

Age- and Sex-Dependent Bone Density Decline in the Calcar Region of the Proximal Humerus: A CT-Based Population Analysis

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Abstract

The inferomedial calcar is a key biomechanical region for proximal humerus fracture fixation, yet large-scale data on calcar bone quality across age and sex are lacking. This retrospective imaging study analyzed CT-derived Hounsfield unit (HU) values in 739 adult left proximal humeri from the Stryker Orthopaedic Modeling and Analytics database. Cylindrical regions of interest (30 mm length, 5 mm diameter) were defined along the calcar, and HU values were extracted at 5% depth increments. Individuals were stratified by age (18–40, 41–65, > 65 years) and sex. Multiple regression (adjusted $R^2 = 0.36$) identified age ($\beta = -1.97$, $p < 0.001$) and sex ($\beta = 53.4$, $p = 0.001$) as independent predictors of calcar density, with no significant interaction. Young males had the highest density (222.5 ± 81.5 HU); elderly females the lowest (65.8 ± 64.6 HU). At 15 mm depth, over 40% of women > 65 had HU values below 100. The calcar undergoes substantial age- and sex-dependent density decline, with implications for implant anchorage in osteoporotic proximal humerus fractures. The clinical relevance of specific HU thresholds remains to be validated against fixation outcomes.

Introduction

Study Design and Data Source

This study was conducted and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. A retrospective cross-sectional imaging study was performed using anonymized computed tomography (CT) data from the Stryker Orthopaedic Modeling and Analytics (SOMA) database. The SOMA platform contains a large collection of adult CT scans acquired for various clinical indications and processed into standardized three-dimensional (3D) bone models using established segmentation software and a validated morphometric registration platform, as described previously [26, 27, 32]. This platform enables high-resolution anatomical alignment and densitometric comparison across specimens.

A total of 739 left proximal humeri from skeletally mature individuals were included. Left humeri were selected to standardize anatomical orientation and region-of-interest (ROI) placement within the SOMA registration framework. Scans were excluded based on database metadata if they showed prior fracture, implant, deformity, tumor, or relevant motion or metal artifact involving the proximal humerus. Specimens with evidence of skeletal immaturity were excluded. Demographic variables included age, sex, ethnicity, and body mass index (BMI); BMI data were not available for all specimens. For subgroup analyses, individuals were stratified into three age groups (18–40 years, 41–65 years, and > 65 years), chosen to approximate pre-menopausal (18–40), peri- to early postmenopausal (41–65), and late postmenopausal (> 65) phases of bone metabolism, broadly aligned with nonlinear biological transition points identified in multi-omics aging studies [28]. In addition, age was modeled as a continuous variable in regression analyses.

All imaging data were fully anonymized before access and analysis. No patient-identifiable information was available. The Ethics Committee of the Hamburg Medical Association (Ethikkommission der Ärztekammer Hamburg; reference number 2023-300394-WF) confirmed that formal ethical approval was not required for this study, as it exclusively used fully anonymized imaging data.

CT Acquisition and Image Processing

CT examinations were acquired between 2008 and 2020 at multiple institutions. Although acquisition parameters varied between scanners and over the 12-year acquisition period (reflecting evolving scanner technology and reconstruction algorithms), all datasets underwent standardized post-processing within the SOMA software to ensure comparability. To mitigate the potential influence of temporal trends in CT technology, uniform inclusion criteria and standardized post-processing were applied across all acquisition years.

To reduce inter-scanner variability, each proximal humerus was registered to a standardized coordinate system using the validated SOMA 3D morphometric alignment workflow [32], ensuring consistent anatomical orientation and uniform ROI placement. Although no external phantom calibration was performed, uniform post-processing reduced, but did not eliminate, systematic inter-scanner differences in absolute HU values.

Bone density was quantified in Hounsfield units (HU). HU values represent CT attenuation and do not equate to absolute bone mineral density, as no external phantom calibration was performed. However, strong correlations between HU and local trabecular bone quality have been demonstrated in multiple skeletal regions [22–25]. HU was therefore used as a validated proxy for regional cancellous bone density, and all values should be interpreted as relative density estimates rather than calibrated mineral density measurements.

