Original Article

The vertebral Hounsfield units can quantitatively predict the risk of adjacent vertebral fractures after percutaneous kyphoplasty

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Background: Measuring the Hounsfield units (HU) of the vertebrae may yield diagnostic information for fracture risk. This study aimed to measure HU of vertebrae in percutaneous kyphoplasty (PKP) patients using computed tomography (CT) imaging to determine the HU measurements threshold for adjacent vertebral fracture and to assess the relationship between HU measurements and the risk of adjacent vertebral fracture.

Methods: A retrospective study was conducted on consecutive patients who underwent PKP between January 2019 and October 2021 in the China-Japan Union Hospital of Jilin University. The HU of the vertebra was measured on the reconstructed CT images by 2 independent spine surgeons. The HU measurements of adjacent vertebrae and the ratio of HU measurements between the surgical vertebra and adjacent vertebrae were statistically analyzed to determine the best critical value and evaluate the prediction effectiveness and accuracy of the best critical value.

Results: A total of 105 patients were identified with complete imaging and follow-up information. Of these, 47 patients (44.8%) had evidence of an adjacent vertebral fracture on follow-up imaging. The mean HU measurements of the fractured adjacent vertebra were significantly different from the mean HU measurements of the unfractured adjacent vertebra (50.94±20.59 *vs.* 81.74±18.97 HU; P<0.001). There was a significant difference in the ratio of HU measurements between the surgical vertebra and the fractured adjacent vertebra and between the surgical vertebra and the unfractured adjacent vertebra (26.34±17.52 *vs.* 14.53±9.40; P<0.001). Interactive scatter plots and receiver operating characteristic (ROC) curve showed that a HU measurement of 66.9 and a HU measurements ratio of 15.18 were the best thresholds for predicting the risk of fracture of adjacent vertebrae after PKP surgery, with an area under the curve (AUC) of 0.901 [95% confidence interval (CI): 0.822–0.953; P<0.001] and 0.874 (95% CI: 0.790–0.934; P<0.001), respectively. The prediction accuracy was 90.4% and 84.0%, respectively.

Conclusions: A low mean HU measurements of adjacent vertebrae or a high ratio of the mean HU measurements of the operated vertebrae to the adjacent vertebrae are risk factors for the vulnerability of adjacent vertebrae to fracture. The risk of fracture in the adjacent vertebrae after PKP can be predicted by measuring HU.

Keywords: Vertebral Hounsfield units; osteoporotic vertebral compression fractures (OVCF); percutaneous kyphoplasty (PKP); adjacent vertebrae fracture

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Introduction

Percutaneous kyphoplasty (PKP) was first proposed as a treatment option for osteoporotic vertebral compression fractures (OVCF) in 1994 by Garfin *et al.* (1). The method uses a puncture catheter to place an expandable balloon inside the compressed vertebrae, through which the lost height of the vertebrae is restored, followed by the injection of bone cement to fix the fractured vertebrae. The increased popularity of the PKP procedure has led to numerous studies examining short- and long-term clinical and radiographic results, which have generally been reported as excellent (2-4). However, there is an increased risk of fractures in adjacent vertebrae of the treated vertebra, which can lead to kyphosis and spinal cord injury. Various clinical and biomechanical studies have evaluated the effect of different cement injection volumes, materials, distribution patterns, bone mineral density (BMD), surgical puncture access, and combined surgical approaches on the occurrence of adjacent vertebral fractures (5-10). In addition, the increasing prevalence of osteoporosis and low BMD in patient populations poses unique clinical challenges for spine surgeons using PKP therapy. Measuring vertebrae in Hounsfield units (HU) has been considered an opportunistic alternative to traditional BMD measurement techniques (11-13). However, to our knowledge, no studies have evaluated the relationship between preoperative HU measurements of adjacent vertebrae and the occurrence of fractures in adjacent vertebrae in the near and distant postoperative period. We aimed to determine whether HU measurements of the preoperative adjacent vertebrae could be used to assess the risk of fracture of the adjacent vertebrae after PKP to minimize the risk of postoperative fracture of the adjacent vertebrae, and whether standardized measurements of HU of the adjacent vertebrae could be performed to determine a critical threshold for the risk of fracture of the adjacent vertebrae and to accurately assess the risk of postoperative fracture of the adjacent vertebrae in patients with PKP. We present the following article in accordance with the STARD reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-22-588/rc).

Methods

The imaging data of all cases with complete imaging data were collected and organized. First, the preoperative reconstructed computed tomography (CT) images were imported into the AW pioneer workstation (version 4.6, General Electric Company, Boston, MA, USA) to measure the HU of the adjacent vertebrae. Then, the postoperative reconstructed CT images of PKP were imported into the AW pioneer workstation to measure the HU of the operated vertebra and the ratio of HU between operated and fractured/unfractured adjacent vertebrae.

