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CLINICAL ARTICLE

Intrinsic Cortical Property Analysis of the Medial Column of Proximal Humerus

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Objective: Adequate mechanical support of the medial column is paramount to maintain fracture reduction in locking plating of proximal humerus fractures. However, intrinsic cortical properties of the medial column are rarely discussed. The purpose of the study is to describe regional variation of cortex in the medial column.

Methods: A total of 147 healthy participants were eligible for enrollment between December 2016 and December 2018. Subjects were divided into three groups: group A (20–39 years), group B (40–59 years), and group C (>60 years). For each individual, a color 3D thickness map for proximal humerus was created by cortical bone mapping (CBM) technique after bilateral shoulders were imaged by computed tomography. Measurement Indices including the cortical thickness (CTh), cortical mass surface density (CM) and the endocortical trabecular density (ECTD) were determined, after six regions of interest (ROI) were defined in metaphyseal region. Regional parameter variations were analyzed by one-way ANOVA.

Results: The CTh, CM and ECTD values were approximately equivalent between genders in the proximal part of the medial column across all ages ($P > 0.05$).The greatest difference between sexes was found in CTh and CM values of middle and distal part ($P < 0.05$). The CTh and CM within medial column were negatively associated with age ($P < 0.05$). The proximal cortical bone of the medial column was thicker and more dense, compared to the lateral column ($P < 0.05$). Significant regional variation was found in all measured parameters in group A, but not in groups B and C.

Conclusion: Our finding proved that regional differences in the distribution of cortical bone in the medial column The attenuation of cortical bone heterogeneity in the medial column was found after the age of 40 years.

Key words: Cortical bone; Cortical bone mapping; Medial column; Proximal humerus; Regional variations

Introduction

Proximal humerus fractures (PHFs) are the third most common fragile fracture in the elderly population following hip and distal radius fractures.[1,2] Internal fixation with locked plate is currently the primary treatment for patients who are fully functional. Despite the improvement in fixation techniques, a large collection of poor outcomes and surgical complications are still prevalent, particularly in the presence of osteoporosis.[3,4] Many factors have been demonstrated to be responsible for the poor outcome of PHFs, including low local bone mineral density, medial calcar comminution, length of metaphyseal segment, and coronal displacement of the fracture at the onset.[3–7] Gardner *et al.*[8] have underlined mechanical support of the medial column was essential to maintain fracture reduction. They concluded that accurate reduction of the medial cortex created a load sharing condition and minimized the forces at the screw-bone interface. In prior publications, mechanical integrity of the medial column was re-established with an endosteal fibular allograft in the comminuted osteoporotic fractures.[9] Most

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recent reports showed that locking plate osteosynthesis of unstable PHFs with medial column disruption augmented with an endosteal fibular grafting had achieved excellent clinical and radiographic results and reduced mechanical failure rate.[4,10–12]

Despite that the importance of the medial column is increasingly underscored by latest literatures, the exact definition and intrinsic structural properties of the medial column were rarely discussed. Sprecher *et al.*[13] presented a histomorphometric study of the proximal humeral trabeculae by coronal sectioning. Their results revealed that the medial metaphyseal region exhibited obvious bone loss in osteoporotic individuals. Tingart *et al.*[14] used peripheral quantitative computed tomography (pQCT) to show that cortical vBMD is 17% higher in the distal part compared to the proximal part of the surgical neck.

Cortical bone mapping (CBM) is a surface-based bone measurement technique which makes accurate estimation of measure cortical and endocortical trabecular properties from clinical CT data. The measurements were repeated at several thousand independent locations over the surface of the proximal femur. Cortical properties can be displayed as a color map over the three-dimensional surface of proximal femur.[15,16] CBM had help to detect focal structural weakness in the hip for predicting an individual's fracture risk, as well as assessing treatment response.[17,18] Poole *et al.*[17] had the contralateral femur inspected by CBM in women with femoral neck fractures. They found that patients with femoral neck fractures presented with a thumbnail-sized patch of cortical thinning at the superior femoral neck. CBM was also efficient in detecting rapid increases in cortical mass at key locations of femur during denosumab therapy in women with osteoporosis.[19] The purpose of this study was: (i) to describe the regional variation of cortex in the medial column using CBM; and (ii) to evaluate age- and gender-related differences in cortical properties of the medial column.

