

# Hounsfield units-based grading of osteoporosis (HUGO) and its association with risk of osteoporotic vertebral compression fractures

## A multicenter study of over 1000 patients

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### Abstract

**Background:** There is a lack of a rapid and convenient quantitative method for assessing the severity of osteoporosis. Thus this study explored the association between Hounsfield unit (HU)-based grading of osteoporosis and the risk of suffering from different levels of osteoporotic vertebral compression fractures (OVCF).

**Materials and methods:** A total of 1463 patients aged  $\geq 60$  years undergoing percutaneous kyphoplasty for OVCF in 4 spine centers were reviewed. We recorded general information including age, gender, height, weight, and the vertebral level of acute and chronic OVCF. The HU value of L1 (L1-HU) was measured with preoperative computed tomography scans. The number of fractured vertebral levels was classified into 3 categories: single level, two level, and multilevel ( $\geq 3$ ). The general risk factors of multilevel OVCF were analyzed.

**Results:** A total of 2358 levels of OVCF were recorded, including 1867 acute OVCF and 491 chronic OVCF. T12 and L1 were the 2 most common fractured vertebral levels. The average L1-HU value was  $71.7 \pm 31.8$  HU. It was significantly different among 3 groups ( $p < 0.05$ ):  $78.8 \pm 30.4$  HU (95% confidence interval [CI]: 76.9–80.8) for single-level group,  $65.0 \pm 31.2$  HU (95% CI: 61.6–68.5) for two-level group, and  $49.6 \pm 25.7$  (95% CI: 46.0–53.1) for multilevel group. The L1-HU of each group showed no significant difference among the 4 spine centers ( $p > 0.05$ ). The numbers of multiples of ten within the 95% CI of average L1-HU values were chosen as cutoffs: cutoff of 80 HU representing the risk of at least single-level OVCF, and the cutoff of 50 HU representing the risk of multilevel OVCF. L1-HU  $< 50$  HU was the independent risk factor of multilevel OVCF, its odds ratio was 4.4 (95% CI: 3.2–6.0,  $p < 0.001$ ).

**Conclusions:** The HUGO method can be used to classify the severity of osteoporosis. Especially patients with L1-HU of  $< 50$  have extremely severe osteoporosis with risk of multilevel OVCF.

**Keywords:** Hounsfield units, osteoporosis, osteoporotic vertebral compression fracture

## 1. Introduction

Hounsfield unit (HU) of vertebral trabecular bone measured with computed tomography (CT) scans has been widely used to evaluate bone mineral density (BMD), identify osteoporosis (OP), and evaluate the risk of OP-related complications following spinal surgery.<sup>[1–3]</sup> The method of CT HU can make full use of preexisting CT

scans performed for other clinical indications. Especially for patients with spinal diseases, the spinal CT scans are usually required for diagnosis or preoperative planning. We can easily measure HU values by reviewing these CT images at no extra cost. The HU value of L1 (L1-HU) is the mostly used standard parameter, because the vertebral level of L1 is included in many types of CT scans, such

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as lumbar CT, thoracic CT, and lung CT.<sup>[4,5]</sup> Additionally, there is sufficient evidence to prove the satisfying efficiency of using L1-HU to screen OP, and 110 HU is the recommended cutoff value.<sup>[1,3,6,7]</sup> However, the diagnosis of OP is not enough for guiding spine surgeons to establish personalized prevention or treatment strategies,<sup>[8,9]</sup> there is a need of developing a quantitative method to judge the severity of OP, particularly based on the simple method of CT HU.

Fragility fractures caused by low-energy injury are the hallmarks of OP, which has become a global public health threat.<sup>[10]</sup> Osteoporotic vertebral compression fracture (OVCF) is the most common type of fragility fractures occurring in human spine.<sup>[11]</sup> It can be asymptomatic and incidentally detected by radiological examinations, but can also cause back pain, spinal kyphosis, and even disability.<sup>[12,13]</sup> The degree of bone loss is associated with the risk of OVCF, and the patients with multilevel OVCF are usually considered to have severe OP.<sup>[14,15]</sup> Therefore, it should be reasonable to establish HU-based grading of OP (HUGO) according to the number of fractured vertebrae.