All CT image sets were reconstructed using advanced modeled iterative reconstruction (ADMIRE) with the same parameters (transverse 1.0 mm slice thickness with 1.0 reconstruction interval, reconstruction filter Br59). CT1, CT2, and CT3 represent the average HU measurements of the fractured adjacent vertebra, unfractured adjacent vertebra, and operated vertebra, respectively. The HU measurements of adjacent vertebrae (CT1 and CT2) and the ratio of HU measurements between the surgical vertebra and adjacent vertebrae (CT3/CT1 and CT3/CT2) were statistically analyzed using interactive scatter plots and using receiver operating characteristic (ROC) curve to determine the best critical value. We applied the best critical values to our study cohort to assess the predictive effectiveness and accuracy of the best critical values.

Study population and criteria

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was conducted with approval from the Ethics Committee of China-Japan Union Hospital of Jilin University. Written informed consent was provided by all participants. In order to ensure the integrity of patient data and adequate follow-up time, we retrospectively reviewed the data of consecutive patients aged 55 years or older with OVCF who had undergone PKP surgery at the same institution (Department of Spine Surgery, China-Japan Union Hospital of Jilin University) between January 2019 and October 2021. Patients were included in the study only if they had the following imaging data: magnetic resonance imaging (MRI) and CT within 1 month before their first PKP treatment, CT and X-ray in the immediate postoperative period, MRI and CT within 1 month after the fracture occurred in the adjacent vertebra, and X-ray in the immediate postoperative period after the fractured adjacent vertebra treated with PKP. The bone cement placement in all patients was polymethylmethacrylate (PMMA). The patients included in the study had a single vertebral fracture for the first OVCF and the adjacent vertebral fracture occurring after PKP, and there was no obvious history of trauma, excluding vertebral

fractures caused by primary or secondary tumorigenic lesions. We also recorded the demographic information and the use of antiosteoporosis medications of the participants. All patients included in this study had no serious adverse effects after PKP surgery. The diagnostic criteria for the first vertebral fracture occurring in each patient and the fracture occurring in the adjacent vertebrae after PKP were assessed and documented by MRI within 1 month after the vertebral fracture.

CT scans

CT scans of the spine were obtained from a General Electric 128-slices CT scanner (General Electric Company, USA) with the following parameters: scan tube voltage, 120 KV; scan tube current, 500 mA; and scan thickness, 1 mm. The scanning area was the operated vertebrae and 2 vertebrae above and below. Other acquisition parameters were: 1 s of rotation time, beam width of 192 detectors with 0.6 mm slice collimation, 512×512 matrix, and 200 mm field of view (FOV).

MRI scans

MRI scans of the spine were obtained from a Siemens Magnetic Aera 1.5T MRI scanner (Siemens, Berlin, Germany). The scanning parameters were as follows: scan thickness, 3.5 mm; FOV, 300 mm; layer spacing, 3.5×0.2 mm. Scanned data imaging included the following: (I) sagittal T1-weighted image time of repetition (TR): 400 ms, and time of echo (TE), 10 ms; (II) sagittal T2-weighted image TR: 3,000 ms, and TE: 100 ms; (III) sagittal T2-weighted lipid suppression image TR: 4,200 ms, and TE: 80 ms; and (IV) axial T2-weighted image TR: 3,600 ms, and TE: 100 ms.

CT image reconstructions

The 47 image sets were reconstructed using ADMIRE with the same parameters (transverse 1.0 mm slice thickness with 1.0 reconstruction interval, reconstruction filter Br59). Then, the 47 reconstructed images were sent and archived in the Picture Archiving and Communication System (PACS) of our institution (CARESTREAM RIS GC version 3.1, Carestream Health, Toronto, Canada).

Quantitative image analysis

HU of the operative vertebrae and adjacent vertebrae for each participant were measured independently and directly by 2 spine surgeons with 7 and 11 years of experience in spine CT imaging, respectively, on the reconstructed images. The 2 spine surgeons were unaware of the details of the participants and adjacent fractured vertebrae. CT images were displayed with the window level/width set to 450/1,500.

Data collection

First, we imported the reconstructed CT images stored in PACS to the AW pioneer workstation. In this workstation, all images showed bone windows, and the bone window position clearly showed the borders of cancellous and cortical bone. The specific measurement methods were as follows: (I) the center point was selected adjusting the cursor to the center point in the sagittal, coronal, and axial positions, respectively; and (II) the region of interest (ROI) was drawn first drawing a rectangular ROI in the transverse position, taking the diagonal intersection of the rectangular ROI as the center point, and then adjusting the rectangular ROI in the coronal position so that the ROI contains as much cancellous bone as possible in the vertebral body. The distance between the ROI and the cortical bone was least great than 0.3 cm to avoid covering the cortical bone and affecting the measurement value. Due to the physiological curvature of the spine, the vertebrae present a certain angle to the horizontal line, and the ROI of the workstation cannot be rotated so that the ROI is parallel to the upper and lower end plates of the vertebrae in the sagittal position, so the rectangular ROI was finally adjusted to the sagittal position. The new diagnostic criteria for vertebral compression fractures on MRI images are low signal on T1-weighted sequences, high or isosignal on T2-weighted sequences, and high signal on lipid-suppressed sequences.