Region of Interest Definition

The primary region of interest was defined along the inferomedial metaphyseal calcar, anatomically corresponding to the dense cancellous bone zone immediately medial and inferior to the articular surface of the humeral head. This region is located at the junction of the humeral head and the medial cortex of the surgical neck, and represents the area typically engaged by inferomedial (calcar) screws in locking plate fixation [10, 14]. A cylindrical ROI with a diameter of 5 mm and a length of 30 mm was positioned along the medial metaphysis, aligned with the humeral shaft axis. The proximal boundary was defined at the inferomedial metaphyseal cortex just distal to the articular margin, using the inferior border of the anatomical neck as a reproducible landmark within the SOMA coordinate system (Fig. 1).

Density values were extracted at 5% increments along the cylinder (0–100%), generating a continuous proximal-to-distal density profile with 21 measurements per specimen. ROIs were placed using standardized anatomical landmarks after 3D registration within the SOMA coordinate framework, which

provides automated morphometric alignment across all specimens. All ROIs were visually inspected to avoid cortical overlap and manually adjusted when required to ensure consistent trabecular sampling.

Outcome Measures

The primary outcome measures were mean HU across the entire calcar ROI, and the proximal-to-distal HU gradient along the cylinder. Secondary outcome measures included HU values at predefined depth increments along the calcar cylinder, age- and sex-specific subgroup differences in calcar density, and the proportion of specimens falling below predefined HU thresholds (100 and 50 HU, based on opportunistic CT screening studies associating low HU values with reduced bone mineral density [22, 23, 31]).

Statistical Analysis

The distribution of continuous variables was assessed using the Shapiro–Wilk test and visual inspection of histograms and Q–Q plots. Although Shapiro–Wilk tests indicated deviations from normality in several subgroups, Q–Q plots showed approximately normal distributions and the large subgroup sizes ensured robustness of parametric methods; parametric analyses were therefore performed.

Homogeneity of variance was assessed using Levene’s test. A simple linear regression model was first constructed with calcar HU as the dependent variable and age as the sole predictor. Subsequently, a multiple linear regression model including age (continuous), sex (binary), and their interaction term as predictors was constructed. Regression coefficients (β), standard errors, 95% confidence intervals, and coefficients of determination (R^2) are reported. Two-way analysis of covariance (ANCOVA) with Type III sum of squares was used to evaluate the independent effects of age and sex on calcar HU. F-values and partial eta squared (η^2p) are reported as effect size measures. Post hoc pairwise comparisons between the three predefined age groups (18–40, 41–65, > 65 years) were performed using Bonferroni-adjusted p values to control for multiple comparisons. All pairwise contrasts were considered (18–40 vs. 41–65, 41–65 vs. >65, and 18–40 vs. >65).

Given the large sample size ($n = 739$), parametric methods were considered robust regardless of minor deviations from normality (central limit theorem). All results are given as mean $\pm$ standard deviation (SD) unless stated otherwise. Statistical significance was defined as a two-sided p value < 0.05 . No formal a priori power analysis was conducted because this study used all available specimens in the SOMA database meeting inclusion criteria. Given the large sample size, the study was adequately powered to detect small-to-medium effects. All analyses were performed using R (version 4.6.0; R Foundation for Statistical Computing, Vienna, Austria). During the preparation of this manuscript, the authors used a generative AI tool to support drafting and editing of the text. The authors take full responsibility for all content.

Results

Demographics

A total of 739 proximal humeri were analyzed, including 424 male and 315 female specimens. The mean age was 59.2 ± 20.7 years (range, 18–101 years). 591 out of 739 specimens were White (80.0%), 125 were Asian (16.9%), and 23 were of other or unknown ethnicity (3.1%). Body mass index data were available for 347 out of 739 specimens (47.0%; mean 22.9 ± 5.3 kg/m²). For subgroup analyses, individuals were stratified into three age groups: 18–40 years (n = 169; 121 male, 48 female), 41–65 years (n = 243; 135 male, 108 female), and > 65 years (n = 327; 168 male, 159 female). Demographic characteristics are presented in Table 1 and Fig. 2.

Table 1
Demographic and densitometric characteristics of the study population.

