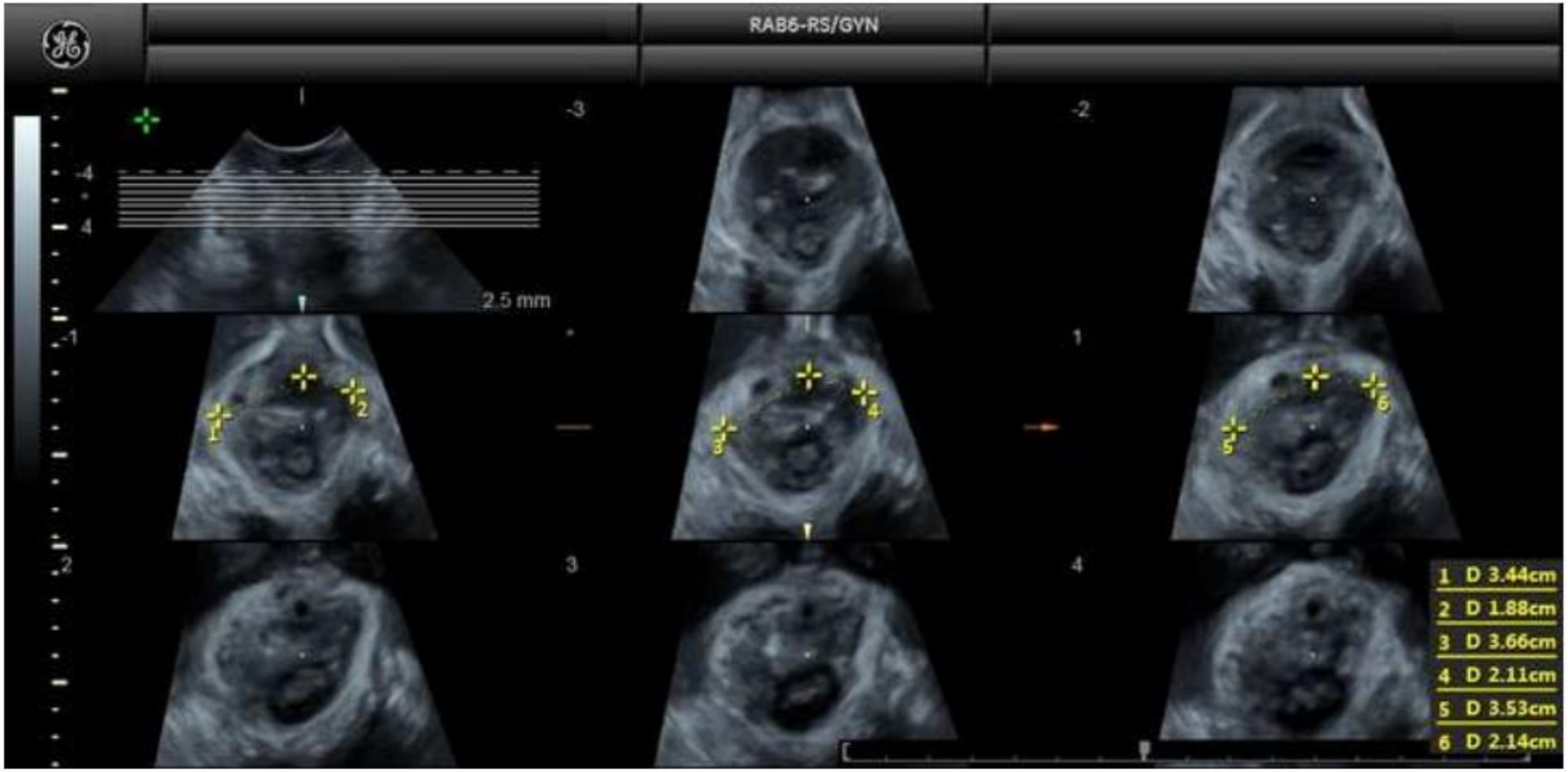
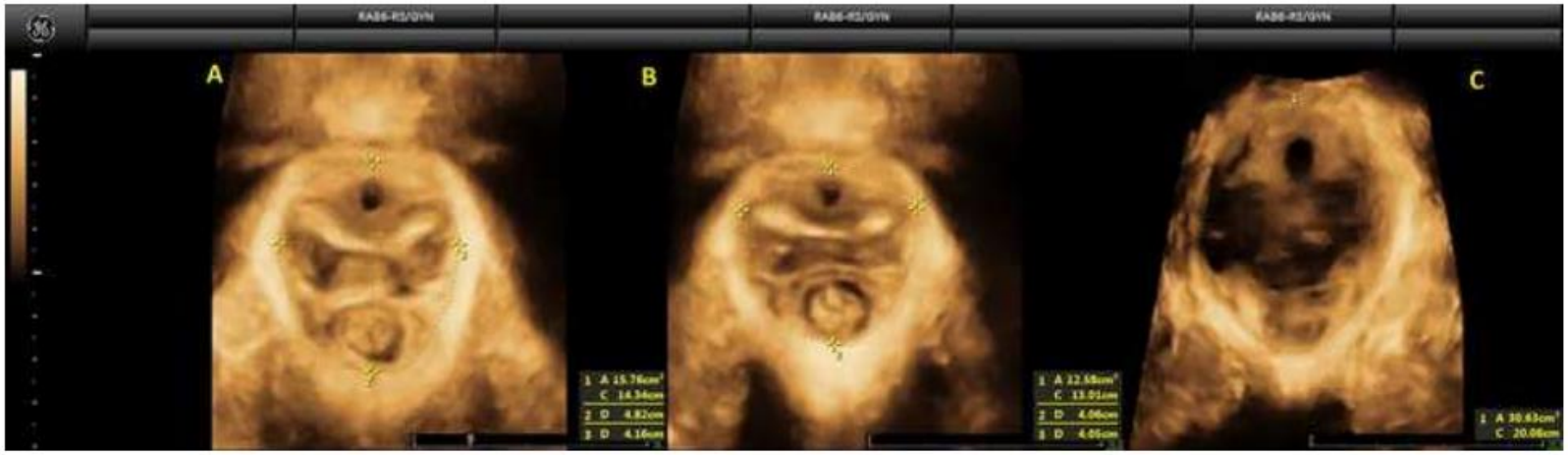


Figure 4

Click here to access/download;Figure;Rest_Contraction_Ballooning_Figure 4.jpg



5. DISCUSSÃO

A FV vem sendo mais frequentemente estudada na última década, principalmente após o advento das terapias à base de energia e da cosmética genital feminina. Essa tendência de valorização da chamada popularmente “estética vaginal” foi reforçada nos últimos anos, com o desenvolvimento de inúmeros equipamentos e técnicas cirúrgicas, empregados, principalmente na ginecologia, uroginecologia e, às vezes, de forma mais apelativa, por profissionais não especializados em cirurgia genital feminina. Os altos custos dos procedimentos e o forte apelo do marketing das empresas, garantindo segurança e eficácia das terapias à base de energia, chamou a atenção dos órgãos reguladores, como, por exemplo, o norte-americano *Food and Drug Administration* – FDA, que em 2018, escreveu um aviso sobre o uso dos lasers para esse fim[75].

Para cumprir com as exigências dos órgãos reguladores, ensaios clínicos randomizados vêm sendo publicados, mesmo que em menor número, quando comparados à quantidade de estudos observacionais realizados. Dessa forma, optamos por desenvolver um ensaio clínico randomizado que comparasse o efeito de uma das terapias à base de energia mais frequentemente estudadas – a radiofrequência, com o treinamento dos músculos do assoalho pélvico, um tratamento já com evidências para outras desordens em assoalho pélvico. O treinamento dos músculos do assoalho pélvico já havia sido estudado em um ensaio clínico randomizado anterior, porém, associado ao laser[76]. Durante a escrita e planejamento do ensaio clínico randomizado, surgiram vários questionamentos sobre o tópico. O primeiro deles foi a falta de padronização da definição da FV. Em uma busca criteriosa da literatura científica encontramos uma variedade de termos, que, a princípio eram sinônimos da FV, mas que também, descreviam outras condições uroginecológicas. Isto nos motivou a fazer a revisão sistemática sobre os vários tratamentos para a FV e a análise das definições encontradas.

A definição da FV (queixa de excessiva flacidez vaginal) surgiu no cenário científico em 2010 com a terminologia da IUGA/ICS, e descrita como

um dos sintomas da disfunção sexual feminina[1]. Em 2016, a FV apareceu novamente como um possível sintoma relacionado ao prolapso genital[71]. Um ano depois, a FV foi novamente relacionada à disfunção sexual feminina e descrita como qualquer desvio da sensação normal e/ou função expressa por uma mulher durante a atividade sexual[77]. Em 2018, retorna como sintoma vaginal e foi definida como sensação de flacidez vaginal[78].

Curiosamente, o termo "*vaginal laxity*" já havia sido usado na década de 80 em um estudo para contracepção em mulheres mais velhas, em que a flacidez vaginal, resultante dos partos vaginais, reduzia o efeito do diafragma[79]. Mais tarde, ao final da década de 90, a FV foi associada ao enfraquecimento da transmissão de forças musculares, interferindo na abertura e fechamento uretral[80]. E em 2010, com o desenvolvimento do *Vaginal Laxity Questionnaire*, a percepção da FV pode ser subjetivamente classificada em níveis de flacidez (*very loose*, *moderately loose*, *slightly loose*)[4].

Outros termos foram usados em pesquisas científicas indicando a sensação de relaxamento ou alargamento vaginal. O termo "*vaginal relaxation*" foi utilizado para se referir a sintomas relacionados ao prolapso genital na década de 50[81] e com maior número de trabalhos a partir da década de 70[82]. Mais tarde, o termo "*vaginal relaxation*" foi associado à perda da estrutura ótima da vagina, com consequente flacidez da parede vaginal[83]. Já o termo "*vaginal relaxation syndrome*" é usado como sinônimo de frouxidão vaginal em alguns estudos[83]. Outro termo utilizado é o "*wide vagina*". Este termo se refere aos defeitos do introito vaginal. Segundo Ostrzenski, a presença de alguns defeitos como: o achatamento do períneo posterior (diminuição da medida do corpo perineal), a ausência parcial ou completa da placa himenal, a perineocele de diferentes tamanhos, o prolapso da parede vaginal posterior distal (compartimento posterior) e o defeito do esfíncter anal podem causar o alargamento do introito vaginal[84]. Diante do exposto, é evidente a necessidade de uma padronização dos termos relacionados à FV. Após a análise de todos os termos, seguimos com a definição inicial da IUGA/ICS para a continuidade da escrita do ensaio clínico randomizado (projeto principal).

Subsequentemente, deparamo-nos com a escassez de instrumentos de avaliação da FV. Somente dois instrumentos, o *ICIQ-Vaginal Symptoms* (pergunta número 4) e o *Vaginal Laxity Questionnaire*, classificavam a percepção da FV. Decidimos então, avaliar a FV de forma abrangente com os instrumentos disponíveis e acrescentar outros instrumentos validados que avaliassem a função sexual feminina e a angústia sexual em nossas participantes. A angústia sexual é caracterizada por um conjunto de sentimentos e emoções que os indivíduos têm sobre sua sexualidade[65]. Difere da disfunção sexual relacionada aos sintomas da função sexual, como excitação, orgasmo e dor, separados das emoções. Curiosamente, não encontramos o *Female Sexual Distress Scale – Revised* (FSDS-R) em língua portuguesa. Assim, planejamos a validação e adaptação cultural deste instrumento. Mais tarde, durante o período de coleta de dados, utilizando o FSDS-R, percebemos que a FV afetava a relação das participantes com elas mesmas, com o parceiro e com a sua sexualidade. A partir daí, um estudo qualitativo fez-se indispensável para compreendermos, com mais detalhes, este cenário. Em geral, a prevalência da disfunção sexual feminina no Brasil é de 67.7%[85]. Mesmo sendo uma condição subnotificada, a prevalência de FV em outros países atinge cerca de 24% a 38% das mulheres. No entanto, até o momento, não foi estimada a prevalência de FV no Brasil. Diante do relato das participantes, no estudo qualitativo, compreendemos as dificuldades que elas apresentavam em lidar com o constrangimento de expor a queixa em si e mesmo o termo “frouxidão vaginal” para os profissionais de saúde e para a parceria. Ficou nítida a importância que as nossas participantes deram à necessidade de promover o prazer do parceiro e o quanto uma “vagina frouxa/flácida” impacta negativamente a sua autoimagem corporal e sua autoestima. O estudo qualitativo enriqueceu grandemente o nosso entendimento sobre a queixa de FV, abrindo possibilidades para o desenvolvimento de outros projetos de pesquisa e clareando o horizonte para a compreensão de sua fisiopatologia. Este estudo talvez possibilite, em um futuro próximo, a elaboração de um instrumento objetivo detalhado para avaliar a FV.

Mesmo sem o conhecimento de sua fisiopatologia, observamos um número crescente de artigos sendo publicados, avaliando os efeitos de terapias

à base de energias, principalmente o laser e outros procedimentos cirúrgicos no tratamento da FV. Após a elaboração de uma pergunta de pesquisa, uma estratégia de busca foi organizada. Pensamos em uma estratégia ampla que encontrasse, em todos os campos de busca, o maior número de trabalhos publicados sobre os tipos de tratamento para a FV. Oitocentos e dezesseis trabalhos foram encontrados. Interessante notar o número elevado de resumos de congressos sobre o tema. Isso significa que o tópico desperta interesse em muitos pesquisadores e que estudos estão sendo desenvolvidos e serão futuramente publicados. Ao realizarmos a busca na literatura para a escrita do projeto de pesquisa principal (ensaio clínico randomizado) encontramos o laser e a radiofrequência como os principais tratamentos publicados para a FV, seguidos pelos procedimentos cirúrgicos e uma opção de tratamento tópico. Em nossa revisão sistemática com meta-análise notamos a mesma tendência. O laser de *Erbium Yag* não ablativo e o Laser de CO_2 ablativo tiveram os seus efeitos avaliados no tratamento da FV. Ambos apresentam o objetivo de promover a remodelação do colágeno nos tecidos conectivos subepiteliais, no entanto, utilizando mecanismos diferentes[86]. O *Erbium Yag* tem mais afinidade para a absorção de água que o CO_2 em um comprimento de onda de 10.600 nm e permite um efeito térmico secundário mais profundo e um aquecimento controlado da mucosa-alvo da parede vaginal, resultando em aquecimento controlado da camada subepitelial sem queimar o epitélio vaginal[87]. Já os lasers de CO_2 (10.600 nm) causam desnaturação tecidual e subsequente remodelação das fibras de colágeno e elastina[57]. Dentre os procedimentos cirúrgicos destacamos o uso do plasma rico em plaquetas e o implante de fios de ouro. O plasma rico em plaquetas é bastante estudado na ortopedia e na dermatologia. O seu uso na uroginecologia é mais recente através das técnicas de cirurgia cosmética genital feminina e das cirurgias de prolapso genital. De acordo com um estudo, as plaquetas liberam cerca de 35 fatores de crescimento, e o seu uso terapêutico promove a cicatrização e regeneração dos tecidos[88]. Em pacientes na pós-menopausa com atrofia vulvovaginal, o plasma rico em plaquetas associado ao ácido hialurônico, melhorou o trofismo e a hidratação da mucosa vaginal[89]. Em pacientes com FV, o plasma rico em

plaquetas tem sido associado à colpoperineorrafia posterior e ao uso da matriz dérmica acelular humana[88,90].