Statistical analysis

The Shapiro-Wilk test was performed to analyze the difference in the D1 of CT1 and CT2 and the difference in the D2 of CT3/CT1 and CT3/CT2. Differences were compared using the paired sample *t*-test for data that conformed to a normal distribution and the Wilcoxon rank sum test to determine the significance of differences for data that did not conform to a normal distribution. Interactive dot plots and ROC were used to determine the critical value, and the closer the area under the curve (AUC) was to 1, the better the prediction accuracy of that critical

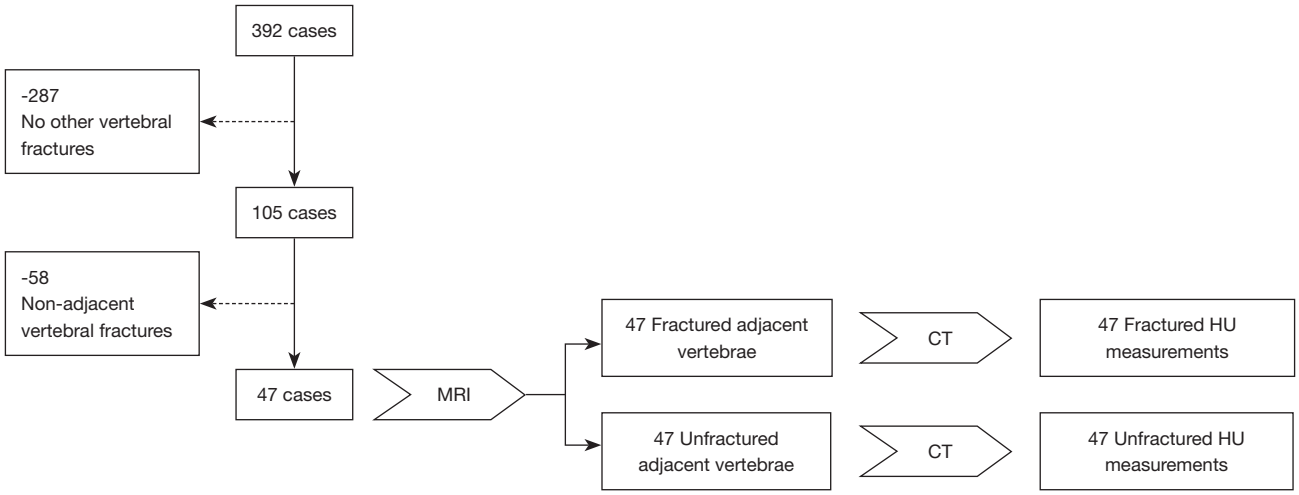

Figure 1 A flow chart showing participant enrollment and analysis. MRI, magnetic resonance imaging; CT, computed tomography; HU, Hounsfield units.

HU measurement. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and prediction accuracy of the corresponding critical HU measurements were also calculated. Statistical analyses were performed using SPSS 27.0 (IBM Corp., Armonk, NY, USA) and MedCalc 20.0 (MedCalc Software Ltd., Ostend, Belgium). A P value less than 0.05 was considered statistically significant. Continuous variables were expressed as mean ± standard deviation (SD).

Results

Among 392 patients, we excluded 287 patients with no other vertebrae fractured postoperatively, and then excluded 58 patients with nonadjacent vertebral fractures from the remaining patient cohort. Finally, we identified a total of 47 patients with complete imaging and follow-up data. Totals of 47 fractured adjacent vertebrae and 47 unfractured adjacent vertebrae were identified by MRI (*Figure 1*). The cohort consisted of 9 male patients and 38 female patients, with a minimum age of 55 years and a maximum age of 91 years (mean age, 74.21±9.74 years). All patients were followed up for a maximum of 24 months and a minimum of 6 months, with a mean follow-up time of 14.61±4.93 months. Antiosteoporotic drugs were used regularly in 25 patients postoperatively, and there was no significant difference in HU measurements of the adjacent vertebrae in the fractured adjacent vertebrae group taking antiosteoporotic drugs compared to those not taking antiosteoporotic drugs (51.12 *vs.* 50.74 HU; P=0.95). The segments of the operated vertebrae were predominantly in the thoracolumbar spine, T10 (n=5, 10.64%), T11 (n=8, 17.02%), T12 (n=11, 23.40%), L1 (n=13, 27.66%), L2 (n=6, 12.77%), L3 (n=3, 6.38%), and L4 (n=1, 2.13%). The postoperative interval between fractures in adjacent vertebrae was less than 3 months in 27 cases, with a mean interval of 1.59±0.10 months, and greater than 3 months in 20 cases, with a mean interval of 6.50±0.53 months (*Table 1*).

