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Complication rates associated with open versus percutaneous pedicle screw instrumentation among patients undergoing minimally invasive interbody fusion for adult spinal deformity

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OBJECTIVE High-quality studies that compare outcomes of open and minimally invasively placed pedicle screws for adult spinal deformity are needed. Therefore, the authors compared differences in complications from a circumferential minimally invasive spine (MIS) surgery and those from a hybrid surgery.

METHODS A retrospective review of a multicenter database of patients with spinal deformity who were treated with an MIS surgery was performed. Database inclusion criteria included an age of ≥ 18 years and at least 1 of the following: a coronal Cobb angle of > 20°, a sagittal vertical axis of > 5 cm, a pelvic incidence–lumbar lordosis angle of > 10°, and/or a pelvic tilt of > 20°. Patients were propensity matched according to the levels instrumented.

RESULTS In this database, a complete data set was available for 165 patients, and after those who underwent 3-column osteotomy were excluded, 137 patients were available for analysis; 76 patients remained after propensity matching (MIS surgery group 38 patients, hybrid surgery group 38 patients). The authors found no difference in demographics, number of levels instrumented, or preoperative and postoperative radiographic results. At least 1 complication was suffered by 55.3% of patients in the hybrid surgery group and 44.7% of those in the MIS surgery group ($p = 0.359$). Patients in the MIS surgery group had significantly fewer neurological, operative, and minor complications than those in the hybrid surgery group. The reoperation rates in both groups were similar. The most common complication category for the MIS surgery group was radiographic and for the hybrid surgery group was neurological. Patients in both groups experienced postoperative improvement in their Oswestry Disability Index and visual analog scale (VAS) back and leg pain scores (all $p < 0.05$); however, MIS surgery provided a greater reduction in leg pain according to VAS scores.

CONCLUSIONS Overall complication rates in the MIS and hybrid surgery groups were similar. MIS surgery resulted in significantly fewer neurological, operative, and minor complications. Reoperation rates in the 2 groups were similar, and despite complications, the patients reported significant improvement in their pain and function.

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KEY WORDS minimally invasive spine surgery; complications; transforaminal lumbar interbody fusion; lateral lumbar interbody fusion; adult spinal deformity; percutaneous instrumentation

ABBREVIATIONS ASD = adult spinal deformity; BMI = body mass index; CCA = coronal Cobb angle; EBL = estimated blood loss; LL = lumbar lordosis; LLIF = lateral lumbar interbody fusion; MIS = minimally invasive spine; PI = pelvic incidence; PT = pelvic tilt; SSI = surgical site infection; SVA = sagittal vertical axis; TLIF = transforaminal lumbar interbody fusion; UTI = urinary tract infection; VAS = visual analog scale.

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Lumbar fusion has been used to treat a variety of spinal pathologies, including tumors, trauma, infection, degenerative disease, and deformity.[1,6,10,13,19,23] The use of lateral interbody techniques offers a number of advantages to the spine surgeon working on deformity from L-2 to L-5. Lateral access provides access to the entire disc space and enables placement of a larger implant, which facilitates greater indirect foraminal and central decompression and higher rates of arthrodesis.[20] The ability to release the annulus fibrosus on either side of the vertebral body enables greater correction of coronal deformity than does a solely posterior approach.[7,24] Anterior and lateral approaches also enable anterior longitudinal ligament sectioning and anterior column release, which is a powerful technique for improving a patient's sagittal deformity.[2–4,15,28] Lateral techniques use less invasive surgical portals, which results in small muscle-sparing incisions, reduced blood loss, and faster postoperative recovery and makes them important tools in a spine surgeon's armamentarium.[5,11,14,16–18,22,26,29]

