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Does vertebral level of pedicle subtraction osteotomy correlate with degree of spinopelvic parameter correction?

Clinical article

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Object. Pedicle subtraction osteotomy (PSO) is a spinal realignment technique that may be used to correct sagittal spinal imbalance. Theoretically, the level and degree of resection via a PSO should impact the degree of sagittal plane correction in the setting of deformity. However, the quantitative effect of PSO level and focal angular change on postoperative spinopelvic parameters has not been well described. The purpose of this study is to analyze the relationship between the level/degree of PSO and changes in global sagittal balance and spinopelvic parameters.

Methods. In this multicenter retrospective study, 70 patients (54 women and 16 men) underwent lumbar PSO surgery for spinal imbalance. Preoperative and postoperative free-standing sagittal radiographs were obtained and analyzed by regional curves (lumbar, thoracic, and thoracolumbar), pelvic parameters (pelvic incidence and pelvic tilt [PT]) and global balance (sagittal vertical axis [SVA] and T-1 spinopelvic inclination). Correlations between PSO parameters (level and degree of change in angle between the 2 adjacent vertebrae) and spinopelvic measurements were analyzed.

Results. Pedicle subtraction osteotomy distribution by level and degree of correction was as follows: L-1 (6 patients, 24°), L-2 (15 patients, 24°), L-3 (29 patients, 25°), and L-4 (20 patients, 22°). There was no significant difference in the focal correction achieved by PSO by level. All patients demonstrated changes in preoperative to postoperative parameters including increased lumbar lordosis (from 20° to 49°, $p < 0.001$), increased thoracic kyphosis (from 30° to 38°, $p < 0.001$), decreased SVA and T-1 spinopelvic inclination (from 122 to 34 mm, $p < 0.001$ and from +3° to −4°, $p < 0.001$, respectively), and decreased PT (from 31° to 23°, $p < 0.001$). More caudal PSO was correlated with greater PT reduction ($r = -0.410$, $p < 0.05$). No correlation was found between SVA correction and PSO location. The PSO degree was correlated with change in thoracic kyphosis ($r = -0.474$, $p < 0.001$), lumbar lordosis ($r = 0.667$, $p < 0.001$), sacral slope ($r = 0.426$, $p < 0.001$), and PT ($r = -0.358$, $p < 0.005$).

Conclusions. The degree of PSO resection correlates more with spinopelvic parameters (lumbar lordosis, thoracic kyphosis, PT, and sacral slope) than PSO level. More importantly, PSO level impacts postoperative PT correction but not SVA. *(DOI: 10.3171/2010.9.SPINE10129)*

Key Words • pedicle subtraction osteotomy • sagittal alignment • pelvic tilt • imbalance • adult deformity

Spinal deformity in the adult is commonly a 3D pathology. However, evidence points toward the clinical impact of deformity being mostly related to the sagittal plane, with little correlation between coronal deformity and self-reported disability. The Classification of Adult Deformity[20] was primarily built on clinical impact parameters, and it highlights lumbar lordosis as well as global sagittal alignment. Work leading to the classification did not identify a significant clinical impact of coronal plane parameters.[20] Additionally, in the commonly known iatrogenic condition of flatback syndrome,

Abbreviations used in this paper: PI = pelvic incidence; PSO = pedicle subtraction osteotomy; PT = pelvic tilt; SPI = spinopelvic inclination; SVA = sagittal vertical axis.

This article contains some figures that are displayed in color online but in black and white in the print edition.

disability has also been tied to global imbalance due to previous instrumentation perturbing sagittal plane alignment.[8] In other studies, it has been shown that the impact of sagittal plane alignment in adults includes spinal parameters and pelvic parameters.[24]

Although the role of sagittal alignment in adults has emerged as a key parameter determining outcome, achieving ideal alignment in the setting of adult deformity remains challenging. There is a growing interest in accurately defining optimal balance in a quantitative manner such that surgical goals can be precisely defined. In moving beyond simply defining alignment by plumbline offsets (for example, SVA), efforts directed at increasing our understanding of standing balance have included analysis of pelvic position (for example, PT). Significant changes in the spinopelvic relationship have been demonstrated in the setting of aging and sagittal deformity.[21,23] In further support of the role of the pelvis in spinal alignment, PI, a morphological character of the pelvis, has been shown to have a strong correlation with lumbar lordosis. Numerous studies have emphasized the importance of spinopelvic balance, whereas the specific impact of realignment techniques has not been fully defined.[2,15]