Age Group	n	Age (years)	Male	Female	Mean HU $\pm$ SD (M)	Mean HU $\pm$ SD (F)
18–40	169	28.9 ± 6.5	121	48	222.5 ± 81.5	174.0 ± 65.4
41–65	243	55.1 ± 6.8	135	108	158.0 ± 67.8	102.2 ± 71.7
> 65	327	77.9 ± 8.3	168	159	122.9 ± 66.4	65.8 ± 64.6
Overall	739	59.2 ± 20.7	424	315	162.5 ± 82.1	94.8 ± 76.8

Values are presented as mean $\pm$ standard deviation. Mean HU = mean Hounsfield units across the entire calcar region of interest. M = male, F = female.

While Shapiro–Wilk testing indicated statistically significant deviations from normality in several subgroups, visual inspection of Q–Q plots showed approximately normal distributions, and the large subgroup sizes ensured robustness of parametric methods (central limit theorem). Levene’s test showed statistically significant but practically small variance differences between sexes in the youngest and oldest age groups (variance ratios < 1.6). Given the large subgroup sizes, parametric analyses were considered robust and were applied throughout.

Bone Density Across Age and Sex

Mean HU values in the calcar region decreased significantly with increasing age ($p < 0.001$ across age groups). Simple linear regression demonstrated a significant negative association between age and calcar density: $HU = 264.86 - 2.218 \times \text{Age}$ ($R^2 = 0.28$; $p < 0.001$) (Fig. 3).

To quantify independent contributions, a multiple linear regression model with age, sex, and their interaction term was constructed. The full model explained 36.3% of the variance in calcar density (adjusted $R^2 = 0.363$). Age was a significant negative predictor ($\beta = -1.969$; $SE = 0.202$; 95% confidence interval [CI]: -2.364 to -1.574 ; $p < 0.001$), and male sex was associated with higher density ($\beta = 53.366$; $SE = 16.476$; 95% CI: 21.073 to 85.659 ; $p = 0.001$). The age $\times$ sex interaction was not significant ($\beta = -0.021$; $SE = 0.258$; 95% CI: -0.526 to 0.484 ; $p = 0.94$), indicating that the overall linear rate of density

decline did not differ significantly between males and females. However, decade-level analysis suggested a more pronounced density reduction in women between 40 and 60 years, that is not captured by the linear interaction term and is further addressed in the Discussion.

Furthermore, two-way ANCOVA (Type III sum of squares) showed significant independent effects of age ($F(1, 735) = 95.26$; partial $\eta^2 = 0.115$; $p < 0.001$) and sex ($F(1, 735) = 10.49$; partial $\eta^2 = 0.014$; $p = 0.001$), with no significant interaction ($F(1, 735) = 0.01$; partial $\eta^2 < 0.001$; $p = 0.94$). Post hoc Bonferroni-adjusted pairwise comparisons revealed significant differences between all three age groups (18–40 vs. 41–65, 41–65 vs. >65, and 18–40 vs. >65; all $p < 0.001$).

Individuals aged 18–40 years showed the highest mean HU values (222.5 ± 81.5 in males and 174.0 ± 65.4 in females). Intermediate values were observed in the 41–65-year group (158.0 ± 67.8 in males and 102.2 ± 71.7 in females), and the lowest values were found in individuals older than 65 years (122.9 ± 66.4 in males and 65.8 ± 64.6 in females). Across all age groups, males exhibited significantly higher HU values than females ($p < 0.001$) (Fig. 4).

Proximal-to-Distal Density Gradient

HU values showed a consistent proximal-to-distal decrease along the calcar (Fig. 4). In younger individuals, trabecular density near the articular surface reached approximately 330 HU and remained above 100 HU up to a depth of 20 mm (67% of ROI length). In contrast, individuals older than 65 years showed lower proximal values (187 HU) and a steeper decline, with mean values in females approaching 100 HU at mid-calcar (15 mm) and falling below 100 by 16.5 mm, before approaching 0 HU in the distal third. At a depth of 22.5 mm (75% of ROI length), mean HU was 8 in the oldest group compared with 107 in the youngest group. Detailed HU values at each 5% depth increment for all subgroups are provided in Supplementary Table S1.