Parece haver, novamente, uma tendência na utilização de procedimentos estéticos na uroginecologia. Identificamos um estudo que utilizou implantes de fio de ouro no tratamento da FV. Implantes de tamanhos variados (dependendo do local de fixação) foram inseridos na derme e na camada subcutânea dos lábios maiores, no introito vaginal e nas paredes vaginais entre a lâmina própria e a camada muscular (posicionados nas 3,6,9 e 12 horas), e ao redor do clitóris e dos lábios menores. Segundo o autor, uma melhora significativa foi observada na queixa de FV das 46 participantes operadas[91]. Fios elásticos de silicone foram utilizados previamente em uma abordagem similar com o objetivo de melhorar a função sexual e corrigir a "largura vaginal" em mulheres com "*wide vagina*"[92].

Outro desafio encontrado no decorrer da escrita do projeto principal foi a escassez de medidas objetivas para avaliar a FV. Os estudos previamente publicados traziam somente o auto-relato das participantes como critério de inclusão para a queixa de FV. Poucos trabalhos apresentaram o toque vaginal como avaliação da FV, mas sem nenhuma padronização, a não ser a medida subjetiva do pesquisador. A partir daí, surgiu uma exitosa e feliz parceria com a equipe de ecografia do CAISM. Não sabíamos se a espessura vaginal diferia entre mulheres com e sem FV. Além disso, não queríamos que as participantes fossem submetidas a biópsias vaginais que causariam desconfortos e que não seriam utilizadas na prática clínica dos profissionais de saúde envolvidos no cuidado destas pacientes. Assim, planejamos um estudo transversal que determinasse se a espessura da parede vaginal, medida por ultrassom, poderia diferir de acordo com as técnicas rotineiramente utilizadas na ginecologia (abdominal e vaginal) em mulheres com FV. As medidas da espessura vaginal poderiam ser facilmente realizadas e incorporadas na rotina do cuidado destas pacientes. Outra abordagem ultrassonográfica, como a avaliação translabial, foi também incluída em nosso planejamento, com o intuito de verificarmos se as pacientes com FV apresentavam macro e/ou microtraumas do assoalho pélvico, contribuindo também para o entendimento da fisiopatologia deste

sintoma. A avaliação ultrassonográfica translabial é amplamente utilizada na avaliação do prolapso genital e em outras desordens do assoalho pélvico na uroginecologia.

Como mencionado anteriormente, o ensaio clínico randomizado que comparou o efeito do treinamento dos músculos do assoalho pélvico e da radiofrequência em mulheres com FV, foi o nosso projeto de pesquisa principal e o instrumento disparador para o planejamento de outros estudos que seguiram uma sequência lógica, à medida que notamos a necessidade de compreender e contribuir com o estudo da FV. O recrutamento das participantes foi feito mediante a divulgação do estudo em mídia social e no site oficial do Hospital da Mulher Prof. Dr. José Aristodemo Pinotti - CAISM. Além disso, contamos com a ajuda dos docentes do Departamento de Tocoginecologia da Faculdade de Ciências Médicas da Unicamp na divulgação do estudo nos postos de saúde. Para garantir a privacidade das participantes, disponibilizamos, além de um contanto telefônico, um email e um número de contato em um aplicativo de mensagem. Este último foi o meio de comunicação mais utilizado. Contamos com as parcerias dos setores de fisioterapia, ecografia e o ambulatório de Uroginecologia do CAISM que foram indispensáveis no desenvolvimento do projeto de pesquisa. Nestes locais realizamos a coleta de dados, a aplicação de questionários, a realização de exames físicos e ultrassonográficos, além das intervenções do estudo.

Com um número considerável de participantes recrutadas e outras já randomizadas e em processo inicial de intervenção, fomos surpreendidos pela pandemia de COVID-19. O estudo foi interrompido e retomado somente após a liberação das atividades de pesquisa na UNICAMP. Dentre as maiores dificuldades que encontramos durante a retomada do estudo, destacamos o receio das participantes em retornarem ao ambiente hospitalar, mesmo com todas as medidas de segurança oferecidas pelo CAISM e pela equipe de pesquisa. Esta insegurança foi contornada com muita paciência e acolhimento. Neste processo, excluímos 77 participantes recrutadas, e mesmo tendo o perfil de inclusão para o estudo, não se sentiram seguras para iniciarem a coleta de dados ou prosseguirem com as intervenções. Problema semelhante

encontramos no período de follow-up, sempre que as novas ondas de contaminação pelo COVID-19 surgiam, impedindo a continuidade do seguimento das participantes. Um total de cinco participantes preferiram não retornar ao período de follow-up de 30 dias pós-intervenção. Outro fato importante foi a não aderência ao treinamento dos músculos do assoalho pélvico. Curiosamente, o nosso estudo teve um índice de não-aderência de cerca de 15%, o que consideramos baixo, diante do cenário de pandemia. As principais razões foram as dificuldades encontradas pelas participantes em adaptarem à nova rotina dos filhos e parceiros em casa. Com os parceiros em *home-office* e os filhos em aulas *on-line*, as participantes não conseguiram cumprir com o protocolo de tratamento que incluía sessões de treinamento dos músculos do assoalho pélvico em casa e uma vez na semana no CAISM.

Conforme apresentado nos resultados desta tese, o projeto de pesquisa principal comparou dois tratamentos para a frouxidão vaginal. A radiofrequência já havia sido estudada em desenhos prospectivos observacionais, mas somente um ensaio clínico randomizado estava disponível no momento da elaboração do projeto de pesquisa.

A radiofrequência utilizada em nosso ensaio clínico randomizado foi a de circuito monopolar, do tipo micro-ablativa, com um probe vaginal com 64 microagulhas que funcionam de forma randômica para evitar superaquecimento e sobreposição tecidual. No circuito monopolar, o eletrodo ativo (probe vaginal) é independente do eletrodo dispersivo (placa em contato com o corpo da participante). Assim, a energia flui do eletrodo ativo, atravessa o corpo da participante e alcança o eletrodo dispersivo. A ação randômica de ativação das microagulhas permite o resfriamento entre os pontos e preservação dos tecidos adjacentes aos pontos vaporizados da mucosa vaginal [93,94]. Este efeito parece promover a estimulação dos fibroblastos com consequente neocolagênese e neoelastogênese[93,94], resultando em um aumento da espessura da mucosa vaginal. Em nossas participantes, o aumento da espessura vaginal foi percebido como a diminuição do calibre vaginal com consequente sensação de “aperto” vaginal. As participantes relataram um melhor conforto durante o intercurso sexual, com a sensação, por

elas descritas, de “preenchimento” do canal vaginal. Algumas participantes relataram ainda, que a sensação de “aperto” vaginal foi também percebida pelo parceiro. Mesmo com estes relatos, optamos por não incluir a percepção do parceiro como variável em nosso estudo inicial. Ao final do estudo (após a coleta de dados do follow-up de seis meses pós-intervenção) as participantes poderiam receber a outra intervenção, sem terem que passar pelo processo de *follow-up*. Mesmo com o apelo comercial da radiofrequência nas mídias, menos participantes do grupo treinamento dos músculos do assoalho pélvico solicitaram a realização da radiofrequência ao final do estudo. Já no grupo radiofrequência, a maioria das participantes solicitaram o treinamento dos músculos do assoalho pélvico ao final do estudo. O principal motivo desta solicitação foi o fato de que o efeito da radiofrequência começou a reduzir após os seis meses da última aplicação, e o alto custo do procedimento, inviabilizava a busca por novas sessões. Nesse caso, faz-se necessário o desenvolvimento de estudos que avaliem o efeito a longo prazo da radiofrequência na queixa de FV.

No que diz respeito ao treinamento dos músculos do assoalho pélvico, pouco se sabia sobre o seu efeito nas mulheres com FV. Somente um ensaio clínico randomizado avaliou a contração destes músculos associados ou não ao laser de Erbium, em um período de treinamento de oito semanas, com cinco séries de 20 repetições cada, duas vezes por semana. A pressão de contração dos músculos do assoalho pélvico foi graduada por um equipamento de medida em centímetro de água[76]. O grupo que associou o treinamento dos músculos do assoalho pélvico com o laser de Erbium apresentou contração muscular superior após quatro e oito semanas de tratamento, quando comparado ao grupo que realizou somente o treinamento dos músculos do assoalho pélvico[76]. O efeito do laser de Erbium nos músculos não foram comentados pelos autores. Outro estudo discutiu o efeito do laser de Erbium no aumento da pressão média de contração dos músculos do assoalho pélvico. Os autores informaram que o aumento da pressão de contração muscular foi devido à realização do treinamento dos músculos do assoalho pélvico que as participantes realizaram durante as medidas de perineometria e que a partir da coleta de dados, as participantes aprenderam como aumentar o suporte de

seus músculos pélvicos[95]. Outro estudo reportou que o efeito do laser de Erbium não atinge diretamente os músculos do assoalho pélvico; portanto, não se espera que a contração muscular melhore[96]. No período de desenvolvimento do projeto de pesquisa principal, encontramos um estudo que mostrou melhora na pressão de contração dos músculos do assoalho pélvico medida pela perineometria. No entanto, este estudo não discutiu o efeito da radiofrequência no mecanismo de melhora da contração muscular[97]. A partir desses achados e da falta de evidências que explicassem o efeito da radiofrequência nos músculos do assoalho pélvico, optamos por fazer um grupo isolado de radiofrequência e um grupo isolado de treinamento dos músculos do assoalho pélvico.

Os nossos resultados mostraram uma melhora significativa da contração dos músculos do assoalho pélvico após 30 dias e seis meses do tratamento com a radiofrequência. No entanto, o valor médio da contração dos músculos do assoalho pélvico permaneceu em grau 2 (contração fraca dos músculos do assoalho pélvico), com uma melhora clínica muito pequena, quando comparada com a linha de base. Infelizmente não foi possível a utilização da perineometria nessas participantes. Mesmo assim, a nossa hipótese para estudos futuros, é que a radiofrequência não teria efeito direto sobre os músculos do assoalho pélvico e que as mudanças observadas em nosso ensaio clínico randomizado foi proporcionado pelos benefícios do calor na musculatura.

Alguns estudos mostraram evidências do efeito dos músculos do assoalho pélvico na função sexual feminina[98,99]. No entanto, mais estudos são necessários para comprovarem a sua importância na FV. O que nos motivou a estudar o efeito dos músculos do assoalho pélvico, foi o fato de não sabermos, a princípio, se a queixa de FV seria uma queixa restrita a um conjunto fatores musculares e conectivos que pudessem contribuir para a percepção do sintoma ou à vagina.

Em nosso estudo, a contração dos músculos do assoalho pélvico melhorou significativamente no grupo de treinamento dos músculos do assoalho pélvico. As participantes relataram uma melhora na sensação de

“aperto” do canal vaginal e se sentiram capazes de controlar as contrações dos músculos do assoalho pélvico durante o intercurso sexual. Esta capacidade de controle da contração foi vista de forma positiva pelas participantes do estudo, melhorando o prazer e a autoconfiança nas relações sexuais.

A vagina recebe inervação parassimpática (S2-S4) com função de transudação e inervação somática (S2-S4), pelo nervo pudendo, em sua porção mais distal, com função contrátil, com maior concentração de nervos na parede anterior que na parede posterior[100]. Possui três camadas formadas pela mucosa (camada epitelial e lâmina própria), camada muscular e camada adventícia[101]. A vagina passa por alterações ao longo da vida da mulher, com mudanças encontradas na composição do epitélio, na produção de secreções, no controle do pH e na microbiota vaginal[102]. No entanto, a vagina não apresenta um mecanismo intrínseco esfincteriano. A zona de alta pressão vaginal é inteiramente relacionada ao músculo puborretal, parte do músculo levantador do ânus[103]. A contração do músculo puborretal eleva o canal anal em direção ventral ou anterior e causa uma compressão no canal anal, na vagina e na uretra contra o osso púbico. Isso significa que, na zona de alta pressão vaginal, a pressão vaginal é superior no sentido ântero-posterior que no látero-lateral[104]. Dessa forma, o hiato do levantador do ânus se torna menor na contração e retorna à posição de repouso no relaxamento. Por receberem a inervação do nervo pudendo, o bloqueio desse nervo pode causar o aumento das dimensões do hiato do levantador do ânus e a redução da pressão vaginal[103]. Assim, as hipóteses relacionadas ao micro e macro-traumas do levantador do ânus, apresentada por Delancey[105] e Dietz et al.[7,26], começaram a fazer sentido no nosso entendimento a respeito da fisiopatologia da FV. Em um modelo computadorizado, o parto vaginal impõe uma taxa de estiramento do levantador do ânus de até 3,3 vezes o seu tamanho e o nervo pudendo sofre tensões de até 33%[106]. Mais tarde, um estudo com ultrassonografia 3D/4D encontrou que a área hiatal do levantador do ânus parece ser a medida de distensibilidade mais preditiva de sintomas da FV[46]. E por fim, mulheres com lesões severas do levantador do ânus, que foram submetidas ao treinamento dos músculos do assoalho pélvico tiveram 45% menos chance de desenvolverem sintomas de FV[107].

Mas como compreender este sintoma em mulheres submetidas ao parto cesariana e, em um cenário ainda mais complexo – nas mulheres nulíparas?

O potencial efeito protetor da cesariana para o assoalho pélvico é controverso e continua em debate. Uma revisão de revisões sistemáticas encontrou que a cesariana foi associada a um risco reduzido para incontinência urinária e prolapso genital[108]. No entanto, outro estudo mostrou que, mesmo com um baixo risco para disfunções do assoalho pélvico na cesariana, as mudanças no hiato genital podem ocorrer, independentemente do modo de parto[109]. Somado a estes fatores, tentamos compreender a variação de crescimento e desenvolvimento humano em relação ao assoalho pélvico. Encontramos que o assolho pélvico cresce e se desenvolve durante a infância, atingindo a sua capacidade máxima de reserva funcional no início da vida adulta[106,110]. A partir daí, com o passar dos anos, ocorre um declínio normal da reserva funcional influenciada por fatores como código genético, nutrição e questões ambientais, além do grau de estresse imposto pelo estilo de vida ao assoalho pélvico[106,110]. Apesar de um pequeno número de participantes, o nosso estudo identificou a queixa de frouxidão vaginal em nulíparas e em participantes submetidas à cesariana. Há necessidade de mais estudos para nos auxiliar na compreensão do mecanismo da frouxidão vaginal nesta população.

Chegando ao final de nossa trajetória de estudo da frouxidão vaginal, surgiu a oportunidade de um doutorado sanduíche, financiado pela Fundação de Amparo à Pesquisa do Estado de São Paulo – FAPESP, e em parceria com o Imperial College London, Londres, Reino Unido.

Após o desenvolvimento de um projeto de pesquisa sob a supervisão dos Professores Luiz Gustavo Oliveira Brito e Rufus Cartwright, as atividades de pesquisa foram iniciadas no *Chelsea and Westminster Hospital*, no departamento de uroginecologia, em julho de 2022 e se estendendo até dezembro do mesmo ano. O *Chelsea and Westminster Hospital NHS Foundation Trust* é uma das fundações hospitalares mais bem classificadas e com melhor desempenho no Reino Unido. O hospital conta com mais de 6.000 funcionários, com 12 clínicas comunitárias no noroeste de Londres e oferece

atendimento a uma comunidade de mais de 1,5 milhão de pessoas. Além disso, é o segundo maior serviço de maternidade da Inglaterra, realizando o parto de mais de 11.000 bebês todos os anos. A clínica de uroginecologia recebe, todos os dias, um grande contingente de mulheres, das mais variadas culturas e etnias. Nesse cenário foi possível recrutar e avaliar 300 participantes para o nosso estudo, além de participar de reuniões multidisciplinares, treinamentos voltados para o manejo de homens-trans, acompanhar os atendimentos médico-uroginecológicos, fisioterapêuticos e de enfermagem. O acompanhamento de cirurgias ambulatoriais, laparoscópicas e robóticas, em uma estrutura de tecnologia avançada também foi possibilitada sob a supervisão do Dr. Cartwright. Dentre as cirurgias citadas, destaco o procedimento de reversão de sequelas de mutilação genital feminina, que nunca havia acompanhado. Curiosamente, a etnia não foi associada à frouxidão vaginal e à disfunção sexual em nossa população. Os diferentes grupos étnicos e as suas relações com a função sexual feminina ainda são pouco explorados na literatura científica. O nosso estudo foi o primeiro a avaliar a frouxidão vaginal nas diferentes etnias atendidas pelo departamento de Uroginecologia do Chelsea and Westminster Hospital.