Corrective surgery to restore sagittal balance in adults is approached in a number of manners dependent on the pathology at hand, comorbidities, patient age, and the experience of the surgeon. With significant demographic shifts occurring in Western societies, deformity in adults will emerge as a significant health care issue. De novo degenerative and iatrogenic deformities will markedly impact the spine surgical practice in the near future. This in turn will drive increased application of realignment surgeries. Although the techniques for the latter are well described, increased application of osteotomies has not met with improved surgical planning tools.

Numerous osteotomy techniques have been described to correct adult deformity. For marked realignment applied focally, the PSO technique has become popular, and several reports have described associated spinal parameter correction.[1,4,5,7,10,17,27] In addition, several reports have documented high complication rates, as high as 50%, associated with this technique.[1,4,5,7,10,17,27] However, to date, there is a paucity of data regarding PSO in terms of its impact on spinopelvic parameters. A large data set and multicenter analysis are lacking. Such a study is of marked significance because it can lead to greater understanding of the increasingly popular PSO surgery with regard to global alignment and pelvic parameters, which are critical for clinical success. Information gained will permit better operative planning for the surgeon and improved outcomes for patients.

The purpose of this study was to quantify the impact of a lumbar PSO on sagittal spinopelvic alignment. More specifically, this study aimed to analyze the correlation between PSO location, the degree of correction achieved at the site of the osteotomy, and the degree of change in common spinopelvic parameters. Enrollment was limited to adults with significant sagittal imbalance who were treated with lumbar PSO. The hypothesis was that the level and degree of correction of a PSO will impact not only regional and global sagittal spinal parameters but also pelvic parameters to a variable degree. A linear correlation between osteotomy degree and pelvic correction was not expected.

Methods

Patient Selection

This is a multicenter retrospective study (8 institutions in the US) that was approved by each institutional review committee. Inclusion criteria included any adult patient (> 20 years old at time of surgery) with a documented regional or global sagittal plane deformity (Table 1) who underwent surgical treatment including a PSO in the lumbar spine (L1–5). Exclusion criteria included any patient with underlying neurological or neuromuscular condition, known hip, knee, ankle, or foot pathology that might affect joint position, more than 1 PSO, or sagittal radiographs without femoral heads or C-7 and T-1 included or without the PSO site clearly visible to calculate degree of correction.

Data Collection

Demographic data were collected for each patient (age, sex, weight, and height). All patients had pre- and postoperative (minimum 3 months of follow-up) radiographic spinal evaluation in the free-standing position.[9] The patients were instructed to assume a comfortable standing posture with feet approximately shoulder width apart and arms positioned at approximately 45° of forward shoulder flexion[9,16] and their fingertips placed on the midclavicular line.

Radiographic films were downloaded from PACS systems (DICOM format) or digitized through a Vidar scanner (Vidar Systems Corp.) with 75-dpi resolution and 12 gray levels.

Radiological Measurements

Preoperative and postoperative sagittal spinopelvic parameters were evaluated using Spineview software (Laboratory of Biomechanics, ENSAM-CNRS), a validated computer-based tool that enables quantitative measurements of the spine and pelvis.[6,19]

The spinal sagittal plane was described by calculating the L1–S1 lumbar lordosis, the T4–12 thoracic kyphosis, the T10–L1 thoracolumbar kyphosis, the SVA, and the T-1 SPI and T-9 SPI, which are the angles between the vertical plumb line and the line drawn from the vertebral bodies of T-1 or T-9, respectively, and the center of the bicoxofemoral axis (Fig. 1).