HU measurements and volumes of a total of 141 vertebrae with ROIs were obtained using quantitative assessment of CT imaging of the operated vertebrae and the adjacent vertebrae in 47 included patients (*Table 2*). The data distribution of the HU measurements of the adjacent vertebrae and the ratio of the HU measurements of the operated vertebrae to the adjacent vertebrae are represented as box plots (*Figure 2*). The difference of the D1 between CT1 and CT2 had a normal distribution (W =0.9741; P=0.38); therefore, a paired sample *t*-test was conducted for CT1 *vs.* CT2. This analysis showed that HU measurements of adjacent vertebrae with fractures were significantly smaller than those of adjacent vertebrae without fractures (50.94±20.59 *vs.* 81.74±18.97 HU; P<0.001). In addition, the proportion of adjacent vertebrae HU measurements less than the median 66.25 HU was significantly higher in the fractured adjacent vertebra group (89.4% *vs.* 10.6%; P<0.001). The difference of the D2 between CT3 and CT1 and between CT3 and CT2 did not conform to a normal distribution (W =0.6545; P<0.001); therefore, the Wilcoxon rank sum test was used to compare CT3 and CT1 *vs.* CT3 and CT2. The ratio of HU measurements of

Table 1 The demographic information, the HU measurements of adjacent vertebrae, and the ratio of HU measurements for 47 patients

Variables	Values
Sex, n	
Male	9
Female	38
Age (years)	
Minimum, n	55
Maximum, n	91
Average, mean ± SD	74.21±9.74
Follow-up time (months)	
Shortest, n	6
Longest, n	24
Average, mean ± SD	14.61±4.93
Use of antiosteoporosis drugs or not	
Yes (n=25), mean ± SD	51.12±3.20*
No (n=22), mean ± SD	50.74±5.38**
P value	0.95
HU	
CT1, mean ± SD	50.94±20.59
CT2, mean ± SD	81.74±18.97
P value	<0.001
HU measurements ratio	
CT3/CT1, mean ± SD	26.34±17.52
CT3/CT2, mean ± SD	14.53±9.40
P value	<0.001
The segments of the operated vertebrae, n (%)	
T10	5 (10.64)
T11	8 (17.02)
T12	11 (23.40)
L1	13 (27.66)
L2	6 (12.77)
L3	3 (6.38)
L4	1 (2.13)
Mean time to diagnosis of adjacent vertebral fractures (months)	
<3 months (n=27), mean ± SD	1.59±0.10
>3 months (n=20), mean ± SD	6.50±0.53
Position of the fractured adjacent vertebrae relative to the operated vertebrae (HU)	
Above (n=31), mean ± SD	44.02±17.84
Below (n=16), mean ± SD	64.37±19.28
P value	<0.001

*, HU measurements of fractured adjacent vertebrae in 25 patients who had used antiosteoporosis drugs; **, HU measurements of fractured adjacent vertebrae in 22 patients who had not used antiosteoporosis drugs. HU, Hounsfield units; SD, standard deviation.

Table 2 HU measurements and volume averages

Adjacent and surgical vertebral	CT1	CT2	CT3
Cases (n)	47	47	47
HU, mean ± SD	50.94±20.59	81.74±18.97	1,058.09±104.82
ROI (cm^3), mean ± SD	4.26±0.34	4.20±0.27	3.29±0.28

HU, Hounsfield units; SD, standard deviation; ROI, region of interest.

the operated spine to the adjacent spine with fracture was significantly different from the ratio of HU measurements of the operated spine to the adjacent spine without fracture (26.34±17.52 *vs.* 14.53±9.40; P<0.001). In addition, the ratio of HU measurements of the operated vertebra to the adjacent vertebra was significantly higher in the group of fractured adjacent vertebrae (85% *vs.* 15%; P<0.001) with a ratio of HU measurements greater than the median of 15.19.

Interactive scatter plot analysis of CT1 and CT2 yielded the critical HU measurements of 66.9 for the ideal fractured adjacent vertebra. A total of 43 of the 47 patients included had HU measurements ≤66.9 in the fractured adjacent vertebrae, with a sensitivity of 91.5%. A total of 5 patients had HU measurements ≤66.9 in the unfractured adjacent vertebrae, with a specificity of 89.4%, a PPV of 89.6%, and an NPV of 91.3%. The accuracy of the critical HU measurements for CT1 ≤66.9 in predicting the risk of adjacent vertebral fracture was 90.4% (*Table 3*). The ROC analysis showed the AUC was 0.901 with a 95% confidence interval (CI) of 0.822–0.953, indicating that this was a good predictor of the risk of adjacent vertebral fracture (*Figure 3*). Interactive scatter plots of CT3/CT1 and CT3/CT2

