



## OPEN CT-based hounsfield unit as an alternative osteoporosis assessment in ankylosing spondylitis patients with bamboo spine

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This retrospective study compared bone mineral density (BMD) measurements assessed by unenhanced computed tomography (CT)-based HU at L1 vertebrae to those by plain spine radiographs in ankylosing spondylitis (AS) patients with or without bamboo spine (BS). We also assessed whether BS affects dual-energy X-ray absorptiometry (DXA)-based osteoporosis diagnosis using unenhanced CT scans at the L1 vertebrae. All patients underwent DXA, unenhanced CT scans, and plain spine radiographs. The cohort of 524 AS patients was classified into BS ( $n = 189$ ) and non-BS ( $n = 335$ ) groups (Hu threshold for osteoporosis, 135). The BS group had significantly higher spine ( $P < 0.001$ ) and hip ( $P < 0.001$ ) T-scores and significantly lower L1 HU values ( $P < 0.001$ ) than the non-BS group. Among non-BS patients, lowest T-scores correlated positively with L1 HU values (R-value, 0.437;  $P < 0.001$ ); in BS patients a weak but significant correlation was observed between L1 HU values and hip T-scores (R-value, 0.341;  $P < 0.001$ ). Using the Hu threshold, 77.8% of BS and 55.2% of non-BS patients were reclassified as osteoporotic despite DXA indicating no osteoporosis. Whether CT-based HU improves the accuracy of BMD evaluation in the AS population requires confirmation in larger cohort studies.

**Keywords** Ankylosing spondylitis, Bamboo spine, Computed tomography, Dual-energy x-ray absorptiometry, Hounsfield units, Osteoporosis, DXA t-score, Ligamentous calcification, Plain spine radiographs, Bone mineral density, Axial spondyloarthritis

### Abbreviations

AP	Anteroposterior
AS	Ankylosing spondylitis
BMD	Bone mineral density
BS	Bamboo spine
CT	Computed tomography
DXA	Dual-energy X-ray absorptiometry
HU	Hounsfield units
ROI	Region of interest
SD	Standard deviation
WHO	World Health Organization

Ankylosing spondylitis (AS), alternatively known as radiographic axial spondyloarthritis, is a persistent inflammatory condition that predominantly affects the axial skeleton<sup>1</sup>. A key feature of AS is calcification of the entheses of the tendons and ligaments due to prolonged inflammation. The majority of patients with AS

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experience bone loss, the most common comorbidity in these patients<sup>2–4</sup>. Bamboo spine (BS) is a potential complication of AS. This inflammatory condition can lead to fusion of the bones of the spine, forming one long bone<sup>4</sup>. Research has shown that AS patients have a higher incidence of vertebral fractures, attendant neurological compromise, and spinal surgery-related complications than does the general population<sup>5–7</sup>. Therefore, accurately identifying AS patients at risk for fracture is crucial.

Osteoporosis is currently diagnosed using dual-energy X-ray absorptiometry (DXA), which evaluates bone mineral density (BMD). DXA of the total hip and the spine in anteroposterior (AP) projections is commonly used for BMD determination<sup>8</sup>. In patients with advanced AS involving ligamentous calcification, DXA of the spine in AP or lateral projections may be inaccurate<sup>9–12</sup>. In such cases, DXA may underestimate BMD due to masking by soft-tissue calcification and bony fusion of the facet joints in the spine. To address this issue, the European League Against Rheumatism recommends that AS patients with BS undergo DXA scan of the hip joint to assess osteoporosis<sup>13</sup>.

Several studies have reported promising results using computed tomography (CT)-based Hounsfield unit (HU) values to diagnose osteoporosis<sup>14–18</sup>. Using CT-based HU values at the L1 level together with corresponding DXA T-scores is an alternative method for diagnosing osteoporosis in the general population<sup>14,16,19</sup>. A threshold of 135 HU at the L1 vertebral body may clinically indicate osteoporosis, as reported by Ahern et al.<sup>20</sup> and Anderson and colleagues<sup>21</sup>.

Clinical studies have yet to confirm whether CT-based HU values can be used to evaluate BMD in AS patients and whether this measurement correlates with DXA T-scores in this population. To address these questions, this retrospective study aims to compare the BMD measured by unenhanced CT-based HU at the L1 vertebral body to that using plain spine radiographs in AS patients with or without BS. The secondary outcome is to determine whether the presence of BS affects DXA-based osteoporosis diagnosis as re-evaluated at a threshold of 135 HU.

