CLINICAL ARTICLE

Correlation of CT Values and Bone Mineral Density in Elderly Chinese Patients with Proximal Humeral Fractures

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Objective: To investigate the correlation between computed tomography (CT) values and bone mineral density (BMD) in elderly Chinese patients with proximal humeral fractures.

Methods: This was a single-center retrospective study involving 166 elderly patients with proximal humeral fractures between January and June 2015 in our hospital. Following the inclusion and exclusion criteria, 89 patients were finally enrolled in this study. The spiral CT scanning was performed on these patients, and the CT images were obtained by using MIMICS software. The CT values in axial, coronal, and sagittal images of healthy proximal humeri were measured using a circular region of interest (ROI) by Image J. The bone mineral density (BMD) of the lumbar spine and femoral neck was measured using dual-energy X-ray absorptiometry (DXA). Spearman rank correlation methods were used for analysis of the association between the proximal humerus average CT value (CT_{Mean}) and the lumbar spine as well as femoral neck BMD in patients with proximal humeral fractures, or osteoporotic patients.

Results: Among the included 89 patients, there were 26 males and 63 females, 69% and 84% of whom were diagnosed with osteoporosis, respectively. The lumbar spine and femoral neck BMD and the CT_{Mean} of the proximal humerus were higher in males than females with proximal humeral fractures ($P < 0.05$). This gender difference was also found in the osteoporotic patient population ($P < 0.05$). The Spearman rank correlation method showed that the lumbar spine and femoral neck BMD was closely related to the proximal humeral CT_{Mean} in males ($r = 0.877$, $P = 0.000$; $r = 0.832$, $P = 0.000$; respectively) and females ($r = 0.806$, $P = 0.000$; $r = 0.616$, $P = 0.000$; respectively) with proximal humeral fractures, as well as osteoporotic male ($r = 0.745$, $P = 0.000$; $r = 0.575$, $P = 0.000$; respectively) and female ($r = 0.613$, $P = 0.000$; $r = 0.629$, $P = 0.000$; respectively) patients.

Conclusions: The CT value of the proximal humerus is a rapid and accurate method by which bone quality can be assessed in elderly patients with proximal humeral fractures. Moreover, the CT value of the proximal humerus is an alternative measurement of BMD that can guide surgeons in selecting the appropriate internal fixation material.

Key words: Bone mineral density; CT value; Osteoporosis; Proximal humeral fracture

Introduction

Proximal fractures of the humerus, which are mainly caused by low-energy trauma, are common osteoporotic fractures[1]. Proximal fractures of the humerus account for approximately 10% of all osteoporotic fractures and rank third in frequency, following spine and hip osteoporotic fractures[2]. The ideal treatment for proximal fractures is debated[3,4]. Clinical studies have reported that poor bone quality is commonly found in elderly patients with proximal humeral fractures, while local bone quality is considered one of the most

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important factors that can influence surgical treatment strategies and prognosis[1,5,6]. Specifically, poor bone quality may reduce the mechanical stability of bone, decrease the holding and supporting functions of an internal fixation apparatus, and thereby increase the risk of internal fixation failure[7,8]. Moreover, Kralinger *et al.*[9] analyzed the effect of local bone quality on prognosis in 150 patients with proximal humeral fractures treated with locking plates and found that poor bone quality was associated with a higher incidence of complications. Therefore, assessment of bone quality is of great importance before surgical treatment of proximal humeral fractures.

Bone mineral density (BMD), as measured using dual-energy X-ray absorptiometry (DXA), is currently one of most common approaches for assessment of bone quality and fracture risk[10,11]. Generally, the sites that are measured include the spine, hip, and femoral neck, while the proximal humerus and other sites are rarely assessed[12,13]. Mather *et al.*[14] determined the correlation between proximal humerus cortical bone thickness, as measured by standard anteroposterior shoulder radiographs, with the spine and femoral neck BMD and concluded that cortical bone thickness measurement could be used to detect the severity of osteoporosis in the clinic; however, the radiography quality is affected by the perspective parameters set by clinical imaging technicians. In addition, a fuzzy inner margin of cortical bone and a significantly reduced cortical bone thickness in the proximal humerus due to osteoporosis makes it difficult to accurately determine the cortical bone inner margin[15,16]. Indeed, these factors may eventually influence the accuracy of BMD measurements. Therefore, an objective method less affected by human factors is still needed in the clinic to improve BMD measurement accuracy.