Durante o período de doutorado, tive também a oportunidade de participar do Programa de Estágio Docente (PED) no ambulatório de Uroginecologia do CAISM, onde desenvolvi atividades de ensino supervisionada para alunos de medicina do quinto ano, principalmente, no manejo conservador do prolapso genital; de ministrar a aula intitulada *Physiotherapy and Obstetric Anal Sphincter Injuries* no 6º Congresso Internacional da Associação Latino-americana de Assoalho Pélvico - ALAP; de ministrar três aulas intituladas “Estratégia de busca, Introdução e Justificativa” na disciplina TG583 - Metodologia de Pesquisa em Reprodução Humana I do curso de Mestrado do Programa de Pós-Graduação em Tocoginecologia da UNICAMP; de ministrar cinco aulas no curso de Especialização em Fisioterapia aplicada à Saúde da Mulher, com os temas “O sistema de quantificação do Prolapso de Órgão Pélvico – POP-Q”, “Frouxidão Vaginal” e “Revisão Sistemática”; de revisar artigos científicos em três jornais: *BioMed Central* (BMC), *International Urogynecology Journal* (IUJ), e *Brazilian Journal of*

Physical Therapy (BJPT); de participar como uma das redatoras do *Journal Club* do *International Urogynecology Journal* (IUJ); de co-supervisionar os projetos de pesquisa de três alunos do curso de medicina do Imperial College London; de receber dois prêmios de segundo melhor estudo no 60º Congresso Brasileiro de Ginecologia e Obstetrícia, 2022 e no 27º Congresso Paulista de Obstetrícia e Ginecologia, 2022; e de publicar outros sete artigos como primeira autora e 12 artigos como co-autora, além dos artigos que se encontram na presente tese.

6. CONCLUSÃO

6.1. Objetivo 1. Revisar sistematicamente as evidências contemporâneas da eficácia e da segurança das intervenções para a FV.

A radiofrequência e o laser apresentaram benefícios na função sexual medida pelo escore total do FSFI em oito estudos observacionais. Estes benefícios não foram observados em três ensaios clínicos randomizados que utilizaram o mesmo instrumento. Tanto o laser quanto a radiofrequência tiveram um efeito benéfico na melhora da contração dos músculos do assoalho pélvico em ensaios clínicos randomizados.

6.2. Objetivo 2. Realizar a adaptação transcultural, tradução e validação da *Female Sexual Distress Scale-Revised* (FSDS-R) em português do Brasil para mulheres com FV.

O *Female Sexual Distress Scale – Revised* na versão traduzida e adaptada para a língua portuguesa brasileira apresentou consistência interna satisfatória para o *ICIQ-Vaginal Symptoms e Female Sexual Function Index*. O *Female Sexual Distress Scale – Revised* pode ser uma ferramenta auxiliar na identificação da angústia sexual das mulheres com FV e contribuir para o cuidado de mulheres brasileiras com outras queixas sexuais.

6.3. Objetivo 3. Determinar se a espessura da parede vaginal medida por ultrassom pode diferir de acordo com as técnicas abdominal ou vaginal e avaliar se as variáveis clínicas estão associadas às medidas vaginais de mulheres com FV.

Uma correlação significativa foi encontrada entre a espessura da parede vaginal e a duração das queixas de FV, a contração dos músculos do assoalho pélvico e os pontos anatômicos do POP-Q. Ambas as técnicas de medida da espessura da parede vaginal parecem ser uma abordagem promissora na

compreensão da fisiopatologia da FV e podem ser facilmente incorporadas à rotina de atendimento de mulheres com esse sintoma.

6.4. Objetivo 4. Compreender os significados que as mulheres atribuem à sensação de FV e seu impacto na percepção de si mesmas, na relação afetiva íntima e na sexualidade.

Os relatos mostram que a sensação de FV impacta negativamente as relações intra e interpessoais das entrevistadas. A melhora nos sintomas de FV foi vista como uma via de recuperar a feminidade das participantes. Este estudo precursor pode contribuir para o desenvolvimento de estratégias para a compreensão da fisiopatologia da FV.

6.5. Objetivo 5. Investigar os fatores associados à FV e à disfunção sexual e suas relações com as desordens do assoalho pélvico em uma população feminina multiétnica.

Mulheres na menopausa, multíparas e em estágios iniciais de prolapso genital foram associadas à uma chance aumentada de apresentarem FV. Além desses fatores, a primiparidade, a laceração perineal, e os tipos de parto também foram associados à FV. Os sintomas vaginais, a qualidade de vida sexual e a angústia sexual foram significativamente piores em mulheres com FV quando comparadas com mulheres sem queixa de FV. Curiosamente, diferenças não foram encontradas entre os quatro grupos étnicos identificados no estudo.

6.6. Objetivo 6. Comparar o efeito da RF e do TMAP no tratamento de mulheres com FV.

6.6.1. Objetivo 6.1.Apresentar o protocolo do ensaio clínico randomizado que compara o efeito de RF e TMAP em mulheres com sintomas de FV.

O protocolo de estudo foi capaz de apresentar as etapas do ensaio clínico randomizado de forma detalhada para garantir a sua reprodutibilidade. Tanto a radiofrequência quanto o TMAP podem auxiliar na abordagem inicial da FV com benefícios nos sintomas sexuais, vaginais e urinários.

6.6.2. Objetivo 6.2. Colaborar com a compreensão da avaliação objetiva de mulheres com FV comparando a espessura da parede vaginal medido pela ultrassonografia 2D transabdominal e transvaginal; e a morfometria e a função dos músculos do assoalho pélvico medidas por ultrassom translabial quadridimensional nos grupos de RF e TMAP após 30 dias e 6 meses de acompanhamento.

A análise secundária foi capaz de auxiliar na avaliação objetiva de mulheres com FV. As medidas da espessura parede vaginal pelos USTA e USTV apresentaram uma correlação fraca com instrumentos clínicos. Mulheres com *ballooning* no 4D-USTL apresentaram pontuação significativamente pior na função sexual e sintomas vaginais; e maiores medições de TVL, Ba e Bp.

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8.ANEXOS

8.1. Formulário de Coleta de Dados do Ensaio Clínico Randomizado

Número da Participante: _____

PESQUISA FROUXIDÃO VAGINAL – UNICAMP

Nome: _____
(o seu nome será substituído por um número no registro da pesquisa)

Data (hoje): ___/___/_____ **Data Nasc:** ____/_____/_____

Telefones: ( ) _____ ( ) _____

Estado Civil: ( ) Solteira ( ) Casada ( ) Divorciada ( ) Viúva
Cor da Pele: ( ) Branca ( ) Negra ( ) Parda
Escolaridade: ( ) Não Alfabetizada ( ) Ens. Fundamental ( ) Ens. Médio
( ) Ens. Superior □ completo □ incompleto
Peso: _____ **Altura:** _____ **Faz atividade física:** ( ) sim ( ) não

Dor para urinar: ( ) sim ( ) não **Levanta a noite para urinar:** ( ) sim ( ) não
Absorvente p/urina: ( ) não ( ) sim Quantos p/dia: _____
Quantas vezes vai ao banheiro por dia (para urinar): _____
Sente que a bexiga não esvazia totalmente: ( ) não ( ) sim
Faz esforço para começar a urinar: ( ) não ( ) sim
Ao terminar de urinar permanece gotejando por um tempo: ( ) não ( ) sim
Tem dificuldade de começar a urinar: ( ) não ( ) sim
Perde urina na relação sexual: ( ) não ( ) sim
Se sim: ( ) no orgasmo (prazer) ( ) na penetração ( ) ambos
Infecção Urinária: ( ) nunca ( ) sim Último Episódio: _____

Data da Última Menstruação: ___/___/_____ **( ) Menopausa**
Nº Gestações: _____ **Nº Partos:** _____ **Nº Abortos:**_____
Nº Partos Normais (vaginal): _____ **( ) Fórceps** **Nº Cesarianas:** _____
Peso dos Bebês: _____
Fez cirurgia no Períneo: ( ) não ( ) sim Quando? _____
Sente peso na Vagina: ( ) não ( ) sim

Vida sexual ativa: ( ) não ( ) sim
Tenho ( ) parceiro ( ) parceira ( ) ambos
Tipos de Relação: ( ) vaginal ( ) anal ( ) vaginal e anal
Queixa de Frouxidão: ( ) minha queixa ( ) queixa do marido ( ) ambos
Há quanto tempo você sente sua vagina frouxa:_____
Como você percebe sua vagina frouxa (descreva com suas palavras):
_____
_____
_____

Hábitos Intestinais: ( ) regular ( ) prisão de ventre _____ dias
Perde Gases sem controle: ( ) não ( ) sim
Perde Fezes sem controle: ( ) não ( ) sim

Número da Participante: _____

Doenças Prévias: ( ) Hipertensão ( ) Diabetes **Outras:** _____
Cirurgias:_____
Medicamentos: _____
Tabagismo: ( ) não ( ) sim **Etilismo:** ( ) não ( ) sim

1) ÍNDICE DE FUNÇÃO SEXUAL FEMININA

PARA CADA ITEM, MARQUE COM X APENAS UMA RESPOSTA

O desejo ou interesse sexual é um sentimento que abrange a vontade de ter uma experiência sexual, a receptividade às iniciativas sexuais do parceiro, e pensamentos ou fantasias sobre o ato sexual.

1. Durante as últimas 4 semanas, com que frequência você sentiu desejo ou interesse sexual?
   (5) Sempre ou quase sempre
   (4) Muitas vezes (mais da metade do tempo)
   (3) Às vezes (aproximadamente a metade do tempo)
   (2) Poucas vezes (menos do que a metade do tempo)
   (1) Nunca ou quase nunca

2. Durante as últimas 4 semanas, como você classificaria seu nível (grau) de desejo ou interesse sexual?
   (5) Muito alto
   (4) Alto
   (3) Moderado
   (2) Baixo
   (1) Muito baixo ou nenhum

A excitação sexual é uma sensação com aspectos físicos e mentais. Pode aparecer uma sensação de calor ou de vibração na genitália, lubrificação (umidade), ou contrações musculares.

3. Durante as últimas 4 semanas, com que frequência você se sentiu excitada durante o ato ou atividade sexual?
   (0) Sem atividade sexual
   (5) Sempre ou quase sempre
   (4) Muitas vezes (mais da metade do tempo)
   (3) Algumas vezes (metade das vezes)
   (2) Poucas vezes (menos da metade do tempo)
   (1) Nunca ou quase nunca

4. Durante as últimas 4 semanas, como você classificaria seu nível (grau) de excitação sexual durante a atividade sexual?
   (0)Sem atividade sexual
   (5) Muito alto
   (4) Alto
   (3) Moderado
   (2) Baixo
   (1) Muito baixo ou nenhum

Número da Participante: _____

5. Durante as últimas 4 semanas, qual foi seu grau de confiança sobre sentir-se excitada durante a atividade sexual?
   (0) Sem atividade sexual
   (5) Altíssima confiança
   (4) Alta confiança
   (3) Moderada confiança
   (2) Baixa confiança
   (1) Baixíssima ou nenhuma confiança

6. Durante as últimas 4 semanas, com que frequência você ficou satisfeita com seu nível (grau) de excitação durante a atividade sexual?
   (0) Sem atividade sexual
   (5) Sempre ou quase sempre
   (4) Muitas vezes (mais da metade do tempo)
   (3) Algumas vezes (aproximadamente a metade do tempo)
   (2) Poucas vezes (menos da metade do tempo)
   (1) Nunca ou quase nunca

7. Durante as últimas 4 semanas, com que frequência você ficou lubrificada ("molhada") durante a atividade sexual?
   (0) Sem atividade sexual
   (5) Sempre ou quase sempre
   (4) Muitas vezes (mais da metade do tempo)
   (3) Algumas vezes (aproximadamente a metade do tempo)
   (2) Poucas vezes (menos da metade do tempo)
   (1) Nunca ou quase nunca

8. Durante as últimas 4 semanas, qual foi o grau de dificuldade para ficar lubrificada ("molhada") durante a atividade sexual?
   (0) Sem atividade sexual
   (1) Extremamente difícil ou impossível
   (2) Muito difícil
   (3) Difícil
   (4) Pouco difícil
   (5) Nada difícil

9. Durante as últimas 4 semanas, com que frequência você manteve sua lubrificação até o final da atividade sexual?
   (0) Sem atividade sexual
   (5) Sempre ou quase sempre
   (4) Muitas vezes (mais da metade do tempo)
   (3) Algumas vezes (aproximadamente a metade do tempo)
   (2) Poucas vezes (menos da metade do tempo)
   (1) Nunca ou quase nunca

10. Durante as últimas 4 semanas, qual foi o grau de dificuldade para manter sua lubrificação até terminar a atividade sexual?
    (0) Sem atividade sexual
    (1) Extremamente difícil ou impossível
    (2) Muito difícil
    (3) Difícil
    (4) Pouco Difícil
    (5) Nada Difícil

Número da Participante: _____

11. Durante as últimas 4 semanas, na atividade sexual ou quando sexualmente estimulada, com que frequência você atingiu o orgasmo (clímax)?
    (0) Sem atividade sexual
    (5) Sempre ou quase sempre
    (4) Muitas vezes (mais da metade do tempo)
    (3) Algumas vezes (aproximadamente a metade do tempo)
    (2) Poucas vezes (menos da metade do tempo)
    (1) Nunca ou quase nunca

12. Durante as últimas 4 semanas, na atividade sexual ou quando sexualmente estimulada, qual foi o grau de dificuldade para atingir o orgasmo (clímax)?
    (0) Sem atividade sexual
    (1) Extremamente difícil ou impossível
    (2) Muito difícil
    (3) Difícil
    (4) Pouco Difícil
    (5) Nada Difícil

13. Durante as últimas 4 semanas, qual foi o grau de satisfação com sua habilidade de chegar ao orgasmo (clímax) durante a atividade sexual?
    (0) Sem atividade sexual
    (5) Muito satisfeita
    (4) Moderadamente satisfeita
    (3) Indiferente
    (2) Moderadamente insatisfeita
    (1) Muito insatisfeita

14. Durante as últimas 4 semanas, qual foi o grau de satisfação com a quantidade de envolvimento emocional entre você e seu parceiro durante a atividade sexual?
    (0) Sem atividade sexual
    (5) Muito satisfeita
    (4) Moderadamente satisfeita
    (3) Indiferente
    (2) Moderadamente insatisfeita
    (1) Muito insatisfeita

15. Durante as últimas 4 semanas, qual foi o grau de satisfação na relação sexual com seu parceiro?
    (5) Muito satisfeita
    (4) Moderadamente satisfeita
    (3) Indiferente
    (2) Moderadamente insatisfeita
    (1) Muito insatisfeita

16. Durante as últimas 4 semanas, de forma geral, qual foi o grau de satisfação com sua vida sexual?
    (5) Muito satisfeita
    (4) Moderadamente satisfeita
    (3) Indiferente
    (2) Moderadamente insatisfeita
    (1) Muito insatisfeita

Número da Participante: _____

17. Durante as últimas 4 semanas, com que frequência você sentiu desconforto ou dor durante a penetração vaginal?
    (0) Não houve tentativa de penetração
    (1) Sempre ou quase sempre
    (2) Muitas vezes (mais da metade do tempo)
    (3) Algumas vezes (aproximadamente a metade do tempo)
    (4) Poucas vezes (menos da metade do tempo)
    (5) Nunca ou quase nunca

