

The association between lower Hounsfield units of the upper instrumented vertebra and proximal junctional kyphosis in adult spinal deformity surgery with a minimum 2-year follow-up

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OBJECTIVE Patients undergoing long-segment fusions from the lower thoracic (LT) spine to the sacrum for adult spinal deformity (ASD) correction are at risk for proximal junctional kyphosis (PJK). One mechanism of PJK is fracture of the upper instrumented vertebra (UIV) or higher (UIV+1), which may be related to bone mineral density (BMD). Because Hounsfield units (HUs) on CT correlate with BMD, the authors evaluated whether HU values were correlated with PJK after long fusions for ASD.

METHODS The authors performed a retrospective study of patients older than 50 years who had undergone ASD correction from the LT spine to the sacrum in the period from October 2007 to January 2018 and had a minimum 2-year follow-up. Demographic and spinopelvic parameters were measured. HU values were measured on preoperative CT at the UIV, UIV+1, and UIV+2 (2 levels above the UIV) levels and were assessed for correlations with PJK.

RESULTS The records of 127 patients were reviewed. Fifty-four patients (19 males and 35 females) with a mean age of 64.91 years and mean follow-up of 3.19 years met the study inclusion criteria; there were 29 patients with PJK and 25 patients without. There was no statistically significant difference in demographics or follow-up between these two groups. Neither was there a difference between the groups with regard to postoperative pelvic incidence (PI), sacral slope (SS), lumbar lordosis (LL), PI minus LL (PI-LL), thoracic kyphosis (TK), or sagittal vertical axis (SVA; all $p > 0.05$). Postoperative pelvic tilt ($p = 0.003$) and T1 pelvic angle ($p = 0.014$) were significantly higher in patients with PJK than in those without. Preoperative HUs at UIV, UIV+1, and UIV+2 were 120.41, 124.52, and 129.28 in the patients with PJK, respectively, and 152.80, 155.96, and 160.00 in the patients without PJK, respectively ($p = 0.011$, 0.02, and 0.018). Three receiver operating characteristic (ROC) curves for preoperative HU values at the UIV, UIV+1, and UIV+2 as a predictor for PJK were established, with areas under the ROC curve of 0.710 (95% CI 0.574–0.847), 0.679 (95% CI 0.536–0.821), and 0.681 (95% CI 0.539–0.824), respectively. The optimal HU value by Youden index was 104 HU at the UIV (sensitivity 0.840, specificity 0.517), 113 HU at the UIV+1 (sensitivity 0.720, specificity 0.517), and 110 HU at the UIV+2 (sensitivity 0.880, specificity 0.448).

CONCLUSIONS In patients undergoing long-segment fusions from the LT spine to the sacrum for ASD, PJK was associated with lower HU values on CT at the UIV, UIV+1, and UIV+2. The measurement of HU values on preoperative CTs may be a useful adjunct for ASD surgery planning.

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KEYWORDS proximal junctional kyphosis; PJK; upper instrumented vertebra; UIV; bone mineral density; Hounsfield units

ABBREVIATIONS ASD = adult spinal deformity; AUC = area under the ROC curve; BMD = bone mineral density; CSVL = central sacral vertical line; DXA = dual-energy x-ray absorptiometry; HU = Hounsfield unit; LL = lumbar lordosis; LT = lower thoracic; PI = pelvic incidence; PI-LL = PI minus LL; PJK = proximal junctional kyphosis; PT = pelvic tilt; ROC = receiver operating characteristic; ROI = region of interest; SS = sacral slope; SVA = sagittal vertical axis; TK = thoracic kyphosis; TPA = T1 pelvic angle; UIV = upper instrumented vertebra; UIV+1 = 1 level above the UIV; UIV+2 = 2 levels above the UIV.