This study hypothesized that L1-HU was lower in the patients with increasing number of fractured vertebrae. The L1-HU was measured with preoperative thoracic-lumbar CT scans of 1463 patients undergoing percutaneous kyphoplasty (PKP).

## 2. Methods

### 2.1. Patients cohort

This study was approved by the institutional review board of our hospital (IRB 00006761). The informed consent was waived because this was a retrospective study. The inpatients undergoing PKP for acute OVCF from January 2021 to December 2023 in the 4 spine centers of our medical alliance were reviewed. The 4 spine centers were numbered from 1 to 4 (Table 1). Inclusion criteria were (1) patients aged 60 years and older; (2) those who underwent PKP for acute thoracic or lumbar OVCF; (3) no history of trauma or history of only low-energy trauma before the occurrence of acute OVCF. The exclusion criteria were (1) lack of preoperative spine CT scans for measuring HU value; (2) other types of fragility vertebral compression fractures, such as vertebral metastatic carcinoma; (3) existence of bone cement or metal implants at target vertebral levels, which may interfere with HU measurement. We recorded all the acute OVCF identified by clinical

manifestation and radiologic characteristics. Meanwhile, if the patients also had chronic OVCF identified by the patients' medical history and radiologic features, the vertebral levels of chronic OVCF were also recorded.

### 2.2. Measurements of L1-HU

L1 was chosen as the standard vertebral level for HU measurements. In case of patients with anomalies of vertebral number (such as 11 or 13 thoracic vertebrae), L1 was identified as the first nonrib-bearing vertebra.

The L1-HU value of vertebral trabecular bone in axial CT images was measured with preoperative 3-dimensional reconstructive spine CT (the tube voltage of all of the CT scans was 120 kV). The oval region-of-interest was placed in the middle-axial CT plane excluding cortical bone and heterogeneous areas.<sup>[5,15-17]</sup> If there was an OVCF at L1, the HU values of adjacent levels (T12 and L2) were used as the alternatives for L1-HU. A typical case of OVCF patient is shown in Figure 1.

### 2.3. Statistical analysis

The statistical analysis in this study was conducted using SPSS version 24 (SPSS, USA). Analysis of variance was used to compare the L1-HU among patients having different levels of OVCF, and the L-HU among different spine centers. Chi-squared test was used for comparing the gender ratio between multilevel OVCF group and control group. The independent samples Student *t* test was used for comparing continuous variables between multilevel OVCF group and control group. Receiver operating characteristic curve analysis and the area under the curve were used to evaluate the performance of using L1-HU to distinguish patients with multilevel OVCF from control patients. *p* < 0.05 was considered to indicate a statistically significant difference.

## 3. Results

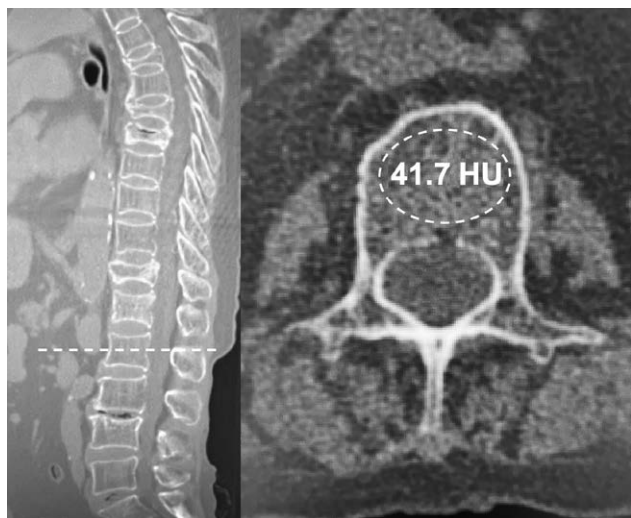
This study included 1463 patients in the final analysis. There were 1135 females and 328 males, and their average age was  $73.5 \pm 8.0$  years (60–97 years). A total of 2358 levels of OVCF were recorded, including 1867 acute OVCF and 491 chronic OVCF. The distribution of these OVCF among different vertebral levels was illustrated in Figure 2. T12 and L1 were the 2 most common fractured vertebral levels, accounting for about 46% (1079/2358) of the whole OVCF.