The sagittal pelvic morphology and orientation were described by the PT, which is the angle between the verti-

TABLE 1: Radiographic inclusion criteria (need to meet only 1)

Parameter	Cutoff Value
SVA	>8 cm
lumbar lordosis	<20°
PT	>25°
thoracolumbar kyphosis	>20°
local lumbar kyphosis	>20°

cal line and the line through the midpoint of the sacral plate to the axis of the femoral head (retroversion is then measured as a PT increase, anteversion as a PT decrease); the sacral slope, defined as the angle between the horizontal and the sacral plate; and the PI, defined as the angle between the perpendicular to the sacral plate at its midpoint and the line connecting this point to the axis of the femoral head (Fig. 2).

The PSO degree of resection (pedicle subtraction angle) was defined as the change of the angle formed by the lower vertebral endplate of the adjacent cephalic vertebra and the upper vertebral endplate of the adjacent caudal vertebra (Fig. 3).

Statistical Analysis

Data were statistically analyzed using SPSS software (SPSS, Inc.). Changes in pre- and postoperative measurements of the spinopelvic parameters were evaluated using a paired Student t-test (level of significance set at 0.05), and the normality of data was evaluated using the Shapiro-Wilk test. Correlation analysis between correction obtained and PSO parameters (vertebral level and degree) was pursued using Spearman (for vertebral levels) and Pearson (for PSO angle) coefficients of correlations.

Results

Data Distribution

Using the Shapiro-Wilk test, all pre- and postoperative parameters were found to be normally distributed ($p > 0.05$), except for the following: weight, height, preoperative thoracolumbar kyphosis ($p = 0.027$), and postoperative T-1 sagittal tilt ($p = 0.004$).

Group Description

The study included 70 adult patients (57 women and 13 men), with a median age of 53 years (Table 2). Among this group of patients, 16 underwent primary surgery and 54 underwent revision surgery. At the time of the PSO surgery, the most common diagnoses were iatrogenic sagittal imbalance (in 56 patients) and kyphoscoliosis (in 8; Table 3). The PSO surgery was performed as part of a revision surgery in 54 patients, and for this subset of patients, the most common original diagnoses were idiopathic scoliosis (in 34 patients), degenerative deformity (in 12), and lumbar degeneration (in 6; Table 4). The PSO distribution by level and mean degree of correction is provided in Table 5. There was no significant difference in the focal correction achieved based on PSO level.

