

Peer Review File

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Reviewer A

Comment 1: This study included 145 patients who underwent ASD surgery during the study period. A total of 121 (83.4%) had CT scans from which a HU was measured. However, even if the value of HU is similar, the force applied to the screw is inevitably different depending on the quality of the bone. In particular, if patients who applied anabolic medication are divided, it is recommended to classify and analyze that part separately or to add more cohort patients if n is insufficient.

Reply 1: The Reviewer raises a crucial point. We wholeheartedly agree that anabolics play a critical role in the bone quality and the force applied to the screw. However, given the low sample size, we were unable to control for more covariates to the multivariable model. In addition, the number of patients receiving anabolics was low (N=30), which prevented any subanalysis in that small group. Regardless of whether the patient was receiving anabolic medication, we sought to determine whether Hounsfield Unit can accurately reflect bone quality and predict outcomes. Furthermore, adding more cohort patients was impossible due to the retrospective nature of the study and lack of patient recruitment. We have elaborated on this important point brought forth by the Reviewer in the limitations, and we thank him/her for the opportunity to further clarify this point.

Changes in the text: Lines 304-305.

Comment 2: Your method part it's separated like this: There were 100 (82.6%) females in the cohort. The mean HU was 153.5 ± 52.8 . A total of 41 (33.9%) patients had osteopenia, 8 (6.6%) had osteoporosis, and 30/56 (24.8%) were on anabolic medication, specifically Teriparatide, for a mean duration of 469.5 ± 259.5 days. In addition, if you have undergone deformity surgery, the strength of the force applied to the UIV screw may be different from the angle of correction before and after surgery, and the presence or absence of PJK should be considered together with the HU by considering the difference depending on the location of the UIV.

Reply 2: The Reviewer makes a valid point, and we thank him/her for the opportunity to improve our analysis. As the Reviewer elaborated, the choice of UIV is important predicting PJK. Since we could not add more covariates, and as per the Reviewer's suggestion, we compared the rate of PJK in patients with thoracic UIV (above T7) vs. thoracolumbar UIV (T7 and below) and found no significant difference in PJK rate between the two groups (23.8% vs. 37%, $p=0.248$). We have added this great point brought forth by the Reviewer to the Results, and we reinforced the limitations regarding UIV location.

Changes in the text: Lines 206-208, 304-305

Comment 3: Your article is described as follows: The UIV was in the upper thoracic spine (above T7) in 21 (17.4%) patients and lower thoracic area (T7 and below) in 100 (82.6%). PJK is an essential part of deformity correction surgery, and your research contributes greatly to the clinical field. However, since there seems to be diversity in the groups that have been analyzed, we request a more controlled type of analysis.

Reply 3: The Reviewer makes a focal point. As per the comment above, we compared PJK rate between patients with thoracic (T7 and above) vs. thoracolumbar UIV (T8 and below) and found no significant difference in PJK rate between the two groups (23.8% vs. 37.0%, $p=0.248$). While

we did not control for UIV in the multivariable regression, the rate of PJK remained similar regardless of the UIV location. We have further elaborated on this point in the Results and limitations, and we thank the Reviewer for raising this important question.

Changes in the text: Lines 206-208, 304-305

Reviewer B

Comment 4: The authors evaluated the association of HU with mechanical complications and reoperation in patients that underwent ASD surgery, and 2) identified an optimal HU threshold to predict the occurrence of mechanical complications. The authors concluded that HU below 163 was associated with increased PJK on ROC curve analysis. Many papers have already investigated HU and PJK in patients with ASD. What is the novelty of this paper? Unless UIV is unified, it is impossible to determine the setting value of HU for PJK. For example, T3 and T10 have different HU values.