Computed tomography (CT) or Hounsfield unit (HU) value is a measure of the density of human local tissues or organs based on a CT examination[17]. This software-defined value expresses the structural characteristics of the local tissues and is not affected by human factors[18]. Until now, CT value measurements have been used clinically to assess fracture risk for patients[18–20]. Schreiber *et al.*[21] confirmed the close relationship between lumbar CT values and BMD in osteoporosis patients. Like the lumbar spine, the proximal humerus mainly consists of cancellous bone. Therefore, a close relationship may also exist between proximal humeral CT values and BMD of the lumbar spine and femoral neck in patients with osteoporosis.

In this study we determined the relationship between healthy proximal humerus CT values and the lumbar spine and femoral neck BMD in a cohort of elderly patients with proximal humeral fractures. The CT values were obtained by spiral CT scanning with high resolution and digital software processing, while the lumbar spine and femoral neck BMD was assessed by DXA. In this study we sought to achieve the following: (i) confirm the correlation between the proximal humerus CT value and lumbar spine and femoral neck BMD; (ii) introduce a more objective method to assess proximal humeral bone quality; and (iii) provide valuable reference data for preoperative planning for proximal humeral fractures using imaging technologies, thus providing guidance to surgeons for selecting the appropriate internal fixation material based on bone quality.

Methods

General Information

This retrospective study was approved by the Ethics Committee of Tianjin Hospital. One hundred and sixty-six patients with proximal humeral fractures who were treated in our hospital between 1 January 2015 and 30 June 2015 were enrolled. Informed consent was obtained from all participants. The inclusion criteria were as follows: (i) age ≥ 60 years; (ii) injury due to low-energy trauma, such as falling on flat ground; (iii) fracture site involving the proximal humerus-to-surgical neck; and (iv) patients who underwent spiral CT and DXA examinations. The exclusion criteria were as follows: (i) co-existing diseases which affect local bone density, such as endocrine diseases affecting calcium and phosphorus metabolism, and metabolic bone diseases; and (ii) pathologic fractures, such as giant cell tumors (GCTs) and myeloma. Eighty-nine patients were eventually included in this retrospective study (Fig. 1).Proximal humeral fractures are commonly caused by an accident, such as an injury by a fall from a standing position, which are not closely correlated with patient age and gender. Therefore, in this retrospective study, the normal distribution test was not performed in this cohort of patients with proximal humeral fractures.

Imaging Instrument

All patients were placed in a supine position with the shoulder joints in a neutral position. A Light Speed Spiral CT (General Electric, Milwaukee, WI, USA) was used to scan the patients from the acromion to the middle of the humerus with the following parameters: 120 kV; 240 mA; 1500 HU (window width); 450 HU (window level); 0.8 mm (scanning layer thickness); and 0.625 mm (scanning interval). The CT image files were stored on a CD using the digital imaging and communications in medicine (DICOM) format for further analysis.

Digital Software

A Materialize interactive medical image control system (MIMICS 11.0; Materialize, Leuven, Belgium) was used to import images, and image segmentation and measurements. The software exports CT scan data in a variety of image formats, such as DICOM and JPEG files. ImageJ, developed by the National Institutes of Health Research, is public image processing software with image editing, analysis, processing, and preservation functions that can perform pixel statistics of specified areas in an image using the DICOM format. In this study MIMICS software was used for coronal, sagittal, and horizontal reconstruction of CT scan images, while ImageJ software was used to measure CT values of bony structures on the axial CT images by extracting and importing the images into the DICOM format.