Materials and Methods

Subjects

Recruitment began in December 2016 and was complete by December 2018. Of 175 Chinese residents screened, 147 were eligible for enrollment and agreed to participate. There were 71 males and 76 females, with range from 20 to 88 years (mean, 49.79 years). Participants were stratified into three groups based on age: group A (aged 20–39 years), group B (aged 40–59 years), and group C (aged>60 years). Group A consisted of 24 males and 22 females, with mean age of 29.35 years (range, 20–39 years). Group B comprised 27 males and 22 females, with average age of 49.67 years (range, 40–59 years). Group C included 20 males and 32 females, with mean age of 67.98 years (range, 60–88 years). Arm dominance was determined as to which arm the subject would throw a ball with. The inclusion criteria included: (i) aged over 20 years; and (ii) local residents who underwent CT scanning of the shoulder for trauma to rule out tiny fractures. The exclusion criteria included: (i) history of metabolic bone disease; (ii) exposure to medications that affect bone metabolism; and (iii) history of previous humeral fractures and shoulder surgeries. The study was approved by the Institutional review Board of Tianjin Hospital (No. 20160300012). All participants provided written informed consent. The early part of study has been reported.[20]

Cortical Bone Mapping

CT scans were performed in a supine position with a GE Light Speed VCT (GE, Milwaukee, WI, USA). Scan parameters were 120 KV, mA Auto, 8.8 s/HE; 1.25 mm slice/39.38 HQ. The scan scope covered the highest point of the acromion to the inferior angle of the scapula. CT values of pixels were recorded in Hounsfield units (HU).

The cortical parameter measurement using the CBM technique has been previously described.[15,16] First, the profile of the bone surface was drawn in the CT slices using Stradwin software (http://mi.eng.cam.ac.uk/∼rwp/stradwin/). A triangular surface mesh with thousands of vertices distributed uniformly over the proximal humerus surface was created. Then, CT data were sampled at each vertex of mesh using an 18 mm transcortical line. This line runs perpendicular to and through the cortical bone and into the trabecular compartment. By fitting a model that accounts for the imaging blur to the data samples, cortical and trabecular parameters including the cortical thickness (CTh, mm),cortical mass surface density (CM), which represents cortical mass per unit surface area of the cortex, and the endocortical trabecular density (ECTD), which is the trabecular density directly adjacent to the cortex, were estimated. Cortical properties can be shown as a color coded map of humeral surface.

Definition of the Regions of Interest

For cortical distribution analysis, specific regions of interest (ROIs) were defined within metaphyseal region. After a single 3D thickness map was created, the height of the head was determined by measurement of the distance between the superior aspect of the humeral head and the most distal edge of the articular surface (Fig. 1). Using the height of the humeral head as the reference length, three isometric planes were constructed at the metaphysis. In each slice, the maximum transverse diameter of the medullary cavity was drawn. The intersection of the maximum transverse diameter and the medial and lateral cortices was the measurement point. The medial and lateral columns each had three points for compact bone lamella measurements (Fig. 2). Thus, ROIs 1–6 were well defined. After data collection, the regional variation of the medial column was analyzed.

Statistical Analysis

Statistical analysis was performed using SPSS ver.20.0 (SPSS, Chicago, IL, USA). Differences between lateral and medial columns were assessed by Student's *t*-test or the Mann–Whitney *U*-test. One-way ANOVA was used to evaluate site

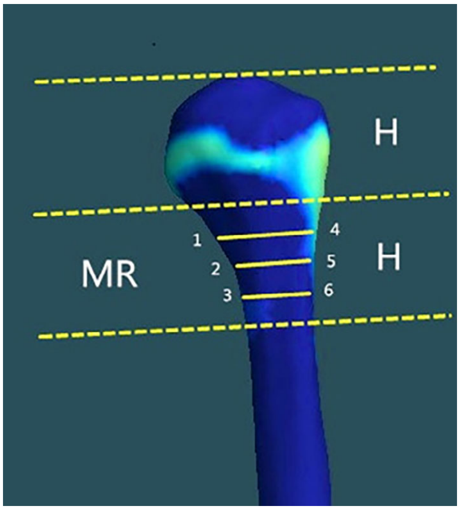

Fig. 1 Cortical thickness color mapping showing ROIs and slices. Using the height of the humeral head as the reference length, three isometric planes were constructed at the metaphysis.

