

The L3 Flexion Angle Predicts Failure of Non-Operative Management in Patients with Tandem Spondylolithesis

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Abstract

Study Design: Retrospective cohort study.

Objective: Determine impact of standard/novel spinopelvic parameters on global sagittal imbalance, health-related quality of life (HRQoL) scores, and clinical outcomes in patients with multi-level, tandem degenerative spondylolisthesis (TDS).

Methods: Single institution analysis; 49 patients with TDS. Demographics, PROMIS and ODI scores collected. Radiographic measurements—sagittal vertical axis (SVA), pelvic incidence (PI), lumbar lordosis (LL), PI-LL mismatch, sagittal L3 flexion angle (L3FA) and L3 sagittal distance (L3SD). Stepwise linear multivariate regression performed using full length cassettes to identify demographic and radiographic factors predictive of aberrant SVA (≥ 5 cm). Receiver operative curve (ROC) analysis used to identify cutoffs for lumbar radiographic values independently predictive of SVA ≥ 5 cm. Univariate comparisons of patient demographics, (HRQoL) scores and surgical indication were performed around this cutoff using two-way Student's t-tests and Fisher's exact test for continuous and categorical variables, respectively.

Results: Patients with increased L3FA had worse ODI ($P = .006$) and increased rate of failing non-operative management ($P = .02$). L3FA (OR 1.4, 95% CI) independently predicted of SVA ≥ 5 cm (sensitivity and specificity of 93% and 92%). Patients with SVA ≥ 5 cm had lower LL (48.7 ± 19.5 vs 63.3 ± 6.9 mm, $P < .021$), higher L3SD (49.3 ± 12.9 vs 28.8 ± 9.2 , $P < .001$) and L3FA (11.6 ± 7.9 vs -3.2 ± 6.1 , $P < .001$) compared to patients with SVA ≤ 5 cm.

Conclusions: Increased flexion of L3, which is easily measured by the novel lumbar parameter L3FA, predicts global sagittal imbalance in TDS patients. Increased L3FA is associated with worse performance on ODI, and failure of non-operative management in patients with TDS.

Keywords

spine, spondylolisthesis, health-related quality of life, global sagittal imbalance

Introduction

Degenerative spondylolisthesis (DS) occurs in 19.1 to 43.1% of elderly patients and is a common cause of spinal stenosis.^{1,2} DS of the lumbar spine most commonly involves a single level,³ however, multi-level degenerative spondylolisthesis, or tandem spondylolisthesis (TDS), is relatively uncommon, representing only 5-12% of all degenerative spondylolistheses.⁴⁻⁶ Most commonly DS occurs at the L4-L5 level, and the literature focuses predominantly on single level disease.⁵

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In addition to classically cited risk factors such as elevated BMI, advanced age and female gender, there is a growing body of literature implicating aberrant sagittal radiographic parameters in the pathogenesis of DS.⁵ In particular, a high pelvic incidence (PI) has been associated with an increased risk of DS.⁷⁻⁹ Additionally, whether or not a patient with DS presents with global, sagittal anterior malalignment has been speculated to be related to various compensatory mechanisms including pelvic retroversion, thoracic flattening, and lower limb responses.^{5,9} Despite this growing body of work, the relationship between focal degenerative changes associated with DS and more global sagittal deformity has not been well defined. A prior work that compared TDS to single-level degenerative spondylolisthesis found that patients with TDS had a significantly greater pelvic incidence, C7 tilt, pelvic tilt (PT), and PI-LL mismatch than those with single-level DS.¹⁰ These findings suggest that TDS may be a distinct clinical entity from single-level DS and may represent a significant, and possibly underappreciated, source of severe global sagittal imbalance. However, there is a paucity of data that evaluates what radiographic parameters may impact the clinical outcomes of patients with TDS.

The purpose of this study was to correlate the novel lumbar radiographic parameters L3 lumbar flexion angle (L3FA) and L3 sagittal distance (L3SD) with global sagittal alignment parameters, patient reported outcomes, and ultimately failure of non-operative treatment in patients with TDS. The hypothesis of this study was that L3FA and L3SD would correlate with SVA and that elevated L3FA and L3SD would correlate with poorer patient reported outcome scores and consequently an increased likelihood of patients with TDS failing non-operative management and requiring surgical intervention.