## Methods

### Study population and demographic data

This study was approved by the Institutional Review Board of Taipei Veterans General Hospital (No. 2023-08-010BC), and informed consent was waived by the Institutional Review Board of Taipei Veterans General Hospital due to the retrospective nature of the analysis. This study was performed in accordance with the Declaration of Helsinki. Analysis included all AS patients treated at our institution between 2003 and 2022 who met the Modified New York Classification criteria for AS, were aged 20 years or above, and underwent both non-enhanced lung, abdominal or lumbar CT examination for any indication (which included the L1 vertebral body in all recruited) and DXA, with a maximum period of 6 months between the two examinations to ensure comparability. All participants were Asian. The medical records of the 811 patients were carefully reviewed, and 287 were excluded due to bone metastasis or tumor ( $n=64$ ), spine instrumentation ( $n=67$ ), infection ( $n=79$ ), trauma ( $n=47$ ), or incomplete medical records ( $n=30$ ). The final study cohort included 524 patients (Fig. 1). Demographic and clinical information including age, sex, body mass index, and medical history, including diabetes and underlying medications, were collected from medical records.

Whether BS was present in these patients was determined using plain spine lateral radiographs analyzed by one orthopedic spine surgeon (3 years of clinical practice) and confirmed by formal radiologic reports (Fig. 2). The 524 enrolled AS patients were categorized into BS ( $n=189$ ) and non-BS ( $n=335$ ) groups. The demographic and clinical characteristics of the two groups were similar (Table 1).

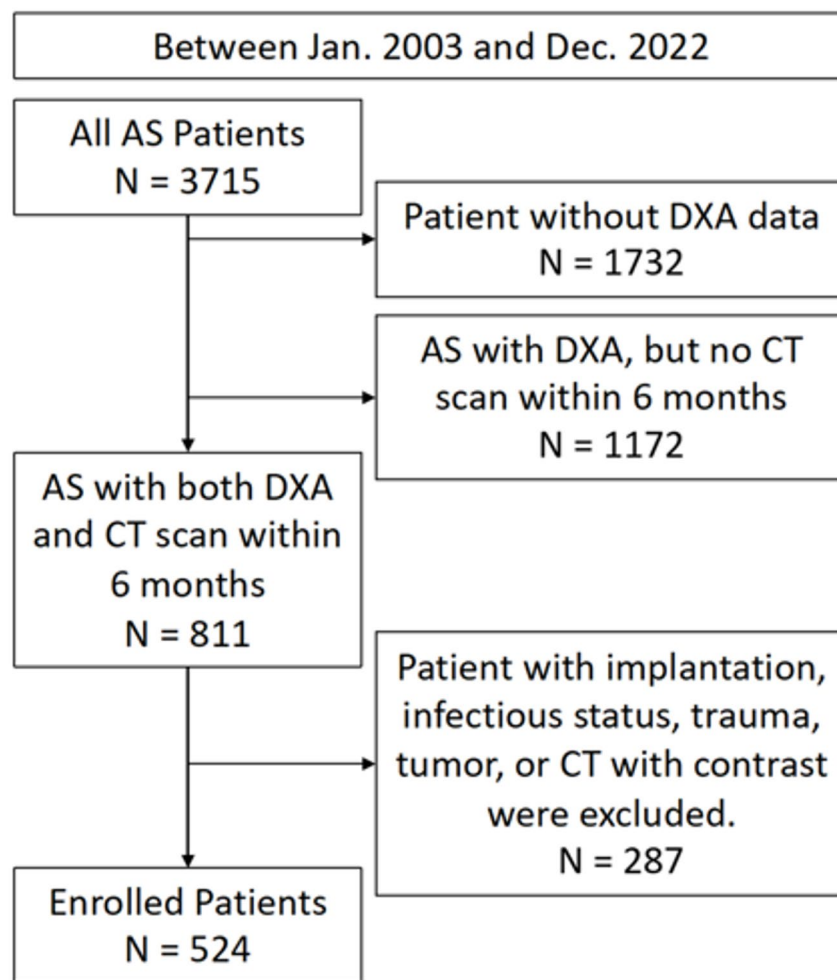
### Dual-energy X-ray absorptiometry (DXA)