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THE treatment of adult spinal deformity (ASD) has become more prevalent, with ASD affecting up to 60% of the elderly population.^{1,2} Despite advances in the surgical treatment of ASD, proximal junctional kyphosis (PJK) is a well-recognized postoperative risk.^{3–7} The prevalence of PJK in ASD patients undergoing long-segment fusions has been reported to be between 5.8% and 62%.^{3,5,8–12} Multiple studies on PJK have been performed, with more and more evidence showing that PJK appears to be a multifactorial phenomenon.^{3,6,10,11,13–17} One mechanism of PJK is fracture of the upper instrumented vertebra (UIV) or the level above (UIV+1).^{3,13,14,18} Maruo et al. reported that fracture at the UIV was the most common mechanism for PJK, especially in the lower thoracic (LT) spine.³ It has also been reported that low bone mineral density (BMD) is a potential risk factor for PJK.^{18–20} Furthermore, other studies have reported that even osteopenia may be a factor in vertebral body fracture, subluxation, and PJK.^{6,21}

BMD is normally evaluated using dual-energy x-ray absorptiometry (DXA).^{18,22} However, DXA scans in the lumbar spine may not always be accurate given the amount of degeneration obscuring the true values, and spinal instrumentation can obfuscate interpretation.^{18,22} Moreover, not all patients obtain a preoperative DXA scan. Hounsfield units (HUs) on CT as a proxy for BMD have been shown to correlate with DXA values.^{18,22–24} Studies have demonstrated a correlation between HUs and DXA scores when comparing osteoporotic and non-osteoporotic patients,^{23,25} with a positive correlation between the T-score on DXA and the HU value on spinal CT.^{18,25} However, these studies have focused on degenerative conditions of the lumbar spine, and it is unclear if HUs reliably reflect the BMD of the LT vertebrae, the often-chosen UIV level in ASD surgery. We evaluated whether the HU values at the UIV, UIV+1, and UIV+2 (2 levels above the UIV) were associated with PJK in ASD patients over 50 years old.

Methods

Patient Cohort

We performed a retrospective study of patients who had undergone ASD correction from the LT spine (T9–T12) as their UIV to the sacrum in the period from October 2007 to January 2018 at the University of California, San Francisco; four spine surgeons had performed the procedures. Patients had to meet at least one of the following inclusion criteria: age > 50 years; scoliotic Cobb angle > 20°; sagittal vertical axis (SVA) > 5 cm; pelvic tilt (PT) > 25°; minimum 2-year follow-up; preoperative CT that included the UIV, UIV+1, and UIV+2; and ASD fusion at ≥ 6 levels for sagittal plane realignment. The majority of patients had a diagnosis of adult idiopathic scoliosis, adult degenerative scoliosis, or flat back deformity. Patients with tumor, trauma, or infection and/or without either long-standing cassette films or a 2-year follow-up were excluded.

Radiographic Measurements

All patients had 36-inch standing anteroposterior and lateral spinal radiographs preoperatively, within 1 month postoperatively, and at the last follow-up. Radiographic

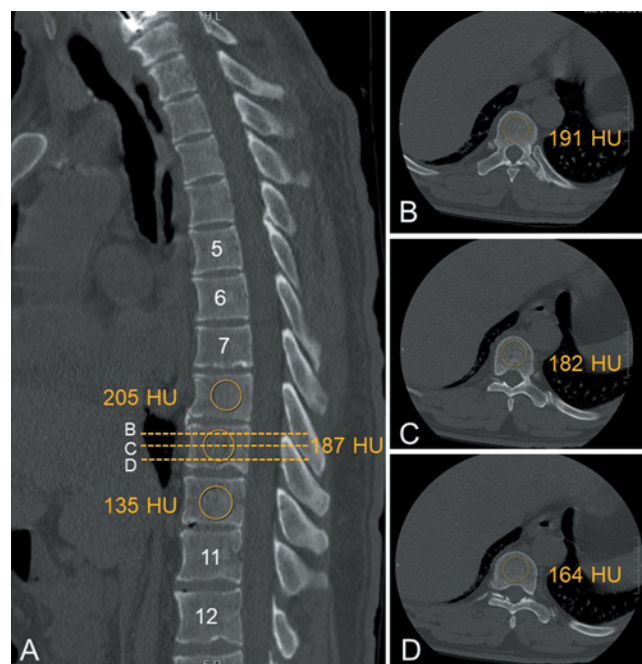


FIG. 1. Illustration of measuring HU values on preoperative CT at the UIV (T10 in this case), UIV+1 (T9), and UIV+2 (T8). The four separate measurements made are in the midsagittal plane (A), at the midbody axial plane (C), in the axial plane just inferior to the superior endplate (B), and in the axial plane just superior to the inferior endplate (D).

spinopelvic parameters measured were as follows: pelvic incidence (PI), PT, lumbar lordosis (LL), PI minus LL (PI-LL), sacral slope (SS), T1 pelvic angle (TPA), T5–12 thoracic kyphosis (TK), SVA, central sacral vertical line (CSVL), and scoliotic Cobb angle.