Lateral lumbar interbody fusion (LLIF) is generally supplemented with posterior fixation (e.g., pedicle screw placement), which can be performed via open or minimally invasive (percutaneous) techniques. The advantages conferred by open instrumentation include direct visualization of anatomical landmarks, the ability to decorticate bony surfaces easily to maximize posterolateral arthrodesis, and reduction of fluoroscopic radiation exposure to the patient and surgeon compared with that necessary during percutaneous fixation. In comparison, the advantages of minimally invasive techniques include less disruption to the paraspinal musculature and stabilizing structures, which results in decreases in blood loss, postoperative pain, length of hospital stay, and iatrogenic morbidity.[5,11,13,16–18,22,26,29]

In this study, we aimed to retrospectively analyze a large multicenter database to determine the effect of open surgery on complications compared with that of using percutaneous screws among patients who underwent minimally invasive interbody fusion procedures with supplemental fixation for adult spinal deformity (ASD).[25]

Methods

Study Design and Patient Population

We performed a retrospective analysis of data collected from a multicenter database of patients with ASD who had been treated with a component of minimally invasive surgical techniques between 2009 and 2013. Eleven participating institutions contributed data, and each site obtained institutional review board approval. Inclusion criteria for entry into the multicenter database were patient age of ≥ 18 years and at least 1 of the following factors: a coronal Cobb angle (CCA) of > 20°, a sagittal vertical axis (SVA) of > 5 cm, a pelvic tilt (PT) of > 20°, a pelvic incidence–lumbar lordosis (PI-LL) angle of > 10°, and/or a thoracic kyphosis (TK) angle ≥ 60°. This database included patients treated with a component of minimally invasive surgery as part of their index surgery. Patients were categorized into 1 of 2 groups: those who underwent minimally invasive spine (MIS) surgery (MIS surgery group) or those who underwent hybrid surgery (hybrid surgery group). The MIS surgery group included patients who had undergone minimally invasive LLIF and/or transforaminal lumbar interbody fusion (TLIF) with percutaneous pedicle screw fixation. The hybrid surgery group consisted of patients who had undergone LLIF with open pedicle screw fixation. The surgical approach for each patient was determined at the discretion of the surgeon; all surgeons in this group perform both minimally invasive and hybrid spine surgeries. Data on decompressions (laminectomies, foraminotomies, etc.) and posterior column osteotomies performed were not collected, nor were data on radiation exposure.

Patients who underwent 3-column osteotomy as part of their open procedure were excluded from the study. In addition, patients who did not have a minimum of 2 years of follow-up were not included in the analysis. To ensure homogenous comparison groups, patients in the MIS and hybrid surgery groups were matched by levels treated.

An initial query of the multicenter database identified 97 patients who had undergone MIS surgery and 68 who had undergone hybrid surgery. Patients were propensity matched based on the number of levels treated, which resulted in a total of 76 patients analyzed, with 38 in each group (MIS and hybrid surgery groups). A flow diagram for patient selection is shown in Fig. 1.

Data Collection

Health-related quality of life measures were assessed at baseline and at the latest follow-up visit. Clinical outcome variables included Oswestry Disability Index (ODI)[8] and visual analog scale (VAS) scores for both back and leg symptoms. Demographic and intraoperative data, including age, body mass index (BMI), estimated blood loss (EBL), operating room time, and number of levels treated, were also analyzed for each outcome group. Thirty-six–inch standing scoliosis radiographs at baseline and at least 2 years after surgery were available for each patient. Measured radiographic parameters included coronal curve, PI, LL, PI-LL mismatch, PT, and SVA. All radiographs were evaluated at a single location for consistency.

Data and Statistical Analysis

Means (± standard deviation) were used to document continuous variables, and frequency analysis was used for categorical variables. Comparisons between the 2 outcome groups were performed using nonparametric Mann-Whitney U-test and chi-square analyses. Because not all data points were distributed normally, a nonparametric test was applied. Nonparametric tests can be applied to normally distributed data and are less sensitive to outliers than their parametric counterparts, which is important in comparisons of small samples. The change between preoperative and postoperative parameters within each group was analyzed using a paired Wilcoxon signed-rank test. A p value of ≤ 0.05 was considered significant.