18. Durante as últimas 4 semanas, com que frequência você sentiu desconforto ou dor após a penetração vaginal?
    (0) Não houve tentativa de penetração
    (1) Sempre ou quase sempre
    (2) Muitas vezes (mais da metade do tempo)
    (3) Algumas vezes (aproximadamente a metade do tempo)
    (4) Poucas vezes (menos da metade do tempo)
    (5) Nunca ou quase nunca

19. Durante as últimas 4 semanas, como você classificaria seu grau (nível) de desconforto ou dor durante ou após a penetração vaginal?
    (0) Não houve tentativa de penetração
    (1) Altíssimo
    (2) Alto
    (3) Moderado
    (4) Baixo
    (5) Baixíssimo ou nenhum

2) ESCALA DE DOR NA RELAÇÃO SEXUAL

Sobre dor na relação sexual

Não possuo relação sexual		Não
Ausência de dor na relação sexual		0
Dor leve, que não obriga a interromper a relação sexual		1
Dor moderada, que dificulta, mas não obriga a interromper a relação sexual		2
Dor intensa, que obriga a interromper a relação sexual		3

QUESTIONÁRIO DE SINTOMAS VAGINAIS

1. Você percebe uma dor em pressão ou peso no seu abdômen inferior (pé da barriga)?

Nunca		0
Ocasionalmente		1
Às vezes		2
Na maior parte do tempo		3
O tempo todo		4

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

Número da Participante: _____

2. Você percebe que sua vagina está dolorida?

Nunca		0
Ocasionalmente		1
Às vezes		2
Na maior parte do tempo		3
O tempo todo		4

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

3. Você sente que tem uma redução de sensibilidade ou amortecimento na sua vagina ou em volta dela?

De jeito nenhum		0
Um pouco		1
Moderadamente		2
Muito		3

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

4. Você sente sua vagina muito frouxa ou larga?

De jeito nenhum		0
Um pouco		1
Moderadamente		2
Muito		3

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

5. Você percebe um "caroço" ou uma "bola" descendo na sua vagina?

Nunca		0
Ocasionalmente		1
Às vezes		2
Na maior parte do tempo		3
O tempo todo		4

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

Número da Participante: _____

6. Você percebe um "caroço" ou uma "bola" saindo de sua vagina de forma que você possa senti-la o vê-la fora dela?

Nunca		0
Ocasionalmente		1
Às vezes		2
Na maior parte do tempo		3
O tempo todo		4

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

7. Você sente que sua vagina é muito seca?

Nunca		0
Ocasionalmente		1
Às vezes		2
Na maior parte do tempo		3
O tempo todo		4

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

8. Você tem que colocar o dedo na sua vagina para ajudar a evacuar (fazer cocô)?

Nunca		0
Ocasionalmente		1
Às vezes		2
Na maior parte do tempo		3
O tempo todo		4

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

9. Você sente que sua vagina é muito apertada?

Nunca		0
Ocasionalmente		1
Às vezes		2
Na maior parte do tempo		3
O tempo todo		4

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

Número da Participante: _____

10) Atualmente você tem vida sexual?

0- Sim

1- Não, por causa dos meus sintomas vaginais

2- Não, por outros motivos

11) O seu problema de vagina interfere na sua vida sexual?

De jeito nenhum		0
Um pouco		1
Moderadamente		2
Muito		3

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

12) Você sente que o seu relacionamento é afetado pelos sintomas vaginais?

De jeito nenhum		0
Um pouco		1
Moderadamente		2
Muito		3

O quanto isso incomoda você? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

13) O quanto você acha que sua vida sexual tem sido prejudicada pelos seus sintomas vaginais?

Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

14) Em geral, quanto os seus sintomas vaginais interferem em sua vida diária?

Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

Número da Participante: _____

ESCALA DE AFLIÇÃO SEXUAL

A Escala de Aflição Sexual Feminina – Revisada é um questionário para medir a sua aflição sexual. Marque com X a resposta que corresponda o que você sente.

Quão frequentemente você se sentiu:

1. Angustiada com sua vida sexual

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

2. Infeliz com o seu relacionamento sexual

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

3. Culpada por dificuldades sexuais

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

4. Frustrada por seus problemas sexuais

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

5. Estressada sobre sexo

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

6. Inferior por causa de problemas sexuais

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

7. Preocupada com sexo

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

8. Sexualmente inadequada

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

9. Lamenta sua sexualidade

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

10. Envergonhada com problemas sexuais

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

Número da Participante: _____

11. Insatisfeita com a sua vida sexual

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

12. Irritada com a sua vida sexual

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

13. Incomodada com baixo desejo sexual

(0) nunca (1) raramente (2) ocasionalmente (3) frequentemente (4) sempre

PERDA URINÁRIA

- **Frequência da perda urinária:**

Nunca		*0*
Uma vez por semana ou menos		*1*
Duas ou três vezes por semana		*2*
Uma vez ao dia		*3*
Diversas vezes ao dia		*4*
O tempo todo		*5*

- **Quantidade de urina perdida:**

Nenhuma		0
Uma pequena quantidade		2
Uma moderada quantidade		4
Uma grande quantidade		6

Em geral, quanto que perder urina interfere em sua vida diária? Circule um número de 0 (não incomoda) a 10 (incomoda muito).

0 1 2 3 4 5 6 7 8 9 10

- **Quando você perde urina?**

Nunca		0
Perco antes de chegar ao banheiro		1
Perco quando tusso ou espirro		2
Perco quando estou dormindo		3
Perco quando estou fazendo atividades físicas		4
Perco quando terminei de urinar e estou me vestindo		5
Perco sem razão óbvia		6
Perco o tempo todo		7

Número da Participante: _____

PESQUISA FROUXIDÃO VAGINAL
AVALIAÇÃO PESQUISADOR

( ) PRIMEIRA AVALIAÇÃO ( ) PRIMEIRO FOLLOW-UP ( ) SEGUNDO FOLLOW-UP

NOME: _____ DATA: ___/___/____

1- CLASSIFICAÇÃO FUNCIONAL DO AP (OXFORD): _____

0- sem função perineal objetiva	3- contração de intensidade regular e elevação cranial da parede vaginal
1- esboço de contração muscular	4- contração de intensidade boa e elevação cranial da parede vaginal
2- contração de intensidade fraca	5- contração de intensidade ótima e elevação cranial da parede vaginal

2- HIPERMOBILIDADE URETRAL: ( ) NÃO ( ) SIM

3- AVALIAÇÃO DO PROLAPSO:

ESTADIO: ____ ANTERIOR ____ APICAL ____ POSTERIOR

GH (cm)	Aa (+3 -3)	Ba (+3 -3)
PB (cm)	Ap (+3 -3)	Bp (+3 -3)
C (cm)	D (cm)	**TVL (cm)**

0- não há prolapso I- o ponto mais distal do prolapso é maior que 1 cm acima do hímen
II- o ponto mais distal do prolapso está entre -1 a +1 do hímen
III- o ponto mais distal do prolapso está além de 1 cm do hímen
IV- eversão completa

4- MEDIDAS GH, PB E RIDGE

Gh: _____ cm

PB: _____ cm

RIDGE: _____ cm

5 – ESPESSURA VAGINAL - ULTRASSONOGRAFIA

TRANSABDOMINAL:

a) Terço proximal: _____mm

b) Terço médio: _____ mm

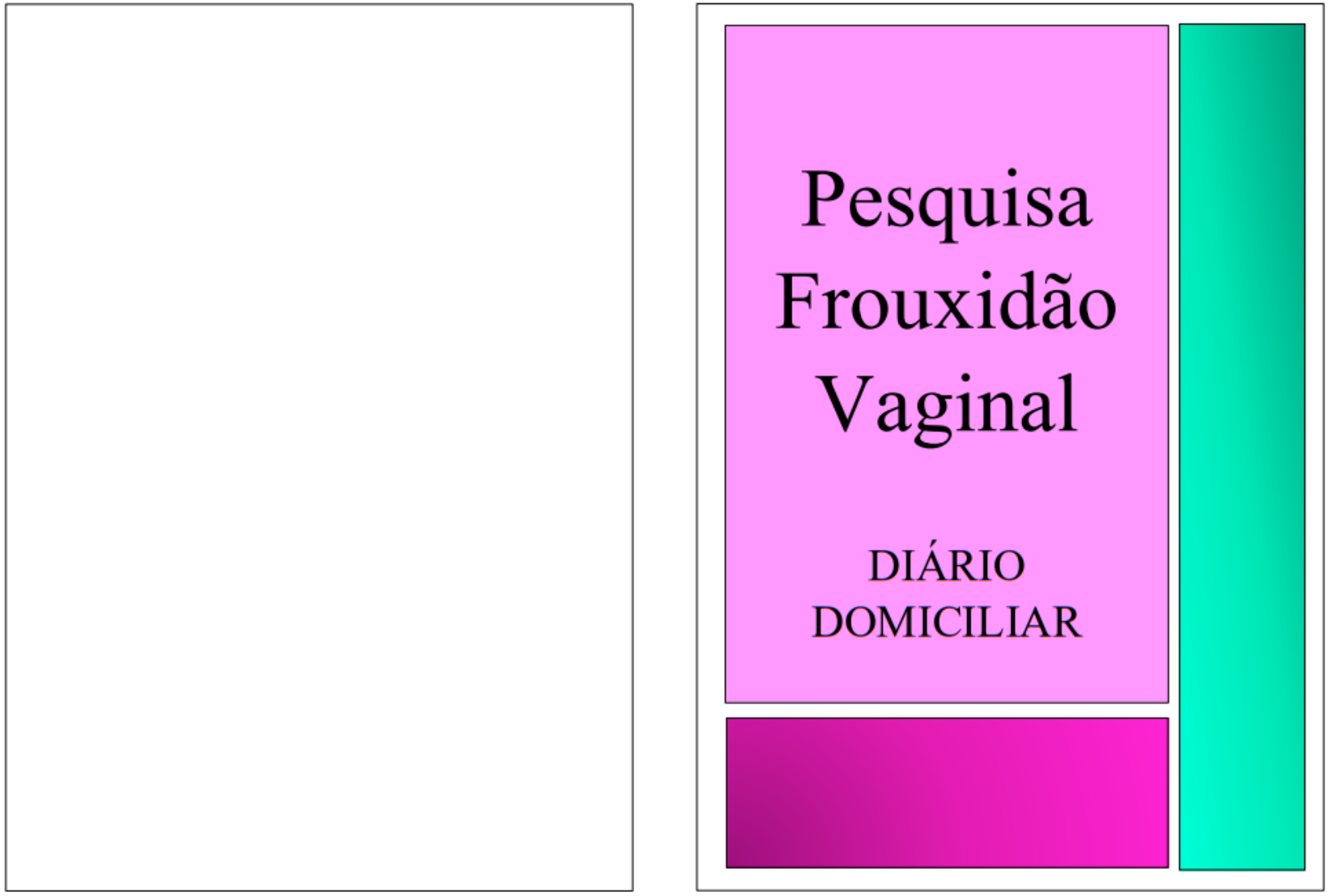
c) Terço distal: _____ mm

TRANSVAGINAL:

a) Terço proximal: _____mm

b) Terço médio: _____ mm

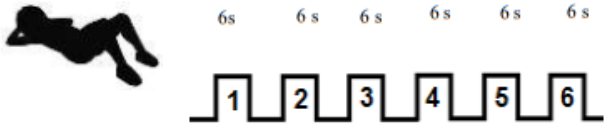
c) Terço distal: _____ mm


Pesquisa
Frouxidão
Vaginal
DIÁRIO
DOMICILIAR

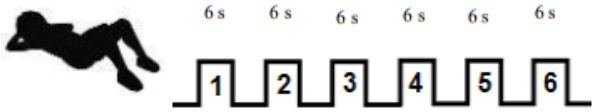
Orientações para as Contrações

Aquecimento - realizar sempre antes de cada programa semanal

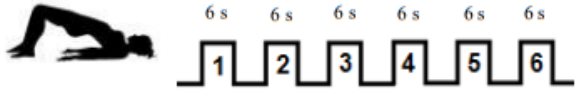
1- Inspire e depois contraia a musculatura do assoalho pélvico expirando.



2- Inspire e depois contraia a musculatura expirando + encostar o abdome na coluna.



3- Inspire e depois contraia a musculatura expirando + eleve o quadril.



5-8 semana: 8 s/ 6 rep.
9-12 semana: 10 s/ 6 rep.

Anotações

Em caso de dúvidas sobre o treinamento dos músculos do assoalho pélvico, entre em contato:

Celular/WhatsApp: (19) 98176 - 7113

Relaxamento – realizar sempre após cada programa semanal

1- Anteversão e Retroversão da Pelve.

2- Movendo a pelve em forma de 8.

3-Inclinando a Pelve para cima e para baixo.

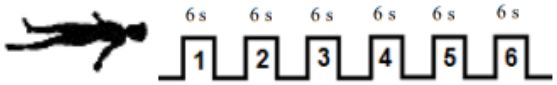
MARQUE AQUI A REALIZAÇÃO DOS SEUS EXERCÍCIOS

DOM	SEG	TER	QUA	QUI	SEX	SAB
SEMANA 1						
SEMANA 2						
SEMANA 3						
SEMANA 4						
SEMANA 5						
SEMANA 6						
SEMANA 7						
SEMANA 8						
SEMANA 9						
SEMANA 10						
SEMANA 11						
SEMANA 12						

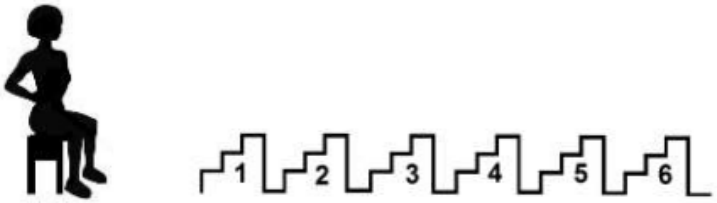
SEMANA 1 A 4

1- Inspire , contraia a musculatura e realize 1 tosse. 3 repetições

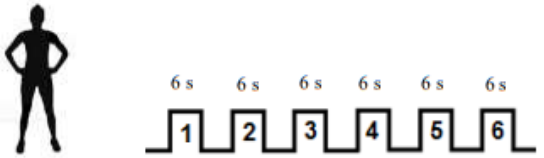
2- Inspire e depois contraia a musculatura expirando. 2 repetições.



3- Inspire e depois contraia em 3 etapas expirando. 2 repetições.



4- Inspire e depois contraia a musculatura expirando.



2 repetições

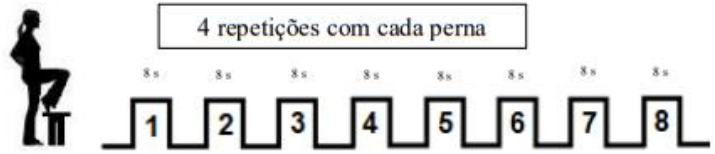
SEMANA 5 A 8

1- Inspire , contraia a musculatura e realize 2 tosses. 3 repetições

2- Inspire e depois contraia a musculatura expirando. 2 repetições.

3- Inspire e depois contraia em 3 etapas expirando. Relaxe em 3 etapas. 2 repetições.

4- Inspire e depois contraia a musculatura expirando. 2 repetições.



5- Inspire e depois contraia expirando e fazendo a postura. 2 repetições.

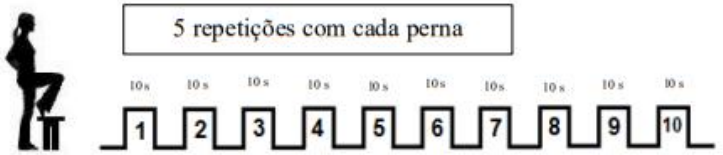
SEMANA 9 A 12

1- Inspire , contraia a musculatura e realize 3 tosses. 3 repetições

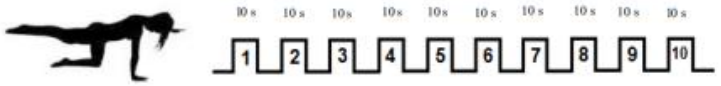
2- Inspire e depois contraia a musculatura expirando. 2 repetições.