HU Measurements

HU values were measured on preoperative CTs at the UIV, UIV+1, and UIV+2 according to the methodology described by Schreiber et al.²⁵ According to this method, an ellipsoid region of interest (ROI) is used on the CT, ideally including the largest possible cancellous bone region while excluding cortical margins, osteophytes, and Schmorl nodes. The ROIs are measured in four separate sections of each vertebra: the midsagittal plane, immediately inferior to the superior endplate, in the middle of the vertebral body, and immediately superior to the inferior endplate. The HU value of each ROI is calculated using the PACS. The mean HU value of the four ROIs is defined as the vertebral body mean HU (Fig. 1).

Proximal Junctional Kyphosis

The proximal junctional angle (PJA) was defined as the sagittal Cobb angle between the inferior endplate of the UIV and the superior endplate of the UIV+2. Radiographic PJK was defined as PJA ≥ 10° and at least 10° greater than the corresponding preoperative measurement.^{8,26}

Statistical Analysis

Continuous variables were presented as means with

TABLE 1. Classification of PJK

Type of PJK	No.
Type 1	11
Type 2	4
Type 3	14

Type 1 = disc and ligament failure; type 2 = bone fracture; type 3 = implant-bone interface failure.

standard deviations, and categorical variables were presented as frequencies and percentages. Pre- and postoperative continuous variables were analyzed with independent-samples t-tests. A p value < 0.05 was considered statistically significant. A receiver operating characteristic (ROC) curve was analyzed to establish separation criteria between patients with PJK and without PJK. The areas under the ROC curve (AUCs) were calculated for preoperative HU assessment at the UIV. The most appropriate threshold (cutoff value) of HU at the UIV with a higher sensitivity and specificity was also established using the ROC curve. Statistical analysis was performed using SPSS Statistics version 24.0 (IBM Corp.).

Results

After evaluating 127 patients who had LT to sacral fusions in the study period, we found a total of 54 patients (19 males and 35 females) who met the inclusion criteria (mean age 64.91 ± 7.59 years) and had a mean follow-up of 3.19 ± 1.14 years. There were 29 patients with PJK and 25 patients without; the overall rate of PJK was 53.7% (29 of 54). Classification of PJK according to Yagi et al. revealed 11 type 1, 4 type 2, and 14 type 3 cases (Table 1).¹⁵ We also categorized the patients using an HU threshold of 110 since that value is the threshold for osteoporotic spines. With this threshold, 73.9% (17 of 23) of patients with HUs lower than 110 had PJK, and 38.7% (12 of 31) of patients with HUs higher than 110 had PJK ($p = 0.014$). Prophylactic methylmethacrylate augmentation was performed at the UIV or UIV+1 in 19 patients. Of these, 10 had PJK, and 9 did not ($p = 0.781$). Only 2 patients had interspinous tethers, and no patients had transitional rods to the UIV. There was no difference in age, BMI, sex, and follow-up between the two groups.

There was no statistical difference between the groups with regard to preoperative PI, SS, PT, LL, PI-LL, TK, TPA, SVA, CSVL, or Cobb angle (all $p > 0.05$; Table 2). Preoperative HUs at UIV, UIV+1, and UIV+2 were 120.41 ± 45.67 , 124.52 ± 45.17 , and 129.28 ± 45.99 in patients with PJK, respectively, and 152.80 ± 43.99 , 155.96 ± 50.87 , and 160.00 ± 46.31 in the patients without PJK ($p = 0.011$, 0.02 , and 0.018 , respectively). Postoperative PT and TPA were significantly higher in patients with PJK than in those without ($p = 0.003$ and 0.014 , respectively). However, there was no statistical difference between the groups with regard to postoperative SS, LL, PI-LL, TK, SVA, and CSVL (all $p > 0.05$; Table 3). Multivariate regression analysis was performed, and there was no statistical correlation with PJK and other common causes of PJK (Table 4).