**Table 1**

**Comparison of L1-HU among the 4 spine centers.**

		Center serial number ( <i>n</i> = 1463)				<i>p</i> value
		No. 1 ( <i>n</i> = 563)	No. 2 ( <i>n</i> = 308)	No. 3 ( <i>n</i> = 296)	No. 4 ( <i>n</i> = 296)	
L1-HU (average ± SD and 95% CI)	Overall	70.4 ± 30.8 (67.8–72.9)	74.3 ± 33.2 (70.6–78.0)	71.4 ± 31.2 (67.8 ± 74.9)	72.1 ± 32.7 (68.3–75.8)	0.38
	Single-level group	78.7 ± 27.2 (75.8–81.6)	81.2 ± 32.5 (76.7–85.8)	81.5 ± 30.7 (76.6–86.3)	75.3 ± 32.6 (71.1–79.4)	0.13
	Two-level group	62.4 ± 30.0 (57.0–67.7)	71.7 ± 32.0 (63.5–80.0)	66.2 ± 29.6 (59.4–73.0)	61.9 ± 29.7 (52.0–71.8)	0.24
	Multilevel group	46.7 ± 28.1 (40.2–53.2)	48.5 ± 23.5 (41.7–55.3)	53.1 ± 23.6 (47.3–59.0)	51.3 ± 28.3 (37.7–65.0)	0.50

CI = confidence interval, HU = Hounsfield unit, L1-HU = HU value of L1, SD = standard deviation.



**Figure 1.** An example of multilevel OVCF: a female patient aged 70 years suffered from acute OVCF of T8, T12, and L1 (detected by MRI). She also has chronic OVCF at T5 and T7. The HU value of L2 is used to represent L1-HU because both L1 and T12 are fractured (such situation has been explained in the Methods section). The HU value is lower than 50 HU. HU = Hounsfield unit, MRI = magnetic resonance imaging, OVCF = osteoporotic vertebral compression fractures.

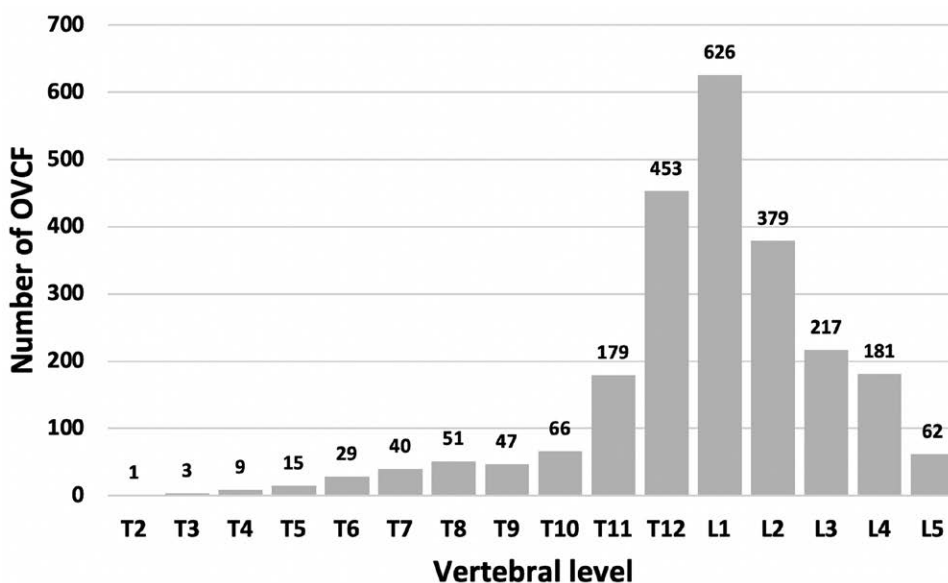
The average L1-HU value was  $71.7 \pm 31.8$  HU. It was  $78.8 \pm 30.4$  HU (95% CI: 76.9–80.8) for single-level OVCF,  $65.0 \pm 31.2$  HU (95% CI: 61.6–68.5) for two-level OVCF, and  $49.6 \pm 25.7$  (95% CI: 46.0–53.1) for multilevel ( $\geq 3$ ) OVCF. It shows a significant difference among these 3 groups ( $p < 0.01$ ). The average L1-HU showed no significant difference among the 4 spine centers (Table 1). Moreover, there is no significant difference between the L1-HU of patients with fracture at L1 and those without fracture at L1 ( $70.6 \pm 32.9$  vs.  $72.6 \pm 30.9$ ,  $p = 0.22$ ). The number of multiples of ten within the 95% CI of average L1-HU value was chosen as