3- Inspire e depois contraia em 3 etapas expirando. Relaxe em 3 etapas. 2 repetições.

4- Inspire e depois contraia a musculatura expirando. 2 repetições.



5- Inspire e depois contraia expirando e fazendo a postura. 2 repetições.



8.2. Termo de Consentimento Livre e Esclarecido

Efeito da radiofrequência microablativa fracionada e do treinamento dos músculos do assoalho pélvico no tratamento de mulheres com queixa de frouxidão vaginal: ensaio clínico randomizado

Gláucia Miranda Varella Pereira; Cássia Raquel Teatin Juliato; Lucia Alves da Silva Lara; Luiz Gustavo Oliveira Brito;

Número do CAAE:12919119.9.0000.5404

A senhora está sendo convidada a participar de uma pesquisa. Este documento, chamado Termo de Consentimento Livre e Esclarecido, visa assegurar seus direitos como participante da pesquisa e é elaborado em duas vias, assinadas e rubricadas pelo pesquisador e pelo participante/responsável legal, sendo que uma via deverá ficar com a senhora e outra com o pesquisador.

Por favor, leia com atenção e calma, aproveitando para esclarecer suas dúvidas. Se houver perguntas antes ou mesmo depois de assiná-lo, você poderá esclarecê-las com o pesquisador. Se preferir, pode levar este Termo para casa e consultar seus familiares ou outras pessoas antes de decidir participar. Não haverá nenhum tipo de penalização ou prejuízo se você não aceitar participar ou retirar sua autorização em qualquer momento. Caso retire sua autorização ou não queira participar a senhora será encaminhada para o tratamento convencional presente no serviço.

Justificativa e objetivos:

A senhora está sendo convidada a participar de um estudo que procura avaliar dois tipos de tratamento para sua queixa de frouxidão vaginal. Uma opção de tratamento será a fisioterapia, através do treinamento muscular do assoalho pélvico, cujo benefício é fortalecer os músculos da região da vagina. O outro tipo de tratamento é chamado de radiofrequência – é um aparelho que será colocado na região da vagina, cujo objetivo é melhorar a elasticidade vaginal. Para isso, a senhora será sorteada para um grupo de tratamento e permanecerá nesse grupo até o final da proposta de tratamento. Não sabemos qual desses tratamentos é melhor para tratar a sua queixa, por isso estamos realizando este trabalho.

Procedimentos:

Participando do estudo a senhora será convidada a:

- responder algumas perguntas gerais como sua idade, peso, número de partos, etc.

Rubrica do (a) Pesquisador(a) _____ Rubrica da Participante _____

-responder questionários sobre perda de urina, prolapsos vaginais, sintomas na vagina e atividade e satisfação sexual, que demorarão em média 15 minutos no total.

-ser submetida a exames físicos para avaliação dos músculos que dão suporte à vagina (via vaginal – toque vaginal e probe vaginal), exame para avaliar o prolapso vaginal (via vaginal com régua graduada) e ultrassom sobre o períneo (sem introduzir na vagina). Os exames físicos demorarão em média 30 - 40 minutos.

Os questionários e todos os parâmetros serão realizados antes do tratamento e 30 dias e 6 meses após o término do tratamento. Um sorteio definirá qual tratamento a senhora fará: radiofrequência isolada ou fisioterapia isolada. A senhora não poderá escolher qual tratamento vai realizar. Se for realizado procedimento de radiofrequência, serão 3 aplicações mensais, indolores e intravaginais. Se for a fisioterapia, serão realizadas sessões individuais 1 vez por semana por 12 semanas. A senhora realizará também o tratamento em casa e receberá as orientações para executá-lo.

Desconfortos e riscos:

A senhora poderá se sentir desconfortável em responder as perguntas e em ser examinada ginecologicamente. Não é esperado nenhum incomodo durante ou após a realização da fisioterapia. A radiofrequência é um procedimento indolor, mas pode ocasionar desconforto leve em algumas pacientes durante sua aplicação. A radiofrequência não possui efeito colateral como secreção, sangramento, dor crônica, infecção ou câncer. A senhora não deverá ter relações sexuais 3 dias antes da radiofrequência, assim como não usar pomadas ou cremes intravaginais. Após cada sessão da radiofrequência a senhora não poderá ter relações sexuais por 10 dias.

Benefícios:

A senhora terá como benefício o acesso a um tratamento especializado para a frouxidão vaginal, com radiofrequência ou fisioterapia, e em contrapartida contribuirá para um melhor entendimento a respeito dos tratamentos para a frouxidão vaginal. Caso os resultados da pesquisa mostrem que um grupo é melhor que o outro para o tratamento, caso a senhora esteja no grupo que não mostrou esse benefício, a senhora terá o direito de tratar no grupo contrário após o término da pesquisa, se a senhora assim desejar.

Acompanhamento e assistência:

Caso haja qualquer problema que não possibilite sua participação no estudo, a senhora será encaminhada para o ambulatório de ginecologia cirúrgica e ou para o setor de fisioterapia do CAISM, mesmo que a senhora não deseje mais participar da pesquisa. A pesquisa não mudará em nada o seu tratamento caso a senhora resolva não participar da pesquisa. A senhora terá o seu acompanhamento garantido, mesmo após o fim da pesquisa, para ser avaliada em caso de queixas que possam estar relacionadas a

pesquisa, independente do término da mesma. Em caso de falta às consultas previamente agendadas para a realização dos exames ou procedimentos de radiofrequência ou fisioterapia sem justificativa, a senhora será desligada da pesquisa e outra voluntária será convidada.

Sigilo e privacidade:

A senhora tem a garantia de que sua identidade será mantida em sigilo e nenhuma informação será dada a outras pessoas que não façam parte da equipe de pesquisadores. Na divulgação dos resultados desse estudo, o seu nome não será citado. Os resultados desta pesquisa não estarão em seu prontuário médico.

Ressarcimento e Indenização:

A senhora não receberá nenhuma ajuda de custo para participar da pesquisa. A pesquisa será realizada durante as sessões de fisioterapia que a senhora teria agendada (rotina de tratamento definida pelo serviço). Desta forma, a senhora não terá gastos extras para participar da pesquisa. A senhora terá direito à indenização em casos de danos diretos e indiretos decorrentes da pesquisa. Não haverá custo para a realização dos exames e tão pouco com o tratamento de radiofrequência (caso seja este o tratamento sorteado). Todos os exames serão realizados no mesmo dia da avaliação ou tratamento fisioterapêutico com objetivo de facilitar seu deslocamento.

Contato:

Em caso de dúvidas sobre a pesquisa, a senhora poderá entrar em contato com os pesquisadores Gláucia Varella ou Luiz Gustavo Brito: Rua Alexandre Fleming, 79 Campinas – SP; telefone (WhatsApp) (19) 9 8176 7113.

Em caso de denúncias ou reclamações sobre sua participação e sobre questões éticas do estudo, a senhora poderá entrar em contato com a secretaria do Comitê de Ética em Pesquisa (CEP) da UNICAMP das 08:00hs às 11:30hs e das 13:00hs as 17:30hs na Rua: Tessália Vieira de Camargo, 126; CEP 13083-887 Campinas – SP; telefone (19) 3521-8936 ou (19) 3521-7187; e-mail: cep@fcm.unicamp.br.

O Comitê de Ética em Pesquisa (CEP).

O papel do CEP é avaliar e acompanhar os aspectos éticos de todas as pesquisas envolvendo seres humanos. A Comissão Nacional de Ética em Pesquisa (CONEP), tem por objetivo desenvolver a regulamentação sobre proteção dos seres humanos envolvidos nas pesquisas. Desempenha um papel coordenador da rede de Comitês de

Rubrica do (a) Pesquisador(a) _____ Rubrica da Participante _____

Ética em Pesquisa (CEPs) das instituições, além de assumir a função de órgão consultor na área de ética em pesquisas

Consentimento livre e esclarecido:

Após ter recebido os esclarecimentos sobre a natureza da pesquisa, seus objetivos, métodos, benefícios previstos, potenciais riscos e o incômodo que esta possa acarretar, aceito participar:
Nome do (a) participante da pesquisa: _____

_____Data: ____/_____/_____
(Assinatura do participante da pesquisa ou nome e assinatura do seu RESPONSÁVEL LEGAL)

Responsabilidade do Pesquisador:

Asseguro ter cumprido as exigências da resolução 466/2012 CNS/MS e complementares na elaboração do protocolo e na obtenção deste Termo de Consentimento Livre e Esclarecido. Asseguro, também, ter explicado e fornecido uma via deste documento ao participante da pesquisa. Informo que o estudo foi aprovado pelo CEP perante o qual o projeto foi apresentado e pela CONEP, quando pertinente. Comprometo-me a utilizar o material e os dados obtidos nesta pesquisa exclusivamente para as finalidades previstas neste documento ou conforme o consentimento dado pelo participante da pesquisa.

_____Data: ____/_____/_____.
(Assinatura do pesquisador)

8.3. Aprovação do Comitê de Ética de Pesquisa

UNICAMP - CAMPUS CAMPINAS

PARECER CONSUBSTANCIADO DO CEP

DADOS DA EMENDA

Título da Pesquisa: Efeito da Radiofrequência Microablativa Fracionada e do Treinamento dos Músculos do Assoalho Pélvico no Tratamento de Mulheres com Queixa de Frouxidão Vaginal: Ensaio Clínico Randomizado

Pesquisador: LUIZ GUSTAVO OLIVEIRA BRITO

Área Temática:

Versão: 3

CAAE: 12919119.9.0000.5404

Instituição Proponente: Hospital da Mulher Prof. Dr. José Aristodemo Pinotti - CAISM

Patrocinador Principal: Universidade Estadual de Campinas - UNICAMP

DADOS DO PARECER

Número do Parecer: 3.495.558

Apresentação do Projeto:

Resumo: Introdução: A frouxidão vaginal, condição raramente discutida entre as pacientes e médicos, é definida como queixa de excesso de flacidez vaginal. Apresenta prevalência de 24% e parece estar associada à idade jovem, partos vaginais, sintomas de prolapso e prolapso objetivo, sendo, portanto, uma disfunção somática e não psicogênica. Um estudo recente mostrou associações entre as áreas hiatal, hiato genital e corpo perineal, sugerindo que a frouxidão vaginal é uma manifestação da hiperdistensibilidade do levantador do ânus. Mulheres com flacidez vaginal podem ser representativas de um estágio inicial no desenvolvimento de prolapso de órgão pélvico; no entanto, isso não foi avaliado anteriormente. Uma definição padronizada e meios para consultar pacientes em relação a tais sintomas ainda não existe. Procedimentos cirúrgicos para frouxidão vaginal com reparo posterior/perineoplastia são mais comumente recomendados, todavia, há riscos de dispareunia. Opções não cirúrgicas e com custo mais baixo podem contribuir para o tratamento da frouxidão vaginal. Entre elas destacam-se o treinamento dos músculos do assoalho pélvico e a radiofrequência. Até o momento, nenhum ensaio clínico foi desenvolvido para avaliar o papel do treinamento dos músculos do assoalho pélvico e da radiofrequência na frouxidão vaginal.Objetivos: Comparar o efeito da radiofrequência microablativa fracionada isolada e do treinamento dos músculos do assoalho pélvico isolado em mulheres com queixa de frouxidão vaginal.Metodologia: Trata-se de um estudo clínico, randomizado, prospectivo, controlado,

Endereço: Rua Tessália Vieira de Camargo, 126
Bairro: Barão Geraldo **CEP:** 13.083-887
UF: SP **Município:** CAMPINAS
Telefone: (19)3521-8936 **Fax:** (19)3521-7187 **E-mail:** cep@fcm.unicamp.br

paralelo e não cego. A pesquisa será desenvolvida no ambulatório de ginecologia cirúrgica da Universidade Estadual de Campinas - UNICAMP/SP. Para o estudo serão incluídas mulheres na pré-menopausa com idade 18 anos, parto vaginal, com queixa de frouxidão vaginal avaliada por pergunta direta (sim/não) e pelo Vaginal Laxity Questionnaire e com disponibilidade para frequentar as terapias na data e locais agendados para a realização do tratamento proposto. Os critérios de exclusão são: uso de marcapasso; doenças cardíacas descompensadas; déficit cognitivo; afecções neurológicas periféricas ou centrais; presença de qualquer tipo de câncer; presença de displasia cervical; história de infecção urinária ou vaginal ativa; doenças metabólicas descompensadas; tratamento fisioterapêutico com treinamento do assoalho pélvico prévio nos últimos 12 meses; uso de estrógeno via vaginal ou terapia hormonal oral nos últimos 6 meses, pacientes já submetidas a cirurgias de correção de prolapso ou de slings; presença de prolapso de órgão pélvico estadio 2 em diante. As participantes selecionadas serão divididas em 2 grupos de protocolos de tratamento: grupo 1 – radiofrequência e grupo 2 – treinamento dos músculos do assoalho pélvico. Após o período de intervenção, os grupos serão reavaliados em 30 e 90 dias. Para o cálculo amostral utilizamos valores da função sexual avaliada por meio do questionário Female Sexual Function Index. Ao se considerar um poder de estudo de 80%, um alfa de 0,05 com teste bicaudal, foi verificado que o número de participantes mínimo necessário em cada grupo será somado a um percentual de 30% de perda na amostra, totalizando 68 mulheres, sendo 34 em cada grupo (radiofrequência isolada e treinamento dos músculos do assoalho pélvico isolado). Será realizada uma análise descritiva dos dados para caracterização das participantes da pesquisa, na forma de valores de frequência absoluta e percentual (relativa) para variáveis categóricas e valores de média e desvio padrão para as variáveis numéricas. Em seguida, será realizada análise estatística de comparação e correlação dos dados obtidos a partir dos seguintes testes estatísticos: Kolmogorov-Smirnov para avaliação da normalidade da amostra. Dependendo dos resultados obtidos no teste de normalidade, serão utilizadas para as análises comparativas entre os grupos as Análises de Variância (se os dados apresentarem distribuição normal) ou Teste de Wilcoxon e Mann-Whitney (se os dados forem não-paramétricos). Da mesma forma, para as análises correlacionais serão utilizados os testes de Pearson ou Spearman. As variáveis categóricas serão analisadas pelos testes qui-quadrado ou pelo teste exato de Fisher. As análises estatísticas serão realizadas por meio do programa estatístico SPSS (Statistical Package for the Social Sciences), adotando nível de significância de 5% ($p< 0,05$). Os dados também serão avaliados através do método de análise da variância para medidas repetidas (ANOVA for repeated measures) com o objetivo de verificar simultaneamente a influência dos 2 grupos de estudo (avaliação intergrupos) e

das 2 avaliações (avaliação intragrupos) para cada uma das variáveis, afim de obter a estimação do efeito interação grupo x tempo. Caso as variáveis numéricas não apresentarem distribuição normal, serão transformadas em ranks ou postos.

Objetivo da Pesquisa:

Objetivo Primário: Comparar o efeito da RF microablativa fracionada isolada e do TMAP isolado em mulheres com queixa de frouxidão vaginal.

Objetivo Secundário:

• Comparar o efeito da RF isolada e do TMAP isolado sobre a função sexual.

• Comparar o efeito da RF isolada e do TMAP isolado sobre os sintomas urinários.

• Comparar o efeito da RF isolada e do TMAP isolado sobre a contratilidade e função dos músculos do assoalho pélvico.

• Comparar o efeito da RF isolada e do TMAP isolado sobre a escala de frouxidão vaginal.