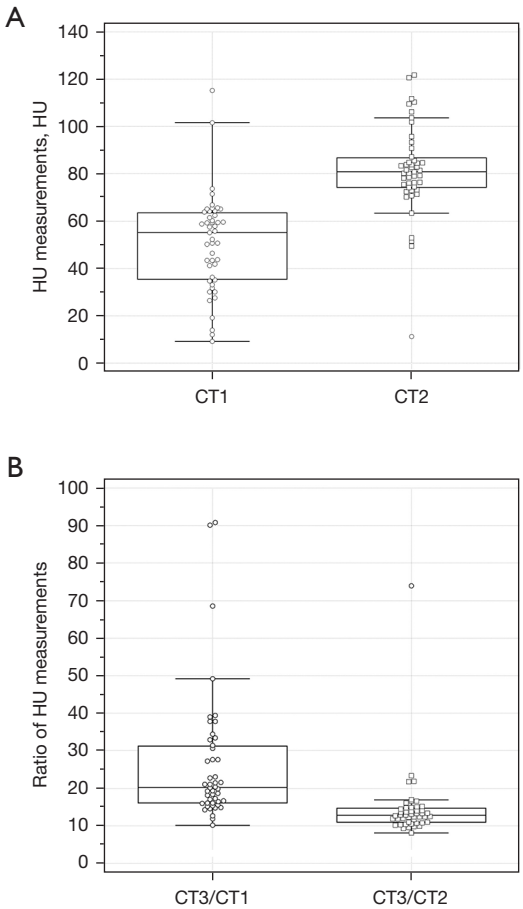

Figure 2 Box plots of HU measurements. The distribution of HU measurements of adjacent vertebrae with and without fracture (A) and HU measurements ratio distribution of operated vertebra to adjacent vertebrae (B). HU, Hounsfield units.

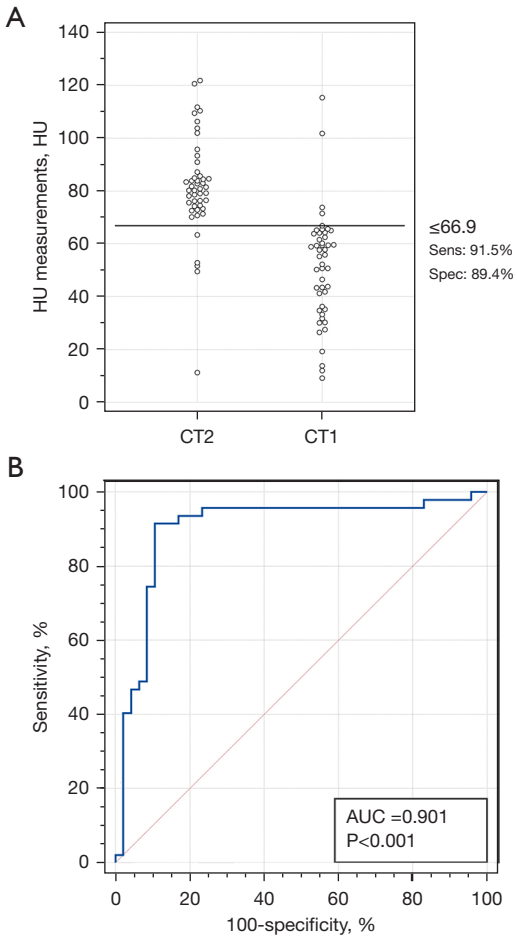

Figure 3 Interactive dot plots and ROC of the threshold values. A HU measurement of ≤66.9 HU in the adjacent vertebrae was used as the predictive threshold, with a sensitivity of 91.5%, specificity of 89.4%, and the AUC of its ROC of 0.901 (P<0.001). HU, Hounsfield units; AUC, area under the curve; ROC, receiver operating characteristic; Sens, sensitivity; Spec, specificity.

Table 3 Diagnostic efficacy of critical HU measurements

Quantitative assessment	CT1 ≤66.9	CT3/CT1 >15.18
True positive, n	43	40
False positive, n	5	8
True negative, n	42	39
False negative, n	4	7
Sensitivity (%)	91.5	85.1
Specificity (%)	89.4	83.0
PPV (%)	89.6	83.3
NPV (%)	91.3	84.8
Prediction accuracy (%)	90.4	84.0

HU, Hounsfield units; PPV, positive predictive value; NPV, negative predictive value.

yielded the ideal critical value of 15.18. Some 40 of the 47 patients included had a ratio of HU measurements for CT3/CT1 of >15.18, with a sensitivity of 85.1%, and 8 patients had a ratio of HU measurements for CT3/CT1 of >15.18, with a specificity of 83.0%, a PPV of 83.3%, and an NPV of 84.8%. The accuracy of the ratio of HU measurements of CT3/CT1 >15.18 in predicting the risk of adjacent vertebral fracture was 84.0% (*Table 3*). The ROC analysis showed that the AUC was 0.874 with a 95% CI of 0.790–0.934, indicating that this was also a good predictor of the risk of adjacent vertebral fracture (*Figure 4*). We cited 1 typical case from the included cases to illustrate the predictive efficacy of the HU measurement thresholds identified

