Oregon Health & Science University
School of Medicine

Scholarly Projects Final Report

Title *(Must match poster title; include key words in the title to improve electronic search capabilities.)*

Bad to the Bone: The Impact of Methamphetamine on Bone Mineral Density

Student Investigator's Name

David Cornwell

Date of Submission *(mm/dd/yyyy)*

03/17/2022

Graduation Year

2022

Project Course *(Indicate whether the project was conducted in the Scholarly Projects Curriculum; Physician Scientist Experience; Combined Degree Program [MD/MPH, MD/PhD]; or other course.)*

Scholarly Projects Curriculum

Co-Investigators *(Names, departments; institution if not OHSU)*

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Mentor's Name

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Concentration Lead's Name

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Project/Research Question

What is the impact of chronic methamphetamine use on bone mineral density?

Type of Project *(Best description of your project; e.g., research study, quality improvement project, engineering project, etc.)*

Clinical Research Study (retrospective cohort)

Key words *(4-10 words describing key aspects of your project)*

Methamphetamine, Bone Mineral Density, Orthopaedics, Substance Use

Meeting Presentations

If your project was presented at a meeting besides the OHSU Capstone, please provide the meeting(s) name, location, date, and presentation format below (poster vs. podium presentation or other).

OHSU Research Week 2022 virtual poster presentation

Publications *(Abstract, article, other)*

If your project was published, please provide reference(s) below in JAMA style.

Not as of yet

Submission to Archive

Final reports will be archived in a central library to benefit other students and colleagues. Describe any restrictions below (e.g., hold until publication of article on a specific date).

N/A

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Next Steps

What are possible next steps that would build upon the results of this project? Could any data or tools resulting from the project have the potential to be used to answer new research questions by future medical students?

This study can be built on with a continuation of chart review (i.e. charleson comorbidity index collection) in order to better remove bias and understand causation/correlation. It can also be expanded on with an evaluation of fracture risk, peri-prosthetic fracture risk, and infection rates in this patient population.

Please follow the link below and complete the archival process for your Project in addition to submitting your final report.

https://ohsu.ca1.qualtrics.com/jfe/form/SV_3ls2z8V0goKiHZP

Student's Signature/Date *(Electronic signatures on this form are acceptable.)*
This report describes work that I conducted in the Scholarly Projects Curriculum or alternative academic program at the OHSU School of Medicine. By typing my signature below, I attest to its authenticity and originality and agree to submit it to the Archive.

X _____

Student's full name

Mentor's Approval *(Signature/date)*

X _____

Mentor Name

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Report: *Information in the report should be consistent with the poster, but could include additional material. Insert text in the following sections targeting 1500-3000 words overall; include key figures and tables. Use Calibri 11-point font, single spaced and 1-inch margin; follow JAMA style conventions as detailed in the full instructions.*

Introduction *(≥250 words)*

Methamphetamine is an illicit psychoactive stimulant with well recognized effects on the cardiovascular, pulmonary, and central nervous systems.[1] The impacts of methamphetamine on these systems is well-researched, and the effects of chronic dopaminergic stimulation on most organ systems are detailed in full. There is however limited understanding as to the effects of methamphetamine use on bone mineral density (BMD). Existing studies on this subject have been performed in limited quantities, but show that osteopenia and osteoporosis exist in the population at rates of 76% and 22% respectively, far higher than expected for their age groups.[2] This is a topic in need of further research as methamphetamine users present with orthopaedic injuries at far higher than expected rates based on their prevalence in the general population.[1] BMD, which is typically measured via dual energy X-ray absorptiometry (DEXA) scans, can also be determined based on CT scans using Hounsfield units (HU) of trabecular bone. BMD's true impact on orthopaedics is debated in the literature, but studies have shown that BMD can be used as both a surrogate marker for fracture risk reduction as well as a tool to predict the success of orthopaedic implants.[3,4] Fractures of the lumbar spine and femur are among the most common fractures associated with osteoporosis, and the BMD of these bone has been found to correlate directly with the BMD of the calcaneus, suggesting that calcaneal BMD can serve as a surrogate for lumbar and femoral osteopenia and osteoporosis.[5] This study attempts to ascertain the implications of chronic methamphetamine use on the BMD of orthopaedic patients, and thus their risk of fracture, orthopaedic hardware failure, and need for supplemental care.