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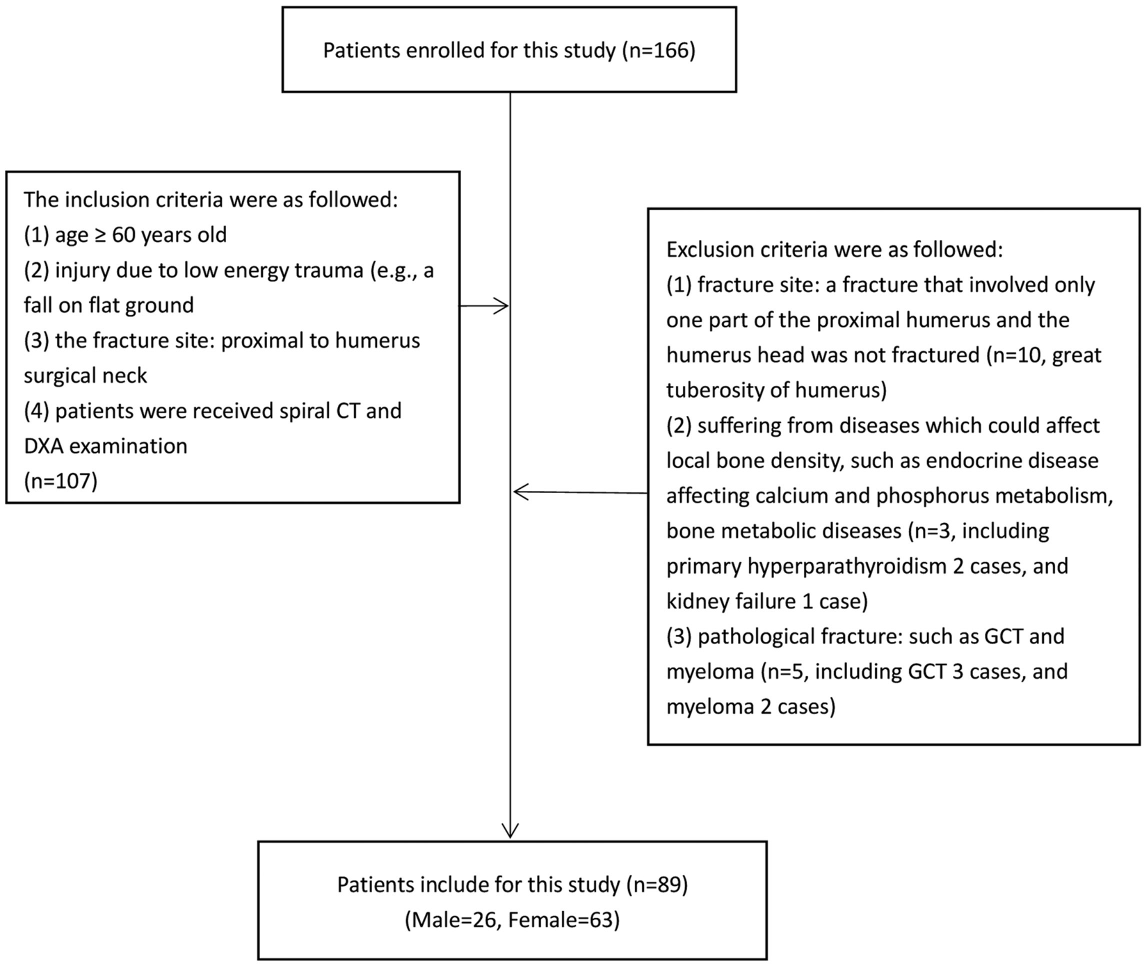

Fig 1 Flow chart of patient inclusion. GCT, giant cell tumors; CT, computed tomography; DXA, dual-energy X-ray absorptiometry.

Mean CT Values in the Proximal Humerus

The above data files in DICOM format were imported into MIMICS11.0 software for coronal, sagittal, and horizontal reconstruction of shoulder joint. The mean CT value of healthy proximal humeri was measured based on the method described by Pervaiz *et al.*[22]. Briefly, a healthy humerus was first set as a measure template and the center of the humerus medullary cavity was used as the axis in the horizontal image (Fig. 2A). Then, the distance between the humerus surgical neck and the upper edge of the humerus head was divided into three equal parts along the axis in the coronal image, and designated as the first, second, and third measuring planes (Fig. 2A). After switching to the horizontal image, the data in DICOM format in the three measuring planes were imported into ImageJ software. The humerus head cortex was then removed and the circular regions of interest (ROIs) were placed (Fig. 2B–D). Following this procedure, the average CT value in the humerus ROIs was obtained and the proximal humerus CT_{Mean} was determined by the average CT value of the above three measured planes.

Bone Mineral Density (BMD) Determination

With patients in the supine position, lumbar vertebrae1-4 and the femoral neck were detected using Discovery-W type DXA (Hologic Company, Bedford, MA, USA) with the following parameters:140 kv; tube rating value, 14 mA; and focus area, 0.4 mm X 1.2 mm. The individual BMD values were compared with BMD values representative of a normal young population, and the results are displayed as standard deviations (SDs). SDs < 0 were associated with a lower BMD and greater risk of fracture. Clinically, a T score < −2.5 is consistent with osteoporosis, −2.5 < T score < −1.0 is consistent with osteopenia (low bone mass), and −1.0 < T score < 1.0 is consistent with normal bone mass.