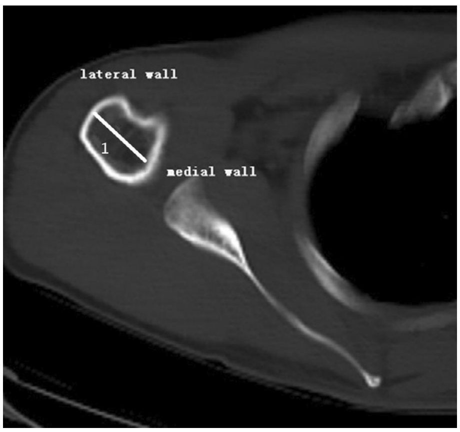

Fig. 2 Location of the measuring points in proximal metaphysis. Line 1, the maximum transverse diameter of the medullary cavity.

differences in cortical parameters at medial columns within each group. Linear regression analyses were performed to investigate the effects of age. For all analyses, the level of statistical significance was established at $P < 0.05$.

Results

Age- and Gender-Related Differences in Cortical Bone Quality

The CTh, CM and ECTD values were approximately equivalent between genders in ROI 1 at all ages ($P > 0.05$). The CTh and CM values were higher for men than for women in ROI 2–3 ($P < 0.05$). The ECTD values were similar between male and female cohorts in ROI 2–3, irrespective of age ($P > 0.05$) (Table 1). It can be seen that men had higher

TABLE 1 Cortical and trabecular parameters of the medial column in three age groups

	Male			Female		
Group	A group ($n = 24$)	B group ($n = 27$)	C group ($n = 20$)	A group ($n = 22$)	B group ($n = 22$)	C group ($n = 32$)
Age (years)	29.54 ± 4.74	50.19 ± 5.69	69.80 ± 8.06	29.13 ± 6.04	49.05 ± 6.62	66.84 ± 5.83
CTh(mm)						
ROI 1	5.47 ± 1.54*	4.43 ± 1.91	4.18 ± 1.84	5.26 ± 1.26	4.86 ± 2.03	4.63 ± 1.84
ROI 2	5.19 ± 1.73†	4.28 ± 1.43	4.08 ± 1.79	4.08 ± 1.33	3.81 ± 1.43	3.71 ± 1.29
ROI 3	4.78 ± 1.48 [a]	4.25 ± 1.35	3.98 ± 1.56	3.81 ± 1.27	3.67 ± 1.59	3.55 ± 1.10
CM (mmHU)						
ROI 1	63266.86 ± 18494.32 [b]	50325.36 ± 22305.26	45614.16 ± 20118.27	59440.87 ± 15524.31	53505.80 ± 24238.10	50782.57 ± 19902.13
ROI 2	59460.35 ± 20126.31 [a]	49097.76 ± 18183.88	46393.31 ± 19425.29	47175.06 ± 16351.62	44896.84 ± 18922.38	40943.19 ± 13496.94
ROI 3	54754.95 ± 16904.71 [a]	49070.44 ± 17015.24	45364.40 ± 16518.95	44063.41 ± 15611.76	43129.94 ± 17221.75	42761.13 ± 12739.64
ECTD (HU)						
ROI 1	10125.90 ± 53.74	9808.47 ± 1483.98	10012.92 ± 300.14	10097.51 ± 89.20	9919.99 ± 874.95	9974.61 ± 234.27
ROI 2	10075.02 ± 66.32	9752.91 ± 1479.20	9926.96 ± 308.13	10033.51 ± 85.83 [b]	10009.13 ± 78.63	9901.33 ± 236.63
ROI 3	10028.29 ± 66.53	9717.48 ± 1482.27	9905.73 ± 299.53	9997.08 ± 60.40 [b]	9996.37 ± 70.51	9895.97 ± 232.79

Notes: The values are given as the mean and the standard deviation.; * $p < 0.05$, between women and men of the same age group.; † $p < 0.05$, between different ROIs of the same sex group.; Abbreviations: CM, cortical mass surface density; CTh, cortical thickness; ECTD, the endocortical trabecular density.