TABLE 2. Comparison of preoperative parameters in patients with and without PJK

Parameter	PJK (n = 29)	No PJK (n = 25)	p Value
Age in yrs	65.18 ± 8.19	64.64 ± 7.20	0.801
BMI in kg/m ²	26.99 ± 5.34	29.49 ± 5.01	0.105
SS in °	32.96 ± 11.32	33.44 ± 14.55	0.895
PT in °	29.00 ± 7.30	26.76 ± 14.32	0.476
PI in °	61.56 ± 11.74	56.72 ± 13.91	0.180
LL in °	36.48 ± 15.99	31.36 ± 17.34	0.273
PI-LL in °	25.59 ± 13.57	25.36 ± 14.47	0.953
TPA in °	29.85 ± 8.23	25.88 ± 9.99	0.123
TK in °	30.07 ± 13.74	23.80 ± 13.95	0.109
SVA in cm	8.71 ± 5.45	9.24 ± 5.10	0.726
CSVL in mm	2.78 ± 2.51	2.33 ± 1.40	0.442
Cobb angle in °	28.07 ± 18.04	20.75 ± 18.76	0.162
HU at UIV	120.41 ± 45.67	152.80 ± 43.99	0.011*
HU at UIV+1	124.52 ± 5.17	155.96 ± 50.87	0.02*
HU at UIV+2	129.28 ± 45.99	160.00 ± 46.31	0.018*

n = number of patients.

* $p < 0.05$.

Three ROC curves for preoperative HU values at the UIV, UIV+1, and UIV+2 as a predictor for PJK were established, with an AUC of 0.710 (95% CI 0.574–0.847) for the UIV, 0.679 (95% CI 0.536–0.821) for UIV+1, and 0.681 (95% CI 0.539–0.824) for UIV+2. The optimal HU cutoff value determined by the Youden index was 104 HU at the UIV (sensitivity 0.840, specificity 0.517), 113 HU at the UIV+1 (sensitivity 0.720, specificity 0.517), and 110 HU at the UIV+2 (sensitivity 0.880, specificity 0.448; Fig. 2).

Discussion

Given the various rates, mechanisms, risk factors, and treatment strategies for PJK, the complication probably has a multifactorial etiology.^{3,6,10–17} Fracture of the UIV or the UIV+1 has been shown to be one of the mechanisms of PJK.^{3,13,14,18} Indeed, Maruo et al. have reported that fracture at the UIV is the most common mechanism.³ Burch et

TABLE 3. Comparison of postoperative parameters in patients with and without PJK

Parameter	PJK (n = 29)	No PJK (n = 25)	p Value
SS in °	34.81 ± 9.47	39.92 ± 10.96	0.084
PT in °	26.65 ± 8.11	19.38 ± 8.31	0.003*
LL in °	53.61 ± 10.99	53.45 ± 15.77	0.967
PI-LL in °	10.92 ± 7.72	8.72 ± 8.73	0.344
TPA in °	24.62 ± 9.25	17.79 ± 9.74	0.014*
TK in °	36.97 ± 10.99	33.67 ± 14.66	0.354
SVA in cm	5.66 ± 4.48	4.52 ± 3.40	0.313
CSVL in mm	2.27 ± 1.63	2.05 ± 1.68	0.635

* $p < 0.05$.