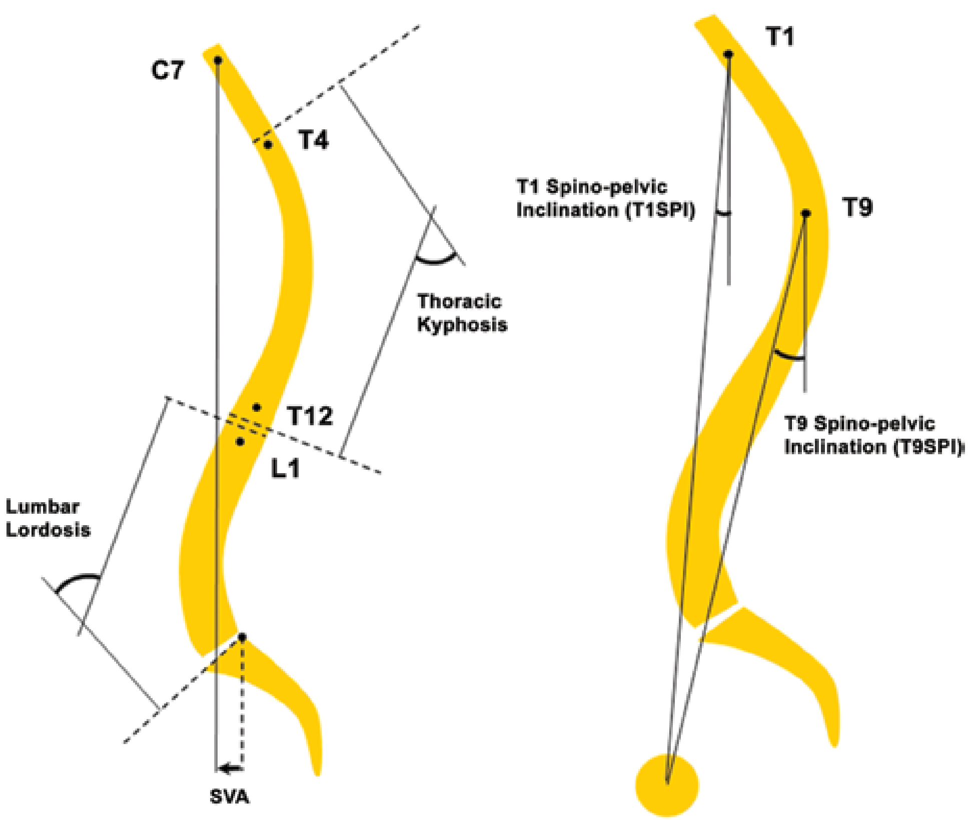

Fig. 1. Measures of sagittal spinal radiological parameters. The SVA is the horizontal distance between a C-7 plumb line dropped vertically from the center of the C-7 vertebral body and the posterior superior aspect of S-1. Positive and negative values of SVA reflect the C-7 plumb line anterior and posterior to the posterior superior aspect of S-1, respectively. Thoracic kyphosis was measured as the Cobb angle from T-4 to T-12, and lumbar lordosis was measured as the Cobb angle from L-1 to S-1. The T-1 SPI and T-9 SPI are the angles between the vertical plumb line and the line drawn from the vertebral bodies of T-1 or T-9, respectively, to the center of the bicoxofemoral axis.

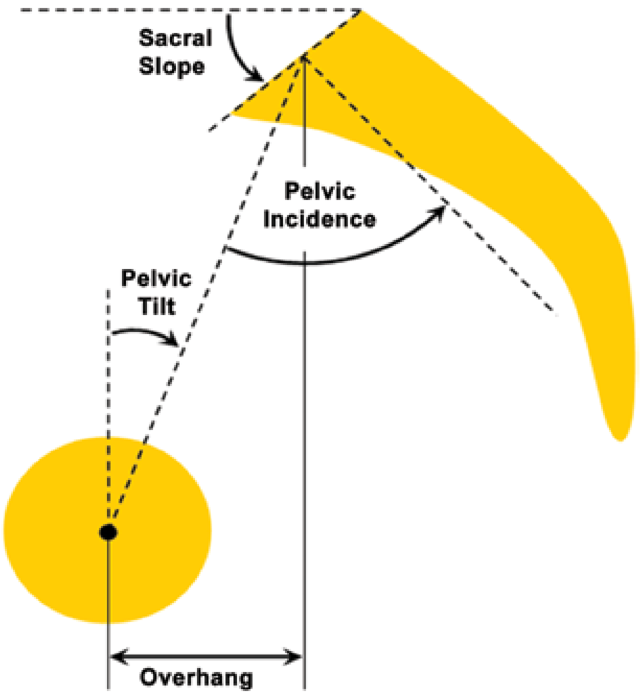

Fig. 2. Pelvic parameters. Sacral slope is defined as the angle subtended by a horizontal reference line and a line drawn parallel to the sacral endplate. Pelvic incidence is the angle subtended by a line dropped perpendicular to the sacral endplate and a line drawn from the center of the sacral endplate to the center of the bicoxofemoral axis. Pelvic tilt is defined as the angle subtended by a horizontal reference line and a line drawn from the center of the sacral endplate to the center of the bicoxofemoral axis. Note that PI = sacral slope + PT.

Change in Regional Curves and Global Balance

In comparison with preoperative measurements, we observed the following statistically significant postsurgical differences: an increase in lumbar lordosis (from 20° preoperatively to 49° postoperatively, $p < 0.001$), a more pronounced thoracic kyphosis (from –30° preoperatively to –38° postoperatively, $p = 0.001$), and a less pronounced thoracolumbar kyphosis (from –10° preoperatively to –7° postoperatively, $p = 0.026$) (Table 6).