Results

Patient Population

After excluding patients who underwent 3-column osteotomy and after propensity matching based on the

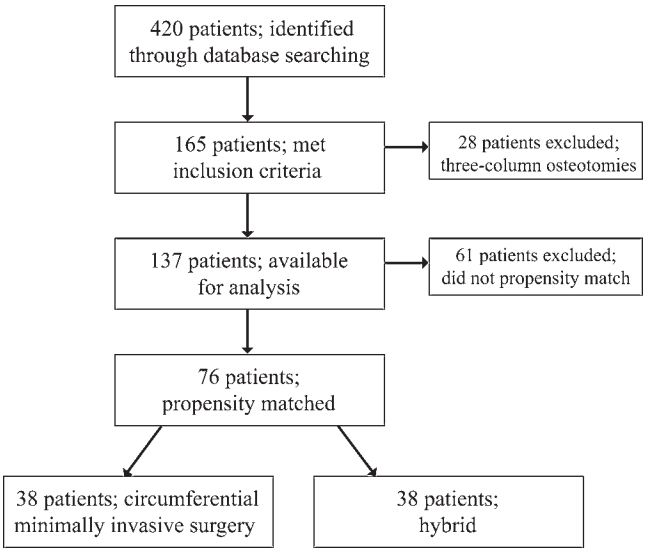

FIG. 1. Flow diagram for patient selection.

number of levels treated, 76 patients were included in this study for analysis (MIS surgery group 38 patients, hybrid surgery group 38 patients). Demographic, radiographic, operative, and clinical outcomes data are displayed in Table 1. Demographically, we found no significant difference between the MIS and hybrid surgery groups in mean age (62.8 vs 57.7 years, respectively; p = 0.147), sex (71.1% vs 86.8% female, respectively; p = 0.091), BMI (27.7 vs 26.2, respectively; p = 0.265), or smoking status (5.3% vs 10.5%, respectively; p = 0.395).

Operative Outcomes

We found no significant difference between the MIS and hybrid surgery groups in the number of levels instrumented (6.1 vs 6.8, respectively; p = 0.622), the percentage of patients who required pelvic fixation (13.2% vs 21.1%, respectively; p = 0.361), or the percentage of patients who underwent staged procedures (i.e., anterior column and posterior column performed on different days) (60.5% vs 52.6%, respectively; p = 0.488). We also found no significant difference in the number of patients who underwent fusion or instrumentation at L5–S1. In the hybrid surgery group, 16 (42.1%) patients underwent an interbody fusion at L5–S1, compared with 21 (55.3%) patients in the MIS surgery group (p = 0.251), and 23 (60.5%) patients in the hybrid surgery group and 24 (63.2%) patients in the MIS surgery group (p = 0.813) had a construct that ended at S-1 or below.

No significant difference was found in preoperative and postoperative PT, PI, PI-LL angle, SVA, or CCA between the groups.

Patients in the MIS surgery group had a lower EBL than those in the hybrid surgery group (673.7 vs 1359.5 ml, respectively; p = 0.001), and operative time was shorter for patients in the MIS surgery group (490.2 vs 623.3 minutes, respectively; p = 0.015). However, we found no significant difference between the 2 groups regarding the requirement for blood transfusion, average length of stay, or average follow-up duration.