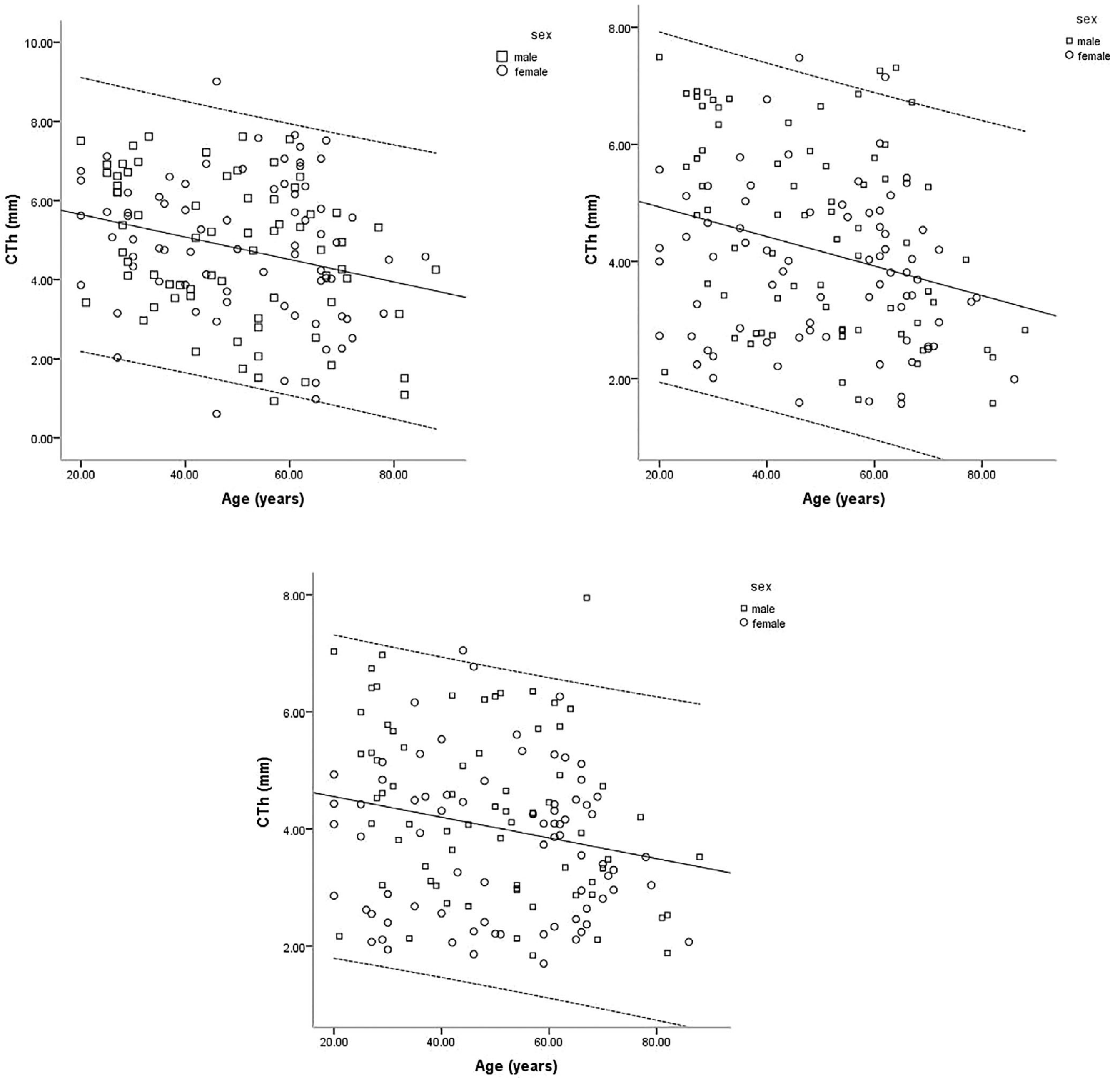

Fig. 3 Age-related changes in cortical thickness at the ROI 1–3. The solid line represents the fitted mean from the regression model, and the dashed lines represent the 95% confidence interval of the prediction.

cortical thickness and cortical mass surface density in the middle and distal part of medial column, whereas no sex-related differences were seen in the proximal segment.

The CTh and CM values in ROI1-2 was significantly different between age groups ($P < 0.05$). Of note, comparison to baseline group A, the CTh value of ROI 1 in group B was lower by 19.2%, and in group C by 23.6% in men ($P < 0.05$). Similarly, the CM values of ROI 1 in group B decreased by 20.5%, group C by 27.9% ($P < 0.05$). Among women, the ECTD values in ROI 2 and ROI 3 decreased significantly over 60 years by 1.3% and 1.0% ($P < 0.05$) (Table 1). Linear regression analysis revealed CTh and CM of the whole cohort were negatively associated with age in ROI 1-3 ($P < 0.05$), but not ECTD (Fig. 3). Collectively, these results showed that age-related bone loss in the medial column varied with sex and measurement site. In men, the loss in bone