TABLE 4. Multivariate regression analysis of the statistical contribution of other risk factors for PJK

Parameter	Exp(B)	95% CI		p Value
		Lower	Upper	
Age	1.006	0.900	1.125	0.910
Sex	0.483	0.051	4.566	0.526
BMI	1.095	0.934	1.285	0.263
Postop SS	0.941	0.183	4.835	0.942
Postop PT	0.745	0.140	3.963	0.730
Postop PI	1.185	0.240	5.843	0.835
Postop LL	0.944	0.803	1.109	0.481
Postop PI-LL	1.026	0.875	1.204	0.750
Postop SVA	0.894	0.616	1.297	0.554
Postop CSVL	1.047	0.561	1.956	0.885
Postop TPA	1.005	0.743	1.358	0.976
Postop TK	0.994	0.906	1.091	0.900

al. have reported that the presence of osteoporosis, which reflects a deterioration of bone strength, not just density, is a key etiological factor for insufficiency fractures, PJK, pseudarthrosis, and screw pullout.²⁷ Other studies have documented similar findings, concluding that age and low BMD are potential risk factors for postoperative PJK.^{18–20} In addition to its PJK risk, Yagi et al. reported that low BMD is also a significant risk factor for proximal junctional failure.²⁰ One reason for these failures may be that poor bone quality either compromises the interface between bone and instrumentation or is insufficiently strong to withstand the new forces of the spine against a long lever arm from a multilevel fusion.^{6,17,21}

Because the high incidence of PJK has become a vexing problem for both the patient and the treatment team,

surgeons are becoming more aware of the importance of assessing BMD prior to surgical correction of ASD. Although DXA is currently considered to be the gold standard to assess BMD and its values have been shown to correlate with fracture risk,^{22,25} DXA is not always part of the routine preoperative workup.²² Furthermore, DXA has been shown to underestimate the magnitude of bone loss in spinal vertebrae,²⁷ leading to false-negative rates of fracture risk.²⁸ Burch et al. have shown that vertebral fractures are highly associated with CT-measured BMD and finite element–estimated vertebral bone strength more so than DXA-measured BMD.²⁷ Hendrickson et al. have shown that CT provides better accuracy and excellent reproducibility for measuring BMD by using HU values.²⁸ However, for ASD surgeries, many surgeons will obtain a preoperative CT, not a DXA scan, and the HU values on the CT may be a proxy for BMD, saving both cost and time.^{22,25} Lewiecki et al. found a linear correlation between HU values and compressive strength of bone.²⁹ HU values can also be used to estimate regional bone strength, and measuring the HU value in the planned screw trajectory may predict the strength of the bone-screw interface prior to screw insertion.²⁵ Furthermore, several studies have reported reasonably good correlation between HUs and DXA values^{18,25,30,31} and between HUs and osteoporosis.^{23,25,32} Thus, the use of HUs on CT as a proxy for a DXA scan may be a reasonable option in the preoperative workup, and formal DXA can be performed if the CT indicates probable poor bone quality.^{18,25,28} Although the spine is the ROI in terms of surgical planning, the hip also needs to be evaluated when obtaining a DXA scan because the spine DXA may not be accurate with degenerative change or deformity, common findings in older patients requiring spine surgery. Moreover, if the lumbar spine is evaluated with DXA, an accurate assessment should be performed from L1 to L4, and the thoracic spine is currently not a standard area to perform DXA.³³