TABLE 1. Clinical, radiographic, and outcome comparisons between the MIS and hybrid surgery groups using the Mann-Whitney U-test and chi-square test

Data Type	Hybrid Surgery Group (n = 38)	MIS Surgery Group (n = 38)	p Value
Demographics			
Age (yrs)	57.7 ± 13.7	62.8 ± 9.2	0.147
Sex, female	33 (86.8)	27 (71.1)	0.091
Follow-up (mos)	32 ± 8.5	35.1 ± 9.6	0.125
BMI (kg/m^2)	26.2 ± 5.8	27.7 ± 5.2	0.265
Smoking	4 (10.5)	2 (5.3)	0.395
Surgical			
Levels instrumented	6.8 ± 3.5	6.1 ± 2.6	0.622
Staged	20 (52.6)	23 (60.5)	0.488
Transfusion	20 (52.6)	17 (44.7)	0.491
Pelvic fixation	8 (21.1)	5 (13.2)	0.361
L5–S1 interbody fusion	16 (42.1)	21 (55.3)	0.251
Construct ending at or below S-1	23 (60.5)	24 (63.2)	0.813
Preop			
PT (°)	22.4 ± 10.4	26.2 ± 12.5	0.32
PI (°)	52.6 ± 14.4	54 ± 13.4	0.762
PI-LL angle (°)	15.1 ± 18.4	16.5 ± 14.7	0.646
LL (°)	37.5 ± 19.0	37.2 ± 14.0	0.25
SVA (mm)	47.3 ± 57.7	47.6 ± 47.1	0.729
Maximum Cobb angle (°)	40.7 ± 15.1	36.7 ± 14.4	0.307
VAS score, back pain	6.8 ± 2.7	6.4 ± 2.3	0.236
VAS score, leg pain	5.5 ± 3.2	5.5 ± 3.0	0.96
ODI	59.1 ± 18.5	46.6 ± 16.5	0.005*
Postop			
PT (°)	22.7 ± 11.3	24.8 ± 11.8	0.574
PI (°)	53.1 ± 14.3	54.2 ± 12.5	0.854
PI-LL angle (°)	9.7 ± 18.6	9.2 ± 13.1	0.858
LL (°)	43.4 ± 15.1	45.6 ± 12.4	0.707
SVA (mm)	49.4 ± 59.8	48.2 ± 55.2	0.94
Maximum Cobb angle (°)	18.3 ± 22.2	9.5 ± 15.0	0.111
VAS score, back pain	4.2 ± 2.8	2.9 ± 2.6	0.037*
VAS score, leg pain	2.8 ± 2.8	1.8 ± 2.2	0.136
ODI	38.3 ± 20.7	25.9 ± 17.9	0.005*
Operative			
EBL (ml)	1359.5 ± 1024.9	673.7 ± 555.4	0.001*
Operating room time (mins)	623.3 ± 232.5	490.2 ± 214.6	0.015*
Length of stay (days)	8.7 ± 5.3	7.7 ± 5.1	0.183

Values are number of patients or mean ± SD.
* Significant result.

TABLE 2. Comparison of complication rates in the MIS and hybrid surgery groups

Complication	No. of Complications (%)		p Value
	Hybrid Surgery Group (n = 38)	MIS Surgery Group (n = 38)	
Total	21 (55.3)	17 (44.7)	0.359
Reoperation	11 (28.9)	10 (26.3)	0.798
Major complication	14 (36.8)	11 (28.9)	0.464
Minor complication	19 (50.0)	10 (26.3)	0.034*
Neurological	11 (28.9)	4 (10.5)	0.044*
Operative complication	7 (18.4)	0 (0.0)	0.005*
Other	1 (2.6)	1 (2.6)	0.999
Perioperative complication	5 (13.2)	1 (2.6)	0.089
Postoperative complication	19 (50.0)	15 (39.5)	0.356

* Significant result.