Methods *(≥250 words)*

A retrospective chart review was completed of 380 patients between the ages of 18-60 who had suffered one of five lower extremity fractures: Intra-articular tibial fracture, extra-articular tibial fracture, talar fracture, calcaneal fracture, and Lisfranc injury. Charts that did not contain an axial CT scan with 2 mm cuts were excluded. CT scans were reviewed for completeness, and scans that did not contain complete cuts of the calcaneus or distal tibia were excluded. After exclusion criteria were applied, 176 charts were selected for further review. Charts were separated by fracture location and reviewed in sequential order. CT scans were opened using *Agfa* and windowed for bone (W:2000 L:500). An ellipse tool was used to measure average HU of trabecular bone. Cortical bone and areas containing fracture were not included in the measurements. Location of measurements for each bone was standardized as follows:

Tibia: The first measurement is taken 10 mm proximal to the tibial plafond. The second and third measurement are taken 6 mm proximal to the prior measurement.

Talus: The first measurement is taken 6 mm distal to the talar dome. The second and third measurements are taken 6 mm distal to the prior measurement.

Calcaneus: The first measurement is taken 12 mm distal to the superior aspect of the posterior facet. The second and third measurements are taken 6 mm distal to the prior measurement.

Following the recording of the raw data, an average of the three measurements was taken to represent bone density. Data was not collected from bones including fracture area in planned cuts. Charts were subsequently reviewed for age, gender, and results of urine toxicology screens. Patients with a urine toxicology screen positive for methamphetamine during the course of the hospitalization associated with the fracture were sorted into a methamphetamine-positive cohort. Patients with no or negative toxicology screens were sorted into the methamphetamine-negative cohort. Results were averaged among the cohorts.

Results *(≥500 words)*

After exclusion criteria were applied and CT scans were reviewed for completeness, 176 charts were included in the final analysis. CTs were examined prior to chart review in order to reduce risk of bias. Methamphetamine use was identified in 15.3% (27/176) of patients. Between the methamphetamine-positive (M+) and methamphetamine-negative (M-) groups, there was no significant difference in average age. The M+ cohort was 41.5 years old on average, while the M- cohort was 40.4 years old on average. One notable but not statistically significant difference between the groups was the gender ratio, which was 18.5% (5/27) female in the M+ cohort while the M- cohort was 30.9% (46/149). This is notable given that the average male BMD is higher than age matched female patients, and even though the difference was not significant with a p-value of greater than 0.05, it is nonetheless a factor in expectations for BMD comparison. The average body mass index (BMI) across all patients was 27.9 and 5% (9) of patients had diabetes. Polytrauma was present in 46% (78) of patients, and the most common methods of injury (MOI) among all groups were falls and motor vehicle collisions (MVC), which accounted for a combined 91% (154) of all fractures. There was no significant difference in rates of polytrauma, MOI, or BMI found between the two groups.

The average BMD of the talus, tibia, and calcaneus were measured for both groups, and are displayed in *Figure 1.* The average BMD of the tibia in the M- cohort was 264.3 HU, while the average BMD of the tibia in the M+ cohort was 220.4 HU, an average reduction of 17%. This data was analyzed using an unpaired t-test and was found to be significant, with a p-value of less than 0.005. This data is displayed in the first column of *Figure 1.* The average BMD of the talus in the M- cohort was found to be 404.9 HU, while the average BMD of the talus in the M+ group was found to be 354.1 HU, an average reduction of 13%. This data was also found to be significant when analyzed using an unpaired t-test, with a p-value of less than 0.001. This data is displayed in column 2 of *Figure 1*. The average BMD of the calcaneus in the M- cohort was 257.7 HU, while the average BMD of the calcaneus in the M+ cohort was found to be 213.6 HU, an average reduction of 17%. This data like the data for the tibia and talus was also found to be significant when examined with an unpaired t-test, with a p-value of less than 0.005. This data is shown in column 3 of *Figure 1*.