Hologic Discovery W DXA (Hologic, Inc., Marlborough, MA, USA) was used to evaluate BMD in the hip or in AP projections of the lumbar spine (vertebrae L1 to L4) according to the European guideline for the diagnosis and management of osteoporosis<sup>22</sup>. For patients who underwent both AP spine and hip DXA scans within 6 months of the CT scan, we compared the lowest T-scores at either the hip or spine. According to World Health Organization (WHO) guidelines, osteoporosis is indicated by a DXA T-score  $\leq -2.5$ , while osteopenia corresponds to a DXA T-score  $\leq -1.0$  and  $> -2.5$ . A DXA T-score  $> -1.0$  is deemed normal<sup>8</sup>.

### Computed tomography and Hounsfield unit (HU) measurements

All CT scans were performed using either a Canon Aquilion Prime SP (Canon Medical Systems, Japan) or a Siemens SOMATOM Definition Flash (Siemens Healthcare, Germany), depending on scanner availability. The scanned regions included the abdomen and lumbar spine. All examinations were performed without the use of intravenous contrast agents.

Standard acquisition parameters included a Tube voltage of 120 kVp with automatic tube current modulation (typically 100–300 mAs), detector collimation of 0.5–0.625 mm, and pitch ranging from 0.8 to 1.2 based on anatomical region and scanner type. For abdominal CT scans, axial images were reconstructed with a slice thickness of 5 mm and an increment of 5 mm, using a soft tissue reconstruction kernel. For lumbar spine CT scans, axial images were reconstructed with a slice thickness of 3 mm and an increment of 3 mm, using both soft tissue and bone kernels, as appropriate. Scans were acquired in the supine position, during breath-hold for abdominal imaging and during free breathing for lumbar spine imaging. On axial images of non-contrast CT scans, the region of interest (ROI) was defined as the trabecular bone within the vertebral body at L1 level, excluding posterior elements (Fig. 3). The largest possible elliptical ROI was drawn in the vertebral body at the L1 level, excluding the cortical margins, lateral walls, endplates, and obvious syndesmophytes to avoid measurement bias. The Hu was measured 3 times and averaged to give a mean Hu to reduce observer bias. All measurements for the 524 patients were conducted by the same orthopedic spine surgeon. We used a threshold of 135 HU at the L1 vertebrae to diagnose osteoporosis, based on Ahern et al.<sup>20</sup> and Anderson et al.<sup>21</sup>



**Fig. 1.** Flowchart of our enrolled population. AS, ankylosing spondylitis; DXA Dual-energy X-ray Absorptiometry; CT, computed tomography.

### Statistical analysis

Demographic variables, medication histories, DXA-based T-scores, and CT-based HU values are presented as counts (percentage) or the mean  $\pm$  standard deviation (SD). The independent t-test was used to compare continuous variables, and the chi-squared test was used to compare categorical variables. Simple linear regression analysis was used to determine the correlation between HU values and DXA T-scores. The significance of Pearson correlation coefficient (R-value) was determined using the t-test, with  $p < 0.05$  considered statistically significant. The correlation strength was interpreted based on R-values, classified as follows: 0–0.19, very weak; 0.2–0.39, weak; 0.40–0.59, moderate; 0.6–0.79, strong; and 0.8–1, very strong<sup>23</sup>. Statistical computations were conducted using SPSS for Windows version 25.0 (IBM Corp., Armonk, NY, USA).

### Results

The DXA-based T-scores and CT-based L1 HU values were compared between the two groups (Table 1). The mean lowest T-scores were significantly higher in the BS group than in the non-BS group ( $-0.59 \pm 2.65$  vs.  $-1.42 \pm 1.38$ ;  $p < 0.001$ ). The mean spine T-score was significantly higher in the BS group than in the non-BS group ( $1.27 \pm 3.03$  vs.  $-0.86 \pm 1.44$ ;  $p < 0.001$ ). The mean CT-based L1 HU values were significantly lower in the BS group than in the non-BS group ( $41.4 \pm 47.53$  vs.  $111.83 \pm 56.34$ ;  $p < 0.001$ ).