Methods

This study was institutional review board (IRB) approved with IRB number STUDY20040115 and was exempt from obtaining informed consent. This study was a retrospective analysis of a prospectively collected database of patients with low back pain or extremity symptoms in the setting of TDS at a single institution from 2016 to 2020. Inclusion criteria were patients with TDS and adequate standing, anterior-posterior (AP) and lateral radiographs of the lumbar spine. Adequate standing lumbar spine radiographs for analysis of spinopelvic parameters have previously been defined as radiographs that include the upper end plate of the L1 vertebra, the sacral dome, and both femoral heads.¹¹ Exclusion criteria were patients with high grade DS, a history of lumbar spine trauma, lumbar spine tumors, any symptoms concerning for cauda equina, conus medullaris, or other reasons to proceed with urgent surgery after the initial clinic visit, prior lumbar spine surgery (all patients with iatrogenic spondylolisthesis were excluded) or abdominal surgery, low-quality radiographic data, congenital malformations of the lumbar spine, or a history of a

spine infections. High grade DS was defined according to the Meyerding classification as a ratio of overhang from the superior vertebral body to the anteroposterior length of the adjacent inferior vertebral body of greater than 50% (above Meyerding Grade 2).¹²

For the purposes of this study, TDS was defined as anterolisthesis of at least 3 mm at two levels of the lumbar spine (L1-S1), which is a definition that has been used in prior work related to TDS.¹ Two non-contiguous, anterior spondylolistheses were still considered TDS (this pattern was only encountered in one patient in this study).¹ This study focused on TDS resulting in anterolisthesis due to posterior TDS being exceptionally rare (no patients with posterior TDS were identified in this study).¹³ SVA was measured on 36" standing full-length spine plain radiographs. LL, PI, L3SD and L3FA were measured on lumbar spine plain radiographs. L3 was chosen as the center of measurements because L3-5 is the most common presentation of TDS and because the apex of physiologic lumbar lordosis is typically near the inferior aspect of L3 (Figure 1).¹⁴ All radiographic measurements were performed manually by two senior orthopaedic surgery residents and subsequently averaged together to obtain the final value. An intra-class correlation coefficient (ICC) was calculated using R statistics software in order to assess intra-rater reliability for all lumbar spinopelvic parameters, and for the novel parameters L3SD and L3FA. All ICC calculations were noted to be excellent (>.9) between the two observers.¹⁵ Philips DICOM Viewer software (Koninklijke Philips N.V.) was used to view radiographs and perform measurements. An inter-rater correlation coefficient was then calculated to determine reliability.

The electronic medical record of included patients was retrospectively reviewed to determine if the patient had failed non-operative treatment and ultimately required surgery at any point during clinical follow-up. All patients initially presented to the same clinical practice for low back and/or extremity pain. All patients were treated with the same treatment algorithm, which includes standing lumbar radiographs at first visit, and a multi-tiered trial of non-operative treatment. First-line nonoperative treatment included physical therapy, non-steroidal anti-inflammatory drugs, and the addition of a Medrol dosepak if the onset of pain was relatively more recent. Second-line treatment was initiated if patients represented with continued pain complaints and included magnetic resonance imaging to identify areas of stenosis for consideration of epidural steroid injection. If patients represented with failure of both first-line and second-line treatments, they were offered repeat steroid injections and discussed surgery with the attending surgeon. Failure of non-operative treatment was defined as patients continuing to have pain and/or neurological complaints after first-line and second-line treatments and deciding to proceed with surgery, rather than re-attempt a second-line treatment. Additional collected demographic and clinical data included age, sex, BMI, co-morbidities as measured with the Age-Adjusted Charlson Comorbidity Index

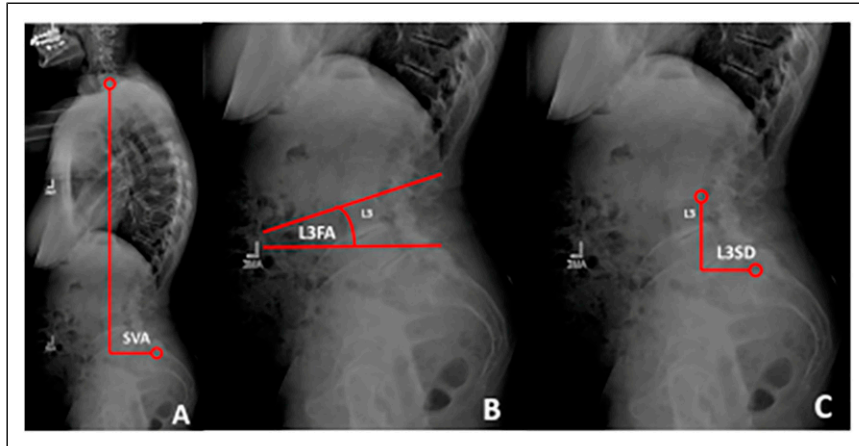


Figure 1. A. SVA was measured as the angle between the posterior-superior corner of S1 to a vertical plumbline drawn from the center of the C7 vertebral body. B. L3FA was measured as the angle between the superior endplate of L3 and a horizontal reference line. C. L3SD was measured as the horizontal distance between a vertical reference from the posterior-superior corner of L3 vertebral body to the posterior-superior corner of S1.