• Comparar o efeito da RF isolada e do TMAP isolado sobre os níveis de ansiedade e depressão em mulheres com frouxidão vaginal.

Avaliação dos Riscos e Benefícios:

Riscos: As participantes serão informadas sobre os exames aos quais serão submetidas bem como a ocorrência de desconfortos em relação aos mesmos. Para os exames de palpação digital e POP-Q, apesar de indolor, será utilizado um gel lubrificante antialérgico para diminuir o desconforto causado pela introdução dos dedos do examinador e da régua graduada. Serão informadas que a aplicação da radiofrequência é um procedimento indolor, via vaginal com duração de 15 a 20 minutos. No vestíbulo e na abertura vaginal, será aplicada lidocaína spray 10% 3 minutos antes do procedimento para evitar qualquer desconforto. Será então introduzido um espéculo vaginal descartável, e posteriormente será realizada a antissepsia com clorexidina aquosa 0,2%, a limpeza com solução salina estéril 0,9% para remover o conteúdo vaginal excedente com gaze. É esperado que o treinamento dos músculos do assoalho pélvico não causará nenhum desconforto. Benefícios: - avaliação gratuita com questionários validados, anamnese criteriosa, realização de exames clínicos e de imagem e tratamento da frouxidão vaginal via Radiofrequencia e treinamento dos músculos do assoalho pélvico (fisioterapia).

Comentários e Considerações sobre a Pesquisa:

Esta versão é solicitação de emenda ao projeto aprovado pelo Parecer Consubstanciado CEP n.o 3.385.615 de 12 de junho de 2019. Apresentou a seguintes juntificativa: "O texto tem o objetivo de divulgar a pesquisa em mídias sociais, em jornais, em rádios e em programas de televisão para

auxiliar no processo de recrutamento de pacientes voluntárias, mediante a leitura do texto, reportagens ou divulgação do texto impresso ou em postagens em mídias sociais. O texto encontra-se na página 38 do projeto de pesquisa no item 10."

Considerações sobre os Termos de apresentação obrigatória:

Nesta versão foram anexados os seguintes documentos:

1- PB_INFORMAÇÕES_BÁSICAS_1398709_E1.pdf

2- Emenda.pdf

3- Projeto_Emenda.pdf

Recomendações:

Sem.

Conclusões ou Pendências e Lista de Inadequações:

Projeto considerado aprovado.

Considerações Finais a critério do CEP:

- O participante da pesquisa deve receber uma via do Termo de Consentimento Livre e Esclarecido, na íntegra, por ele assinado (quando aplicável).

- O participante da pesquisa tem a liberdade de recusar-se a participar ou de retirar seu consentimento em qualquer fase da pesquisa, sem penalização alguma e sem prejuízo ao seu cuidado (quando aplicável).

- O pesquisador deve desenvolver a pesquisa conforme delineada no protocolo aprovado. Se o pesquisador considerar a descontinuação do estudo, esta deve ser justificada e somente ser realizada após análise das razões da descontinuidade pelo CEP que o aprovou. O pesquisador deve aguardar o parecer do CEP quanto à descontinuação, exceto quando perceber risco ou dano não previsto ao participante ou quando constatar a superioridade de uma estratégia diagnóstica ou terapêutica oferecida a um dos grupos da pesquisa, isto é, somente em caso de necessidade de ação imediata com intuito de proteger os participantes.

- O CEP deve ser informado de todos os efeitos adversos ou fatos relevantes que alterem o curso normal do estudo. É papel do pesquisador assegurar medidas imediatas adequadas frente a evento adverso grave ocorrido (mesmo que tenha sido em outro centro) e enviar notificação ao CEP e à Agência Nacional de Vigilância Sanitária – ANVISA – junto com seu posicionamento.

- Eventuais modificações ou emendas ao protocolo devem ser apresentadas ao CEP de forma clara e sucinta, identificando a parte do protocolo a ser modificada e suas justificativas e aguardando a aprovação do CEP para continuidade da pesquisa. Em caso de projetos do Grupo I ou II apresentados anteriormente à ANVISA, o pesquisador ou patrocinador deve enviá-las também à mesma, junto com o parecer aprovatório do CEP, para serem juntadas ao protocolo inicial.

- Relatórios parciais e final devem ser apresentados ao CEP, inicialmente seis meses após a data deste parecer de aprovação e ao término do estudo.

-Lembramos que segundo a Resolução 466/2012 , item XI.2 letra e, "cabe ao pesquisador apresentar dados solicitados pelo CEP ou pela CONEP a qualquer momento".

-O pesquisador deve manter os dados da pesquisa em arquivo, físico ou digital, sob sua guarda e responsabilidade, por um período de 5 anos após o término da pesquisa.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_1398709_E1.pdf	16/07/2019 15:14:03		Aceito
Outros	Emenda.docx	16/07/2019 15:13:04	LUIZ GUSTAVO OLIVEIRA BRITO	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_Emenda.docx	16/07/2019 15:11:26	LUIZ GUSTAVO OLIVEIRA BRITO	Aceito
Outros	PB_PARECER_CONSUBSTANCIADO_CEP_3376836.pdf	07/06/2019 12:23:43	LUIZ GUSTAVO OLIVEIRA BRITO	Aceito
Outros	Carta_resposta.docx	07/06/2019 12:20:53	LUIZ GUSTAVO OLIVEIRA BRITO	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.pdf	07/06/2019 12:12:53	LUIZ GUSTAVO OLIVEIRA BRITO	Aceito
Outros	CrachaUnicampLuizBrito.pdf	26/04/2019 09:13:06	LUIZ GUSTAVO OLIVEIRA BRITO	Aceito
Parecer Anterior	ParecerCPDTGCAISM.pdf	26/04/2019	LUIZ GUSTAVO	Aceito

Parecer Anterior	ParecerCPDTGCAISM.pdf	09:06:05	OLIVEIRA BRITO	Aceito
Folha de Rosto	Folhaderosto.pdf	26/04/2019 09:05:48	LUIZ GUSTAVO OLIVEIRA BRITO	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

CAMPINAS, 08 de Agosto de 2019

Assinado por:
Renata Maria dos Santos Celeghini
(Coordenador(a))

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8.4. Protocolo da Radiofrequência e do Treinamento dos Músculos do Assoalho Pélvico do Ensaio Clínico Randomizado

Table 1. Pelvic floor muscle training and radiofrequency sessions according to the treatment duration.

Period	Interventions			
	Radiofrequency	**Pelvic Floor Muscle Training**		
1 to 4 weeks	1st application	1st phase	2nd phase	3rd phase
	• 2% Lidocaine Gel • Vaginal Examination with speculum • Whiff Test • 10% lidocaine spray • Cleaning: 2% aqueous chlorhexidine and sterile 0.9% saline • RF: 45Watts, Low Energy program (40 milliseconds) • Post-procedure orientation: 10-day sexual abstinence	• PFM maximum contraction (6 r / sustained 6 s/ 6 s rest: 1 time). Supine position. • PFM maximal contraction + transverse contraction (6 r / sustained 6 s/ 6 s rest: 1 time). Supine position. • PFM maximal contraction + hip elevation (6 r / sustained 6 s/ 6 s rest: 1 time). Supine position.	• PFM maximum contraction (1 cough / 3 r). Supine position. • PFM maximal contraction with the lower limbs extended and abducted (6 r / sustained 6 s/ 6 s rest: 2 times). Supine position. • PFM contraction in three stages—mild, moderate, maximum (6 r: 2 times). Sitting position. • PFM maximal contraction (6 r / sustained 6 s/ 6 s rest: 2 times). Standing position.	• Pelvic mobilization (anterior and posterior tilts, lateral tilts and rotation of the pelvis). Standing position. No PFM contraction in this phase. 10 repetitions each pelvic movement.
5 to 8 weeks	2nd application Same procedure (above)	• PFM maximum contraction (6 r / sustained 8 s/ 8 s rest: 1 time). Supine position. • PFM maximal contraction + transverse contraction (6 r / sustained 8 s/ 8 s rest: 1 time). Supine position. • PFM maximal contraction + hip elevation (6 r / sustained 8 s/ 8 s rest: 1 time). Supine position.	• PFM maximum contraction (2 cough / 3 r). Supine position. • Fast PFM maximal (8 r: 2 time). Supine position. • PFM contraction in six stages—mild, moderate, maximum–maximum, moderate, mild (8 r: 2 times). Sitting position. • PFM maximal contraction (8 r /sustained 8 s/ 8 s rest: 2 times). Standing position. • PFM maximal contraction (8 r /sustained 8 s/ 8 s rest: 2 times). Four supports (hands and knees).	• Same Intervention (above)
9 to 12 weeks	3rd application Same procedure (above)	• PFM maximum contraction (6 r / sustained 10 s: 1 time). Supine position. • PFM maximal contraction + transverse contraction (6 r / sustained 10 s/ 10 s rest: 1 time). Supine position. • PFM maximal contraction + hip elevation (6 r / sustained 10 s/10 s rest: 1 time). Supine position.	• PFM maximum contraction (3 cough / 3 r). Supine position. • Fast PFM maximal (10 r: 2 time). Sitting position. • PFM contraction in six stages—mild, moderate, maximum–maximum, moderate, mild (10 r: 2 times). Sitting position. • PFM maximal contraction (10 r /sustained 10 s/10 s rest: 2 times). Standing position. • PFM maximal contraction (10 r /sustained 10 s/10 s rest: 2 times). Four to two supports (right hand and left knee/ left hand and right knee).	• Same Intervention (above)

https://doi.org/10.1371/journal.pone.0259650.t001

8.5. Autorização para a Adaptação Transcultural e Validação da Escala *Female Sexual Distress Scale-Revised* pela empresa *Mapi Research Trust.*

TIMELINE

MM

Hi Glaucia,

Thank you for the signature on the MULA! It was uploaded perfectly.

If you need further authorization regarding providing a translation or a cross-cultural adaptation of this questionnaire to your research, note that it is identified by the copyright that translations and adaptations of this questionnaire is allowed by each academic institution. Below is a screenshot of our copyright table, indicating that academic translations are allowed:

Acronym	Name	PARENT Questionnaire	Copyright holders	academic translations allowed?
FSDS-R	FSDS-R - Female Sexual Distress Scale – Revised		Derogatis Measurement Assessments, LLC (US)	Yes

This documentation should serve as authorization to process any translations or adaptations needed.

Please let me know if more information is needed.

Kind regards,

Maggie

8.6. Registro da Revisão Sistemática no International prospective register of systematic reviews – PROSPERO

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

To enable PROSPERO to focus on COVID-19 submissions, this registration record has undergone basic automated checks for eligibility and is published exactly as submitted. PROSPERO has never provided peer review, and usual checking by the PROSPERO team does not endorse content. Therefore, automatically published records should be treated as any other PROSPERO registration. Further detail is provided here.

Citation

Luiz Gustavo Oliveira Brito, Glaucia Miranda Varella Pereira, Cássia Raquel Teatin Juliato. Treatment of Vaginal Laxity Symptoms - a Systematic Review. PROSPERO 2021 CRD42021252686 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021252686

Review question

What are the treatment modalities for vaginal laxity complaints in women?
Population: Women complaining of vaginal laxity.
Intervention: Any treatment modality

Comparator: Other treatment different from the main intervention (non-treatment, sham, other treatment)

Outcomes: Improvement in sexual activity, improvement in vaginal laxity symptoms

Study Design: Randomized Controlled Trials or Observational Studies

Searches

PubMed (02/05/2021) – All Fields

("vaginal laxity" OR "vaginal looseness" OR "vaginal relaxation" OR "wide vagina" OR "vaginal flaccidity" OR "vaginal flatus" OR "vaginal gas" OR "vaginal noise" OR "vaginal winds" OR "flatus vaginalis")

Ref. 125

Embase (02/05/2021) – All Fields

'vaginal laxity' OR 'vaginal looseness' OR 'vaginal relaxation' OR 'wide vagina' OR 'vaginal flaccidity' OR 'vaginal flatus' OR 'vaginal gas' OR 'vaginal noise' OR 'vaginal winds' OR 'flatus vaginalis'

Ref. 259

Scopus (02/05/2021) – Title/Abstract/Keynotes

(TITLE-ABS-KEY ("vaginal laxity") OR TITLE-ABS-KEY ("vaginal looseness") OR TITLE-ABS-KEY ("vaginal relaxation") OR TITLE-ABS-KEY ("wide vagina") OR TITLE-ABS-KEY ("vaginal flaccidity") OR TITLE-ABS-KEY ("vaginal flatus") OR TITLE-ABS-KEY ("vaginal gas") OR TITLE-ABS-KEY ("vaginal noise") OR TITLE-ABS-KEY ("vaginal winds") OR TITLE-ABS-KEY ("flatus vaginalis"))

Ref. 161

Web of Science (02/05/2021)

TÓPICO: ("vaginal laxity") OR TÓPICO: ("vaginal looseness") OR TÓPICO: ("vaginal relaxation") OR TÓPICO: ("wide vagina") OR TÓPICO: ("vaginal flaccidity") OR TÓPICO: ("vaginal flatus") OR TÓPICO: ("vaginal gas") OR TÓPICO: ("vaginal noise") OR TÓPICO: ("vaginal winds") OR TÓPICO: ("flatus vaginalis")

Ref. 134

Cochrane Library (02/05/2021)

(("vaginal laxity" OR "vaginal looseness" OR "vaginal relaxation" OR "wide vagina" OR "vaginal flaccidity" OR "vaginal flatus" OR "vaginal gas" OR "vaginal noise" OR "vaginal winds" OR "flatus vaginalis")):ti, ab, kw; Any MeSH descriptor in all MeSH products.

Ref. 36

Clinical Trials (02/05/2021)

("vaginal laxity" OR "vaginal looseness" OR "vaginal relaxation" OR "wide vagina" OR "vaginal flaccidity" OR "vaginal flatus" OR "vaginal gas" OR "vaginal noise" OR "vaginal winds" OR "flatus vaginalis")

Ref. 10

No restriction of date, language, or study designs.

Types of study to be included

We will be looking for randomized controlled trials of interventions, however, once they will not be available, we will include observational studies.

Condition or domain being studied

Vaginal laxity as well as other described terms such as 'vaginal looseness', vaginal flaccidity', 'vaginal relaxation', or 'wide vagina' in women. The pathophysiology of the vaginal laxity is not well stated, however, some treatment options have already been described in the literature.

Participants/population

Women complaining of vaginal laxity, mainly during sexual intercourse.

Intervention(s), exposure(s)

We are looking for any treatment for vaginal laxity symptoms. Some energy treatment modalities have been described in the scientific literature. We will be also looking for other treatment modalities (surgery, pelvic floor muscle training, etc.)

Comparator(s)/control

This section can include another intervention (treatment modalities) or a non-exposed group (sham, no treatment, etc).

Context

Inclusion Criteria: Randomized Clinical Trials (or Observational Studies) of intervention comparing types of treatments (or intervention with non-treatment, or intervention with sham, etc) for vaginal laxity symptoms in women.

Exclusion Criteria: Studies that do not present treatments for the complaint of vaginal laxity will be excluded, as well as, studies comparing the treatment of other sexual dysfunctions other than vaginal laxity.

Main outcome(s)

Primary outcomes: clinical improvement in vaginal laxity symptoms (It can be measured by Vaginal Laxity Questionnaire or Question number 4 of ICIQ- Vaginal Symptoms (Vaginal laxity symptoms).

Secondary Outcomes: Sexual activity improvement, quality of life improvement by questionnaires.

Measures of effect

Dichotomous variables through Odds Ratio, Relative Risk or Risk Difference. In cases of continuous variables through mean difference and standardized mean difference.

Additional outcome(s)
In this stage of the systematic review, we will not be able to describe any additional outcome. We will analyze the possibilities to include any additional outcome in the future.