The distribution of CT-based L1 HU values across study groups is shown in Fig. 4. The CT-based HU values at the L1 level were significantly lower in the BS group than in the non-BS group ( $p < 0.001$ ). Additionally, patients with osteoporosis in both groups had lower CT-based HU values, which aligns with clinical observations. Using the CT-based HU cut-off value of  $< 135$ <sup>20</sup> identified an additional 147 (77.8%) patients in the BS group and 185 (55.2%) patients in the non-BS group as having osteoporosis, as compared to using the DXA-based classification (Table 2).

The relationship between DXA T-scores and HU values was examined using linear regression analysis (Fig. 5). All scatterplots show a positive association. Subgroup analysis in non-BS patients revealed a significant moderate correlation between the lowest DXA T-scores and HU values at the L1 level (R, 0.437;  $p < 0.001$ ). In the BS group, no significant correlation was found between the lowest DXA T-scores and HU values at the L1 level



**Fig. 2.** Radiographic appearance of bamboo spine (BS) and non-bamboo spine (non-BS) on lateral plain spine radiographs. (a, left) The white arrow indicates characteristic features of BS, with fusion of both the anterior and posterior longitudinal ligaments; (b, right) No radiographic evidence of BS is observed (non-BS).

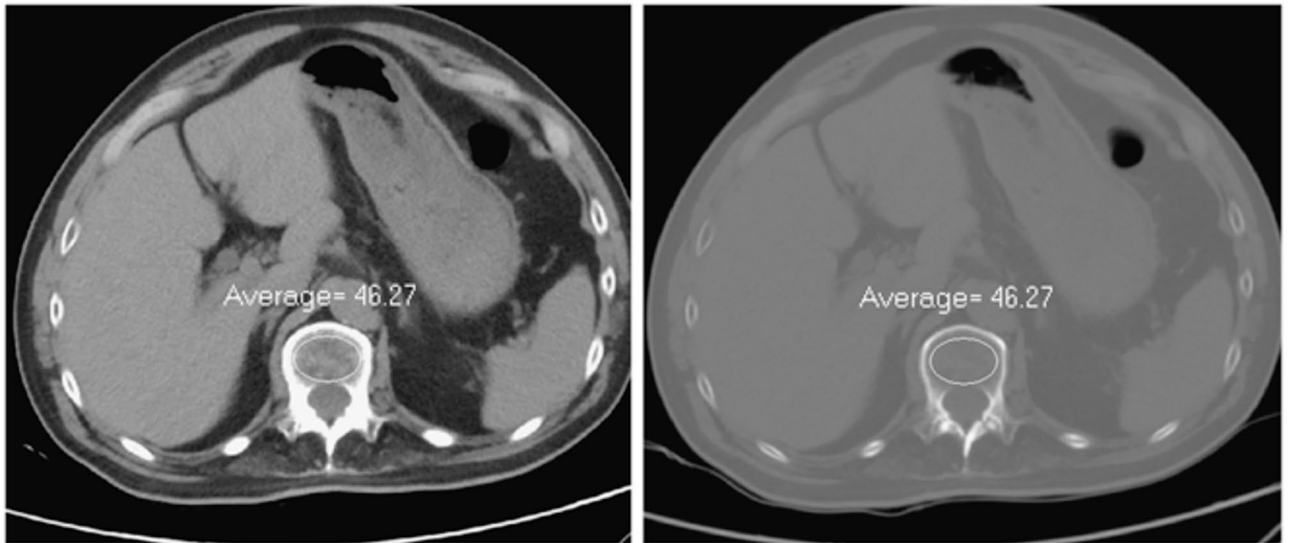
Variables	Non-bamboo spine (non-BS)	Bamboo spine (BS)	<i>p</i>
Cases, N	335	189	
Mean age (years)	63.16 ± 12.50	66.97 ± 14.89	0.107
Sex, N (%)			
Men	91 (27.2%)	36 (19.0%)	
Women	244 (72.8%)	153 (81.0%)	
BMI (kg/m <sup>2</sup> )	22.92 ± 4.23	26.16 ± 5.15	0.341
Smoking, ever	26 (7.8%)	28 (14.8%)	0.158
DM history	85 (25.4%)	64 (33.9%)	0.159
Lowest DXA <i>T</i> -score	-1.42 ± 1.38	-0.59 ± 2.65	<0.001
DXA Spine <i>T</i> -score	-0.86 ± 1.44	1.27 ± 3.03	<0.001
DXA Hip <i>T</i> -score	-2.03 ± 0.95	-1.27 ± 1.86	0.013
CT-based HU at L1	111.83 ± 56.34	41.40 ± 47.53	<0.001
History of medication use			
Glucocorticoids <sup>†</sup>	97 (29.0%)	60 (31.7%)	0.679
Anti-osteoporotic agents	23 (6.9%)	17 (9.0%)	0.248