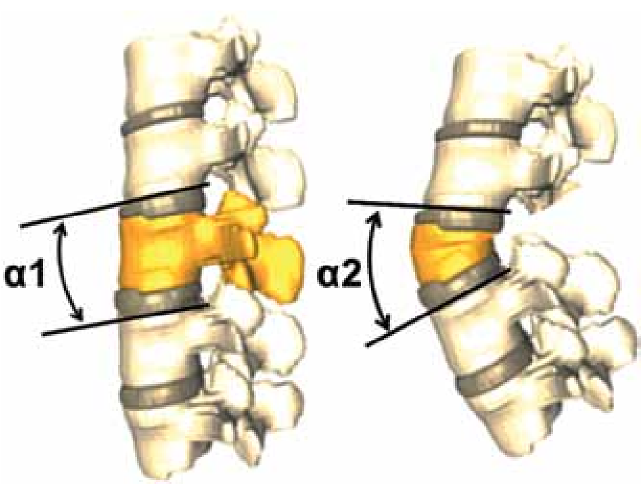

Fig. 3. Measurement of the pedicle subtraction angle, which is the variation of the angle formed by the lower vertebral endplate of the adjacent cephalic vertebra and the upper vertebral endplate of the adjacent caudal vertebra.

TABLE 2: Demographic data in 70 patients who underwent PSO*

Parameter	Age (yrs)	Weight (kg)	Height (cm)	BMI
median	53	68	163	25
25th percentile	44	59	157	23
75th percentile	63	76	168	28

* BMI = body mass index.

A subdivision of the study group by number of fused levels (short fusion below T-10 [in 24 patients] vs long fusion above T-10 [in 46 patients]) led to the same conclusions in terms of change in thoracic kyphosis. Specifically, the short fusion group's thoracic kyphosis was 12° greater postoperatively than preoperatively ($p = 0.001$), whereas there was an increase of 5° ($p = 0.02$) for the long fusion group.

In terms of global sagittal balance, a significant decrease in the SVA was observed between pre- and postoperative measurements (from 122 mm preoperatively to 34 mm postoperatively, $p < 0.001$). Similarly, a decrease in the T-1 SPI (from +3° preoperatively to –4° postoperatively, $p < 0.001$) was also observed, suggesting that the T-1 vertebra moved behind the femoral heads (negative value of T-1 SPI). Notably, there were no statistically significant differences in the preoperative, postoperative, or change from pre- to postoperative SVA between the subset of patients who underwent a shorter instrumented fusion (upper-most instrumented vertebra caudal to T-9) and the subset of patients who underwent a longer instrumented fusion (uppermost instrumented vertebra cephalad to T-5).

Change in Pelvic Parameters

For the pelvic parameters, as expected, the PSO surgery did not affect the PI, because it is a morphological parameter. In contrast, a significant PT decrease was noted postoperatively (from 31° preoperatively to 23° postoperatively, $p < 0.001$), suggesting that the PSO surgery reduced pelvic retroversion (Table 7).

Pedicle Subtraction Osteotomy Versus Change in Radiographic Parameters

In terms of regional changes of spinal curvatures,

TABLE 3: Diagnosis at the time of the PSO surgery

Diagnosis at PSO	No. of Patients (%)
iatrogenic sagittal imbalance	56 (80)
kyphoscoliosis	8 (11)
ankylosing spondylitis	2 (3)
trauma	1 (1)
posttramatic kyphosis	1 (1)
infectious spondylolitis	1 (1)
idiopathic scoliosis	1 (1)

TABLE 4: Original diagnosis for the 54 patients who underwent a revision surgery

Original Diagnosis	No. of Patients (%)
idiopathic scoliosis	34 (63)
degenerative deformity	12 (22)
lumbar degeneration	6 (11)
ankylosing spondylitis	1 (2)
posttraumatic kyphosis	1 (2)

lumbar lordosis and thoracic kyphosis were correlated with the PSO degree of resection (r = −0.66 and r = 0.42, respectively) but not with the PSO vertebral level. None of the parameters related to the sagittal global balance (SVA, T-1/T-9 SPI) were correlated with the PSO vertebral level or degree of resection (Table 8).