(ACCI), which has been used previously in orthopaedic spine literature.¹⁶ Health-related quality of life (HRQoL) scores collected at the initial clinical visit included Oswestry Disability Index (ODI) and the PROMIS Global-10 physical function and mental health sub-scores.

Statistical Testing

Statistical analysis was performed using SPSS 28 (IBM, Armonk, NY, USA). Missing values were inputted 5 times to permit adequate pooled analysis.¹⁷ A stepwise linear multivariate regression was performed using those patients with full length cassettes to identify demographic and radiographic factors independently predictive of $SVA \geq 5$ cm.¹⁸ A Receiver operative curve (ROC) analysis was used to identify an ideal cutoff for lumbar radiographic values independently predictive of $SVA \geq 5$ cm. Univariate comparisons of patient demographics, HRQoL scores and surgical indication were then performed around this cutoff using two-way Student's t-tests for continuous variables and Fisher's exact test for categorical variables.

Significance was defined as $P < .05$ in all cases. A post-hoc power analysis was performed for both the global sagittal malalignment and clinical outcome cohort cohorts. Power was found to be $>95\%$ and $>80\%$ for detecting statistically significant differences in the global sagittal malalignment cohort's average SVA and the clinical outcome cohort's average L3FA, respectively.

Results

A total of 49 patients met our inclusion criteria, of whom 26 had 36" full length cassettes. Mean age was 70.1 ± 7.4 years, 43/49 (87.8%) were female, mean BMI was 29.9 ± 6.1 and mean ACCI was 3.9 ± 1.9 . Mean ODI at presentation was 41.8

± 14.1 , and the mean PROMIS physical and mental sub-scores were 12.1 ± 3.0 and 13.5 ± 3.6 , respectively. Mean SVA was 5.1 ± 2.1 cm, mean PI was 68.1 ± 11.9 , mean PT was 27.6 ± 9.6 and mean LL 54.4 ± 15.8 (mean PI-LL mismatch 13.7 ± 15.9). Mean L3SD was 36.6 ± 18.7 mm while mean L3FA was 4.7 ± 9.9 . The majority of patients had either L3-L5 (26/49, 53.1%) or L4-S1 (18/49, 36.7%) TDS. Other presentations included L2-L4 (2/49, 4.1%) and L3-L4 + L5-S1 non-contiguous TDS (3/49, 6.1%). Meyerding grading was performed for all levels.¹² For L2-L3, 2/2 (100%) of patients were grade 1. For L3-L4, the average grade was $1.1 \pm .3$ (28/31 (90.3%) of patients were grade 1, and 3/31 (9.7%) were grade 2). For L4-L5, the average grade was $1.1 \pm .4$ (38/44 (86.4%) of patients were grade 1, and 6/44 (13.6%) were grade 2). For L5-S1, 21/21 (100%) of patients were grade 1.

In a stepwise multivariate logistic regression of those patients with full length cassettes ($n = 26$), only L3FA (OR 1.4, 95% CI) was independently predictive of $SVA \geq 5$ cm (area under the curve = .96). ROC analysis indicated a cutoff of L3FA cutoff of ≥ 2.5 was optimally predictive of $SVA \geq 5$ cm (Figure 2). When patients with a pre-operative SVA above and below 5 cm were compared, standing PI, SS, and PT were equivalent between groups. The LL of the elevated SVA group was significantly lower than in the normal SVA group (48.7 ± 19.5 vs 63.3 ± 6.9 mm, $P < .021$). L3SD was significantly higher in the elevated SVA group than in the normal SVA group (49.3 ± 12.9 vs 28.8 ± 9.2 , $P < .001$), as was L3FA (11.6 ± 7.9 vs -3.2 ± 6.1 , $P < .001$). Sensitivity and specificity analyses demonstrated that an L3FA threshold greater than 2 degrees yielded a sensitivity and specificity for predicting an $SVA > 5$ cm of 93% and 92%, respectively. When comparing the subgroup of patients with full length cassettes to the entire clinical cohort by demographics, radiographic parameters, and level of spondylolisthesis, there were no significant differences between the two groups (Table 1).