Exploratory Threshold Analysis

In an exploratory analysis using a reference threshold of 100 HU (a value supported by opportunistic CT screening studies associating low HU values with reduced bone mineral density [22, 23, 31]; no validated threshold currently exists for the proximal humerus), at mid-calcar (15 mm), more than 40% of women older than 65 years had HU values below 100. At a depth of 22.5 mm, the large majority of elderly females had HU values below 50. By comparison, fewer than 2% of individuals in the youngest group (3 out of 169) fell below 100 HU at mid-calcar depth (15 mm), whereas the physiological distal density decline resulted in 32.5% falling below 50 HU at 22.5 mm depth even in this young cohort. These observations are descriptive and should be confirmed in future clinical studies.

Qualitative Heatmap Evaluation

Composite density maps visually confirmed these findings (Figs. 5 and 6). Young male humeri showed extensive high-density regions along the calcar axis, whereas elderly female specimens showed high-

density areas limited to the proximal calcar, with minimal density in the distal region. Across all age groups, male specimens demonstrated larger and more pronounced high-density regions than female specimens, and increasing age was associated with a progressive reduction and attenuation of the dense region.

Discussion

The most important finding of this study is that the inferomedial calcar, while representing the densest cancellous region of the proximal humerus in young adults, undergoes a substantial age- and sex-dependent density decline. Using standardized 3D registration and density profiling in 739 specimens, it was shown that this difference is most pronounced in elderly women, in whom mean calcar density approaches or falls below clinically relevant thresholds.

In the present analysis, the full regression model explained 36.3% of variance in calcar density, with age and sex as independent predictors. The absence of a significant age×sex interaction ($p = 0.94$) indicates that the second hypothesis was only partially supported: while females demonstrated consistently lower calcar density across all ages, the rate of decline was comparable between sexes. It can be argued that the sex difference reflects a lower baseline rather than accelerated bone loss in females. The remaining unexplained variance likely reflects biological, behavioral, and methodological factors not captured in this dataset, including physical activity, smoking status, hormonal status, and inter-scanner variability.

The magnitude of density loss is clinically relevant: in younger individuals, dense subchondral cancellous bone extended well into the metaphysis, whereas elderly specimens showed rapid density reduction beyond the proximal third of the ROI. At mid-calcar level, more than 40% of women aged > 65 years had HU values below 100 – which is clinically relevant given the reported association between osteoporotic bone and higher fixation failure rates [6, 7, 9].

These results are in line with previous cadaveric and biomechanical studies. Tingart et al. identified the central and posterior regions of the humeral head as areas of relatively high cancellous density [15–17], and subsequent studies were able to show that inferomedial calcar screws increase construct stability and resistance to varus collapse [10, 12]. Clinical series were able to show that insufficient medial support is associated with screw cutout, secondary displacement, and fixation failure [7, 11]. Furthermore, Osterhoff et al. were able to show that calcar comminution independently predicts poor clinical outcome after locking plate fixation [9]. The feasibility and clinical utility of this standardized SOMA-based mapping approach have previously been demonstrated for the posterior pelvic ring [26] and the distal tibia [27]. However, previous studies on proximal humeral bone density were predominantly limited by small cohorts and the absence of comprehensive demographic stratification. Reeves et al. mapped trabecular apparent density across 13 cross-sections of the proximal humeral canal in 98 specimens, confirming significantly lower values in females and identifying the medial region as the zone of highest density [33]. Oh et al. used quantitative CT in 65 patients with rotator cuff tears to evaluate volumetric bone mineral density across seven proximal humeral regions, reporting consistently

lower values on the symptomatic side and a significant sex difference [34]. Yu et al. used dual-energy CT to characterize bone quality in four humeral head regions in 65 patients [20], and Arentsen et al. assessed 23 skeletal sites in 20 female cadavers using dual-energy CT and identified the proximal humerus as the location with the lowest marrow-corrected volumetric bone mineral density of all sites examined [19]. Spross et al. validated the deltoid tuberosity index as a radiographic surrogate for local bone quality in 71 patients [18], but this approach assesses a single cortical ratio rather than volumetric cancellous density profiling. The present study extends this evidence by providing the first large-scale ($n = 739$), standardized three-dimensional density mapping of the inferomedial calcar with comprehensive age and sex stratification, using automated morphometric alignment to ensure anatomical consistency across the entire cohort.