Statistical Analysis

SPSS statistical software (version 13.0; SPSS Inc., Chicago, IL, USA) was used for statistical processing. A normality test was performed for the proximal humerus CT_{Mean} and the lumbar spine and femoral neck BMD. A comparison of normally distributed data between groups was

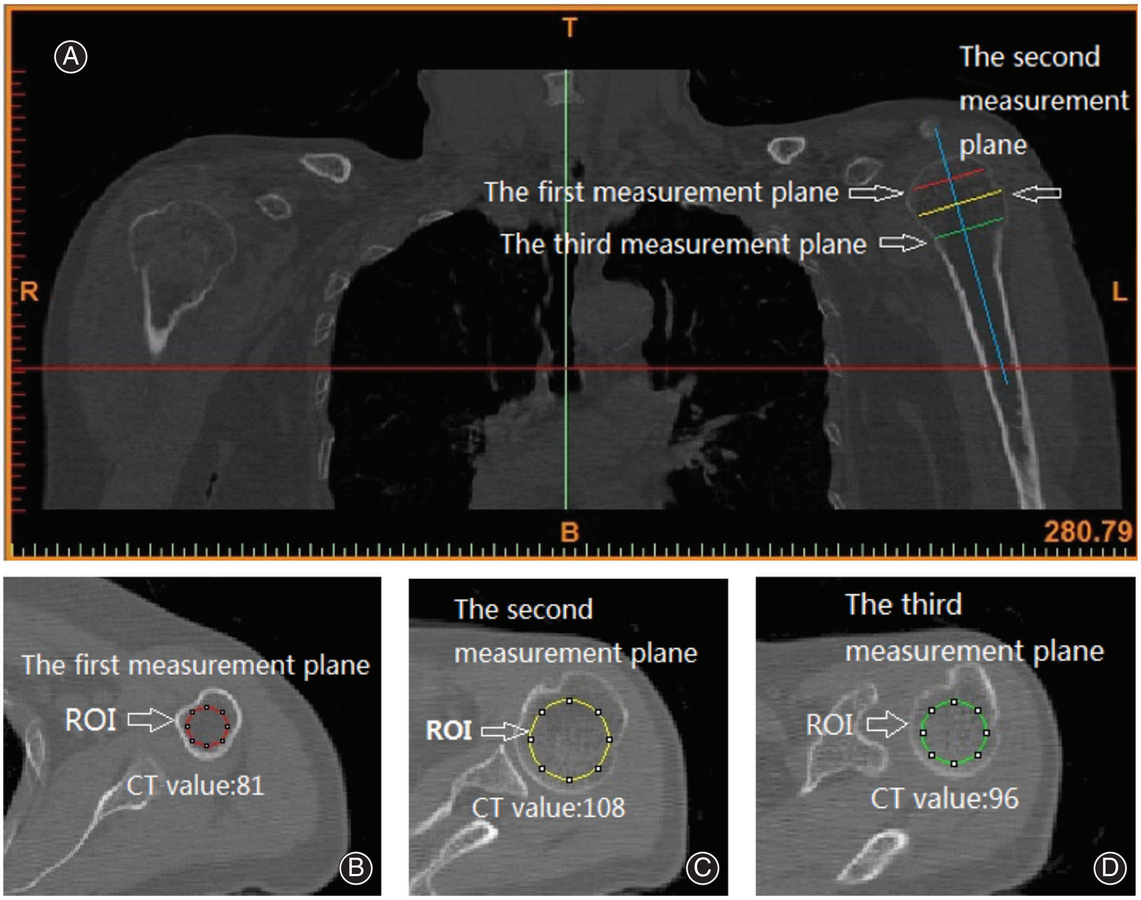

Fig 2 Method of measuring the proximal humerus average CT value (CT_{Mean}). (A) In a horizontal CT image, the center of the humerus medullary cavity was determined first. Then, the proximal humerus was divided equally into three measuring planes along the humerus medullary cavity. The ROI was placed in the proximal humerus and the CT value of the bony structure inside ROI was obtained by ImageJ software; (B) CT value inside the ROI in the first measuring plane; (C) CT value inside the ROI in the second measuring plane; (D) CT value inside the ROI in the third measuring plane. CT, computer tomography; ROI, region of interest.

performed using a *t*-test and a comparison of non-normally distributed data was performed using a rank-sum test. Linear and Spearman rank correlation methods were used for analysis of the association between the proximal humerus CT_{Mean} and the lumbar spine and femoral neck BMD in normally and non-normally distributed data, respectively. A *P* value (two-tailed) < 0.05 indicated a significant difference.

Results

General Results

In this retrospective study, 89 elderly patients with proximal humeral fractures who met the inclusion criteria were included. Of the 89 patients, there were 26 men and 63 women with an average age of 71.5 ± 5.2 years. The detailed information of the 89 patients is shown in Table 1.