Measures of effect
Not applicable

Data extraction (selection and coding)
Two researchers (LGOB and GMVP) will independently screen records according to our inclusion criteria. A third researcher (CRTJ) will be available for any disagreements during the study selection.

In data extraction, the researchers will organize the data (year, study design, country, methodology, intervention types, etc.) into a spreadsheet. Any disagreements related to data extraction will be discussed in a meeting with the participation of the three researchers.

Risk of bias (quality) assessment
ROB (Cochrane Group - Handbook) will be used for assessing the risk of bias.

GRADE will be used for assessing the quality of evidence and recommendation.

Strategy for data synthesis
We expect to include at least two studies in this systematic review. Questionnaires' scores will be selected and mean difference analysis will be indicated to compare data before and after the intervention and follow-ups. In cases of selecting dichotomous variables for analysis, the Odds ratio will be used for comparative analysis.

Analysis of subgroups or subsets
Subgroups analysis can be planned in case of finding studies using questionnaires with different domains (for example FSFI questionnaire with 6 different domains of sexual dysfunction) that would allow this sort of analysis.

Contact details for further information
Glaucia Pereira
glauciavarella@gmail.com

Organisational affiliation of the review
UNICAMP
Rua Alexander Fleming, 101 - Cidade Universitária - Campinas - Sao Paulo - Post Code: 13083-881

Review team members and their organisational affiliations
Professor Luiz Gustavo Oliveira Brito. UNICAMP
Miss Glaucia Miranda Varella Pereira. UNICAMP
Professor Cássia Raquel Teatin Juliato. UNICAMP

Type and method of review
Systematic review

Anticipated or actual start date
02 May 2021

Anticipated completion date
30 October 2021

Funding sources/sponsors
FAPESP - Sao Paulo Research Fundation

Grant number(s)
State the funder, grant or award number and the date of award

Grant 2019/26723–5

Conflicts of interest
None known

Language
English

Country
Brazil

Stage of review
Review Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
MeSH headings have not been applied to this record

Date of registration in PROSPERO
02 June 2021

Date of first submission
02 May 2021

Details of any existing review of the same topic by the same authors
Not applicable

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.
The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions
02 June 2021
02 June 2021

8.7. STROBE Checklist para o Artigo Measurement of the vaginal wall thickness by transabdominal and transvaginal ultrasound of women with vaginal laxity: a cross-sectional study

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

Title: Measurement of the vaginal wall thickness by transabdominal and transvaginal ultrasound of women with vaginal laxity: a cross-sectional study

	Item No	Recommendation	Pages
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2-3
Objectives	3	State specific objectives, including any prespecified hypotheses	2-3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6-7
		(*c*) Explain how missing data were addressed	6-7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	6-7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7-8
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-8
		(b) Indicate number of participants with missing data for each variable of interest	7-8
Outcome data	15*	Report numbers of outcome events or summary measures	7-8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7-8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other	9-13

		relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

8.8. CONSORT Checklist – Artigo Pelvic Floor Muscle Training Versus Radiofrequency for Women with Vaginal Laxity: Randomized Clinical Trial

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	6
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6-7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	7-10
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	10-11
	6b	Any changes to trial outcomes after the trial commenced, with reasons	10-11
Sample size	7a	How sample size was determined	11-12
	7b	When applicable, explanation of any interim analyses and stopping guidelines	11-12
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	11-12
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	11-12
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	11-12
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	11-12
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	11-12

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	11-12
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	12-13
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	12-13
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	13-15
	13b	For each group, losses and exclusions after randomisation, together with reasons	13-15
Recruitment	14a	Dates defining the periods of recruitment and follow-up	13-15
	14b	Why the trial ended or was stopped	n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	13-15
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	13-15
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	13-15
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	13-15
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	n/a
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	15
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	16
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	16
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	16
Other information			
Registration	23	Registration number and name of trial registry	6
Protocol	24	Where the full trial protocol can be accessed, if available	6
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	1

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

8.9. Roteiro de Entrevista – Artigo Qualitativo

UNIVERSIDADE ESTADUAL DE CAMPINAS

HOSPITAL DA MULHER PROF. DR. JOSÉ ARISTODEMO PINOTTI – CAISM

TÍTULO DO PROJETO: A mulher com frouxidão vaginal: uma análise temática

Pesquisador Responsável: Prof. Dr. Luiz Gustavo Oliveira Brito

Pesquisadora Principal: Gláucia Miranda Varella Pereira

Iniciais:	**Tempo de entrevista**:

Dados Sociodemográficos:

Idade:

Estado Civil:

Etnia:

IMC:

Escolaridade:

Gestação:

Tipo de Parto:

Paridade:

Parto Instrumental:

Menopausa:

Tabagismo:

Etilismo:

Entrevista:

Respostas da participante em azul.

Observações da pesquisadora em preto e entre parênteses ao longo do texto.

1- O que você sentiu quando um profissional de saúde disse a você que seus sintomas podiam ser chamados de frouxidão vaginal?

O que a expressão "frouxidão vaginal" sugere para você? **Quando você a ouve, o que vem à sua cabeça?** **O que você sente?**
2- Como você percebe a sensação de frouxidão vaginal? Descreva com as suas palavras essa percepção?
3- Em qual momento você percebeu a sua sensação de frouxidão vaginal **Como você lidou inicialmente com essa sensação?**
4- Como você buscou ajuda para entender essa sensação que apareceu em você? **Você consegue descrever em detalhes como isso foi ficando cada vez mais presente em sua vida?**
5- Como a sua sensação de frouxidão vaginal interfere ou interferia na sua relação sexual? **Após o início de sua sensação de frouxidão vaginal, como era a forma que você enxergava as suas relações sexuais? Se houve mudança durante o momento da prática sexual, de que forma você notou isso?**
6- Como a sua sensação de frouxidão vaginal interferia em sua relação consigo mesma? Sobre o seu olhar sobre si mesma? E sobre a sua autoestima? **E sobre a sua autoimagem corporal?** **Quando você olha para a sua genitália, você sente que o seu ponto de vista mudou em relação ao que você pensa do seu funcionamento corporal?**
7- Como a frouxidão vaginal influenciou na duração da penetração?

Nas preliminares da relação sexual? **Na forma de início da prática sexual?** **Na frequência da prática sexual?**
8- Como você acha que a frouxidão vaginal impactou na sua vida com a parceria?
9- No que diz respeito às relações sexuais, você começou a ter algum tipo de prática que não fazia antes do início da sua sensação de frouxidão vaginal? Conte-me um pouco mais sobre isso.
10- Como a sensação de frouxidão vaginal interfere ou interferia em sua vida?
11- O que a motivou buscar tratamento? **Você tentou outros tratamentos anteriormente? Se sim, fale sobre eles e o que deu certo ou errado. O que você imagina que possa ser o melhor tratamento?**
12- Descreva as suas expectativas sobre a possibilidade de tratar a sua sensação de frouxidão vaginal. **Como você vê o futuro da sua queixa? Como você vê a chance de sucesso desse tratamento?** **Gostaria de complementar algo:**

8.10. Formulário de Coleta de Dados do Estudo Transversal – Chelsea and Westminster Hospital

NHS
Chelsea and Westminster Hospital
NHS Foundation Trust

https://www.chelwest.nhs.uk Tel: 020 3315 8000

Measures of vaginal laxity and sexual function in a multiethnic population: a cross-sectional audit

Consent Form

1. I confirm that I have read and understood the information sheet for the above study

2. I understand that my involvement is voluntary and I am free to withdraw at any time, without giving any reason, without my future medical care or legal rights being affected.

3. I agree that my medical and research notes/data can be accessed by responsible individuals from Chelsea and Westminster NHS Foundation Trust where it is relevant to my taking part in the audit.

Name of Clinician	Date	Signature

Name of Participant	Date	Signature

NHS
Chelsea and Westminster Hospital
NHS Foundation Trust
https://www.chelwest.nhs.uk Tel: 020 3315 8000

Measures of vaginal laxity and sexual function in a multiethnic population: a cross-sectional audit

Patient Information Sheet

You have been invited to take part in an audit of one aspect of our service in the Urogynaecology Department. Before you decide it is important for you to understand why the audit is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the audit?

This audit investigates the main physical, psychological and social factors that affect the quality of life of women and their relationships, as well as understanding how urine/stool leakage and genital prolapse influence these factors. We aim to enrol 200 women attending urogynaecology and physiotherapy clinics.

Do I have to take part?

It is up to you to decide whether or not to take part. Participation will not have any effect on your current or future care from our department. If you decide to take part you are still free to change your mind at any time and without giving a reason.

What will happen to me if I take part?

If you agree to participate you should sign the consent form after having any questions answered by a member of our team. You will have been examined as part of your routine clinical care, and we will record that information. We will then help you to complete a number of short questionnaires about your sexual function, which will take an average of 20 minutes in total.

Will my taking part in this study be kept confidential?

All information collected about you during the course of the audit will be kept strictly confidential. This information will not be recorded in your medical records. Any information that leaves the hospital will be anonymised to remove all your personal details.

What will happen to the results of the audit?

The audit is being conducted as part of research degree for one of the investigators. We expect to publish the results of the study in a medical journal, as well as presenting the results at conferences. You will not be identified in any report/publication.

Contact for Further Information

If you have any further questions, please contact us:

Dr Rufus Cartwright – Consultant Gynaecologist **Dr Glaucia Varella** – PhD Student

NHS
Chelsea and Westminster Hospital
NHS Foundation Trust
https://www.chelwest.nhs.uk Tel: 020 3315 8000

Introduction of new sexual function questionnaires to the urogynaecology service.

Initials: _____ **Date of Birth:** ____/_____/_____

Hospital Number: _____

Recording patients' own perspective on their symptoms is important to help us provide individual treatment options. We would be grateful if you could answer the following questions about your medical history, and then complete a series of questionnaires related to your sexual activity. Your answers will be completely confidential, and used to help us understand what is important to patients about their sex lives. All data will be stored in an anonymous database. Thank you for your help.

Demographics

☐ English, Welsh, Scottish, Northern Irish or British ☐ Irish ☐ Roma

☐ Gypsy or Irish Traveller ☐ Indian ☐ Pakistani ☐ Bangladeshi

☐ Chinese ☐ Caribbean ☐ African ☐ Arab

☐ Any other Asian background ☐ Any other White background

☐ Any other Black, Black British, or Caribbean background ☐ Other: _____

Marital Status: ☐ Single ☐ Married ☐ Divorced ☐ Widowed

Height: _____ **Weight:** _____ **Years of Education:** _____

Menopausal Status:

☐ Premenopausal ☐ Menopausal (If so, when: _____)

Hormone Use: ☐ Tablets ☐ Patch ☐ Gel ☐ Implant ☐ None

Medication Use: _____

Comorbidities: ☐ None ☐ High Blood Pressure ☐ Diabetes ☐ Other

Deliveries

Number of Children: ☐ None ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5+

Types of Deliveries: ☐ Vaginal Delivery ☐ C-Section ☐ Forceps ☐ Vacuum

Did you need any stitches in your perineum after childbirth? ☐ Yes ☐ No

Date of last delivery (Month _____, Year _____)

Are you currently breast-feeding: ☐ No ☐ Yes

FUNCTION QUESTIONNAIRE (PISQ-IR)

Please check the box that best answers the questions for you. While answering the questions, consider your sexual function over the past six months. Thank you for your help.

1.Which of the following best describes you:

Not sexually active at all **1** ☐ → Go to item 2 (Section 1)

Sexually active with or without a partner **2** ☐ → Skip to item 7 (Section 2)

Section 1: For those who are not Sexually Active

2.The following are a list of reasons why you might not be sexually active, for each one please indicate how strongly you agree or disagree with it as a reason that you are not sexually active.

a **No partner** ☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

b **No Interest** ☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

c **Due to bladder or bowel problems (urinary or faecal incontinence) or due to prolapse (a feeling of or a bulge in the vaginal area)**

☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

d **Because of my other health problems**

☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

e **Pain** ☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

3.How much does the fear of leaking urine and/or stool and/or a bulging in the vagina (either the bladder, rectum or uterus falling out) cause you to avoid or restrict your sexual activity?

☐ Not at all ☐ A little ☐ Some ☐ A lot

4.For each of the following, please indicate the number between 1 and 5 that best represents how you feel about your sex life.

	Rating					
a. Satisfied	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	Dissatisfied
b. Adequate	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	Inadequate

5.How strongly do you agree or disagree with each of the following statements:

a **I feel frustrated by my sex life**

☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

b **I feel sexually inferior because of my incontinence and/or prolapse**

☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

c **I feel angry because of the impact that incontinence and/or prolapse has on my sex life**

☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

6.Overall, how bothersome is it to you that you are not sexually active?

☐ Not at all ☐ A little ☐ Some ☐ A lot

END OF ITEMS FOR NOT SEXUALLY ACTIVE

Section 2: For those who are sexually active

7.How often do you feel sexually aroused (physically excited or turned on) during sexual activity?

☐ Never ☐ Rarely ☐ Sometimes ☐ Usually ☐ Always

8.When you are involved in sexual activity, how often do you feel each of the following:

a. Fulfilled	☐ Never	☐ Rarely	☐ Sometimes	☐ Usually	☐ Almost Always
b. Shame	☐ Never	☐ Rarely	☐ Sometimes	☐ Usually	☐ Almost Always
c. Fear	☐ Never	☐ Rarely	☐ Sometimes	☐ Usually	☐ Almost Always

9.How often do you leak urine and/or stool with <u>any type</u> of sexual activity?

☐ Never ☐ Rarely ☐ Sometimes ☐ Usually ☐ Always

10.Compared to orgasm you have had in the past, how intense are your orgasm now?

☐ Much less intense ☐ Less intense ☐ Same intensity ☐ More intense ☐ Much more intense

11.How often do you feel pain during sexual intercourse?

☐ Never ☐ Rarely ☐ Sometimes ☐ Usually ☐ Always

12.Do you have a sexual partner?

☐ Yes ⟶ Go to item 13

☐ No ⟶ Skip to 15

13.How often does your partner have a problem (lack of arousal, desire, erection, etc.) that limits your sexual activity?

☐ All of the time ☐ Most of the time ☐ Some of the time ☐ Hardly ever/Rarely

14.In general, would you say that your partner has a positive or negative impact on each of the following:

a. Your sexual desire

☐ Very Positive ☐ Somewhat Positive ☐ Somewhat Negative ☐ Very Negative

b. The frequency of your sexual activity

☐ Very Positive ☐ Somewhat Positive ☐ Somewhat Negative ☐ Very Negative

15.When you are involved in sexual activity, how often do you feel that you want more?

☐ Never ☐ Rarely ☐ Sometimes ☐ Usually ☐ Always

16.How frequently do you have sexual desire, this may include wanting to have sex, having sexual thoughts or fantasies, etc.?

☐ Daily ☐ Weekly ☐ Monthly ☐ Less often than once a Month ☐ Never

17.How would you rate your level (degree) of sexual desire or interest?

☐ Very high ☐ High ☐ Moderate ☐ Low ☐ Very low or none at all

18.How much does the fear of leaking urine, stool and/or a bulging in the vagina (prolapse) cause you to avoid sexual activity

☐ Not at all ☐ A little ☐ Some ☐ A lot

19.For each of the following, please indicate the number between 1 and 5 that best represents how you feel about your sex life.