As for the pelvic parameters, the change in PT was found to be correlated with the PSO degree of resection (r = 0.44) and the PSO vertebral level (r = −0.41). In other words, a wide resection and a more caudal PSO were correlated with greater PT reduction (r = −0.41, $p < 0.05$). The PSO vertebral level is a categorical data set that numerically assigns the vertebral levels, with L-1 corresponding to a value of 1, L-2 with 2, and so forth. To test the correlation of this categorical variable with PSO degree of resection, the Spearman rho was used (see Table 5).

Discussion

By training, spine specialists tend to focus analysis and treatment purely on the vertebral column, with the aim of achieving standing balance for patients suffering from deformity. However, it is increasingly evident that balance involves a complex interaction between the lower extremities, the pelvis, and the spine. Treatment of a spinal deformity will impact the entire standing axis, and operative intervention must thus be carefully planned to anticipate the impact beyond the immediate surgical field. A number of formulas and alignment guides have emerged to help optimize spinal realignment. It is notable that the data set used in this study reveals patients with low lumbar lordosis (mean 20°) and that a preoperative mismatch to the measured PI is present. The formula for matching lordosis in a patient-specific manner has been proposed as follows: lumbar lordosis = PI + 10°.[22] Thus, the theoretical optimal lordosis for the patients in this study, with a mean PI of 55°, is 65°. This suggests that, in light of PI considerations, the lordosis abnormalities for the patients in this study were not as mild as they may initially appear. The amount of segmental correction obtained in the study patients was variable, with a subset of fairly modest corrections, ranging up to several very large corrections. This is likely reflective of the multicenter study design and the perceived surgeon needs for extent of resection.

The most immediate measurable impact of surgical treatment for spinal deformity relates to the regional curvature of the spine across an instrumented region. Beyond the regional alignment, compensation through adjacent

TABLE 5: Pedicle subtraction osteotomy distribution by vertebral level and focal correction (pedicle subtraction angle)*

PSO Level	No. of Patients	Focal Correction (°)	
		Mean ± SD	Range
L-1	6	24 ± 7	10–30
L-2	15	24 ± 12	8–42
L-3	29	25 ± 9	12–54
L-4	20	22 ± 12	8–46

* The degree of focal correction provided by the PSO did not differ significantly based on the level at which the PSO was performed (p = 0.91, ANOVA analysis).

alignment changes can occur. The increase in thoracic kyphosis may be due both to a compensatory mechanism (short fusion group) and to a direct surgery-related change (long fusion group). In turn, the change in contour of the spine will lead to modifications in mass distribution around the pelvis in the standing position. This will then impact the relative version (rotation of the pelvis around the acetabulum, measured as PT) of the pelvis and the translational offset from the feet.[13] Finally, this will then impact relative hip, knee, and ankle flexion and position. Although the distribution of mass and alignment of parts around the standing axis may appear very theoretical, the clinical impact of poor postoperative alignment is very real, leading to clinical failures and often a series of operative interventions attempting to recapture proper alignment of the patient. Mastering techniques of realignment through complex and risky osteotomies is insufficient to ensure good outcome. It is only through measured application that these tools can be put to use in the best interests of the patient suffering from spinal deformity. Thus, we must improve our understanding of increasingly common realignment methods such as the PSO.

Recent work by Lafage et al.[14] has started to define the impact of regional alignment change on global balance, pelvic position, and pelvic version. Most notably, the high clinical impact on self-reported function (Scoliosis Research Society outcomes, Oswestry Disability Index, 12-item Short Form Health Survey) by PT has been established.[12] Within that context, the current study offers important analyses related to level and degree of significant spinal realignment (via PSO) on these pertinent spinopelvic measures. The data in this study confirm that increasing degrees of vertebral resection by a PSO will permit increasing amounts of change in regional alignment in the lumbar spine and an increase in thoracic kyphosis. The finding that increasing degrees of resection are only weakly correlated with change in SVA (r = 0.23) is not entirely intuitive and supports clinical application of refined predictive formulas for planning realignment surgery. Interestingly, the multicenter data also indicate a rather consistent range of correction afforded through a 1-level PSO in the lumbar spine. The mean correction of 24° at L-1 and L-2, 25° at L-3, and 22° at L-4 can thus offer benchmarks when planning to use this osteotomy technique. Although other single-center reports have