**Table 1.** Demographic data of study participants with ankylosing spondylitis. BMI, body mass index; DM, diabetes mellitus; DXA, dual-energy X-ray absorptiometry; CT, computed tomography; HU, Hounsfield unit score. <sup>†</sup>History of glucocorticoid use equivalent to ≥ 5 mg of prednisolone daily for more than 3 months.

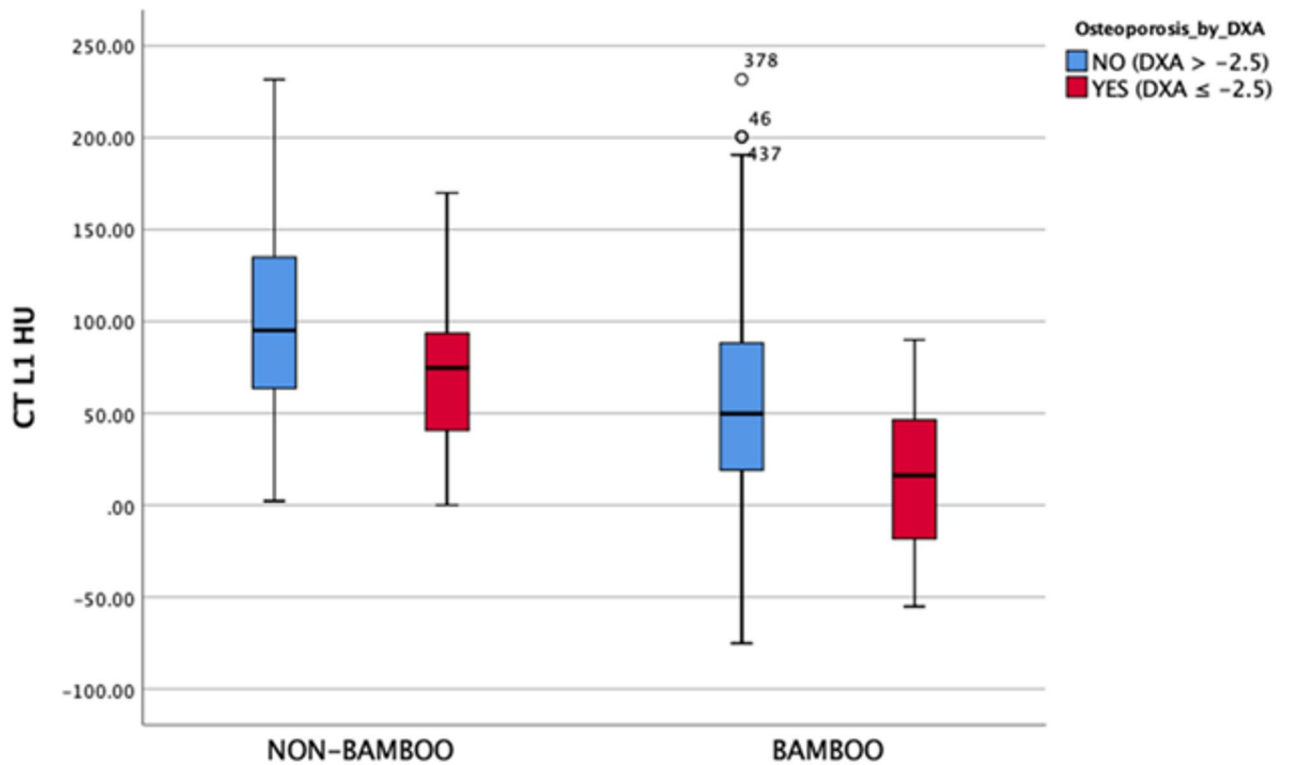
(*R*, 0.160; *p* = 0.129). A weak but significant correlation was observed between DXA *T*-scores at the hip and HU values at the L1 level in the BS group (*R*, 0.341; *p* < 0.001), but no significant correlation was seen between DXA *T*-scores at the spine and HU values at the L1 level.

