Metacarpal Cortical Index: An Accessible Alternative for Assessing Wrist Bone Health and Fracture Risk

Anthony Yosick, MS[1,2], Sophia Turbide, MD[3], Hani Awad, PhD[1,2]
[1]Department of Biomedical Engineering, [2]Center for Musculoskeletal Research, Department of Orthopaedics, University of Rochester, Rochester, NY
[3]Department of Internal Medicine and Pediatrics, University at Buffalo, Buffalo, NY
ayosick@ur.rochester.edu

Disclosures: Anthony Yosick (N), Sophia Turbide (N), Hani Awad (N)

INTRODUCTION: Osteoporosis (OP) is a silent bone disease. Without effective screening, diagnosis, and treatment, bone mineral density (BMD) loss often goes unnoticed leading to a fragility fracture. BMD is assessed using dual-energy X-ray absorptiometry (DXA), which serves as the basis for calculating a T-score, indicating the number of standard deviations from normal healthy BMD. The diagnostic threshold for OP is 2.5 standard deviations (T-score ≤ -2.5). Although T-score is the World Health Organization's (WHO) gold standard for diagnosing OP, it has limitations in accurately capturing overall fracture risk. Moreover, its utility is further undermined by woefully low screening rates in clinical practice, meaning that many at-risk individuals remain undiagnosed and untreated. Alternative tools such as the Fracture Risk Assessment Tool (FRAX) have attempted to address these limitations by incorporating BMD with relevant clinical risk factors to estimate a 10-year probability of a major osteoporotic fracture (wrist, hip, humerus, and spine). While FRAX is established as a clinical standard for predicting fracture risk, it is most commonly performed with femoral neck BMD to improve predictive accuracy; however, this reliance on BMD can limit its accessibility. Additionally, FRAX inputs primarily rely on the accuracy of patient-reported clinical risk factors, which may affect the accuracy of fracture risk estimation. Alternative objective prediction methods have been proposed to investigate bone size and geometry, microarchitecture, and composition. One method, metacarpal cortical index (MCI), offers a practical and accessible option by using a standard hand radiograph to quantify normalized cortical thickness of the second metacarpal. Given the potential of these alternative modalities, this study aims to evaluate whether MCI can reliably diagnose OP and to assess the performance of MCI in estimating fracture risk compared to DXA T-score and FRAX.

METHODS: Human cadaveric specimens were obtained through Anatomy Gifts Registry (AGR). This cohort comprised of 39 female non-paired cadaver arms (disarticulated at the elbow) with a mean age of 68.7±13.5 years and a mean BMI of 28.2±8.6 kg/m^2. Given that biological female sex is a known risk factor for OP, a female-only study cohort was selected to enhance the statistical relevance and specificity of the findings. Inclusion criteria included HIV-negative serology, less than 3-year postmortem recovery, and available medical history. Exclusions include known arm fractures, nonambulatory for more than 1 year, musculoskeletal impairments (paralysis or paresis), neoplasm, or prosthetic hardware. Specimen BMD category was based upon a DXA scan of the wrist (1/3 radius) provided by Advanced Radiology on a Horizon Ci DXA System (Hologic). Of the 39 specimens, n=14 were normal (N), n=10 were osteopenic (OPE), and n=15 were OP. Biomechanical testing protocols for wrist fracture induction were adapted from previous studies [1,2]. Forearm specimens were mounted to simulate a fall on an outstretched hand (FOOSH) with the forearm in pronation and a 15° radial abduction (Figure 1A). Biomechanical testing was conducted using an Instron ElectroPuls E10000 by applying a compressive load to the palm at a rate of 3.3 mm/s to simulate a FOOSH. Force-displacement data was used to determine work to fracture force to measure fracture risk (Figure 1B). Posterior–anterior hand radiographs were acquired using the Hologic UltraFocus Faxitron X-Ray system to assess fracture locations, most commonly distal radius fractures, and measure MCI (Figure 1C and 1D). A threshold for low (≥19 J) versus high (<19 J) wrist fracture risk was established based on a previously published simulated FOOSH model [3]. Statistics: Wrist work to fracture was compared across WHO classifications using one-way ANOVA with Tukey's post hoc test. Fracture risk groups were compared using Welch's t-test. A two-sample, two-sided t-test was performed to estimate the required sample size per group based on observed effect sizes (Cohen's d) and a significance level of 0.05 for the wrist work to fracture results. Optimal cutoffs for T-score, FRAX, and MCI were determined using receiver operating characteristic (ROC) curves and the area under the curve (AUC).