TABLE 1 Neer classification for patients with proximal humeral fractures

			Side		Neer classification			
	Patients	Average age (Years)	Left	right	I	II	III	IV
Male	26	67.2 ± 6.3	16	10	3	6	7	10
Female	63	73.8 ± 4.9	35	28	8	9	22	24
Total	89	71.5 ± 5.2	51	38	11	15	29	34
Percentage	100%	-	57%	43%	12%	17%	33%	38%

TABLE 2 Proportion of bone mineral density (BMD) in elderly males and females with proximal humeral fractures

	Patients	Osteoporosis	Low bone quality	Normal bone quality
Male	26	18	6	2
Female	63	53	10	0

BMD, bone mineral density.

As the Neer classification is based on a four-segment classification system[23] and is widely used for assessment of proximal humeral fractures, we used it to define the fracture population in this study. Generally, there were 11 patients with Neer I fractures (12%), 15 patients with Neer II fractures (17%), 29 patients with Neer III fractures (33%), and 34 patients with Neer IV fractures (38%; Table 1). Based on the diagnostic criteria for osteoporosis, there were 71 patients with osteoporosis (80% [male, n = 18; and female, n = 53]), 16 patients with osteopenia (18% [male, n = 6; and female, n = 10]), and two patients with normal bone mass (2% [male, n = 2; and female, n = 0]; Table 2).

Comparison of CT_{Mean} and Bone Mineral Density (BMD) between Male and Female Patients with Proximal Humeral Fractures

The lumbar and femoral neck BMD and the proximal humerus CT_{Mean} were compared between elderly men and women with proximal humeral fractures using a rank-sum test. Because a $T < 2.5$ is indicative of osteoporosis and $-2.5 < T < -1.0$ is indicative of osteopenia, the lumbar and femoral neck BMD was significantly better in elderly men than women (Table 3). More importantly, the proximal humerus CT_{Mean} in men was also significantly higher in elderly men than women, which was consistent with the BMD results, as determined by DXA measurements (Table 3). Similarly, when comparing these indices between men and women with osteoporosis, a lower BMD and proximal humerus CT_{Mean} were more common in women than men (Table 4).

Correlation of CT_{Mean} and Bone Mineral Density (BMD) in Patients with Proximal Humeral Fractures

Because the lumbar and femoral neck BMD and proximal humeral CT_{Mean} were higher in elderly males than females, the correlation between these two indices was further analyzed by scatter plots. A close relationship existed between the lumbar BMD and proximal humeral CT_{Mean} ($r_{male} = 0.877$, $P = 0.000$; $r_{female} = 0.806$, $P = 0.000$; Fig. 3), and between the femoral neck BMD and proximal humeral CT_{Mean} ($r_{male} = 0.832$, $P = 0.000$; $r_{female} = 0.616$, $P = 0.000$; Fig. 4) in males and females, suggesting that the lumbar spine and femoral neck BMD were closely related to the proximal humerus CT_{Mean} in patients with proximal humeral fractures.

Correlation of CT_{Mean} and Bone Mineral Density (BMD) in Patients with Osteoporosis

The correlation between the proximal humeral CT_{Mean} and lumbar and femoral neck BMD was also analyzed in patients with osteoporosis. Similarly, the scatter plots indicated a close relationship between the lumbar BMD and proximal humeral CT_{Mean} ($r_{male} = 0.745$, $P = 0.000$; $r_{female} = 0.613$, $P = 0.000$; Fig. 5), and between the femoral neck BMD and proximal

TABLE 3 Comparison of lumbar and femoral neck bone mineral density (BMD) with the proximal humerus CT_{Mean} between elderly males and females with proximal humeral fractures

	Patients	Lumbar BMD (T value)	Femoral neck BMD (T value)	Proximal humerus CT_{Mean}
Male	26	−2.33 ± 0.68	−2.31 ± 0.80	96.04 ± 8.39
Female	63	−2.69 ± 0.44	−2.64 ± 0.46	91.10 ± 7.91
Z	-	1.548	1.469	2.182
P	-	0.017	0.027	0.029

BMD, bone mineral density, CT_{Mean}, average computed tomography value; SD, standard deviation.

TABLE 4 Comparison of lumbar and femoral neck bone mineral density (BMD) with the proximal humerus CT_{Mean} between elderly males and females with osteoporosis

	Patients	Lumbar BMD (T value)	Femoral neck BMD (T value)	Proximal humerus CT_{Mean}
Male	18	−2.71 ± 0.10	−2.73 ± 0.16	91.39 ± 3.91
Female	53	−2.85 ± 0.22	−2.80 ± 0.21	89.74 ± 3.23
Z	-	1.464	1.456	1.587
P	-	0.028	0.029	0.020

BMD, bone mineral density, CT_{Mean}, average computed tomography value; SD, standard deviation.