TABLE 3. Comparison of minor complication rates in the MIS and hybrid surgery groups

Minor Complication	No. of Complications (%)	
	Hybrid Surgery Group (n = 38)	MIS Surgery Group (n = 38)
Infection, UTI	4 (10.5)	0 (0.0)
Implant, painful	2 (5.3)	0 (0.0)
Implant, prominence	2 (5.3)	0 (0.0)
Implant, screw-bone interface loosening	3 (7.9)	4 (10.5)
Radiographic, screw malposition	0 (0.0)	1 (2.6)
Radiographic, adjacent-segment degeneration	1 (2.6)	1 (2.6)
Radiographic, DJK w/o symptoms	1 (2.6)	0 (0.0)
Radiographic, PJK w/o symptoms	0 (0.0)	1 (2.6)
Surgical site, dehiscence	0 (0.0)	0 (0.0)
Neurological, femoral cutaneous neuralgia	0 (0.0)	1 (2.6)
Neurological, sensory deficit	4 (10.5)	1 (2.6)
Neurological, pain/radiculopathy	8 (21.1)	1 (2.6)
Cardiological, plural effusion	1 (2.6)	1 (2.6)
Gastrointestinal tract, ileus	1 (2.6)	1 (2.6)
Operative, dural tear	3 (7.9)	0 (0.0)
Operative, vertebral body fracture	2 (5.3)	0 (0.0)

DJK = distal junctional kyphosis; PJK = proximal junctional kyphosis; UTI = urinary tract infection.

Clinical Outcomes

No significant difference between preoperative and postoperative VAS leg pain scores was found between the study groups. However, we did find a statistically significant improvement in VAS back pain scores in the MIS surgery group compared with that in the hybrid surgery group (2.9 vs 4.2, respectively; p = 0.037), even though both groups started with similar values (6.4 vs 6.8, respectively; p = 0.236). The postoperative ODI was lower in the MIS surgery group than in the hybrid surgery group (25.9 vs 38.3, respectively; p = 0.005). However, the preoperative ODI was also lower in the MIS surgery group than in the hybrid surgery group (46.6 vs 59.1, respectively; p = 0.005). The changes between the preoperative and postoperative status in ODI were similar between groups (20.8 [hybrid surgery group] vs 20.7 [MIS surgery group]).

Complication Rates

Complication rates are detailed in Table 2. We found no statistically significant difference in the numbers of overall, major, radiographic, cardiac, gastrointestinal, perioperative, or postoperative complications between the MIS and hybrid surgery groups. There was also no difference in the numbers of reoperations, implant failures, or surgical site complications, which included dehiscence, erythema, drainage, hematoma, and seroma.

Six (15.8%) patients in the hybrid surgery group suffered 9 incidental radiographic complications, whereas 10 (26.3%) patients in the MIS surgery group suffered 12 radiographic complications. The radiographic complications in the MIS surgery group included distal junctional kyphosis, proximal junctional kyphosis, and pseudarthrosis. The radiographic complications in the hybrid surgery group included the same 3 complications and adjacent-segment disease and sagittal imbalance.

The MIS surgery group experienced fewer minor complications (26.3% vs 50.0%, respectively; p = 0.034), neurological complications (10.5% vs 28.9%, respectively; p = 0.044), and operative complications (0.0% vs 18.4%, respectively; p = 0.05) than the hybrid surgery group (Table 3). Neurological complications included cerebrovascular accident/stroke, femoral cutaneous neuralgia, motor paralysis, sensory deficit, and pain/radiculopathy. Operative complications included retained sponge/instrument, vascular injury, visceral injury, dural tear, fixation failure (hook/screw), implant failure, pedicle fracture, posterior element fracture, and vertebral body fracture.

We found a strong trend toward decreased perioperative and intraoperative complications in the MIS surgery group (2.6% [MIS surgery group] vs 13.2% [hybrid surgery group]; p = 0.089); however, these data did not reach statistical significance, likely because of the low patient numbers within each group. An identical trend toward fewer infections in the MIS surgery group than in the hybrid surgery group (2.6% vs 13.2%, respectively; p = 0.089) was found, but the number of affected patients might have left the analysis insufficiently powered for the trend to reach significance. Infections tracked for these groups included deep infection, pneumonia, sepsis, superficial infection, and urinary tract infection (UTI).