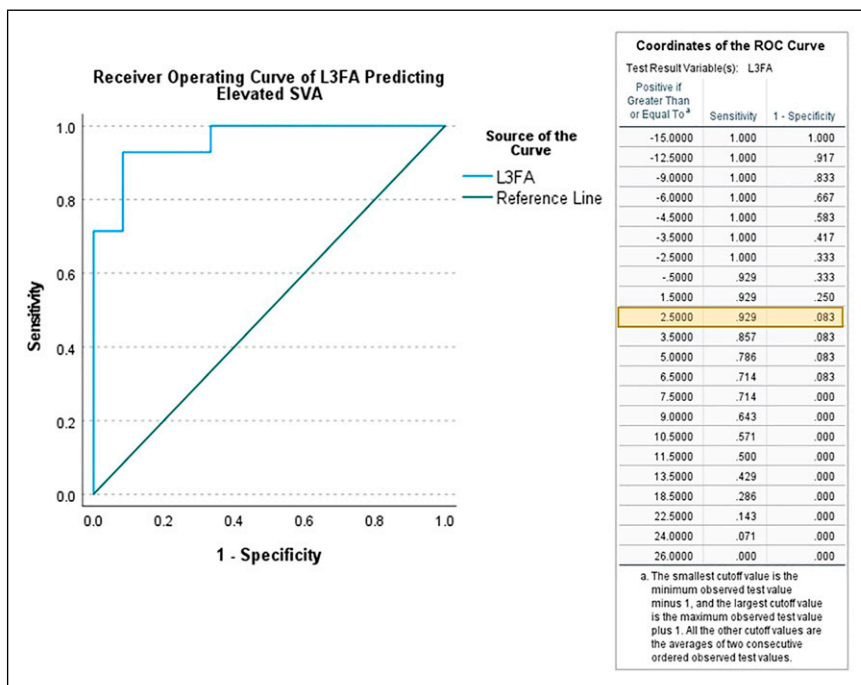


Figure 2. Receiver operating curve analysis demonstrating the ideal cutoff value of 2.5 degrees for lumbar radiographic values independently predictive of SVA ≥ 5 cm Legend: SVA = Sagittal Vertical Axis L3FA = Flexion angle of the L3 vertebral body.

Table 1. Comparison of demographic, radiographic and HRQoL parameters of patients with lower vs elevated L3FA.

	Lower L3FA (N = 21)	Elevated L3FA (N = 28)	Univariate P-value
Patient demographics			
Age	72.7 ± 6.9	68.2 ± 7.3	0.03
Sex (% female)	20 / 21	23 / 28	0.2
BMI	29.1 ± 5.6	30.5 ± 6.5	0.4
Age-adjusted	4.0 ± 1.7	3.9 ± 2.1	0.9
Charlson score			
Radiographic parameters			
Pi	65.1 ± 9.1	70.3 ± 13.4	0.1
Pelvic tilt	26.3 ± 10.8	28.4 ± 8.6	0.4
Sacral slope	39.8 ± 9.8	41.5 ± 12.3	0.6
PI-II mismatch	5.0 ± 12.1	20.1 ± 15.4	< 0.001
L3 SD	21.7 ± 11.6	47.7 ± 14.7	< 0.001
Patient reported outcomes			
ODI	33.2 ± 13.1	44.1 ± 13.0	0.006
Promis physical subscore	12.8 ± 2.6	11.5 ± 2.9	0.1
Promis mental subscore	13.7 ± 3.8	13.7 ± 3.6	0.5
Surgical indication			
Offered surgery	7 / 21 (33.3%)	19 / 28 (67.9%)	0.02

In a univariate analysis of the entire cohort (n = 49), among patient factors only younger age was associated with an increased L3FA (68.2 ± 7.3 years vs 72.7 ± 6.9 years in low L3FA group, P = .03). Increased L3SD (47.4 ± 14.7 mm vs 21.7 ± 11.6 mm, P < .001), decreased LL (50.1 ± 18.2° vs 60.1 ± 9.6, P = .03) and increased PI-LL mismatch (20.1 ± 15.4 vs

5.0 ± 12., P < .001) were also associated with increased L3FA. While PROMIS scores were equivalent between high vs low L3FA groups, an increased L3FA was associated with an elevated ODI (44.1 ± 13.0 vs 33.2 ± 13.1, P = .006, Table 1).