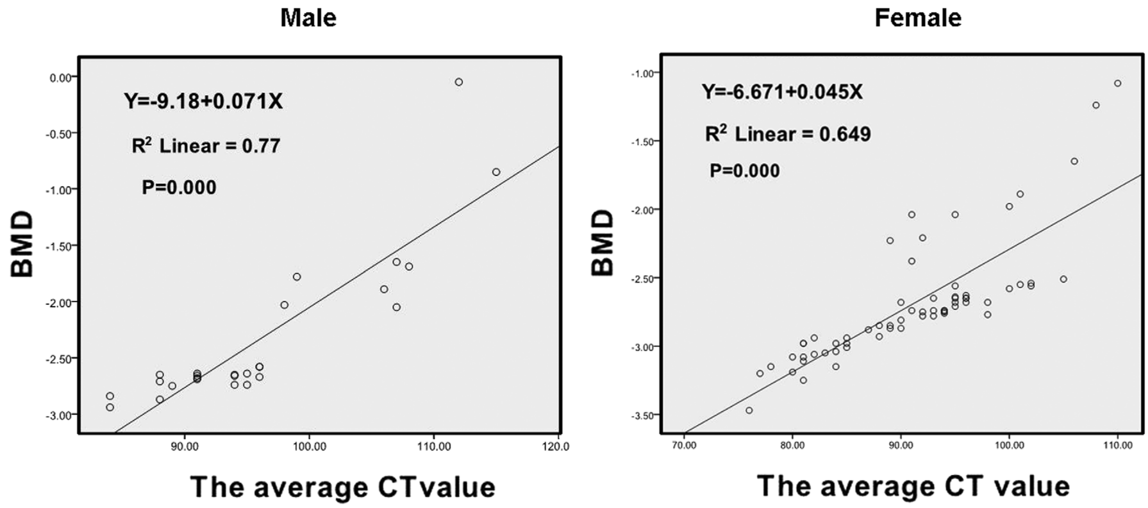

Fig 3 Scatter diagram showing a close correlation between lumbar vertebrae and proximal humeral average CT value. BMD, bone mineral density; CT, computed tomography.

humeral CT_{Mean} ($r_{male} = 0.575$, $P = 0.013$; $r_{female} = 0.629$, $P = 0.000$; Fig. 6) in males and females. These results further confirmed that the lumbar spine and femoral neck BMD was closely related to the proximal humerus CT_{Mean} in patients with osteoporosis, and measurement of proximal humeral CT values is an alternative method to assess bone quality in patients with proximal humeral fractures.

Discussion

Characteristics of Proximal Humeral Fractures in the Elderly Population

Proximal humeral fracture in the elderly population is a common osteoporotic fracture due to low-energy trauma, such as a fall on flat ground, and the incidence increases with age[24,25]. It has been predicted that the population with proximal humeral fractures would be more than twice the current level by 2030 owing to the trend in aging[1,26]. At present, >70% of proximal humeral fractures occur in patients >60 years of age, and proximal humeral fractures occur more frequently in women than men[13,27]. It has been shown that this gender difference may be attributed to severe osteoporosis caused by an early and rapid drop in estrogen levels in females[27,28]. In this retrospective study we also found a higher proportion of female patients with proximal humeral fractures than male patients (63 *vs* 26), as well as a higher incidence of osteoporosis in elderly females with proximal humeral fractures than elderly males (84% *vs* 69%). A common cause of proximal humeral fractures is an accidental injury, and the high random nature of the injury may also