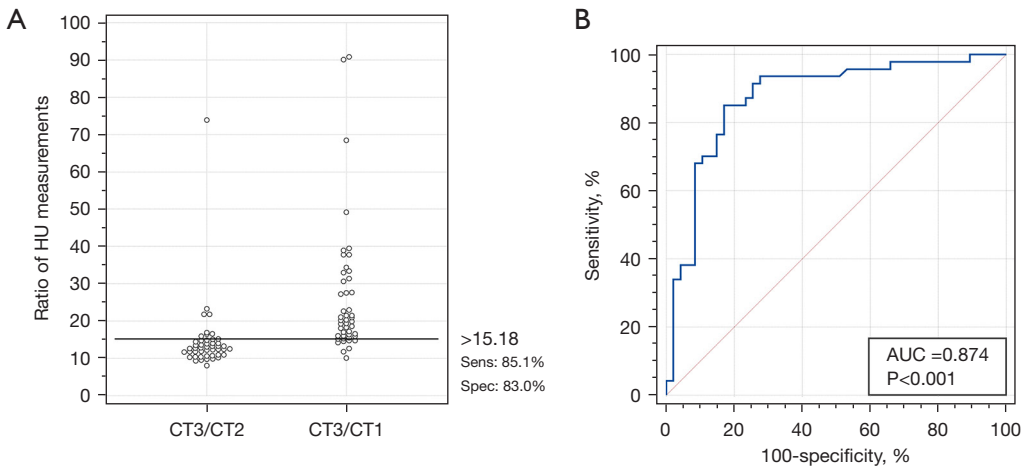

Figure 4 Interactive dot plots and ROC of the threshold values. The ratio of HU measurements between the operated vertebra and the adjacent vertebrae >15.18 was used as the predictive threshold, with a sensitivity of 85.1%, specificity of 83.0%, and the AUC of its ROC of 0.874 (P<0.001). HU, Hounsfield units; Sens, sensitivity; Spec, specificity; AUC, area under the curve; ROC, receiver operating characteristic.

in this study (*Figure 5*). *Figure 5* shows a 68-year-old female patient with an OVCF in L1 after treatment with PKP, and an OVCF in the upper adjacent vertebra T12 during the follow-up period. We measured the HU measurements of the upper and lower adjacent vertebrae on the preoperative CT images of her first OVCF (*Figure 5A*; T12: 33.2 HU; L2: 74.5 HU). We compared these with the critical HU measurements of 66.9 HU identified in our paper for fractured adjacent vertebrae. The results showed that the HU measurements of T12 could be less than the critical value (T12: 33.2 HU <66.9 HU), which suggested that the patient was at a higher risk of subsequent fracture of the adjacent vertebrae during the follow-up period. We then measured the HU measurements of the operated vertebra on the CT image of the first post-PKP (*Figure 5C*; L1: 1,044 HU). We calculated the HU measurements ratios of the operated vertebra L1 to the adjacent vertebrae T12 and L2 (L1/T12: 31.45; L1/L2: 14.01) and compared them with the critical HU measurements ratios of 15.18 determined in our paper. The results showed that the HU measurements ratio of L1/T12 was greater than the critical value (L1/T12: 31.45>15.18), which also suggested that the patient was at a higher risk of subsequent fracture of the adjacent vertebrae during the follow-up period.

Discussion

PKP, when applied to OVCF, is usually recommended for more severely compressed fractured vertebrae. In addition to providing rapid relief of painful symptoms caused by the fracture and fixation of the fractured vertebrae, the height restoration of the fractured vertebrae allows for the improvement of the patient's kyphotic deformity (14). However, vertebrae that have been strengthened with PKP have a very significant increase in vertebral strength and stiffness, which undoubtedly increases the risk of fracture of the adjacent vertebrae, potentially leading to continued fracture of the adjacent vertebrae (15). If a fracture occurs in the adjacent vertebrae, it may lead to the possibility of more severe kyphotic deformity or even spinal cord injury. We found a 12% incidence of adjacent vertebral fractures, which is generally consistent with data from previously published studies; Ding *et al.* obtained a 12.8% incidence of postoperative adjacent vertebral fractures from a meta-analysis of 8,047 patients (16). Multiple studies have validated the correlation between HU as measured on CT and dual-energy X-rays for assessing BMD to determine the degree of osteoporosis and the risk of fracture, as well as the efficacy of HU measurement for quantitative assessment of BMD (17-20). Hendrickson *et al.* (21) reported good accuracy and reproducibility of HU measurements of the vertebrae for identifying osteoporosis in the spine. In our study, reduced HU measurements of adjacent vertebrae were found to be a risk factor for fracture of adjacent vertebrae, with a significant difference in HU measurements between fractured and unfractured adjacent vertebrae (50.94±20.59