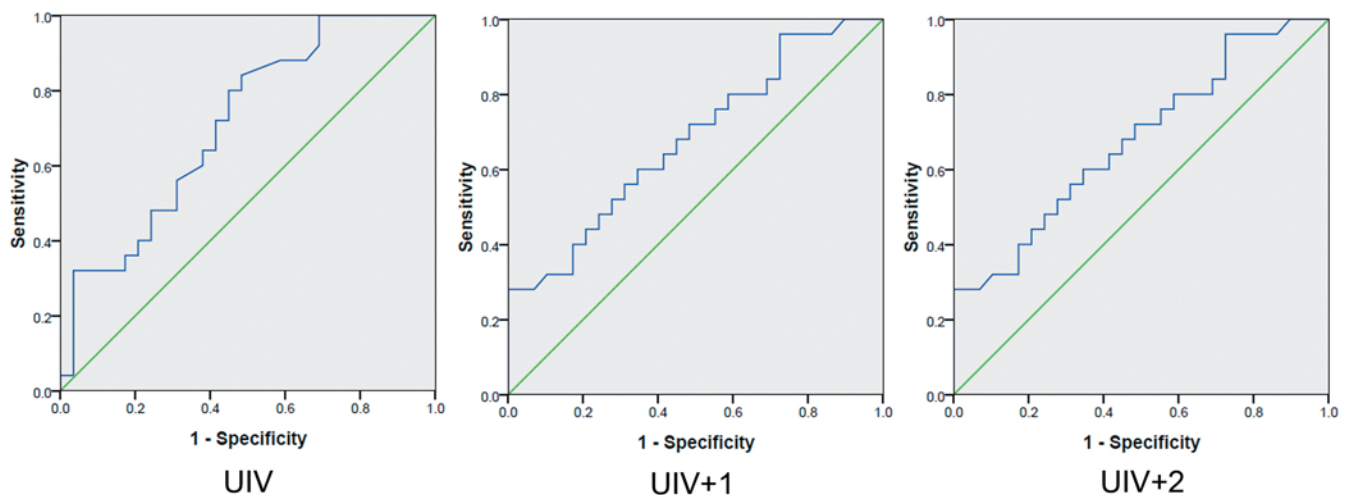


FIG. 2. Three ROC curves for preoperative HU values at the UIV, UIV+1, and UIV+2 as a predictor for PJK were established, with an AUC of 0.710 (95% CI 0.574–0.847) for the UIV, 0.679 (95% CI 0.536–0.821) for the UIV+1, and 0.681 (95% CI 0.539–0.824) for the UIV+2. The optimal HU cutoff value determined by the Youden index was 104 HU at the UIV (sensitivity 0.840, specificity 0.517), 113 HU at the UIV+1 (sensitivity 0.720, specificity 0.517), and 110 HU at the UIV+2 (sensitivity 0.880, specificity 0.448).

PJK has been defined as a sagittal Cobb angle of more than 10° or 10° greater than the preoperative angle between the inferior endplate of the UIV and the superior endplate of the UIV+2.^{8,26} It has been shown that one mechanism by which PJK occurs is fixation failure at the bone-implant interface, resulting in proximal screw loosening.^{3,4,17} Recent studies have shown that HU values measured on preoperative CT are independent predictors of implant loosening, and lower HU values are significantly correlated with a higher risk of pedicle screw loosening after lumbar fusion.^{34–36} Schwaiger et al. demonstrated that HU values on CT adequately differentiated patients with and without osteoporotic fractures, and they showed that HU values could predict pedicle screw loosening after fusion.³⁶ However, previous studies have focused on the lumbar spine, establishing thresholds of 135 HU for osteopenic spines, 120 HU for the risk of pedicle screw loosening, 110 HU for osteoporotic spines, and 90 HU for the risk of vertebral body fracture.^{32,37,38} Although these numbers may be useful in identifying osteoporosis in patients undergoing spinal surgery for degenerative pathology, the same correlation has not been clearly shown in patients undergoing ASD correction, especially at the UIV in the thoracic spine.³⁹ Thus, in ASD patients, the HUs of the LT spine may be more critical than the HUs of the lumbar spine. Although the reports on HU values at the UIV in PJK cases have been rare, Uei et al. evaluated the HUs at the UIV vertebral bodies in their series of ASD patients.¹⁸ They concluded that the mean BMD of vertebral bodies at T8 and T9 was significantly lower in elderly patients who required revision surgery. With regard to their study compared to ours, there are some differences. First, Uei and colleagues studied UIV levels from T8 to L2, incorporating the HU values of the lumbar spine and not focusing exclusively on the LT spine. Our study evaluated only the UIVs of the LT spine (T9 to T12) without any lumbar spine involvement. Second, they measured HU values from T8 to S1, and they did not focus their findings specifically on the UIV as we did. Despite these differences, however, our findings corroborate those of Uei et al., noting that decreased HUs on CT is associated with PJK.

Regardless of these findings, PJK remains a multifactorial phenomenon. Some possible reasons for PJK are long fusions to the sacrum, overcorrection of sagittal plane deformities, poor bone density, disruption of the posterior ligamentous tissues, or extreme rod stiffness. Although we have classified the types of PJK into ligamentous, bone-implant interface, or fracture, there may be multiple reasons for PJK, and they may not be clearly elucidated from the data. Although we controlled for PI-LL mismatch and SVA, there were patients who had increased TPA and PT, indicating that there was probably a higher proportion of patients who did have some degree of imbalance in addition to the lower HU values.