## Discussion

This study is the first to report a poor correlation between the DXA-based *T*-score at the hip or lowest value at hip or spine and CT-based HU at the L1 level in AS patients, especially those with BS. Accordingly, DXA alone may not reflect the true BMD in those with advanced stage AS; CT-based HU at the L1 level may assist in the evaluation of BMD in the AS population. The underestimation of BMD by DXA might be caused by masking



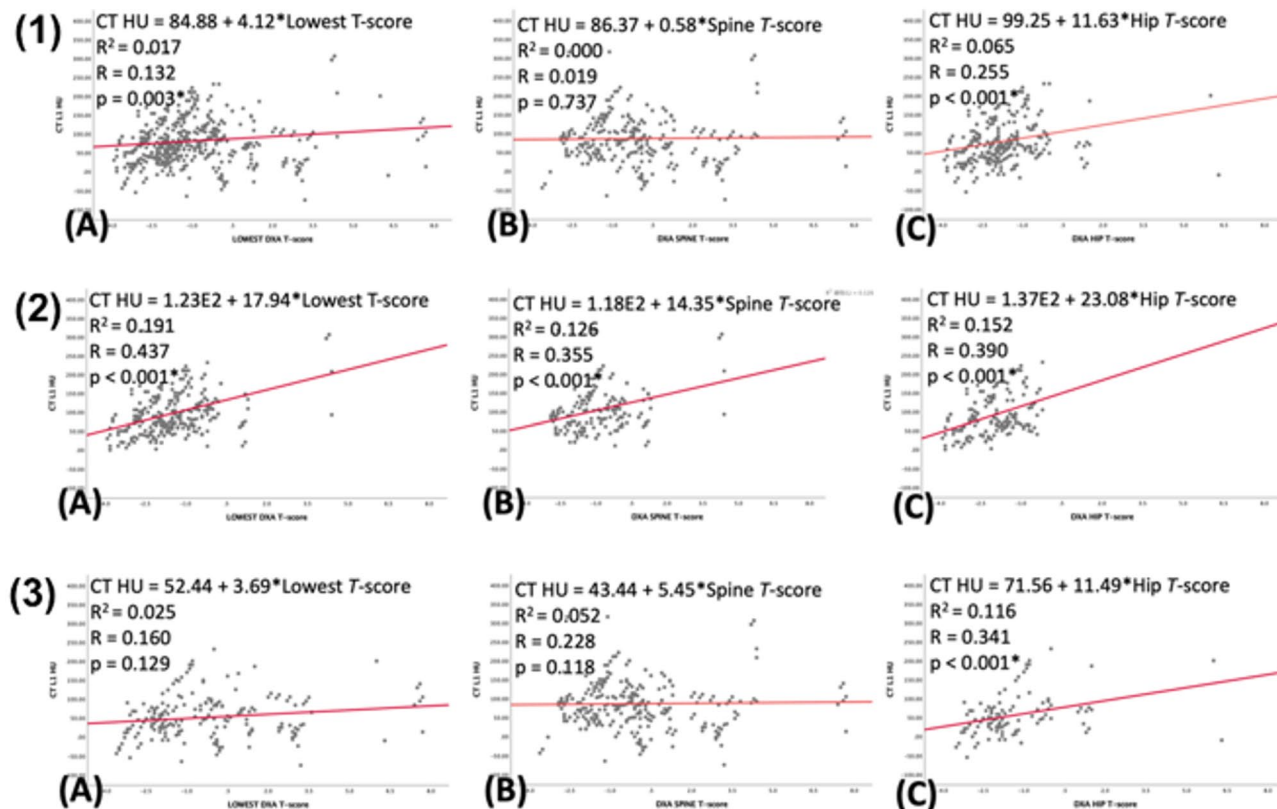
**Fig. 3.** Illustration of region of interest (ROI) for Hounsfield Unit measurement at the L1 vertebrae level in the unenhanced abdominal computed tomography scan. ROI = circle.



**Fig. 4.** Decrease in Hounsfield Unit (HU) value at the L1 vertebrae in those with osteoporosis, as determined by Dual-energy X-ray Absorptiometry (DXA) T-score at the hip. Blue bars, non-osteoporosis subgroup (T score > -2.5 on DXA); red bars, osteoporosis subgroup (T score ≤ -2.5 on DXA) in patients with and without bamboo spine (BS).