TABLE 2 Cortical and trabecular parameters of the medial and lateral column in three age groups

Groups	Group A (n = 46)		Group B (n = 49)		Group C (n = 52)	
	Medial column	Lateral column	Medial column	Lateral column	Medial column	Lateral column
Plane 1						
CTh (mm)	5.38 ± 1.40*	4.20 ± 1.56	4.62 ± 1.96*	3.42 ± 1.66	4.45 ± 1.83*	2.94 ± 1.09
CM (mmHU)	61437.04 ± 17059.39*	48469.71 ± 18434.86	51753.31 ± 23002.03*	39261.41 ± 21040.27	48602.41 ± 20267.46*	33320.72 ± 12550.65
ECTD (HU)	10112.32 ± 73.44*	10071.89 ± 63.67	9858.54 ± 1237.30	9884.47 ± 1105.18	9989.35 ± 259.38	9923.42 ± 267.07
Plane 2						
CTh (mm)	4.66 ± 1.63	4.39 ± 1.59	4.07 ± 1.43	3.69 ± 1.72	3.85 ± 1.49	3.36 ± 1.22
CM (mmHU)	53584.78 ± 19245.37	50487.67 ± 18769.38	47211.63 ± 184444.80	42928.46 ± 22411.10	43039.39 ± 16077.19	37899.85 ± 13438.14
ECTD (HU)	10055.17 ± 78.28	10049.51 ± 67.97	9867.95 ± 1097.48	9865.23 ± 1109.87	9911.19 ± 263.76	9913.03 ± 264.99
Plane 3						
CTh (mm)	4.32 ± 1.45	4.41 ± 1.46	3.99 ± 1.48	3.83 ± 1.60	3.80 ± 1.27	3.63 ± 1.31
CM (mmHU)	49641.60 ± 16998.71	49925.46 ± 17057.49	47015.52 ± 18211.56	45159.41 ± 20899.08	43762.39 ± 14210.81	41342.83 ± 14551.98
ECTD (HU)	10011.84 ± 66.30	10022.55 ± 72.29	9842.69 ± 1100.88	9851.33 ± 1107.82	9989.73 ± 257.65	9909.18 ± 262.82

Notes: The values are given as the mean and the standard deviation.; * $P < 0.05$, between medial and lateral column of the same age group.; Abbreviations: CM, cortical mass surface density; CTh, cortical thickness; ECTD, the endocortical trabecular density.

cortical thickness and density at the proximal end of the medial column was marked, whereas in women, the decrease in endocortical trabecular bone density at the mid-distal end was pronounced.

Regional Analysis

The cortical parameters of the metaphyseal cortex were measured medially and laterally at three points each in plane 1–3. Cortical thickness and cortical mass surface density values were higher than the corresponding portion of lateral sides in plane 1 regardless age ($P < 0.05$), showing that the proximal part of medial columns had thicker and denser cortices. The ECTD value was 4% higher in ROI 1 than in ROI 4 of the group A ($P < 0.05$). The ECTD value of medial column were similar to those of lateral one in group B–C ($P > 0.05$) (Table 2).

In group A, the highest CTh CM and ECTD values were seen in ROI 1. Compared to ROI 1, CTh CM and ECTD in ROI 2 was lower by 13.3%, 19.7% and 6.0%, in ROI 3 by 12.8%, 19.2% and 1.0% ($P < 0.05$). However the medial columns had approximately equivalent CTh CM and ECTD in ROI 1–3 of group B and C ($P > 0.05$, Fig. 4). This implied a gradual decrease in cortical thickness, cortical mass surface density and endocortical trabecular density from the proximal to the distal end of the medial column in subjects aged 20–29 years, but this was not observed in individuals older than 40 years.

Discussion

In this study, we have identified regional variances in the cortical properties of the medial column by CBM technique. Significant age- and sex-related differences were found in cortical parameters at different measurement points of the medial column. Our major findings are: (i) higher-quality indices of cortex were found in the proximal part of medial columns, compared to the lateral column; (ii) in the age group of 20–39 years, spatial variability of cortical bone in the medial column was evident, where the maximum values of cortical thickness and density were seen in the proximal portion. However, similar regional variation was not found in subjects aged above 40 years; (iii) no gender-related differences regarding cortical parameters were seen in the proximal segment of medial columns; and (iv) age-related bone loss in the medial column varied with sex and measurement site.

