Anxiety, Depression, and SSRI Use in Patients with Chronic Bone Diseases

Sophia Caputo BS[1], Hannah Dieterle PhD[1], Dr. Edward Fox MD[1]
[1]Penn State College of Medicine, Hershey, PA
scaputo@pennstatehealth.psu.edu

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INTRODUCTION: It has been well established that patients with chronic bone diseases are at an increased risk for fracture, chronic pain, and permanent joint deformities. These significant complications can lead to mental health issues and subsequent prescription of SSRIs. Current evidence has studied the association between higher rates of mental health disorders in patients with some metabolic bone diseases, like osteoporosis, but little literature has looked at rates of mental health disorders in other populations with chronic genetic and metabolic bone diseases. The aim of this study is to investigate if there is a higher prevalence of depression, anxiety, and SSRI use in patients with chronic bone diseases as compared to patients without chronic bone disease. A disclaimer should be noted that this study is not comprehensive of all known metabolic or genetic bone diseases.

METHODS: The TriNetX Global Collaborative Network was queried to create seven cohorts of patients with chronic bone diseases of renal osteodystrophy (n=102,907), osteoporosis with a current fracture (n=325,428), osteoporosis without a current fracture (n=2,308,889), osteomalacia (n=35,758), Paget's disease of bone (osteitis deformans) (n=21,978), x-linked hypophosphatemic rickets (n=132,111), or osteogenesis imperfecta (n=13,350). Each bone disease cohort was propensity matched with a cohort of patients who do not have a diagnosis of any of the above bone diseases. Cohort balancing was done based on the primary covariates of age and gender due to computational constraints of large cohort sizes. The bone disease cohorts were created based on their corresponding ICD-10 codes for renal osteodystrophy (N25.0), osteoporosis with a current fracture (M80-M80.08, M80.8-M80.88), osteoporosis without a current fracture (M81, M81.0, M81.6, M81.8), osteomalacia (M83.0, M83.9), Paget's disease of bone (M88-M88.9), x-linked hypophosphatemic rickets (E83.31), and osteogenesis imperfecta (Q78.0). The propensity matched cohorts were created based on a general adult medical examination (Z00.0) and exclusion of all of the aforementioned bone disease codes. Outcomes evaluated between the bone disease cohort and its propensity matched cohort included anxiety (F41), depression (F32, F33), and SSRI prescription of sertraline, escitalopram, citalopram, paroxetine, and fluoxetine (2556, 321988, 32937, 36437, 4493) rates within 5 years after the index event (diagnosis of the initial bone disease or the general physical exam). Only outcomes occurring after the index date were included in the seven chi-square analyses with statistical significance set at $p < 0.05$.

RESULTS: Within 5 years of diagnosis, patients with renal osteodystrophy, osteoporosis with and without fracture, osteomalacia, x-linked hypophosphatemic rickets, and Paget's disease of bone were significantly more likely to have anxiety or depression when compared to patients without a diagnosis of a bone disease (Figure 1A, $p \leq 0.001$). Similarly, these same patient populations showed significantly higher rates of SSRI use in comparison to patients without a diagnosis of a chronic bone disease (Figure 1B, $p \leq 0.001$). There was no statistically significant difference in rates of anxiety, depression, or SSRI use in patients with osteogenesis imperfecta versus patients without bone diseases (Figure 1A and 1B, $p > 0.05$).

DISCUSSION: There is a high prevalence of anxiety, depression, and SSRI use observed in the majority of the chronic bone diseases highlighted in this study. This supports the need for implementing the best screening practices to address mental health issues within these patient populations. Additionally, given the high rates of SSRI use, the negative effects of these medications on bone healing outcomes should be analyzed in these diseases as well. Osteogenesis imperfecta, a genetic bone disease, was the only condition included in this study to not show significantly higher rates of anxiety, depression, or SSRI use. This could be indicative of many underlying factors such as increased resilience in these patients or initial diagnosis occurring at a younger age, but ultimately serves as a point of question for future research. Limitations of this study include computational constraints of large sample sizes within TriNetX, inclusion of only a limited subset of ICD-10 codes for anxiety and depression, and underdiagnosis of mental health disorders.

CLINICAL RELEVANCE: This study emphasizes the importance of increased mental health awareness and screening tools within chronic bone disease populations. In consideration of the recent literature detailing the negative impacts of SSRIs on bone healing, prescription of these medications in patient populations with preexisting poor bone health should be carefully considered.
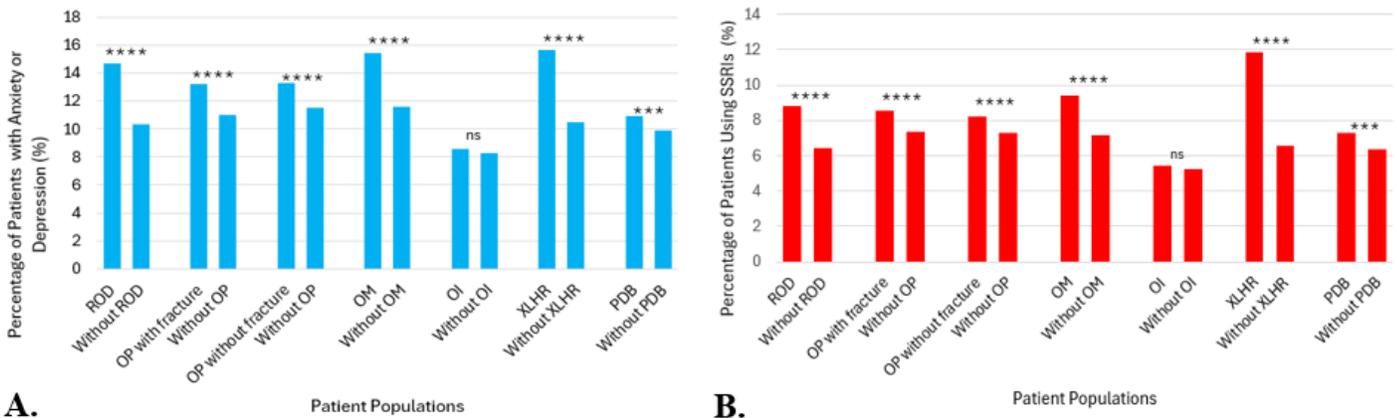
IMAGES AND TABLES:

Figure 1. Mental Health Disorders (A) and SSRI Medication Use (B) in Patients with Bone Disease Compared to Patients Without Bone Disease.
ROD = renal osteodystrophy; OP = osteoporosis; OM = osteomalacia; OI = osteogenesis imperfecta; XLHR= x-linked hypophosphatemic rickets; PDB = Paget's Disease of the Bone. The statistical significance when comparing cohorts is shown as follows: * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$. "ns" indicates there is no significant difference ($p > 0.05$).