cutoff value. The cutoff of 80 HU is chosen to represent the patients with severe OP who is at risk of at least single level of OVCF, and the cutoff of 50 HU is chosen to represent the patients with extremely severe OP who are at risk of multilevel OVCF. In summary, the cutoffs of 80 and 50 HU are used to grade the severity of OP.

To further identify the relationship between HU and multilevel OVCF, the 1463 patients were divided into 2 groups: multilevel OVCF group and the control group of  $< 3$  levels of OVCF. First, we performed receiver operating characteristic curve analysis, and the area under the curve was 0.74 (95% CI: 0.71–0.78,  $p < 0.001$ ) for using L1-HU to predict multilevel OVCF. The comparison of general information of these 2 groups was summarized in Table 2. The gender ratio, height, weight, BMI, and L1-HU showed significant differences between the 2 groups. Being female, height, weight, and L1-HU  $< 50$  HU were chosen as the possible influencing factors in the logistic regression, only L1-HU  $< 50$  HU was the independent risk factor of multilevel OVCF, its odds ratio was 4.4 (95% CI: 3.2–6.0,  $p < 0.001$ ).

#### 4. Discussion

In recent years, the CT HU value of vertebral trabecular bone has been widely used in bone density assessment of spine. There is sufficient evidence to prove that HU value is effective in OP screening and predicting postoperative OP-related complications. The method of CT HU has the most advantage in patients requiring spine surgery, such as PKP for OVCF, because spine CT is usually performed preoperatively. The CT scans can be conveniently used to measure HU value at no extra cost. The literature reviews recommend to use the cutoff of 110 HU at L1 vertebral level to identify OP, but there is a lack of research on methods of evaluating the severity of OP based on CT HU. Patients with different severities of OP should have different risk



**Figure 2.** The distribution of these OVCF among different vertebral levels. OVCF = osteoporotic vertebral compression fractures.

**Table 2****The comparison of general information between multilevel OVCF group and control group.**

	Multilevel group	Control group	<i>p</i> value
Age	74.0 ± 7.7	73.4 ± 8.0	0.334
Female:male	172/35 (83.1%)	963/293 (76.7%)	0.04
Height	159.3 ± 6.9	160.8 ± 7.2	0.006
Weight	58.6 ± 9.8	61.3 ± 10.2	<0.001
BMI	23.1 ± 3.6	23.7 ± 3.4	0.026
L1-HU	49.6 ± 25.7	75.4 ± 31.2	<0.001

BMI = body mass index, HU = Hounsfield unit, L1-HU = HU value of L1, OVCF = osteoporotic vertebral compression fracture.

degrees of OP-related complications. OVCF is the most common pathological result of spinal OP, and multilevel OVCF is more hazardous because of the higher risk of spinal kyphosis and even spinal imbalance. According to the results of this study, the cutoff of 80 HU represents severe OP with risk of at least single level of OVCF, and the cutoff of 50 HU represents extremely severe OP with risk of ≥3 levels of OVCF. This HUGO method may help spine surgeons to offer specific treatment strategies according to the severity of OP in the future.

OP is often called the “silent disease” because the osteoporotic patients are always unaware of their impaired bone quality until they suffer a broken bone from low-energy injury. In other words, the osteoporotic bone is characterized by high risk of fragility fractures, and patients with multilevel OVCF usually have lower BMD. This is the reason why this study uses the risk of suffering from different levels of OVCF to identify the patients with different severities of OP. *In vitro* research suggests that HU value of vertebral body is positively correlated with vertebral body compression strength.<sup>[18]</sup> In clinical studies, low vertebral BMD measured by different CT-based techniques has been proved to be the independent risk factor of OVCF.<sup>[13,19]</sup> A retrospective cohort study of 1966 older adults reveals that the L1-HU measured by chest or abdominal CT has modest effect on fracture-free survival after adjusting for other influencing factors.<sup>[20]</sup> The research of Fang et al.<sup>[21]</sup> shows that the HU value of thoracic-lumbar spine in abdominal and pelvic CT can identify women at higher risk of osteoporotic fractures. In addition, lower L1-HU of <50 HU can also predict refracture of thoracic-lumbar vertebrae after the treatment for OVCF.<sup>[11,22]</sup>