Reply 4: The Reviewer's raises a vital point, and we appreciate the opportunity to provide further explanation of our research. While multiple studies examined the impact of HU on PJK or PJK requiring reoperation, we investigated many more outcomes, including overall mechanical complications, DJK, implant failure, rod fracture, pseudarthrosis, and overall reoperation. Regarding UIV, as a retrospective study with limited sample size, it was nearly impossible to unify the UIV location. Practically, one HU threshold at the UIV might be easier for spine surgeons to utilize preoperatively. Therefore, to simplify the methodology, HU was taken on three axial slices of one vertebra, either at the UIV itself or at a vertebra within $UIV \pm 4$ from CT scans preoperatively, and HU around the UIV were analyzed for all patients. We have reinforced the discussion and limitations to accommodate for the Reviewer's excellent points.

Changes in the text: Lines 286-288, 302-303.

Comment 5: Line 101-103, "Inclusion criteria were: Cobb angle $\geq 30^\circ$, sagittal vertical axis (SVA) ≥ 5 cm, coronal vertical axis (CVA) ≥ 3 cm, pelvic tilt (PT) of $\geq 25^\circ$, thoracic kyphosis (TK) $\geq 60^\circ$, or pelvic incidence-lumbar lordosis mismatch of $\geq 10^\circ$." Why did the authors make this indication? Please include the ref and add it.

Reply 5: The Reviewer makes a valid point. In keeping with prior literature (PMIDs: 33007745, 36728801), and according to the spinal deformity registry at our institution, patients were retrospectively included if the listed inclusion criteria were met. While sagittal/coronal malalignment can have multiple connotations, these criteria were chosen by the senior authors according to the spinal deformity literature to facilitate patients' recruitment. We have added to the Methods the references according to the Reviewer's excellent recommendation.

Changes in the text: Line 129.

Comment 6: Line 110-113, "The primary exposure variable was HU taken on three axial slices of one vertebra, either at the UIV itself or at a vertebra within $UIV \pm 4$ from CT scans preoperatively.[20] This method is similar to previous reports in the literature [21] and was chosen due to the average of different levels throughout the spine." Since the readers do not understand, please show the evaluation method concretely with a figure.

Reply 6: The Reviewer raised a great point. We apologize for this oversight. As per his/her excellent suggestion, we provided **Figure 1** to illustrate the methodology used to capture HU.

Changes in the text: Line 143, **Figure 1**.

Comment 7: I don't understand the meaning of "Hounsfield Units UIV/UIV+4" shown in Table 1. please explain.

Reply 7: The Reviewer raised an important point. As per our Method section, HU was taken on three axial slices of one vertebra, either at the UIV itself or at a vertebra within UIV±4 from CT scans preoperatively. The mean, median, and range of HU was reported in Table 1 as a result of the three axial HU recorded from the UIV/UIV±4. We removed the "UIV/UIV+4" from **Table 1** to avoid confusion.

Changes in the text: Table 1.

Comment 8: Line 162-163, "A total of 41 (33.9%) patients had osteopenia, 8 (6.6%) had osteoporosis, and 30/56 (24.8%) were on anabolic medication" What is the definition of each, osteopenia or osteoporosis?

Reply 8: The Reviewer brings forth a valid point, and we thank him for the opportunity to expand on the methodology used to classify patients as osteopenic or osteoporotic. In keeping with prior literature, osteopenia was determined by the WHO criteria when the lowest T-score (radius, lumbar spine, femur) was between -1 to -2.5, while osteoporosis was determined when a T score was lower than -2.5. The lowest T-score was recorded. We have expanded our Methods regarding osteopenia and osteoporosis and provided the appropriate citations.

Changes in the text: Lines 145-147.

Comment 9: Line 168-170, "The UIV was in the upper thoracic spine (above T8) in 21 (17.4%) patients and lower thoracic area (T8 or below) in 100 (82.6%)." How did the authors decide on UIV settings? Please add to the methodology who decided UIV based on what criteria.