Seven patients in the hybrid surgery group suffered an operative complication, which included 3 dural tears, 2 vertebral body fractures, 1 incisional hernia, and 1 case of excessive blood loss (> 4 L). No operative complications were identified in the MIS surgery group (p = 0.005).

Discussion

In this study, we compared the complication profiles

of patients who underwent hybrid surgery for ASD (LLIF with open posterior instrumentation) with those who underwent circumferential MIS surgery (minimally invasive LLIF and/or minimally invasive TLIF with percutaneous posterior instrumentation). In these well-matched groups, we found that patients in the MIS surgery group experienced fewer minor complications, neurological complications, and operative complications than those in the hybrid surgery group. Patients in the MIS surgery group also experienced shorter operative time and less blood loss. We found no statistically significant difference in the numbers of major complications, reoperations, implant failures, or surgical site complications between the 2 groups. To our knowledge, this is the first study to have examined the difference in complication rates between MIS surgery and hybrid surgery in patients with ASD.

A paucity of studies exist in the literature that compared complications between open and minimally invasive fusion surgery for ASD. Previous work has compared complications in patients with ASD treated via open surgery, hybrid surgery, or MIS surgery after propensity matching the groups for age, preoperative SVA, number of levels fused, and lumbar CCA.[27] The authors found that blood loss was significantly lower in the MIS surgery group than in the open-surgery group (669 vs 2322 ml, respectively; $p = 0.001$). No difference was found in the total, postoperative, or major complication rates among the 3 surgery groups. However, there were decreases in the numbers of intraoperative complications experienced during MIS and hybrid surgeries (0% [MIS], 5.3% [hybrid], and 25% [open]; $p < 0.03$). Our study had similar findings and the additional advantage of propensity matching according to number of levels.

A small number of systematic reviews have compared complication rates associated with open and minimally invasive TLIFs. Khan et al.[12] performed a meta-analysis of 30 studies and found minimally invasive TLIF to result in statistically significantly less blood loss, shorter lengths of stay, and fewer complications than open TLIF. Goldstein et al.[9] similarly analyzed 26 studies and found that patients who underwent minimally invasive surgery were less likely than those who underwent open surgery to experience medical adverse events (risk ratio 0.39, 95% confidence interval 0.23–0.69, $p = 0.001$) but not surgical adverse events. Medical adverse events included UTI, respiratory complications, cardiac complications, and need for transfusion. Patients who underwent minimally invasive surgery had statistically significantly less blood loss, faster times to ambulation, and shorter lengths of stay. Last, in a study that lacked adequate statistical analysis, Hu et al.[11] systematically reviewed 14 studies and also found lower complication rates associated with minimally invasive TLIF than with open TLIF (11.87% vs 14.35%, respectively).

Two studies reported that surgical site infection (SSI) rates were lower after minimally invasive TLIF than after open TLIF. In a literature review, Parker et al.[21] compared 10 cohorts of patients who underwent minimally invasive TLIF (362 patients) with 20 cohorts of patients who underwent open TLIF (1133 patients) and found a significantly lower incidence of SSI in the MIS surgery group (0.6% vs 4.0%, $p = 0.0005$). In a retrospective review of a large administrative database, McGirt et al.[16] identified 5173 patients who underwent 1- or 2-level open or minimally invasive posterior lumbar fusion. Although the incidences of SSI and associated costs were similar in those who underwent 1-level minimally invasive fusion and those who underwent open fusion, the authors found significant differences when they compared 2-level fusions. Specifically, the incidence of SSI was 4.6% in their MIS surgery group and 7.0% in their open-surgery group ($p = 0.037$), and the mean SSI-associated cost per fusion was also lower in their MIS surgery group ($756 vs $1140, respectively; $p = 0.030$).

The infection rates in our study were 2.6% in the MIS surgery group and 13.2% in the hybrid surgery group, and the average number of levels instrumented in both groups was greater than 6, substantially more than that found in the 1- and 2-level fusion studies previously reported.