Diagnosis of osteoporosis	By DXA	By hounsfield units (HU)
BS ( <i>n</i> = 189)	24 (12.7%)	171 (90.5%)
Non-BS ( <i>n</i> = 335)	76 (22.7%)	261 (77.9%)

**Table 2.** Diagnosis of osteoporosis by DXA and CT scan between BS and non-BS groups. DXA, dual-energy X-ray absorptiometry; CT, computed tomography; BS, bamboo spine. DXA-based osteoporosis was defined as T-score  $\leq -2.5$ . CT-based osteoporosis was defined as HU  $< 135$  as adopted by Ahern et al.<sup>20</sup> and Anderson et al.<sup>21</sup>.



**Fig. 5.** Scatter plots illustrating positive correlations between Hounsfield Unit (HU) values and Dual-energy X-ray Absorptiometry (DXA) T-scores in different groups. (1) All ankylosing spondylitis (AS) patients; (2) AS patients without bamboo spine (BS); (3) AS patients with BS. (A) Lowest T-score; (B) spine T-Score; (C) hip T-score.

from calcification of the soft tissue and bony fusion of the facet joints in the AS spine. Our results may provide valuable information for spine surgeons treating AS patients with chance fracture or correcting ankylosing spine deformations.

The reported prevalence of osteoporosis in AS varies widely, ranging from 18.7–62%<sup>24</sup>. Explanations for the high prevalence of osteoporosis in the AS population include systemic inflammation and decreased mobility<sup>25</sup>. Because low BMD increases fracture risk, it is important for primary care physicians to accurately diagnose osteoporosis in AS patients to allow for patient counseling and education to reduce the risk of fracture. The use of a more accurate diagnostic tool will therefore improve patient care by allowing clinicians to better identify individuals within this population who are at increased risk. While we do not recommend using the CT-based HU value instead of the DXA-based T score for screening or assessing BMD in AS patients, we believe that HU values may provide valuable additional information for AS patients who undergo CT scans for other reasons.

Schreiber et al. observed a significant correlation between CT-based HU and BMD, suggesting clinical applications for CT-based HU to assess fracture risk, diagnose osteoporosis, and promote early initiation of needed treatment<sup>17</sup>. Several clinical investigations have used CT-based HU values to predict cage subsidence or screw loosening in lumbar fusion surgery<sup>26,27</sup>. CT-based HU is less affected by lumbar degeneration than DXA, as it avoids cortical bone and degenerative changes and also indicates the local surrounding bone quality at the index level<sup>28</sup>. However, the optimal cut-off value at the L1 level for diagnosing osteoporosis is still unclear. The current CT-based Hu threshold for diagnosing osteoporosis ranges from 78.5<sup>17</sup> to 135<sup>20</sup> and

is a major limitation in our clinical investigation. Study results may vary depending on the HU threshold used to diagnose osteoporosis. Applying the 135 HU threshold<sup>20</sup> to an Asian cohort may result in over-diagnosis of osteoporosis. Determination of the optimal HU cut-off for osteoporosis screening in this population requires further investigation through larger prospective cohort studies.

We found that CT-based HU at the L1 level (< 135) led to the re-classification of 157 AS patients with BS as having osteoporosis as compared to the original classification based on the DXA-based T-score (< -2.5). This result suggests that DXA examination alone may underestimate the incidence of osteoporosis in the AS population. Artifacts related to the presence of syndesmophytes or other structural lesions such as an ankylosed posterior arch or a periosteal bone formation may increase the DXA-based BMD value<sup>25</sup>. In other words, the use of DXA alone to diagnose osteoporosis in advanced AS patients may not reflect the actual BMD. The use of CT-based HU in addition to DXA may improve BMD evaluation after prospective datasets are used to determine a cut-off value to re-define osteoporosis in the AS population.