Across the board, a reduction in BMD was found in the M+ cohort when compared to an age matched control group of patients with similar fractures and no history of methamphetamine use. The average BMD was reduced by between 13-17%, with the talus exhibiting the least reduction in BMD while the tibia and calcaneus both displayed similar reductions in BMD.

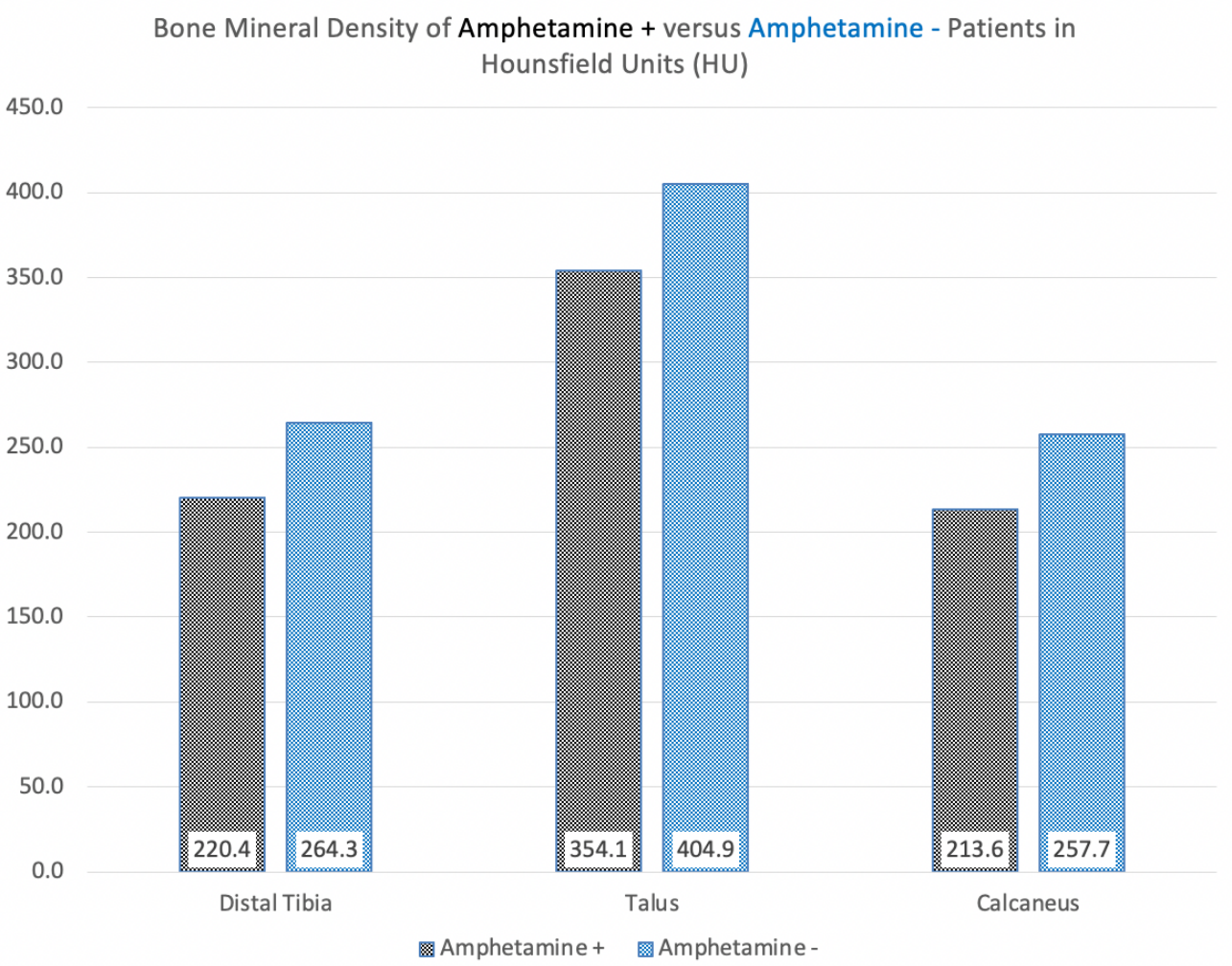

Figure 1. Reduction in the average BMD of the tibia, talus, and calcaneus of patients with positive urine toxicology screens for methamphetamine, as compared to patients with no or negative toxicology screens.

Discussion *(≥500 words)*

The impacts of methamphetamine on organ systems such as the cardiovascular, pulmonary, and central nervous system are well-researched, however the understanding of the impacts of methamphetamine use on bone health and BMD have yet to be elucidated. The results of this study display that there is a significant reduction in BMD in patients with a history of methamphetamine use as compared to age matched comparisons with similar orthopaedic injury profiles. There was a significant reduction in BMD of between 13-17% across all categories. This reduction in BMD portends a greater risk of fracture as well as a significantly increased risk for implant failure following fracture repair.[3,4] This data is notably important to orthopaedics as patients with a history of methamphetamine use are more likely to present as patients of the orthopaedic trauma service than would be expected for their demographic.[1]

The implications of reduced BMD on orthopaedics are not yet fully elucidated, and there is debate within the literature as to the relevancy of BMD on fracture risk and orthopaedic outcomes. While some studies have not found significant data to correlate low BMD to increased fracture risk, osteopenia and osteoporosis are known risk factors for increased frequency and severity of fractures.[5] Other studies have shown significant data linking reduced BMD to fracture risk, with one study showing that periprosthetic fractures following total ankle arthroplasty were significantly ($p=0.018$) increased in patients with tibial HU of lower than 200.