Study Limitations

This study's primary limitations were its retrospective design and the data review of a relatively small number of patients from a multicenter study. The retrospective nature limited the level of available detail, such as the costs, specific decompressions, and/or osteotomies performed in each group. The multicenter nature of the study introduced a level of variability that is difficult to control for with respect to data collection but provides more generalizable results. Because of the lower number of patients in each group, we were unable to achieve the gold standard 80% power. Because this was a multicenter study, we attempted to enroll as many patients with ASD who were undergoing minimally invasive correction as possible. However, because of the specific inclusion criteria and creation of homogenous cohorts for the 2 procedure types, our sample size decreased significantly. In addition, because 10 institutions contributed for the total of 76 patients in the propensity-matched cohort, we had insufficient power to determine statistical differences in the complication rates among institutions.

The results of this study improve our current understanding of complications after spine surgery. Future prospective studies that involve larger numbers of patients will help support and confirm the findings presented here.

Conclusions

In this study, 76 patients who underwent either MIS or hybrid surgery were followed up for at least 2 years, and we retrospectively compared their surgical outcomes. Overall complication rates between the MIS and hybrid surgery groups were similar. MIS surgery resulted in significantly fewer neurological, operative, and minor complications. Reoperation rates were similar, and despite complications, the patients reported significant improvement in their pain and function. Although the results of this study provide insight into complications after spine surgery, the paucity of studies from the literature that compared complications between these groups and the relatively small number of patients in our multicenter database reveal a need for future prospective studies that involve larger numbers of patients to support and confirm the findings presented here.

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Disclosures

Dr. Anand has direct ownership of stock in Globus Medical and Medtronic, is a patent owner (Medtronic), and has received royalty payments from Globus Medical. Dr. Chou has served as a consultant for Medtronic and Globus. Dr. Eastlack has direct ownership of stock in NuVasive, SeaSpine, and Alphatec Spine; has served as a consultant for NuVasive, Alphatec, Titan, Aesculap, SeaSpine, and K2M; is a patent holder (Invuity, Globus, Spine Innovation, and NuTech); and is part owner of Spine Innovation.

Dr. Kanter is a patent holder (Zimmer Biomet) and has served as a consultant for NuVasive. Dr. La Marca has served as a consultant for Globus Medical, Zimmer, DePuy Synthes, and RTI and has received royalty payments from Globus Medical and Zimmer. Dr. Mummaneni has served as a consultant for DePuy Spine and Stryker; has direct ownership of stock in Spinicity/ISD; has provided statistical analysis for study/writing or editorial assistance on manuscripts for ISSG; has received royalty payments from DePuy Spine, Thieme Publishing, and Springer Publishing; and has received honoraria from AOSpine and Globus. Dr. Mundis has served as a consultant for NuVasive, AlloSource, and K2M. Dr. Nunley has direct ownership of stock in Amedica, Paradigm, and Spineology; is a patent holder (K2M and LDR Spine); has served as a consultant for K2M; and has served on the speakers' bureau for K2M and LDR Spine. Dr. Park has served as a consultant for Globus, Medtronic, NuVasive, Biomet Zimmer, and Bioventus and has received royalty payments from Globus. Dr. Uribe has served as a consultant for NuVasive.

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Conception and design: Than, Mummaneni, Tran, Park, Chou, La Marca, Uribe, Vogel, Nunley, Eastlack, Anand, Okonkwo, Kanter, Mundis. Acquisition of data: Than, Mummaneni, Park, Chou, La Marca, Uribe, Vogel, Nunley, Eastlack, Anand, Okonkwo, Kanter, Mundis. Analysis and interpretation of data: all authors. Drafting the article: Than, Bridges. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Than. Statistical analysis: Tran. Administrative/technical/material support: Tran. Study supervision: Mummaneni, Mundis.

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