The influence of L3FA on failure of non-operative treatment was evaluated. A significantly larger number of patients

with elevated L3FA angles (19/28, 67.9%) were offered surgery than those with lower L3FA angles (7/21, 33.3%, $P = .02$).

Discussion

TDS is an uncommon multi-level spondylolisthesis with unclear sagittal alignment and clinical severity implications. In a retrospective analysis of 49 patients with TDS managed over a 4-year period, we found that increased L3FA, or downward flexion of the L3 vertebral body, was independently associated with elevated SVA. A L3FA cutoff of ≥ 2.5 was predictive of a SVA ≥ 5 cm. Patients in the present study with TDS had a mean SVA of 51.3 ± 38.8 mm (range: -12.8 – 135.8 mm), which is markedly greater than that of 22.0 ± 8.0 mm previously measured in patients with single-level DS.¹⁹ Patients above the L3FA cutoff had an increased PI-LL mismatch, elevated ODI scores and were more likely to fail nonoperative treatment. Findings suggest that the relative flexion of the L3 vertebra in the setting of TDS may be associated with global spinal balance and patient reported outcomes.

Native spinopelvic morphology is thought to play a significant role in dictating mechanical stresses at the lumbosacral junction, thereby predisposing certain individuals to the development of DS.²⁰ It has been previously hypothesized that a higher PI requires increased LL to maintain a neutral sagittal alignment, thereby placing higher forces on the posterior articular joints and excess mechanical stresses on the posterior facets.^{8,21,22} The resulting accelerated posterior arthritis, in conjunction with increased baseline inclination of the vertebral endplate of L5 due to increased PI, has been postulated to be a significant predisposing factor to vertebral slippage.^{23,24} All of these parameters have been noted in prior research to be more severely aberrant in patients with TDS compared with single-level DS.¹⁰ Thus, it is reasonable to speculate that TDS may occur due to more severely abnormal native spinopelvic morphology, more severe degenerative facet changes and vertebral slippage and, ultimately, compensatory flattening of LL and elevated SVA. Roussouly et al.²¹ classified the normal spine into four morphotypes based on increasing PI and sacral slope (SS). It has been previously speculated that Roussouly morphotype 4, which includes a SS of >45 degrees with hyperlordosis and a high PI, may predispose to posterior arthritis and degenerative spondylolisthesis.²⁵ Interestingly, the apex of lumbar curvature of Roussouly Type 4 spines has been reported to be most typically centered at L3, which is more proximal than the average apex of lumbar lordosis in the general population.²¹ Another recent work concurred with Roussouly regarding the proximal migration of the apex towards L3 in high PI individuals.²⁶ However, the authors posited that this finding was due to a higher PI requiring the recruitment of more proximal lumbar segments to contribute a large proportion of the lumbar spine's total lordosis, which ultimately drove the apex proximally.²⁶ This finding is

somewhat in contrast to Roussouly, because it emphasizes the importance of the proximal lordotic segments, rather than the lower lumbar arc, in terms of determining the shape of the global lumbar lordosis.^{21,26} These works indicate a connection between a high PI and a more proximal lumbar apex, namely at L3. As previously mentioned, a high PI has also been associated in prior work with TDS. It is difficult to draw mechanistic conclusions between increased L3FA and worse clinical outcomes amongst TDS patients noted in the present work. However, it is possible that the loss of the natural L3 apex via increased L3FA (downward flexion) reflects deterioration of a crucial structural element of the lumbar spine, which both drives the apex further proximally and places further lordotic demand on the proximal lumbar spine until it is unable to compensate further. This specific pathologic cascade, detected via increased L3FA, may be linked to deterioration of both the harmonious balance of the lumbar spine and global sagittal balance in patients predisposed to TDS.

