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https://academic.oup.com/ndt/article/38/Supplement_1/gfad063c_2700/7196333

DOI: https://doi.org/10.1093/ndt/gfad063c_2700

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RENAL OSTEODYSTROPHY AND CLINICAL OUTCOMES: RESULTS FROM THE BRAZILIAN REGISTRY OF BONE BIOPSY

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Background and Aims: Mineral and bone disorders caused by chronic kidney disease (CKD-MBD) encompass biochemical/hormonal abnormalities, soft tissue calcifications and bone morphological changes known as renal osteodystrophy (ROD). Data from prior studies have consistently shown that patients with CKD-MBD are susceptible to an increased risk of mortality, bone fractures and major cardiovascular outcomes. This study is a sub analysis of the Brazilian Registry of Bone Biopsy (REBRABO), a prospective, national

multicenter cohort of patients with CKD who underwent bone biopsy, aimed at addressing the relationship between ROD type and the occurrence of bone fractures, hospitalizations, cardiovascular events, and a composite of all-cause mortality.

Method: During the period from August 2015 to December 2021, 511 patients with CKD who underwent bone biopsy and with diagnosis of ROD were included in REBRABO. Bone biopsy was indicated by medical reasons or research protocol. Were excluded from this analysis patients who lost their follow-up (N = 111), had no bone biopsy report (N = 40), had an estimated glomerular filtration rate > 90 mL/min (N = 28), not signed their consent (N = 24), had bone fragments inadequate for diagnosis (N = 23), had a bone biopsy indicated by a specialty other than nephrology (N = 6), or were < 18 years old (N = 4). Baseline was defined as the time when the patient underwent bone biopsy. The prospective analysis included data from patients who completed at least 12 months of follow-up. The mean follow-up was 1242 (693-1508) days. The following events were adjudicated: bone fractures, hospitalization, major cardiovascular events - MACEs (unstable angina, nonfatal acute myocardial infarction, elective or emergency coronary revascularization, transient ischemic attack, stroke, and cardiovascular death), and death. Bone fragments were obtained via transiliac bone biopsies using an electrical trephine after prelabeling with tetracycline (3 days) administered over two separate periods. The samples were classified as osteitis fibrosa (OF), mixed uremic osteodystrophy (MUO), adynamic bone disease (ABD), osteomalacia (OM) and normal/minor alterations, according to TMV system. Cox regression analysis was performed to detect independent determinants of clinical outcomes.

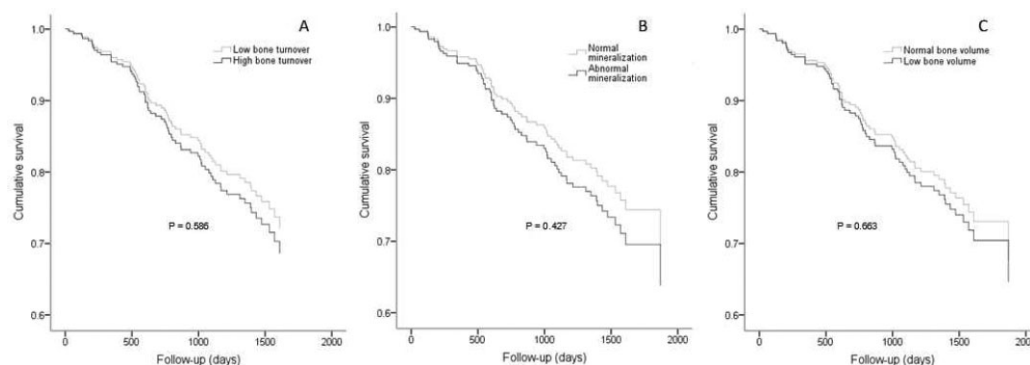


Figure 1: Effects of bone turnover, mineralization, and volume on death outcome.

Cox regression analysis survival curves for death outcome. Variables tested in the models: age, previous cardiovascular disease, previous parathyroidectomy, proportion of patients out of the normal range for serum phosphate levels, plus: bone turnover (reference: high bone turnover) in (A), or bone mineralization (reference: abnormal bone mineralization) in (B), or bone volume (reference: low bone volume) in (C). Overall $p = 0.0001$.

Results: A total of 275 patients were included. This was a population with a mean age of 52 (42– 60) years, 143 (52%) were men, 39 (14%) had diabetes, and 248 (90%) were on dialysis. During follow-up, a total of 28 bone fractures, 97 hospitalization events, 44 MACEs, and 70 deaths were reported, with incidence of 15.1% (4.4%/year), 49.5% (14.6%/year), 23.3% (6.85%/year) and 25.5% (7.5%/year), respectively. Patients who presented MACEs had lower serum hemoglobin levels [11.1 (9.6–12.6) vs. 12 (10.8–13.5; $p = 0.026$], higher prevalence of diabetes mellitus [11 (25%) vs. 15 (10%); $p = 0.013$] and previous cardiovascular disease [8 (18%) vs. 8 (5%); $p = 0.008$]. Age, previous cardiovascular disease, and proportion of serum phosphate levels out of the normal range were independent predictors for death [OR 1.046 (CI: 1.024–1.069), $p = 0.0001$; OR 1.856 (CI: 1.009–3.413), $p = 0.04$; OR: 1.942 (CI: 1.116–3.379), $p = 0.019$; respectively]. Participants were grouped according to the ROD subtype as: OF ($n = 113$; 41%), ABD ($n = 79$; 29%), MUO ($n = 59$; 21%), OM ($n = 12$; 4%), and normal/minor alterations ($n = 12$; 4%). ROD subtypes were not related to incident outcomes.

Conclusion: The incidence of bone fractures, hospitalizations, cardiovascular events, and of a composite of all-cause mortality did not differ between the types of ROD.