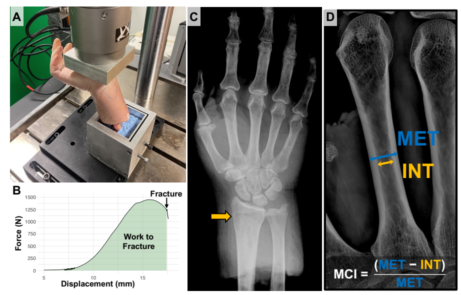

Figure 1. Experimental setup and radiographic assessments. (A) Forearm mounting setup and (B) representative force-displacement curve. Radiograph illustrating (C) common FOOSH fracture location and (D) MCI measurement.

RESULTS: DXA scans and biomechanical measurements were obtained for all donors, while FRAX measurements were available for 37 donors, as two exceeded the FRAX upper age limit of 90 years. Comparison of wrist work to fracture across WHO classifications showed a significant difference between N and OP (P= 0.0110; Figure 2A). Power analysis between N and OP yielded a power of 0.8 with an effect size of 1.08. Comparisons involving the OPE group (N vs. OPE or OPE vs. OP) showed the expected trends but were not statistically significant and did not reach a power of 0.8. MCI differentiated between N and OP (AUC= 0.986, cutoff = 0.395), N and OPE (AUC=0.779, cutoff = 0.462), and OPE and OP (AUC=0.940, cutoff = 0.409) (Figure 2B). Work to fracture force was significant between low and high wrist fracture risk (p=0.0002; Figure 3A). For distinguishing low from high wrist fracture risk, performance was highest for MCI (AUC = 0.855, cutoff = 0.524), followed by T-score (AUC = 0.796, cutoff = –1.6) and FRAX (AUC = 0.713, cutoff = 21.5%) (Figure 3B).

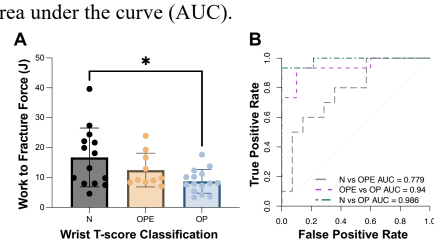

Figure 2. Work to fracture force and diagnostic performance of metacarpal cortical index (MCI) across WHO classifications. (A) Comparison of work to fracture force among N, OPE, and OP donors based on 1/3 radius WHO classification, *P < 0.05. (B) Receiver operating characteristic (ROC) curves for MCI between groups.

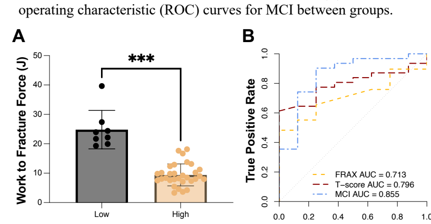

Figure 3. Fracture risk stratification and predictive performance of screening modalities. (A) Work to fracture force for donors classified as low (≥19 J) or high (<19 J) fracture risk, ***P < 0.001. (B) Receiver operating characteristic (ROC) curves for predicting low versus high wrist fracture risk using FRAX, wrist T-Score, and MCI.

DISCUSSION: Our findings demonstrate that MCI serves as an accessible and effective tool for diagnosing OP, even outperforming DXA T-score and FRAX in our limited cohort. Among all modalities assessed, MCI showed the highest predictive performance. Notably, both MCI and T-score outperformed FRAX in distinguishing wrist fracture risk as defined by our FOOSH biomechanical testing. These results suggest that MCI may serve as a viable alternative to DXA T-score and as a practical option for OP screening in rural areas that lack access to DXA. This study has several limitations. Although health histories provided through AGR were derived from medical records at time of death, certain details were incomplete. Some medications appear to reflect hospice or comfort care rather than long-term medical management, familial history of fracture is not documented, and information on smoking and alcohol consumption was not consistently reported. Calculation of FRAX values was completed using the 1/3 radius BMD, which may not be in concordance with femoral neck BMD. Our future studies will aim to address this limitation by incorporating femoral assessments, another major site of osteoporotic fracture.

SIGNIFICANCE/CLINICAL RELEVANCE: Worldwide, osteoporosis affects more than 200 million women with 1 in 3 over the age of 50 expected to experience a fragility fracture, yet DXA screening rates are woefully dismal, necessitating the exploration of alternative screening strategies [4,5].

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