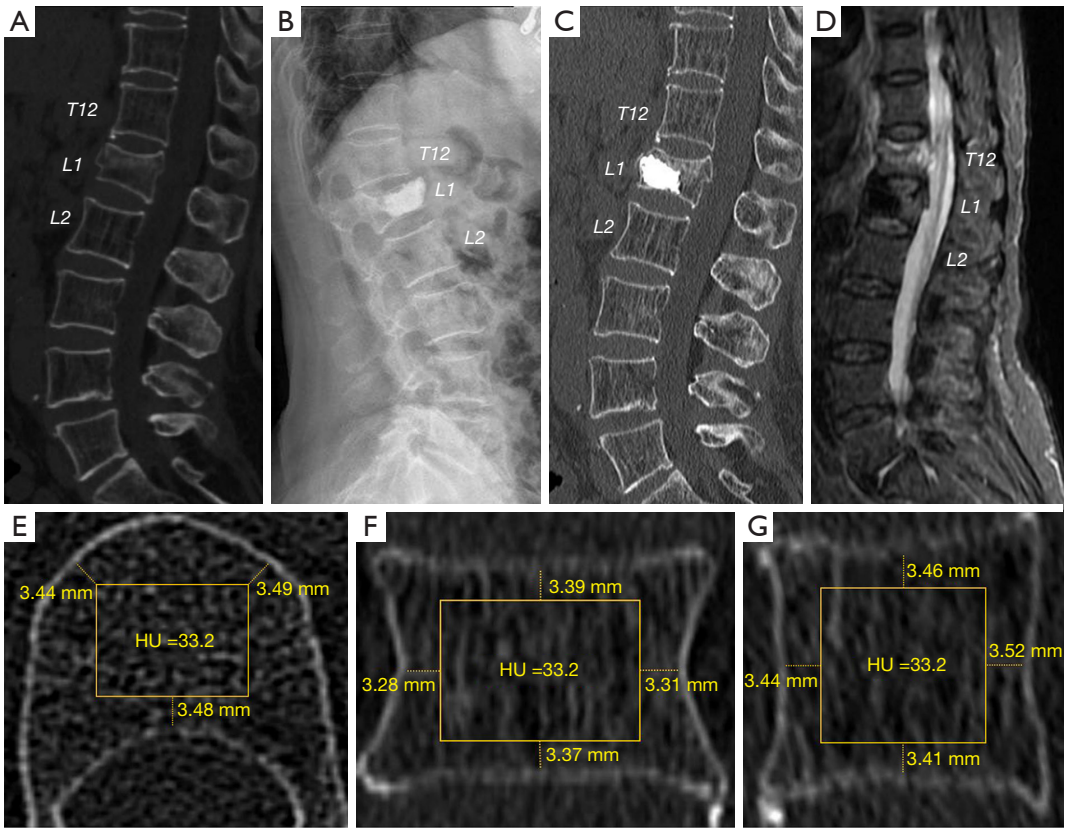

Figure 5 The ROI used for data analysis in a typical case. CT of the thoracolumbar spine of a 68-year-old female patient after OVCF in L1 (A), X-ray (B), and CT (C) of the thoracolumbar spine after PKP in L1, and MRI after the occurrence of OVCF in the adjacent vertebral T12 (D). (E-G) The 3 images show the process of ROI measurement in T12 of the adjacent vertebra. (A) The HU measurements of the adjacent vertebrae are T12: 33.2 HU and L2: 74.5 HU. (C) The HU measurement of the operated vertebra is L1: 1,044 HU. HU, Hounsfield units; ROI, region of interest; CT, computed tomography; OVCF, osteoporotic vertebral compression fractures; PKP, percutaneous kyphoplasty; MRI, magnetic resonance imaging.

vs. 81.74±18.97; P<0.001), which is consistent with some previous studies (22,23). In our study, we also found that an increased ratio of the operated vertebra to the adjacent vertebra was a risk factor for fracture of the adjacent vertebra, with a significant difference between the HU measurements ratio of the operated vertebra to the fractured adjacent vertebra and the unfractured adjacent vertebra (26.34±17.52 *vs.* 14.53±9.40; P<0.001). We have not found a study published with similar findings. Schreiber *et al.* (24) chose a 2-dimensional ROI to measure the HU measurements of the vertebrae by selecting 3 ROIs at the upper, middle, and lower levels of the vertebrae and calculating the arithmetic mean of the HU measurements of the 3 ROIs as the HU measurements of the vertebrae. A similar approach was used by Zaidi *et al.* (13), where the difference was in the selection of 5 levels of ROI of the vertebrae. Although 3 or 5 levels of ROI were selected and the arithmetic mean was calculated to reduce the error, there was still a large difference between this and the true HU measurements of the vertebrae. Since HU measurements refer to the attenuation of X-rays as they pass through the tissue, the HU measurements measured by 2-dimensional ROI represent the absorption of X-rays by cancellous bone at only 1 level within the vertebrae. Therefore, in our study, we added vertebral thickness as an important influencing factor and chose a 3-dimensional ROI to measure the vertebral HU. We believe that the ROI should include as much cancellous bone as possible in the vertebrae because only by including as much cancellous bone in the vertebrae as possible in the ROI can the true HU measurements of the vertebrae be more closely approximated. Furthermore, the assessment of HU after setting up a volumetric ROI is somewhat comparable to

quantitative CT, whereby the volumetric HU measurements can be converted to volumetric BMD (vBMD) using specific measurement software and a conversion formula after calibration equations. This is an advantage that is not available with 2-dimensional ROI measurements of HU (25).

As our results indicate, vertebrae with smaller HU measurements in adjacent vertebrae and vertebrae with larger HU measurement ratios between the operative and adjacent vertebrae were more likely to fracture. The calculated interactive dot plots and ROC of HU measurements in adjacent vertebrae yielded a critical value of 66.9 with a sensitivity of 91.5% for fracture occurring in adjacent vertebrae. In addition, we calculated a PPV of 89.6% for a critical value of 66.9 and an NPV of 91.3%, and the overall predictive accuracy was 90.4%. We also performed an interactive dot plot and ROC calculation of the HU measurements ratio of the operative vertebra to the adjacent vertebrae, yielding a critical HU measurements ratio of 15.18, a sensitivity of 85.1% for the occurrence of fracture in the adjacent vertebra, a PPV of 83.3%, and an NPV of 84.8%, with an overall predictive accuracy of 84.0%. This may be a useful predictive tool for the risk of subsequent adjacent vertebral fractures in PKP patients.