Furthermore, the proximal-to-distal density gradient has additional implications. Cancellous density was highest beneath the articular surface and declined toward the metaphyseal–diaphyseal transition, in accordance with density gradients described in other skeletal regions [26, 27, 29]. In young adults, HU values remained above 100 up to 20 mm depth (67% of the ROI), indicating adequate trabecular support across the proximal two-thirds of the metaphysis. In elderly women, mean HU approached 100 by 15 mm (50%) and fell below 50 by 18–19.5 mm, and this study suggests that the effective fixation zone for calcar screws may be limited to the proximal 10–15 mm. Although derived from density data rather than biomechanical testing, these observations are relevant for screw length and trajectory planning in osteoporotic patients.

The sex-specific differences reflect established patterns in osteoporosis [1, 2]. These differences likely result from postmenopausal estrogen decline, lower peak bone mass in women, and differential rates of trabecular resorption. As hormonal and treatment data were not available, the relative contributions of these factors could not be assessed separately. Consequently, elderly female patients appear to have a substantially reduced bone stock even before fracture, which supports the concept of demographic stratification in surgical planning.

CT-derived HU measurements provide a practical proxy for site-specific bone quality, with known correlations between HU and bone mineral density in multiple skeletal regions [22–25]. Unlike systemic dual-energy X-ray absorptiometry (DXA), HU mapping provides localized information relevant for implant anchorage. To date, however, a direct correlation between calcar HU and screw pullout strength has not yet been established. Future biomechanical studies should validate this relationship. With this caveat, opportunistic CT-based assessment offers a clinically accessible method for preoperative risk stratification.

Based on the present data, elderly female patients with calcar HU below 100 at mid-metaphyseal depth may be at increased risk of fixation failure despite adequate screw placement. The 100 HU threshold used in this analysis is supported by opportunistic CT screening studies associating low HU values with reduced bone mineral density [22, 23, 31]; however, no validated HU threshold currently exists for the proximal humerus, and this value should be confirmed against fixation outcomes in future clinical

studies. Importantly, the standardized cylindrical ROI measurement used in SOMA cannot be directly replicated in routine clinical CT reporting; future studies should define a simplified set of reproducible measurement locations (e.g., two to three defined axial levels) to facilitate clinical translation.

In patients with markedly reduced calcar density, augmentation strategies such as cement augmentation [30] and optimization of screw trajectory toward preserved subchondral bone should be considered [10, 11]. This study provides population-level reference values to guide future outcome-based validation of such thresholds.

Strengths of this study include the large sample size ($n = 739$), standardized 3D anatomical registration, consistent ROI methodology based on automated morphometric alignment, and comprehensive stratification by age and sex. Compared with small cadaveric series, this dataset captures broad demographic variability and allows robust modeling of age and sex effects.

This study has several limitations. One of the limitations of this study is that HU was used as a proxy for bone mineral density without external phantom calibration. Although standardized reconstruction protocols were applied, systematic inter-scanner differences cannot be fully excluded; however, the relative density patterns remain robust because they represent within-dataset comparisons using consistent methodology. Another limitation is that no direct biomechanical testing or clinical outcome analysis was performed, so associations between HU thresholds and fixation failure are derived from prior literature rather than prospective validation. Additionally, CT examinations were acquired over a 12-year period, during which scanner technology evolved, potentially introducing temporal variability; furthermore, clinical indications for CT scanning were not available, and selection bias toward symptomatic patients cannot be excluded. Furthermore, the cohort was predominantly White (80%) and Asian (17%), all specimens were left humeri, and BMI data were available for only 47% of specimens, which may limit generalizability.

Future studies should correlate calcar HU profiles with prospective fixation outcomes. Integration of HU-based density mapping into finite element models and digital preoperative planning platforms may support screw trajectory optimization according to local bone quality.

Conclusions

Proximal humerus fractures account for approximately 4–6% of all fractures and represent the third most common osteoporotic fracture after distal radius and hip fractures [1, 2]. Their incidence increases substantially with advancing age [3], and women are disproportionately affected, reflecting higher rates of osteoporosis in this population [1, 3]. Although many minimally displaced proximal humerus fractures can be treated nonoperatively, unstable fracture patterns often require surgical fixation with locking plates, intramedullary devices, or arthroplasty, depending on fracture morphology, patient age, and bone quality [4–6].