The tendency toward poor global spinal balance has been more commonly noted in patients with high-grade DS vs low-grade DS.^{27,28} Mechanistic factors that have been proposed for the association between higher grade DS and poor global spinal balance include a pathologic cascade that involves more severe anterior vertebral slippage, which leads to flattening of the lumbar spine via decreased LL.⁸ Given that PI is an anatomic feature and thus fixed after birth, decreased LL leads to increased PI-LL mismatch and ultimately results in a flexion moment of the lumbar spine and the anterior displacement of SVA.^{8,29} This emphasis on the important relationship between PI-LL and elevated SVA is consistent with the present work, which found an SVA >5 cm in 54% of TDS patients and increased PI-LL mismatch in patients above the L3FA cutoff. However, it should be noted that an increased SVA may also be representative of the severe degree of stenosis in patients with TDS. Shin et al. reported that patients with increased SVA and PI-LL mismatch in the setting of spinal stenosis often have improved alignment following decompressive surgery because they no longer need to lean forward to unbuckle their ligamentum flavum and decrease their stenosis symptoms.³⁰ This concept of spinal alignment improving by virtue of decompression alone is well established in the adult spinal deformity literature, in which patients with sagittal malalignment and a flexible spine may achieve improved alignment with a decompression alone rather than a multilevel fusion.^{31,32} It is therefore possible that the SVA in TDS patients with an elevated L3FA is inflated by the patient's response to stenosis rather than a purely mechanical problem. This can be better understood by comparing pre- and post-operative imaging, which was not analyzed by the present work.

The preliminary clinical findings of this work suggest that a relatively flexed L3 in patients with TDS is correlated with both elevated SVA and worse ODI scores. This association is not surprising given that prior work has commented on the association between SVA above 4.7 cm and the presence of

severe disability as measured by ODI above 40 in the setting of adult spinal deformity.³³ It may be speculated that ODI is a sensitive tool for assessing relative disability within the TDS population and that L3FA may be a primary driver behind poor ODI scores.

Associating TDS with more severe SVA elevation and predicting poor global sagittal balance via L3FA in the setting of TDS is important for a number of reasons. In comparison with single-level DS, TDS may be best seen as existing more commonly in the category of true adult spinal deformity, rather than as a focal, lumbar degenerative spinal pathology. Surgical treatment of TDS is often targeted at restoring LL and sagittal balance, and frequently requires much more extensive instrumentation and more frequent use of osteotomies compared with single-level DS. Surgical intervention for TDS thus incurs risks specific to adult spinal deformity. Elevated SVA is a significant risk factor for proximal junctional kyphosis and proximal junctional failure in adult spinal deformity patients after fusion.^{34,35} An unrecognized elevated SVA prior to a fusion can lead to a locked position of fused lumbar vertebrae and subsequent fixed forward inclination of the trunk.³⁶⁻³⁹ This alteration in sagittal alignment parameters and spinopelvic angulation have been shown to be related to significantly worse postoperative back and leg pain, increased rates of radicular symptoms, and a higher rate of adjacent segment degeneration.⁴⁰⁻⁴³ L3FA appears to reliably correlate with elevated SVA in the TDS population and can be measured on lumbar films, which avoids the need for 36-inch full length cassette films that are both expensive, and inconsistently available in the community setting.⁴⁴⁻⁴⁶

The retrospective nature of this work creates a limitation in terms of assessing how L3FA and L3SD may change or improve after successful non-operative treatment, because routine follow-up imaging is not routinely obtained in these patients. Future work may prospectively assess how L3FA and L3SD change or improve over time in patients who are successfully treated non-operatively. This work has several limitations beyond those intrinsic to retrospective studies. A critical limitation of this work is its small sample size. Given the relative rarity of TDS in the general population, the number of patients (N = 49) available from a single institution was proportionately similar to that of a prior multicenter (13 institutions) study of TDS patients (n = 78).¹⁰ Additionally, a post-hoc power analysis demonstrated that this study was adequately powered. Another limitation is the lack of full length 36" cassettes for all patients. This is the result of recent increased utilization of full length imaging as routine standard of practice at our institution due to the availability of full length imaging (EOS). More consistent imaging availability would be preferred in future work. Additional future work may include in vivo biomechanical studies to establish a causal link between L3 deformity and global sagittal malalignment. We also seek to understand the utility of L3FA in patients with single-level spondylolisthesis, as the present work sought to initially evaluate this metric with patients with

TDS alone due to the relative severity of this group's pathology. Finally, it is important to note that we are only discussing patients with TDS who have symptomatic spinal stenosis. These were only TDS patients whose pathology was severe enough to warrant surgery. This highlights that we are not describing TDS as a singular pathology, but only TDS within the surgical stenosis population. Describing TDS more fully would likely require a large multi-institutional prospective study.

In conclusion, L3FA ≥ 2.5 in patients with TDS can serve as a surrogate for SVA ≥ 5.0 cm and is predictive of poor patient reported outcome scores and the failure of non-operative management. L3FA may be a rapid way to evaluate the clinical impact of TDS on these potentially vulnerable patients as well as a target for surgical correction in the future.

Declaration of Conflicting Interests

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IRB Approval

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