Ultimately, our results suggest that low HU measurements of the adjacent vertebrae and high HU measurements ratio of the operative vertebrae to the adjacent vertebrae may increase the risk of fracture of the adjacent vertebrae. We assume that a HU measurement of 66.9 for the adjacent vertebrae and a HU measurement ratio of 15.18 for the operated vertebrae to the adjacent vertebrae are the critical HU measurements for the risk of fracture of the adjacent vertebrae and that the risk of fracture of the adjacent vertebrae can be minimized by more aggressive antiosteoporosis treatment and protection with over-extension braces (26). In this study, 27 patients (57.4%) experienced adjacent vertebral fractures within less than 3 months after their operation, which was consistent with the previous research results (27). Improving BMD is a very important factor in reducing the risk of fracture, and past literature suggests that the time to meaningful improvement in BMD after initiation of antiosteoporosis medication is greater than the time to fracture in most adjacent vertebrae (28). Therefore, we need to develop a more comprehensive and individualized antiosteoporosis regimen for these patients. This includes regular, adequate, and full course of currently FDA-approved osteoporosis drugs (bisphosphonates: alendronate, ibandronate, risedronate, zoledronic acid; estrogen-related therapy: ET/HT, raloxifene conjugated estrogens/bazedoxifene; parathyroid hormone analogs: teriparatide, abaloparatide; RANK-ligand inhibitor: denosumab; sclerostin inhibitor: romosozumab; and calcitonin salmon); providing osteoporosis counseling; recommending adequate calcium intake; maintaining adequate levels of serum vitamin D; identifying and addressing modifiable risk factors associated with falls; providing guidance on smoking and alcohol cessation; and providing guidance on safe exercise strategies (29). We hypothesize that the degree of osteoporosis in the adjacent vertebrae leads to a decrease in HU measurements, which reduces the stiffness and strength of the vertebrae and becomes more fragile, thus predisposing them to fracture. In addition, the operative vertebrae strengthened by PKP become stronger, which dramatically affects the transmission of stress between the adjacent vertebrae, which can also contribute to the fracture of the adjacent vertebrae (30). The vertebral strengthening materials used in our included subcases were all PMMA; therefore, our findings are specific to the risk of adjacent vertebral fractures in patients using these types of vertebral strengthening materials. Furthermore, age was not a limiting factor in our study, as the mean age of our included cases was 74.21±9.74 years, which is consistent with the age profile of the population with a high prevalence of OVCF (31). The CT images we used were very common in clinical work, making it easier to obtain measurement data. As shown in *Table 2*, the prediction accuracy of the critical value of 66.9 HU was 90.4%, and the prediction accuracy of the critical ratio value of 15.18 was 84.0%. This does not mean that the critical ratio value of 15.18 is not important, but it provides us with another option when we encounter the HU measurements of the adjacent vertebra that are both greater than the critical value of 66.9 HU.

Our study was subject to multiple limitations, and clinical information and imaging data measurements were limited by the accuracy of the recordings. There must be a difference between the HU measurements responding to CT in the preoperative period and the vertebral HU measurements when the fracture occurs in the adjacent vertebrae. This is because there is a time span between the fracture in the subsequent adjacent vertebrae and the first PKP surgery, during which the degree of osteoporosis in the vertebrae gradually increases, even though antiosteoporosis drugs were applied. However, in our study, patients who applied antiosteoporosis drugs and those who did not use antiosteoporosis drugs in the fracture adjacent vertebrae group did not differ significantly (51.12 *vs.* 50.74 HU;

P=0.95). In addition, we could not predict the time of fracture of the adjacent vertebrae, so we could not obtain the HU measurements of the moment before the fracture of the adjacent vertebrae. Furthermore, some important limitations affected the extension of the results of this study, such as the generalizability of using the same CT system in different hospitals and the potential use of contrast medium in patients. Imaging data we used to measure were obtained after the case had developed OVCF and lacked the vertebral height of the case prior to the development of OVCF, so the amount of vertebral compression after the vertebrae has developed OVCF is also an important influencing factor for the subsequent development of adjacent vertebral fractures. The final cutoff HU measurements we determined were obtained from the analysis of a total of 141 vertebral HU measurements in 47 patients. Further increases in the number of included cases and longer follow-up studies are needed to obtain more accurate HU measurements. Despite these limitations, our study still provides a reliable predictive tool for the risk of fracture occurring in the adjacent vertebrae after surgery in PKP patients.

Conclusions

In conclusion, we found a significant association between HU measurements of the adjacent vertebrae and the occurrence of adjacent vertebrae fractures after PKP surgery, likewise the HU measurements ratio of the operated vertebrae compared to the adjacent vertebrae and the occurrence of adjacent vertebrae fractures after PKP surgery. Our findings suggest that the risk of fracture in the adjacent vertebrae after PKP can be predicted by using HU measurements.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-588/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was conducted with approval from the Ethics Committee of the China-Japan Union Hospital of Jilin University. Written informed consent was provided by all participants.

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