Reply 9: The Reviewer raised a valid question. The choice of the UIV is often debated among spine surgeons, and no consensus was reached thus far in the spine deformity literature regarding optimal UIV location. UIV selection in each case was left up to the treating surgeon, with no formally accepted guidelines or criteria to choose the UIV. Our data belongs to a retrospective, multi-surgeon registry. Therefore, the choice of the UIV could not be tracked through a retrospective chart review and was most likely based on each surgeon's practice. We expanded on this notion in the Methods and reinforced the limitations regarding the thoughtful point brought forth by the Reviewer.

Changes in the text: Line 149, 307-309.

Comment 10: In this study, mechanical complications and reoperation appear to be more common than previously reported. In particular, the reoperation rate is over 50%, which is unacceptable.

Reply 10: The Reviewer raises a valid concern. We wholeheartedly agree that the reoperation rate is eccentrically high. This data belongs to a multi-surgeon registry and goes back to 2013-2017, which might not reflect the current practice at our institution. However, through the encountered clinical and operative outcomes, we found value in reporting the institution's experience even though it's partially outdated. As a retrospective study based on chart review, it was difficult to ascertain the reasons of the high reoperation rate. We further expanded our limitations regarding the crucial point brought forth by the Reviewer. Overall, we agree the complication rate is very high, but we believe first and foremost to be honest and transparent with our findings as possible. In the more recent 4-6 years, our complication rate and reoperation rate is much lower.

Changes in the text: Lines 309-313.

Comment 11: Although the authors target PJK, it is PJF that is clinically relevant. Please add the following paper evaluating HU in PJF for your ref. “Hiyama A, et al. Relationship Between Hounsfield Units of Upper Instrumented Vertebrae, Proximal Junctional Failure, and Global Alignment and Proportion Score in Female Patients with Adult Spinal Deformity. World Neurosurg 2022.”

Reply 11: The Reviewer raised a valid concern. We agree that PJF is particularly important and is considered a clinically relevant outcome. According to the Reviewer excellent recommendation, we expanded on the citation provided in the Discussion to highlight the relationship between HU and PJK.

Changes in the text: Lines 277-281.

Comment 12: Line 225-227, In addition, most of these studies have pursued a different methodology when it comes to HU measurement (UIV/UIV+1), as opposed to the current study (UIV/UIV+4).” This is a funny sentence; if the authors are aware of this, they should revise their papers.

Reply 12: The Reviewer brings forth an important point. While other previous reports have used different HU measurements such as the average of UIV/UIV+1 and UIV/UIV+2, and given the lack of consensus regarding the location of the HU measurement, we have chosen UIV/UIV±4 to maximize the sample of vertebral bodies, as stated in the Methods. However, we believe that the statement mentioned by the Reviewer may be irrelevant to the Discussion and was subsequently removed. We thank the Reviewer for his/her thoughtful comment and for the opportunity to enhance the quality of our Discussion.

Changes in the text: Lines 252-253.

Comment 13: -Line 233-235, “Furthermore, the authors found that HU was superior to DEXA scan in predicting mechanical complications.” What data results support this observation?

Reply 13: The Reviewer raises a valid question. According to St. Jeor et al., the multivariable regression showed a significant association between HU and osteoporosis related complications, but not with DEXA-measured t-score. While we objectively reported their results, the retrospective nature of their study prevented ultimate conclusions. We expanded the Discussion regarding the findings of St. Jeor et al, and we thank the Reviewer for the thoughtful concern.

Changes in the text: Lines 260-262.

Comment 14: Line 250, “our study found no association between HU and reoperation.” This is a funny sentence, and it is because bone density and HU are not the direct factors determining revision surgery.

Reply 14: The Reviewer raises a valid concern. We agree that this sentence might have been an overstatement, and we apologize for this oversight. Even though a multivariable regression was performed, conclusions drawn from a retrospective study require confirmation from prospective studies with larger sample size. Therefore, we toned down this sentence according to the Reviewer’s excellent suggestion.

Changes in the text: Lines 273-275.