For patients with severe AS who have received a CT examination for other indications, the use of CT HU may help evaluate their BMD without additional radiation exposure or the extra burden of time and cost for other DXA bone density examinations. Several studies also have reported a high incidence of osteopenic and normal DXA T-scores among AS patients with vertebral fractures<sup>18,29</sup>. This result echoes those we observed for CT-based HU, proving that CT-based HU more accurately reflects the true BMD than does DXA in AS patients. Our findings align with previous studies reporting that CT attenuation might serve as a more precise clinical indicator of fragility fractures<sup>30</sup>. These findings highlight the limitations of DXA, especially in patient with AS. In contrast, CT HU measurements are unaffected by spinal ligamentous calcification, a characteristic of AS, indicating that CT HU may provide a more accurate measure of bone quality in these patients. Although the most effective way to implement CT screening in AS patients remains to be determined, CT HU could potentially be incorporated into clinical practice as an opportunistic screening method, depending on the specific clinical objectives. These pivotal results highlight the usefulness of HU values in the advanced AS population and suggest that it may serve as a complementary tool for evaluating BMD.

Substantial evidence indicates that the false-negative rate for DXA of the spine in AP projections is higher among AS patients; therefore, follow-up studies are recommended to evaluate alternative assessment sites, such as lateral projections of the spine, femoral neck, or total hip<sup>12,31</sup>. However, these methods may still be affected by ligamentous calcification in those with advanced disease. Recent studies suggest that the trabecular bone score (TBS) is superior to DXA in detecting osteoporosis<sup>32,33</sup>. TBS is a textural parameter that measures variations in pixel gray-levels in DXA images of the lumbar spine<sup>34</sup>. However, TBS assessment is not widely available in clinical practice, and syndesmophytes may falsely increase the TBS<sup>35</sup>. Another tool for diagnosing BMD is quantitative computed tomography (QCT). However, QCT-derived T-scores do not align directly with DXA T-scores, thereby restricting the practical usefulness of this method<sup>16,36</sup>.

Although previous clinical investigations vary in the CT HU values used to diagnose osteoporosis, the L1 vertebral body serves as an excellent site for CT-based assessment of osteoporosis for several reasons. First, as the first non-rib-bearing vertebra, the L1 vertebral body is easily identifiable, increasing the efficiency of its clinical use. Second, all chest, abdominal, pelvic, and lumbar CT scans include the L1 level, allowing for its wide application in opportunistic screening without additional radiation exposure. Moreover, L1 has been comprehensively studied, and evidence suggests that lumbar spine HU values obtained from CT scans correlate with BMD and can predict osteoporosis<sup>14</sup>.

## Limitations

While our study results indicate the use of CT-based HU as an alternative tool to assist BMD assessment in AS patients, it is important to note the potential limitations associated with this approach. First, the availability of CT equipment and the cost of CT scans may be prohibitive in some settings. Furthermore, the radiation exposure associated with CT scans is a critical consideration, particularly when these scans are used for routine or repeated assessment of bone density. However, if patients with severe AS have undergone CT screening for other indications, CT-based HU measurements can be used without additional radiation exposure, time, or cost. Second, this retrospective study with a small sample size may have some selection bias, and a larger prospective study is warranted to validate our results. Third, we were unable to determine a cut-off point for predicting fracture risk in the AS group based on our results using CT-based HU values at the L1 level. Fourth, due to the retrospective nature of our analysis, we did not evaluate the effect of osteoporosis drugs on changes in CT-based HU values<sup>37</sup>. Treatment with romosozumab (mean treatment time, 10.5 months) significantly increased the mean Hu by 26%, from a baseline of 85 to 107. Patients treated with teriparatide for > 12 months (mean treatment time, 23 months) had a significant improvement in the mean Hu of 25%, from 106 to 132<sup>37</sup>. Fifth, not all patients completed both the DXA and CT scan examinations simultaneously within 6 months due to retrospective analysis, and DXA examinations were not routinely performed at both the hip and the spine. By acknowledging these limitations and providing direction for future research, we hope to encourage continued exploration in this field to ultimately improve diagnostic accuracy and patient outcomes in the AS population.

## Conclusions

Using the CT-based HU cut-off value of < 135, an approximate additional 78% of BS and 55% of non-BS patients were classified as having osteoporosis, as compared with using the DXA-based classification. The appearance of BS in plain spine radiographs plays an important role in affecting DXA-based BMD assessment. The use of CT-based HU as a more accurate diagnostic tool for BMD evaluation in the AS population may be recommended after further validation by studies with prospective datasets and larger patient cohorts.

## Data availability

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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### Declarations

### Competing interests

The authors declare no competing interests.

### Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Taipei Veterans General Hospital (No. 2023-08-010BC), and informed consent was waived by the Institutional Review Board of Taipei Veterans General Hospital due to the retrospective nature of the analysis.

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