TABLE 6: Preoperative and postoperative radiological parameters*

Measurement	Lumbar Lordosis (°)	Thoracic Kyphosis (°)	Thoracolumbar Kyphosis (°)	SVA (°)	T-1 SPI (°)	T-9 SPI (°)
preop	20 ± 20	−30 ± 21	−10 ± 16	122 ± 82	3 ± 8	−8 ± 9
postop	49 ± 15	−38 ± 18	−7 ± 10	34 ± 57	−4 ± 5	−11 ± 6
change	29 ± 17	−8 ± 12	3 ± 12	−88 ± 57	−7 ± 6	−3 ± 6
p value†	<0.001	0.001	0.026	<0.001	<0.001	<0.001

* Values are presented as mean ± 1 SD.
† Paired t-test between pre- and postoperative measurements.

described significantly greater degrees of realignment with a PSO, this multicenter study demonstrates that this should be considered uncommon.[3–5,11]

An important finding in this study relates to the level of PSO in relation to change in spinopelvic alignment. No significant correlation between osteotomy level and global spinal balance, quantified by SVA, has been observed. However, correlation between PSO level and PT was established (r = −0.41). This indicates that changing the distribution of mass above the pelvis impacts the version, measured by PT, of the pelvis. The lack of correlation between PSO level and SVA requires further investigation but may relate to the pelvis acting as principal regulator for subtle changes in lumbar alignment (for example, PSO at L-1 vs L-4). Significant changes in lumbar lordosis by PSO were linked to increasing thoracic kyphosis (r = 0.42) and would appear to reflect a compensatory alignment or positional modification in the operative position. The SVA was found to change significantly through the applied osteotomies, but a linear correlation with degree or level of PSO was not identified.

Prior reports have suggested that simple trigonometric calculations can be made preoperatively based on the C-7 plumb line and the level of the osteotomy to accurately predict the necessary osteotomy size required to achieve a specific sagittal alignment.[18,25,26] Our findings contrast with these prior reports in that no linear association between PSO level and degree of change in the SVA was identified following PSO in the present study. Possible explanations are that a nonlinear correlation may exist and that pelvic version accommodation is more significantly impacted, leaving a variable modification of the SVA. The previously reported simple trigonometric calculations are based on static measures of the spine that are assessed in isolation of the dynamic changes of the thoracic spine and pelvis that occur following PSO. For example, patients may partially accommodate for significant positive sagittal imbalance with pelvic retroversion (increased PT),[21] and following PSO, a change in PT occurs, with greater reduction in PT occurring with a more caudal PSO, as demonstrated in the present study.

A larger study group and application of nonlinear correlation analyses will follow to clarify. In addition, the correlations observed will be further analyzed from a clinical outcomes perspective. The latter has been performed for baseline malalignment and more recently in the context of adult spinal deformity through multicenter work. However, a focused analysis in the setting of PSO by region and degree of spinopelvic realignment is lacking (Fig. 4).

TABLE 7: Spinopelvic parameters and p values*

Measurement	PI (°)	PT (°)	Sacral Slope (°)
preop	55 ± 13	31 ± 12	24 ± 12
postop	56 ± 13	23 ± 10	32 ± 10
change	0 ± 2	−8 ± 10	8 ± 10
p value†	0.517	<0.001	<0.001

* Values are presented as mean ± 1 SD.
† T-test between pre- and postoperative measurements.

Conclusions

Spinal deformity in the adult population is largely tied to a concern over maintaining alignment of the spine and global balance in the sagittal plane. In addition to the SVA, pelvic parameters including the PI and PT are recognized as important in the quantification of balance. Osteotomies are increasingly applied in the setting of adult deformity such that balance can be reestablished. The PSO is one commonly used technique, although to date the impact of degree and level of osteotomy has not been defined. Predictive formulas for anticipating postoperative alignment following deformity surgery are emerging. This study has demonstrated that the degree of resection by PSO is not correlated in a linear fashion with change

TABLE 8: Correlation between PSO parameters and change in radiographic parameters

Measurement	PSO Vertebral Level*	PSO Degree of Resection†
Δ T4–12	−0.21	0.42‡
Δ L1–S1	0.25	−0.66‡
Δ SVA	0.11	0.23
Δ T-1 SPI	0.17	0.19
Δ T-9 SPI	0.04	0.10
Δ sacral slope	0.32§	−0.47§
Δ PT	−0.41‡	0.44§

* Evaluated using the Spearman rho.
† Evaluated using the Pearson rho.
‡ $p < 0.001$.
§ $p < 0.05$.