Regional Variation of Cortex in the Medial Column

The mechanical behavior of the medial calcar is of utmost importance in locking plating of proximal humerus.[8–12] A recent multivariable regression analysis found that medial comminution and insufficient medial support were independent risk factors for reduction loss in the proximal humerus fractures surgery.[21] An essential finding of our study was that cortical shell of medial column adjacent to articular surface was thicker and denser, compared with the lateral column in metaphyseal region. Spatial variability of cortical bone in the

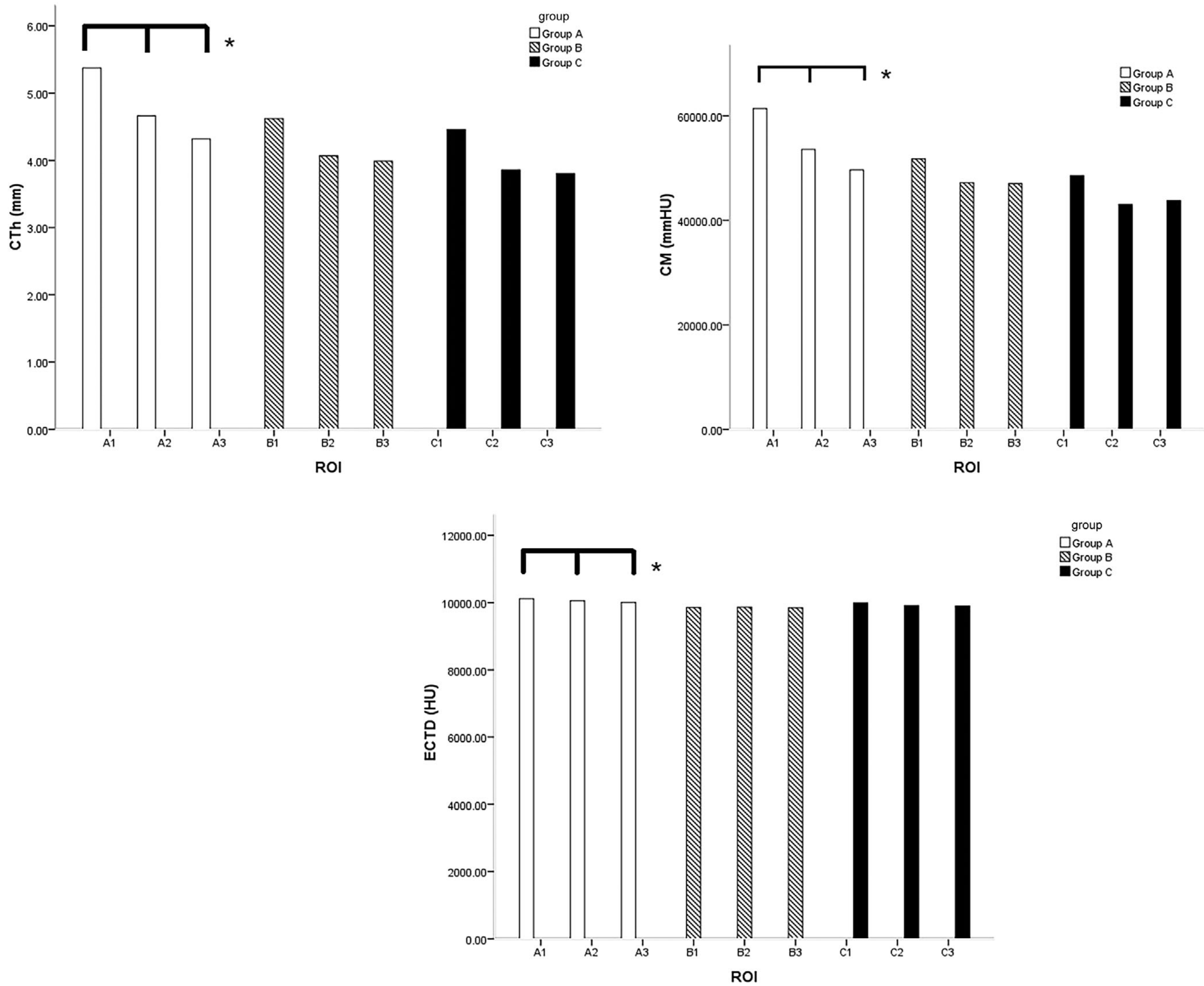

Fig. 4 Regional variation of cortical parameters in cortical thickness (CTh) (A), cortical mass surface density (CM) (B), and endocortical trabecular density (ECTD) (C). Data for the ROI 1 in group A were labeled as A1, and so on.* marks differences between ROI 1–3 ($P < 0.05$).