	Rating					
a. Satisfied	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	Dissatisfied
b. Adequate	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	Inadequate
c. Confident	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	Not Confident

20.For each of the following, please indicate the number between 1 and 5 that best represents how you feel about your sex life.

a **I feel frustrated by my sex life**

☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

b **I feel sexually inferior because of my incontinence and/or prolapse**

☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

c **I feel embarrassed about my sex life**

☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

d **I feel angry because of the impact that incontinence and/or prolapse has on my sex life**

☐ Strongly Agree ☐ Somewhat agree ☐ Somewhat Disagree ☐ Strongly Disagree

---

VAGINAL SYMPTOMS QUESTIONNAIRE

We would be grateful if you could answer the following questions, thinking about how you have been, on average, over the PAST FOUR WEEKS. Thank you for your help.

a.Vaginal symptoms:

1. Are you aware of dragging pain in your lower abdomen?

☐ Never ☐ Occasionally ☐ Sometimes ☐ Most of the time ☐ All of the time

2. Are you aware of soreness in your vagina?

☐ Never ☐ Occasionally ☐ Sometimes ☐ Most of the time ☐ All of the time

3. Do you feel that you have reduced sensation or feeling in or around your vagina?

☐ Not at all ☐ A little ☐ Somewhat ☐ A lot

4. Do you feel that your vagina is too loose or lax?

☐ Not at all ☐ A little ☐ Somewhat ☐ A lot

5. Are you aware of a lump or bulge coming down in your vagina?

☐ Never ☐ Occasionally ☐ Sometimes ☐ Most of the time ☐ All of the time

6. Do you feel a lump or bulge come out of your vagina, so that you can feel it on the outside or see it on the outside?

☐ Never ☐ Occasionally ☐ Sometimes ☐ Most of the time ☐ All of the time

7. Do you feel that your vagina is too dry?

☐ Never ☐ Occasionally ☐ Sometimes ☐ Most of the time ☐ All of the time

8. Do you have to insert a finger into your vagina to help empty your bowels?

☐ Never ☐ Occasionally ☐ Sometimes ☐ Most of the time ☐ All of the time

9. Do you feel that your vagina is too tight?

☐ Never ☐ Occasionally ☐ Sometimes ☐ Most of the time ☐ All of the time

b.Sexual matters:

10. Do you have a sex life at present?

☐ Yes ☐ No, because of my vaginal symptoms ☐ No, because of other reasons

11. Do worries about your vagina interfere with your sex life?

☐ Not at all ☐ A little ☐ Somewhat ☐ A lot

12. Do you feel that your relationship with your partner is affected by vaginal symptoms?

☐ Not at all ☐ A little ☐ Somewhat ☐ A lot

13. How much do you feel that your sex life has been spoilt by vaginal symptoms?

Please ring a number between 0 (not at all) and 10 (a great deal)
0 1 2 3 4 5 6 7 8 9 10

c.Quality of life:

14. Overall, how much do vaginal symptoms interfere with your everyday life?

Please ring a number between 0 (not at all) and 10 (a great deal)
0 1 2 3 4 5 6 7 8 9 10

VAGINAL LAXITY QUESTIONNAIRE (VLQ)

How would you rate your current level of vaginal looseness? or laxity during intercourse sexual?

☐ Very loose ☐ Moderately loose ☐ Slightly loose ☐ Neither loose nor tight

☐ Slightly tight ☐ Moderately tight ☐ Very tight

SEXUAL QUALITY OF LIFE QUESTIONNAIRE – FEMALE (SQoL-F)

This questionnaire consists of a set of statements, each asking about thoughts and feelings that you may have about your sex life. All your answer will be completely confidential.

1.When I think about my sex life, it is an enjoyable part of my overall life.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree

☐ Moderately disagree ☐ Completely disagree

2.When I think about my sex life, I feel frustrated.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree

☐ Moderately disagree ☐ Completely disagree

3.When I think about my sex life, I feel depressed.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree

☐ Moderately disagree ☐ Completely disagree

4.When I think about my sex life, I feel like less of a woman.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

5.When I think about my sex life, I feel good about myself.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

6.I have lost confidence in myself as a sexual partner.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

7.When I think about my sex life, I feel anxious.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

8.When I think about my sex life, I feel angry.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

9.When I think about my sex life, I feel close to my partner.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

10.I worry about the future of my sex life.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

11.I have lost pleasure in sexual activity.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

12.When I think about my sex life, I feel embarrassed.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

13.When I think about my sex life, I feel that I can talk to my partner about sexual matters.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

14.I try to avoid sexual activity.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

15.When I think about my sex life, I feel guilty.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

16.When I think about my sex life, I worry that my partner feels hurt or rejected.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

17.When I think about my sex life, I feel like I have lost something.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

18.When I think about my sex life, I am satisfied with the frequency of sexual activity.

☐ Completely agree ☐ Moderately agree ☐ Slightly agree ☐ Slightly disagree
☐ Moderately disagree ☐ Completely disagree

FEMALE SEXUAL DISTRESS SCALE – REVISED (FSDS-R)

How often that problem has bothered you or caused you distress during the past 30 days including today.

How often did you feel:

1.Distressed about your sex life

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

2.Unhappy about your sexual relationship

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

3.Guilty about sexual difficulties

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

4.Frustrated by your sexual problems

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

5.Stressed about sex

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

6.Inferior because of sexual problems

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

7.Worried about sex

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

8.Sexually inadequate

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

9.Regrets about your sexual functioning

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

10.Embarrassed about sexual problems

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

11.Dissatisfied with your sex life

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

12.Angry about your sex life

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

13.Bothered by low sexual desire

☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Always

THE BRIEF SEXUAL ATTITUDES SCALE - BSAS

Listed below are several statements that reflect different attitudes and cultural aspects about sex. For each statement select the response on the answer scale, that indicates how much you agree or disagree with that statement.

1. I do not need to be committed to a person to have sex with him/her.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

2. Casual sex is acceptable.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

3. I would like to have sex with many partners.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

4. One-night stands are sometimes very enjoyable.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

5. It is okay to have ongoing sexual relationships with more than one person at a time.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

6. Sex as a simple exchange of favors is okay if both people agree to it.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

7. The best sex is with no strings attached.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

8. Life would have fewer problems if people could have sex more freely.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

9. It is possible to enjoy sex with a person and not like that person very much.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

10. It is okay for sex to be just good physical release.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

11. Birth control is part of responsible sexuality.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

12. A woman should share responsibility for birth control.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

13. A man should share responsibility for birth control.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

14. Sex is the closest form of communication between two people.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

15. A sexual encounter between two people deeply in love is the ultimate human interaction.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

16. At its best, sex seems to be the merging of two souls.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

17. Sex is a very important part of life.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

18. Sex is usually an intensive, almost overwhelming experience.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

19Sex is best when you let yourself go and focus on your own pleasure.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

20. Sex is primarily the taking of pleasure from another person.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

21. The main purpose of sex is to enjoy oneself.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

22. Sex is primarily physical.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

23. Sex is primarily a bodily function, like eating.

☐ Strongly agree ☐ Moderately Agree ☐ Neutral ☐ Moderately Disagree ☐ Strongly Disagree

THIS IS THE END OF THE FORM. WE ARE GRATEFUL FOR YOUR HELP.

THANK YOU VERY MUCH.

8.11. STROBE Checklist para o Artigo Predictors of vaginal laxity and sexual function in a multi-ethnic population: a cross-sectional study

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

Title: Measurement of the vaginal wall thickness by transabdominal and transvaginal ultrasound of women with vaginal laxity: a cross-sectional study

	Item No	Recommendation	Pages
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those	7-8

		used to control for confounding	
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	7-8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9
		(b) Indicate number of participants with missing data for each variable of interest	8-9
Outcome data	15*	Report numbers of outcome events or summary measures	8-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-10
		(*b*) Report category boundaries when continuous variables were categorized	8-10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-10
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13

Generalisability	21	Discuss the generalisability (external validity) of the study results	11-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

8.12. Outros Artigos e Capítulos de Livros Publicados durante o período do Doutorado

1-Frederice CP, Brito LGO, **Pereira GMV**, Lunardi ALB, Juliato CRT. Interventional treatment for myofascial pelvic floor pain in women: systematic review with meta-analysis. Int Urogynecol J. 2021 May;32(5):1087-1096. doi: 10.1007/s00192-021-04725-x. Epub 2021 Feb 27. PMID: 33640993.

2-Brito LGO, **Pereira GMV**. Racism and urogynecology: what is the connection? Int Urogynecol J. 2020 Dec;31(12):2455-2456. doi: 10.1007/s00192-020-04507-x. Epub 2020 Sep 8. PMID: 32897462; PMCID: PMC7477731.

3-Pereira GMV, Driusso P, Ferreira CHJ, Brito LGO. Multidisciplinary approach between physicians and physiotherapists in urogynecology: how can we make it stronger? Int Urogynecol J. 2020 Nov;31(11):2187-2188. doi: 10.1007/s00192-020-04417-y. Epub 2020 Jul 17. PMID: 32681346.

4-D'Almeida Lucas Macharet DV, Mendes LN, **Pereira GMV**, de Castro Monteiro MV. Implementing telemedicine in urogynecology: A feasibility study. Int Urogynecol J. 2022 Nov 4:1–7. doi: 10.1007/s00192-022-05392-2. Epub ahead of print. PMID: 36331581; PMCID: PMC9638453.

5-Pereira GMV, de Araújo CC, Juliato CRT, Brito LGO. Incarcerated Ring Pessary Repair under Local Anesthesia. J Minim Invasive Gynecol. 2021 Jun;28(6):1121-1122. doi: 10.1016/j.jmig.2020.11.011. Epub 2020 Nov 22. PMID: 33238209.

6-Miranda Varella Pereira G, Oliveira Brito LG, Slongo H, Carvalho de Araújo C, Benedito de Castro E, Teatin Juliato CR. Rectovaginal Fistula in Women

With Pessary for Pelvic Organ Prolapse: A Case Series and Literature Review. J Low Genit Tract Dis. 2021 Oct 1;25(4):318-325. doi: 10.1097/LGT.0000000000000629. PMID: 34542087.

7-Brito LGO, **Pereira GMV**, Moalli P, Shynlova O, Manonai J, Weintraub AY, Deprest J, Bortolini MAT. Age and/or postmenopausal status as risk factors for pelvic organ prolapse development: systematic review with meta-analysis. Int Urogynecol J. 2022 Jan;33(1):15-29. doi: 10.1007/s00192-021-04953-1. Epub 2021 Aug 5. PMID: 34351465.

8-Albuquerque RC, **Pereira GMV**, Luz AG, Nóbrega MA, Lajos GJ, Brito LGO. Risk factors for mediolateral episiotomy at a tertiary hospital: a cross-sectional study. Rev Assoc Med Bras (1992). 2022 Apr;68(4):463-469. doi: 10.1590/1806-9282.20211251. PMID: 35649068.

9-Pereira GMV, Pimentel VM, Surita FG, Silva AD, Brito LGO. Perceived racism or racial discrimination and the risk of adverse obstetric outcomes: a systematic review. Sao Paulo Med J. 2022 Sep-Oct;140(5):705-718. doi: 10.1590/1516-3180.2021.0505.R1.07042022. PMID: 36043663; PMCID: PMC9514866.

10-Nóbrega MA, **Pereira GMV**, Brito LGO, Luz AG, Lajos GJ. Severe Perineal Trauma in a Brazilian Southeastern Tertiary Hospital: A Retrospective Cohort Study. Female Pelvic Med Reconstr Surg. 2021 Feb 1;27(2):e301-e305. doi: 10.1097/SPV.0000000000000910. PMID: 32576733.

11-Pereira GMV, Hosoume RS, de Castro Monteiro MV, Juliato CRT, Brito LGO. Selective episiotomy versus no episiotomy for severe perineal trauma: a systematic review with meta-analysis. Int Urogynecol J. 2020 Nov;31(11):2291-2299. doi: 10.1007/s00192-020-04308-2. Epub 2020 Apr 24. PMID: 32333062.

12-Macharet DVDL, Mendes LN, Oliveira WCS, **Pereira GMV**, Monteiro MVC. Patient Acceptance of Telemedicine in Urogynecology Consultations - A Cross-Sectional Study Performed at a Brazilian Public Institution. Rev Bras Ginecol Obstet. 2022 Aug;44(8):755-760. English. doi: 10.1055/s-0042-1748971. Epub 2022 Jun 27. PMID: 35760361.

13-Fante JF, Ferreira CHJ, Juliato CRT, Benetti-Pinto CL, **Pereira GMV**, Brito LGO. Pelvic floor parameters in women with gynecological endocrinopathies: a systematic review. Rev Assoc Med Bras (1992). 2020 Dec;66(12):1742-1749. doi: 10.1590/1806-9282.66.12.1742. PMID: 33331587.

14-de Albuquerque Coelho SC, **Pereira GMV**, Brito LGO, Juliato CRT. Cross sectional study on assessment of ring pessary cleaning and removal every six months: adverse events and complications. Int Urogynecol J. 2022 Feb;33(2):397-403. doi: 10.1007/s00192-021-04775-1. Epub 2021 Apr 8. PMID: 33830303.

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Capítulos de Livros

1. Brito, L.G.O. **Pereira, G.M.V**. (2021). Episiotomia sim ou não? Eis a Questão. In R. B. Machado (Ed.). Manual de Ginecologia da SOGESP (volume 2, pp.87-90). São Paulo: Editora dos Editores.

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8.13. Prêmios em Congressos

60º CBGO
CONGRESSO BRASILEIRO DE GINECOLOGIA E OBSTETRÍCIA
O congresso de todos os brasileiros
16-19/Nov, 2022 • Rio de Janeiro, RJ
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Certificamos que

o ESTUDO ORIGINAL intitulado **Fisioterapia Versus Radiofrequência em Mulheres com Frouxidão Vaginal: Ensaio Clínico com 6 meses de seguimento**

dos autores **LUIZ GUSTAVO OLIVEIRA BRITO, GLAUCIA MIRANDA VARELLA PEREIRA, CRISTIANE MARTINS DE ALMEIDA, KLEBER CURSINO DE ANDRADE, NATALIA MARTINHO, CASSIA RAQUEL TEATIN JULIATO**

foi apresentado por **LUIZ GUSTAVO OLIVEIRA BRITO** no **60º Congresso Brasileiro de Ginecologia e Obstetrícia**, realizado no **Rio de Janeiro**, **16 a 19 de novembro de 2022**, na forma de apresentação: **Apresentação Oral**.

Rio de Janeiro, 19 de novembro de 2022.

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FISIOTERAPIA VERSUS RADIOFREQUÊNCIA EM MULHERES COM FROUXIDÃO VAGINAL: ENSAIO CLÍNICO COM 6 MESES DE SEGUIMENTO

Autores: **Luiz Gustavo Oliveira Brito, Glaucia Miranda Varella Pereira, Cristiane Martins de Almeida, Kleber Cursino de Andrade, Natalia Martinho, Cassia Raquel Teatin Juliato**,

foi agraciado com o **Prêmio FEBRASGO**, classificado em **2º lugar** na categoria **Estudo Original: GINECOLOGIA**, como estímulo à comunidade científica associada, durante o **60º Congresso Brasileiro de Ginecologia e Obstetrícia**, ocorrido entre os dias 16 e 19 de novembro de 2022, na cidade do Rio de Janeiro – RJ.

Rio de Janeiro, 19 de novembro de 2022.

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participaram do **27º Congresso Paulista de Obstetrícia e Ginecologia 2022** , realizado de 11 a 13 de agosto de 2022

com o trabalho **G056 – "EFEITO DA RADIOFREQUENCIA VERSUS TREINAMENTO MUSCULAR DO ASSOALHO PÉLVICO NO TRATAMENTO DE MULHERES COM FROUXIDÃO VAGINAL: ENSAIO CLÍNICO RANDOMIZADO"**

Luciano de Melo Pompei
Presidente

Rogério Bonassi Machado
Diretor Científico

Lucia Helena Simões da Costa Paiva
Coordenadora Científica de Ginecologia

Rosiane Mattar
Coordenadora Científica de Obstetrícia

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Luciano de Melo Pompei
Presidente

Rogério Bonassi Machado
Diretor Científico

Lucia Helena Simões da Costa Paiva
Coordenadora Científica de Ginecologia

Rosiane Mattar
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