As mentioned above, previous studies have reported HU thresholds of 135 HU for osteopenic spines, 120 HU for the risk of pedicle screw loosening, 110 HU for osteoporotic spines, and 90 HU for the risk of vertebral body fracture. However, these studies have not specifically evaluated the HU threshold for PJK in ASD patients, nor

did they evaluate HU thresholds specifically in the thoracic spine. In our study, we found that the optimal preoperative HU at the UIV cutoff value determined by the Youden index was 104 HU (sensitivity 0.840, specificity 0.517; Fig. 2). Given this information, our data reflect that the preoperative LT spine HU value of less than 104 HU may be a risk factor for PJK after ASD correction. In addition, our results suggest that preoperative HUs at the UIV, UIV+1, and UIV+2 were significantly lower in the patients with PJK than in those without ($p = 0.011$, 0.02 , and 0.018 , respectively). Thus, the HUs at the UIV, UIV+1, and UIV+2 may be specifically associated with PJK. One point of note is that the Youden index was fairly low, but patients who demonstrated PJK had higher values. One reason is that there was a large range of HU values in the cohort with PJK. Because of this, a low cutoff was used, although some patients with PJK had higher HU values. It must also be kept in mind that per The International Society for Clinical Densitometry position statement, it is important to ensure that these HU values are valid “only if validated machine-specific cutoff values and scanner stability have been established” (<https://www.iscd.org/official-positions/>).

With regard to clinical management, patients who have suspiciously low HU values on CT are sent for DXA to formally evaluate their bone density. If they are osteoporotic, their surgery is delayed, and they are placed on teriparatide or another medication for 3–6 months. If the patient is osteopenic ($T\text{-score} < -2.0$), they will generally have their surgery postponed, and they will be placed on teriparatide if they will be undergoing a large, corrective surgical procedure. However, if the patient is in severe, disabling pain and the surgery will not involve tremendous corrective forces but only a stabilization procedure, then they may be considered to proceed with surgery and given medication after surgery. Generally, the surgical UIV is not taken up into the upper thoracic spine unless there is significant TK, but this is considered as an option in patients with poor bone density.

There are several limitations to this study. First, it is a single-center retrospective study with a relatively small number of patients. Second, the presence of osteotomies (three column or posterior column) was not matched for because of the relatively small number of patients. Such a delineation would have probably made the study underpowered if the patients were divided into these two different groups. However, our data should be interpreted with the understanding that it has been shown that significant sagittal correction is associated with significant stress to the proximal adjacent disc and vertebrae.³ Nonetheless, we did not find a difference between the two groups with regard to pre- and postoperative PI-LL mismatch and SVA, indicating that the corrective magnitude in the sagittal plane between the two groups was not different. However, the PT and TPA were different, indicating that there may still have been some sagittal parameter that acted as a confounding variable with these data. Another limitation to this study that should be considered is the number of patients who were excluded, which may have led to selection bias. Despite these limitations, however, we did find statistical differences in HUs between the PJK and non-

PJK cohorts, which is consistent with previous studies that have shown that a decreased HU is associated with both PJK and implant failure.

Conclusions

In patients undergoing sagittal correction with fusions from the LT spine to the sacrum for ASD, PJK was associated with lower HU values in the LT spine at the UIV, UIV+1, and UIV+2. The measurement of HU values on preoperative CTs may be a useful adjunct when planning surgical correction of ASD.

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Disclosures

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Conception and design: Chou. Acquisition of data: Duan, Rivera, Guinn, Wang, Xi, Li, Wu. Analysis and interpretation of data: Duan. Drafting the article: Duan. Critically revising the article: Mummaneni, Burch, Berven, Chou. Reviewed submitted version of manuscript: Chou. Approved the final version of the manuscript on behalf of all authors: Duan. Statistical analysis: Duan. Administrative/technical/material support: Mummaneni, Rivera, Ames, Burch, Berven, Chou. Study supervision: Chou.

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