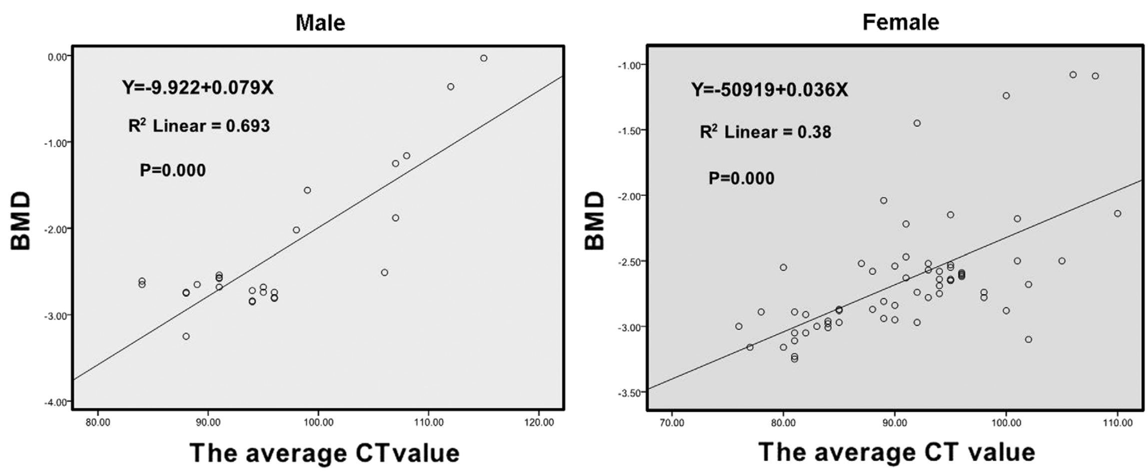

Fig 4 Scatter diagram showing a close correlation between femoral neck BMD and proximal humeral average CT value. BMD, bone mineral density; CT, computed tomography.

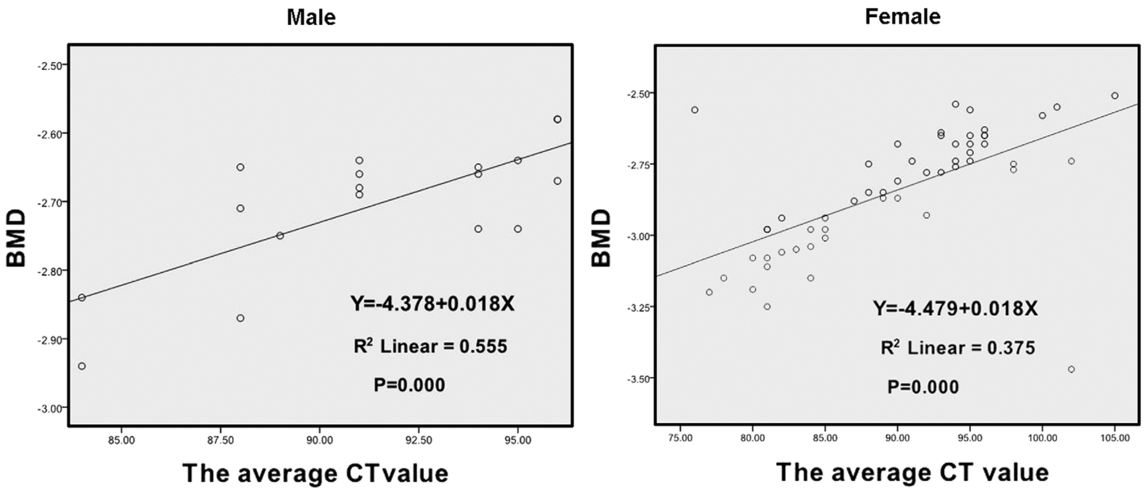

Fig 5 Scatter diagram showing a close correlation between lumbar BMD and proximal humeral average CT value in osteoporotic patients. BMD, bone mineral density; CT, computed tomography.

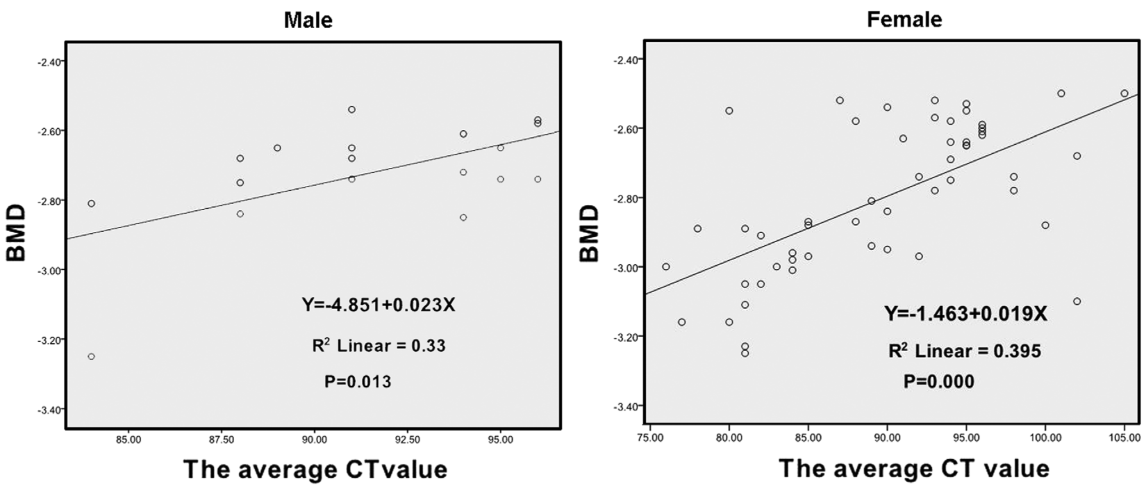

Fig 6 Scatter diagram showing a close correlation between femoral neck BMD and proximal humeral average CT value in osteoporotic patients. BMD, bone mineral density; CT, computed tomography.