Despite advances in implant design and surgical technique, fixation failure after locking plate fixation occurs in 13–23% of cases, particularly in osteoporotic bone [6, 7, 9]. Varus collapse resulting from insufficient medial column support has been consistently identified as a primary mechanism of failure [10, 11], and reduced trabecular mineralization compromises screw anchorage and resistance to cyclic loading [7–9, 13]. The inferomedial calcar region, comprising dense cortical and cancellous bone beneath the articular surface, serves as the principal medial buttress against varus forces [10, 12]. Clinical and biomechanical evidence has demonstrated that inferomedial calcar screws significantly increase construct stability and load to failure [10, 12], and placement of calcar screws has become a widely accepted principle in current fixation strategies [10, 14].

Despite its established mechanical relevance, comprehensive population-level data on calcar bone quality remain limited. Previous studies have largely relied on cadaveric specimens, small cohorts, or indirect radiographic proxies [15–18]. Although dual-energy CT studies have identified notably low mineral density at the proximal humerus and relatively higher calcium content in the posteromedial quadrant [19, 20], these analyses lacked systematic demographic stratification across a broad adult population. Computed tomography–derived Hounsfield unit (HU) measurements have emerged as a practical proxy for local trabecular bone density [21], with demonstrated correlations between HU values and bone mineral density in multiple skeletal regions [22–25]. Using the Stryker Orthopaedic Modeling and Analytics (SOMA) platform, standardized CT-based bone density mapping has been applied to the posterior pelvic ring [26] and the distal tibia [27], demonstrating the feasibility of large-scale population-level density analysis. To the best of our knowledge, this approach has not been applied to the proximal humeral calcar.

Therefore, the aim of the present study was to quantitatively characterize trabecular bone density along the inferomedial calcar in a large and demographically diverse adult population using standardized three-dimensional registration and region-of-interest mapping in 739 proximal humeri. It was hypothesized that calcar density decreases with increasing age, with lower values in females. By defining demographic density gradients and clinically relevant HU thresholds, this study aims to provide population-level data to inform implant design, preoperative planning, and risk stratification in the surgical management of proximal humerus fractures.

Methods

The inferomedial calcar represents the region of highest trabecular density in the proximal humerus of young adults but undergoes a pronounced age- and sex-dependent density reduction. In elderly patients, particularly women, the zone of dense cancellous bone is substantially reduced, limiting the effective bone stock for inferomedial screws. CT-derived HU measurements provide a practical proxy for regional bone quality, though specific thresholds require prospective validation against fixation outcomes. The population-level reference values reported in this study can inform preoperative risk stratification and individualized fixation strategies in the surgical treatment of proximal humerus fractures.

Abbreviations

ANCOVA

Analysis of covariance

BMI

Body mass index

CI

Confidence interval

CT

Computed tomography

DXA

Dual-energy X-ray absorptiometry

HU

Hounsfield units

ROI

Region of interest

SD

Standard deviation

SOMA

Stryker Orthopaedic Modeling and Analytics

STROBE

Strengthening the Reporting of Observational Studies in Epidemiology

3D

Three-dimensional

Declarations

Ethics approval and consent to participate:

The Ethics Committee of the Hamburg Medical Association (Ethikkommission der Ärztekammer Hamburg; reference number 2023-300394-WF) confirmed that formal ethical approval was not required for this study, as it exclusively used fully anonymized imaging data. Informed consent was not applicable as all data were fully anonymized before access.

Consent for publication:

Not applicable. This study exclusively used fully anonymized imaging data; no individual patient data or images are presented.

Competing Interests

LEJG was an employee of Stryker Trauma GmbH at the time of the study. BH is an employee of Stryker Trauma GmbH. The remaining authors declare that they have no conflicts of interest related to this study.

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Author Contribution

LFH contributed to conceptualization, methodology, formal analysis, data curation, and writing. FS and SIS contributed to investigation and data curation. LEJG and BH contributed to data acquisition and technical support for the SOMA platform. DT contributed to methodology, writing (review and editing), and resources. HK contributed to methodology and writing (review and editing). KHF contributed to supervision and writing (review and editing). MFF contributed to conceptualization, methodology, and formal analysis. All authors read and approved the final manuscript.

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Data Availability

The datasets analyzed during the current study are not publicly available due to proprietary restrictions of the SOMA database (Stryker Trauma GmbH). Data access requires permission from the database custodian. Requests may be directed to the corresponding author

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