medial column was pronounced in the 20–39 year age group, with the maximum in cortical thickness and density occurring proximally and showing a progressive decrease from the calcar to shaft. Leng *et al.*[22] reported that when an axial load of 600 N was exerted to glenohumeral joint surface in a biomechanical test using finite element method, a maximum stress of 5.2 MPa was found in the calcar region. Based on previous literature and our regional analysis, we have inferred that the medial column is a physiological load-bearing structure. Its function might be similar to that of femoral calcar, where load is transferred from the trabecular bone in femoral head to cortical shell of shaft. However, cortical measurement results of different sites in medial column tended to be similar in subjects aged over 40 years. The main reason for this is due to the varing rates of age-related bone loss at different parts of the medial column. We believe that the loss of anisotropy in the medial column may be an indication of its decreased mechanical behavior. Our findings could be useful for the elucidation of the mechanism of development and effective fixation of varus-type proximal humerus fractures.

Age- and Gender-related Differences in Cortical Properties of the Medial Column

Cortical bone sustains a large proportion of axial loads in the proximal humerus.[20,23] It can withstand much greater stresses than trabecular bone and experience minimal deformation before failure. The results of our study suggest there was no difference in proximal part of medial column regarding cortical quality between both sexes across all ages. This finding is in line with previous studies that found no gender differences in the cortical thickness of the weight-bearing region of the femoral neck.[23,24] In this study, reduced cortical thickness and density in medial column were significantly associated with age. This was very consistent with a cadaveric QCT study of Helfen *et al*.[25] who found that a high cortical porosity and a concurrent reduced cortical thickness at the surgical neck with aging, which started after 45 years. However, this age-related bone loss had gender and site differences. In men, the sustained reduction of cortical thickness and density at the proximal end of the medial column were seen after age 40 years. This might be one of the contributing factors to the loss of anisotropy in the cortical bone of the medial column. In women, the decrease in endocortical trabecular bone density at the mid-distal end was pronounced over 60 years. This revealed that there was a predominance of age-related cortical loss in men, whereas in women aged over 60 years, trabeculae loss caused by estrogen deficiency was more common.

Strengths and Limitations

The primary strength of this analysis is its focus on the medial column of proximal humerus. To our knowledge, this is the first study to evaluate the inherent attributes of cortical bone in the medial column, although the mechanical role of the medial column in maintaining fracture reduction was widely recognized. Our results are helpful in elucidating the mechanism of proximal humeral fractures. However, there are limitations in the study design worth considering. First, our study included a predominantly Chinese Han population representative of the Tianjin region, thus our findings may not generalize to other ethnic groups. Second, is that height and weight data for all participants were not available, so it was not possible to make statistical corrections for these confounding factors. Third, the sample size was modest, as well as a cross-sectional design, which limits the power of observations related to age effects. Finally, regional distribution of cortical bone within the medial column had been assessed without biomechanical strength data. Nevertheless, this study yielded insight into the changes in cortical parameters with age and sex, which contribute to the mechanical capacity of bone.

Conclusions

In summary, the current study proved regional differences in the distribution of cortical bone in the medial column. Furthermore, our results demonstrated that cortical parameters in the medial column, as measured by CBM, displayed significant age- and gender-related differences. The thickest and highest density of cortex was found in proximal part of medial calcar in participants aged 20–40 years. The attenuation of cortical bone heterogeneity in the medial column was found after the age of 40. These data offer new insight into the intrinsic characteristics of cortical bone in medial column and may prove to provide useful information on surgical fixation. Future work should determine the loading of the medial column during different states of motion of the shoulder.

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Authors Contributions

All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Conceptualization, Yeming Wang; methodology, Yeming Wang and Yutao Men; investigation, Yeming Wang, Yutao Men and Jian Li; formal analysis Yeming Wang and Yutao Men; resources, Jian Li and Wanfu Wei; Writing—original Draft, Yeming Wang and Yutao Men; Writing—review & Editing, Yeming Wang and Wanfu Wei; visualization, Jian Li; supervision, Wanfu Wei; funding acquisition, Yutao Men.

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