result in a low ratio of male-to-female patients with proximal humeral fractures. In addition, the gender difference in BMD was shown among the osteoporosis, osteopenia, and normal bone mass groups, and female patients had more severe degrees of bone mass loss than male patients, which is consistent with the results reported in the literature[1,14,29]. Similarly, the proximal humerus CT_{Mean} was higher in males than females, indicating better bone quality in elderly males than females.

Correlation between Proximal Humeral CT_{Mean} and Bone Mineral Density (BMD)

Lumbar vertebral compression and hip fractures are the most common osteoporotic fractures in the elderly population[30,31]. Therefore, these two sites are currently of greatest clinical value for assessment of whole-body bone quality. Generally, DXA is the most widely used approach for BMD determination at lumbar and femoral neck sites because these two sites present a comprehensive representation of the whole-body bone quality[32]. In the clinic, DXA can predict fracture risk among patients with osteoporotic fractures and is considered to be the "gold standard" for the diagnosis of osteoporosis[11,33]; however, the bone quality at a particular site, such as the proximal humerus, cannot be accurately evaluated by DXA. Therefore, it is of clinical significance to find an objective alternative method to measure bone quality other than DXA.

CT value measurements have been widely used in the evaluation of spinal BMD[18,34,35], while measurements of the shoulder joint have rarely been reported. Pervaiz *et al.*[22]

performed shoulder CT scan and hip DXA examinations before total shoulder arthroplasty in 230 patients with senile shoulder joint osteoarthritis and showed a close relationship between the CT value and BMD ($P < 0.001$). In addition, because a higher fracture risk is related to a lower CT value in patients, they strengthened the clinical significance of CT values as a strategy. Similarly, this retrospective study evaluated the correlation between the proximal humeral CT_{Mean} with BMD in elderly patients with proximal humeral fractures. Generally, the cancellous bone of the humeral head in different layers of the proximal humerus is uniformly presented and the BMD of the layers chosen for CT value analysis theoretically had no significant differences. In this study, we analyzed the CT_{Mean} of uninjured proximal humeri in patients with proximal humeral fractures compared to the lumbar and femoral neck BMD, the latter of which are commonly measured for bone quality assessment in the clinical setting.

This study showed that both lumbar and femoral neck BMD had a positive correlation with proximal humeral CT value ($P = 0.000$ and $P = 0.000$, respectively). Moreover, this association existed in both males (n = 26) and females (n = 63). Specifically, in the patients with osteoporosis, including 18 males and 53 females, the lumbar spine and femoral neck BMD was positively related to the proximal humerus CT value ($P = 0.000$ and $P = 0.000$, respectively). All these results confirmed the close relationship between the lumbar and femoral neck BMD, and the proximal humeral CT_{Mean} ($P < 0.05$), suggesting that the proximal humeral CT value could be used to assess whole-body bone quality. These findings are also consistent with the study reported by Pervaiz *et al.*[22], which demonstrated a positive correlation between the CT value and BMD in patients with senile shoulder joint osteoarthritis. In addition, the Neer classification (the most commonly used fracture classification system) was applied for these 89 patients. Generally, among the patients with Neer I–IV fractures, the lumbar spine and femoral neck BMD was positively correlated to the proximal humerus CT value ($P = 0.000$ [data not shown]). It should be noted that during the software processing of CT value, this method has few artificial measuring errors, which could be used as an objective alternative method to improve the accuracy of bone quality assessment. In addition, hospitalization costs would be reduced because the CT value was obtained after the CT examination. Taken together, the important role of the preoperative CT value in the development of operation planning and in choosing suitable internal fixation materials was confirmed.

Limitations

There were some limitations in this study. First, the size of the proximal humerus may vary among individuals, which in turn may influence the ROI measurements of CT values. In addition, DXA measurements were obtained on the lumbar vertebrae and proximal femurs of patients, the BMD on these sites might be different from the proximal humerus. Further investigations with larger sample sizes are required to reinforce the current findings.

Conclusions

In conclusion, based on the post-processing function of spiral CT and digital software, we confirmed the close correlation between the proximal humeral average CT value with BMD, thus the proximal humeral average CT value could be used as an objective alternative method for DXA in the assessment of bone quality for patients with proximal humeral fractures.

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