[4] The average tibial HU of methamphetamine patients was only 220.4, and many patients fell below an average HU of 200, further indicating that caution and risk management should be preemptively applied when considering surgical management of orthopaedic patients with a history of methamphetamine use. The 17% reduction in calcaneal BMD is additionally concerning due to research that has indicated that calcaneal BMD can act as a surrogate for BMD of the femur and lumbar spine.[5] Osteoporosis of the femur and lumbar spine are especially concerning as they increase risk for fracture due to ground level falls, and ground level fractures, especially of the femur and pelvis, are associated with poor mortality rates.[6]

There are a variety of factors that could play a role in this outside of the impact of methamphetamine's dopaminergic stimulation and catecholamine depletion on BMD. Patients who use methamphetamine are also more likely to be suffering from houselessness, and with that malnutrition and lack of regular weight-bearing exercise which are known to play a role in BMD.[1] These comorbid conditions and their impact on BMD should be explored in order to remove potential confounding variables. Other comorbidities such as those in the Charlson Comorbidity Index such as history of cardiovascular disease, peptic ulcer disease, and kidney and liver disease should also be recorded and quantified in further studies in order to remove bias and confounding effects. In addition to the potential risk for bias conferred by the presence of confounding variables, other limitations on the study exist due to small sample size, and indeterminate precision in administration of urine toxicology screens.

Conclusions *(2-3 summary sentences)*

Methamphetamine abuse may be a causative factor of, or may be correlated with, the development of osteopenia and osteoporosis. Due to its impact on BMD, methamphetamine use may increase rates of fracture and portend lower implant success rates following fracture repair. Further studies on the effectiveness of orthopaedic implants and complication rates following fracture repair are vital for improving care for this population.

References *(JAMA style format)*

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