As mentioned above, CT HU value is effective in evaluating the risk of developing OVCF or even secondary OVCF. Nevertheless, there are few studies focusing on the correlation between BMD and the number of fractured thoracic-lumbar vertebral levels. Shen et al.<sup>[14]</sup> found that lower BMD measured by dual energy X-ray absorptiometry (DXA) is associated with more vertebral levels of OVCF, the BMD was 0.51 g/cm<sup>2</sup> for multilevel and 0.68 g/cm<sup>2</sup> for single level. Zou et al.<sup>[15]</sup> found that the L1-HU value decreased as the number of fractured vertebral levels increased, and the average L1-HU is especially lower than 50 HU in patients with multilevel OVCF. However, the effects of age and sex were not adjusted in these 2 studies. Wang et al.<sup>[23]</sup> found that only females aged 70 to 80 years old with multilevel OVCF showed lower baseline BMD than that of patients with a

lower number of OVCF. The possible reason is that they measured BMD with DXA instead of CT HU, and the DXA results are available in only 387 patients. In our work, the results show that the effect of lower L1-HU on suffering multilevel OVCF is independent of age, sex, and BMI, and the L1-HU alone has moderate predictive value on multilevel OVCF. Further, the average L1-HU of patients with the same number of OVCF (single level, two level, or multilevel) was comparable among different spine centers, suggesting that L1-HU has potential in multicenter application. Based on the 95% CI of L1-HU of patients with different numbers of OVCF, we chose a cutoff of 80 HU to identify patients with at least single-level OVCF, and 50 HU for multilevel OVCF. These 2 cutoffs can be used to assess the severity of spinal OP, which is the HUGO method.

In conclusion, the L1-HU is effective in representing the risk of multilevel OVCF. The 2 cutoffs of 80 and 50 HU of HUGO are used to identify patients with different severities of OP characterized by suffering different numbers of OVCF.

This study has several limitations. First, this is a retrospective cross-sectional study, and it included both acute and chronic OVCF. Although the existence of different levels of chronic OVCF can also reflect the degree of OP, it is better to conduct a prospective cohort study focusing on the association between HU value and the occurrence of acute OVCF. Second, L1 is a common vertebral level of OVCF, and it is inappropriate for HU measurements when OVCF occurs at L1. Therefore, we used the HU values of adjacent levels (T12 and L2) as the alternatives for L1-HU. In this research, the alternatives showed no significant difference to the L1-HU (70.6 ± 32.9 *vs.* 72.6 ± 30.9, *p* = 0.22). Third, we did not include all of the influencing factors because of the inaccessibility of concerning data. There are still some other factors, which may affecting the risk of multilevel OVCF, such as the history of spinal kyphosis or degeneration of paravertebral muscles.

### Acknowledgments

None.

### Ethical statement

This study was approved by the institutional review board of our hospital (IRB 00006761). The informed consent was waived because this was a retrospective study.

## Conflicts of interest

The authors have no conflicts of interest to disclose.

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## Data availability statement

The research data supporting this study are available from the corresponding author upon reasonable request.

## Abbreviations:

BMD = bone mineral density, CI = confidence interval, CT = computed tomography, HU = Hounsfield units, HUGO = HU-based grading of osteoporosis, L1-HU = HU value of L1, OP = osteoporosis, OVCF = osteoporotic vertebral compression fractures, PKP = percutaneous kyphoplasty.

## Author contributions

Writing original draft, Conceptualization, Methodology, Project administration, Supervision, Review & editing: Weishi Li.

Writing original draft, Conceptualization, Methodology, Project administration, Formal analysis, Review & editing: Da Zou.

Investigation, Resources: Lidi Liu, Hong Wang, Shuncheng Jiao.

Software, Validation, Resources: Yuefeng Sun, Jiazhen Duan.

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