Sex Differences in Distal Tibial 3D Bone Microstructure Explained by Body Size

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I. INTRODUCTION

Females are at a greater risk of sustaining lower extremity skeletal injuries than males in motor vehicle crashes [1]. In frontal crashes, the distal tibia represents the most affected injury site in both sexes [2]. Previous studies have reported sex-based differences in volumetric bone mineral density (vBMD) at the distal tibia, with males generally exhibiting higher bone density than females [3]. However, these studies have not examined detailed cortical and trabecular bone microstructure in the context of sex differences. In addition, the distal tibia may be influenced by body size-related factors. Body weight contributes substantially to mechanical loading at this site [4], while its nature as a long bone suggests an additional association with height [5]. These considerations suggest the microstructural properties of the distal tibia likely reflect a complex interplay between sex and body size. Therefore, this study investigated sex differences in cortical (Ct) and trabecular (Tb) bone parameters of the distal tibia and evaluated their relationships with body weight and height.

II. METHODS

Distal tibiae were ethically obtained from 30 post-mortem human subjects (PMHS) (15 males and 15 females with similar age distributions ($p = 0.63$, 58.7 ± 23.1 and 62.7 ± 22.5 years, respectively)). Mean body weight and height were greater in males (71.8 ± 10.4 kg and 175.9 ± 6.8 cm) than females (61.3 ± 16.7 kg and 164.3 ± 7.7 cm) ($p < 0.05$). Nano-computed tomography (nanoCT) scans were acquired with an isotropic resolution of 27 µm at the University of Michigan Integrative Musculoskeletal Health Core (MiMHC). Dragonfly 3D World software (v.2025) was used to define a volume of interest (VOI) corresponding to 4% of the total tibial length from the tibial plafond. A convolutional neural network was used to segment Ct and Tb (Fig. 1) for quantification of six bone parameters: total area (Tt.Ar), Ct area (Ct.Ar), Ct thickness (Ct.Th), bone volume fraction (BV/TV), Tb number (Tb.N), and Tb thickness (Tb.Th). Statistical analyses were performed in Python using SciPy (v1.17), pandas (v3.0.1), and statsmodels (v0.14.6) [6][7]. Sex differences in bone parameters were assessed using Welch's t-tests. Two multiple linear regression approaches were used to evaluate the effects of sex, body weight, and height on each bone parameter: models including main effects only and models including both main effects and interaction terms (Weight*Height, Weight*Sex, Height*Sex, and Weight*Height*Sex). To account for multiple comparisons, p-values were adjusted using the Benjamini–Hochberg false discovery rate (FDR) correction. Alpha was set *a priori* at 0.05.

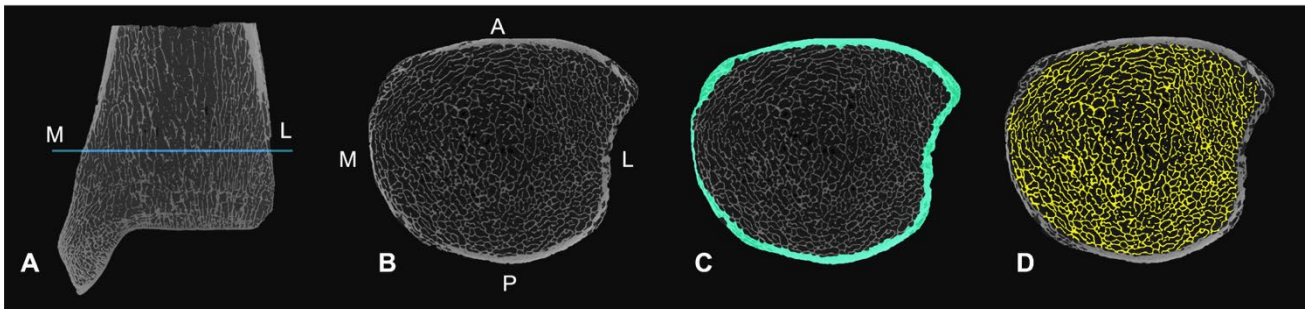

Fig. 1. (A) Coronal view of distal tibia with 4% location (blue line). (B) Axial view at blue line. (C) Ct mask (green). (D) Tb mask (yellow).

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III. RESULTS

Males exhibited significantly larger Tt.Ar compared to females (1286.22 ± 64.93 mm² vs 1039.60 ± 116.80 mm²; $t = 4.726$, $p < 0.001$). Similarly, Ct.Ar was significantly greater in males than in females (113.52 ± 27.56 mm² vs 88.30 ± 22.51 mm²; $t = 2.744$, $p = 0.011$). No significant sex differences were identified for Ct.Th ($p = 0.28$), BV/TV ($p = 0.19$), Tb.N ($p = 0.13$), or Tb.Th ($p = 0.11$).

For multiple regression models with interaction terms, no significant main effects or interaction effects were observed in these models ($p > 0.05$). Given the relatively small sample size in this study, additional multiple regression models without interaction terms were also examined to evaluate main effects more robustly (Table I). In this multiple regression, only height was significantly associated with Tt.Ar ($p = 0.011$), while weight was significantly associated with Tb.N and Tb.Th (both $p = 0.017$). No significant associations were observed for sex with any outcome variables.

TABLE I

MULTIPLE REGRESSION ANALYSIS OF MICROSTRUCTURAL PARAMETERS (FDR-ADJUSTED)

Model Terms		Tt.Ar (mm²)	Ct.Ar (mm²)	Ct.Th (mm)	BV/TV	Tb.N (1/mm)	Tb.Th (mm)
Weight	β	-1.750	0.307	0.005	0.001	-0.004	0.001
	p (FDR)	0.447	0.447	0.245	0.167	**0.017**	**0.017**
Height	β	12.769	1.290	0.005	-0.001	0.004	-0.001
	p (FDR)	**0.011**	0.167	0.447	0.492	0.262	0.262
Sex	β	115.743	6.935	-0.025	0.015	-0.057	0.010
	p (FDR)	0.167	0.565	0.776	0.447	0.307	0.262
R^2		0.651	0.381	0.216	0.198	0.355	0.362

IV. DISCUSSION

This study identified significant sex differences in distal tibial size (Tt.Ar and Ct.Ar) for this sample, however, no sex differences in Ct.Th or Tb microstructural parameters were apparent. These differences were no longer significant after accounting for body size, suggesting that the observed sex differences could be driven by variation in height and weight rather than sex-specific biological (e.g., developmental, hormonal) factors. The significant association between height and Tt.Ar, and between weight and trabecular parameters (Tb.N and Tb.Th), is likely related to bone functional adaptation at this weight-bearing location. In contrast, the lack of association with sex after body size adjustment suggests sex alone may not independently influence distal tibial microstructure. However, the absence of significant main or interaction effects may either reflect shared variance among body size predictors or limited statistical power. These findings highlight the importance of accounting for body size when interpreting sex differences in skeletal morphology, particularly in weight-bearing bones. This may have important implications for understanding injury mechanisms in motor vehicle crashes, where variations in bone structure could influence load distribution and fracture tolerances. Future work should incorporate larger sample sizes with more diverse body sizes and expanded biological variables (e.g. age, vBMD). Additionally, biomechanical data from experimental testing and corresponding computational modelling will be critical to understanding the role of distal tibia microstructure in sex-specific injury tolerances.

V. REFERENCES

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