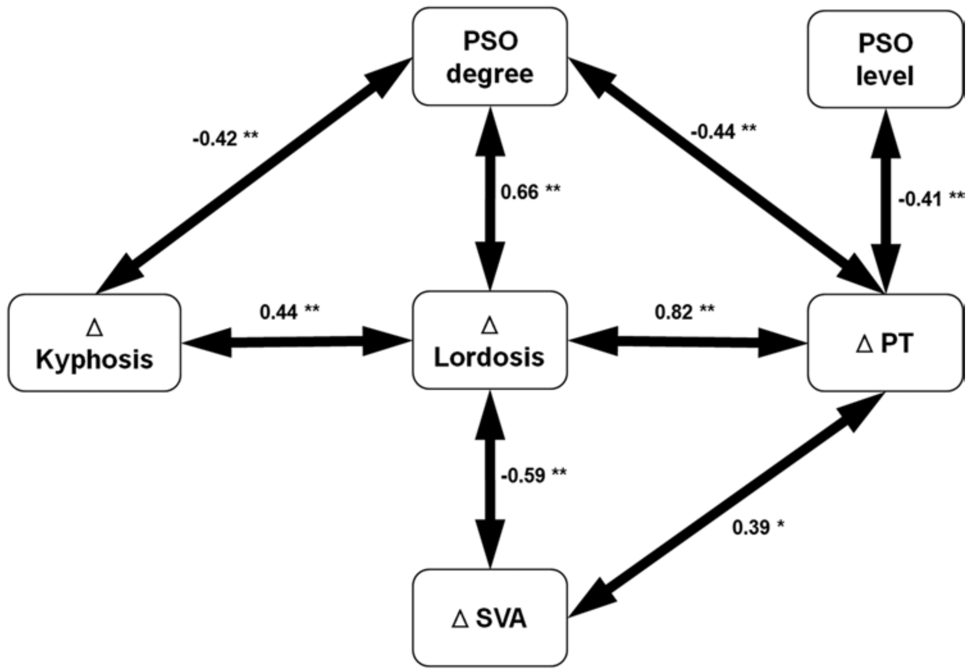

Fig. 4. Chain of correlation among the entire set of measured parameters. Correlation coefficients reflect the degree of correlation between the indicated parameters. Values between 0 and 0.3 (0 and –0.3) reflect a weak positive (negative) linear relationship. Values between 0.3 and 0.7 (–0.3 and –0.7) reflect a moderate positive (negative) linear relationship. Values between 0.7 and 1.0 (–0.7 and –1.0) reflect a strong positive (negative) linear relationship. *p < 0.05; **p < 0.001.

in SVA, whereas level of osteotomy and degree of correction are correlated with change in PT. These data will permit refinement of surgical planning for adult spinal deformity and permit the surgeon to better anticipate outcome, thus improving patient care.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Lafage, Schwab, Vira, Hart, Burton, Boachie-Adjei, Shelokov, Hostin, Shaffrey, Gupta, Akbarnia, Bess, Farcy. Acquisition of data: Lafage, Schwab, Hart, Burton, Boachie-Adjei, Shelokov, Hostin, Shaffrey, Gupta, Akbarnia, Bess. Analysis and interpretation of data: Lafage, Schwab, Vira, Smith, Boachie-Adjei, Shelokov, Hostin, Shaffrey, Gupta, Akbarnia, Bess, Farcy. Drafting the article: Lafage, Schwab, Vira. Critically revising the article: Lafage, Schwab, Vira, Smith, Shelokov, Hostin, Shaffrey, Gupta, Akbarnia, Bess, Farcy. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Lafage, Vira. Administrative/technical/material support: Schwab. Study supervision: Lafage, Schwab.

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