Five-year adjacent-level degenerative changes in patients with single-level disease treated using lumbar total disc replacement with ProDisc-L versus circumferential fusion

Clinical article

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Object. The authors report the 5-year results for radiographically demonstrated adjacent-level degenerative changes from a prospective multicenter study in which patients were randomized to either total disc replacement (TDR) or circumferential fusion for single-level lumbar degenerative disc disease (DDD).

Methods. Two hundred thirty-six patients with single-level lumbar DDD were enrolled and randomly assigned to 2 treatment groups: 161 patients in the TDR group were treated using the ProDisc-L (Synthes Spine, Inc.), and 75 patients were treated with circumferential fusion. Radiographic follow-up data 5 years after treatment were available for 123 TDR patients and 43 fusion patients. To characterize adjacent-level degeneration (ALD), radiologists at an independent facility read the radiographic films. Adjacent-level degeneration was characterized by a composite score including disc height loss, endplate sclerosis, osteophytes, and spondylolisthesis. At 5 years, changes in ALD (Δ ALDs) compared with the preoperative assessment were reported.

Results. Changes in ALD at 5 years were observed in 9.2% of TDR patients and 28.6% of fusion patients ($p = 0.004$). Among the patients without adjacent-level disease preoperatively, new findings of ALD at 5 years posttreatment were apparent in only 6.7% of TDR patients and 23.8% of fusion patients ($p = 0.008$). Adjacent-level surgery leading to secondary surgery was reported for 1.9% of TDR patients and 4.0% of fusion patients ($p = 0.6819$). The TDR patients had a mean preoperative index-level range of motion ([ROM] of 7.3°) that decreased slightly (to 6.0°) at 5 years after treatment ($p = 0.0198$). Neither treatment group had significant changes in either ROM or translation at the superior adjacent level at 5 years posttreatment compared with baseline.

Conclusions. At 5 years after the index surgery, ProDisc-L maintained ROM and was associated with a significantly lower rate of Δ ALDs than in the patients treated with circumferential fusion. In fact, the fusion patients were greater than 3 times more likely to experience Δ ALDs than were the TDR patients. Clinical trial registration no.: NCT00295009.

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KEY WORDS • degenerative disc disease • adjacent-level degeneration • lumbar spine • fusion • total disc replacement • randomized controlled trial

FUSION has long been considered a viable surgical treatment for painful lumbar spinal conditions. Russell Hibbs was the first surgeon to perform spinal fusion in 1911. Patients treated with fusion generally experience reduced back pain and improved function. However, the potential for increased rates of ALD years after fusion has been reported. Degeneration is of particular concern for fusions performed in a younger patient

Abbreviations used in this paper: ALD = adjacent-level degeneration; AP = anterior/posterior; DDD = degenerative disc disease; Δ ALD = change in ALD; ODI = Oswestry Disability Index; ROM = range of motion; SF-36 PCS = 36-Item Short Form Health Survey physical component score; TDR = total disc replacement; VAS = visual analog scale.

population. In the 1980s, in biomechanical and clinical studies, Lee¹² and Lee and Langrana¹³ demonstrated increased stress on the adjacent segments following fusion. Since then, multiple biomechanical studies using a variety of fusion constructs and methodologies have demonstrated that fusion causes increased disc pressure^{3,5,17,21} and altered motion^{5,17,18} of segments adjacent to the fusion site.

Reports on the incidence of radiographic findings of ALD and its clinical impact vary. Adjacent-level degeneration has been observed after fusion more often than occurs naturally in nonfused segments.¹¹ Ekman et al.⁶ reported results from the 10-year follow-up of a randomized study, noting that ALD occurred significantly more

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often in fusion patients than in nonoperative controls, although ALD was only clinically significant in patients with severe changes at the adjacent segment.

While patients generally have good clinical outcomes following fusion, newer surgical interventions have evolved. Total disc replacement has been developed to treat functionally disabling lumbar DDD with the theoretical potential to reduce ALD as well. To date, few authors have studied the radiographic incidence of ALD and its clinical consequences in patients with lumbar DDD treated with fusion versus TDR. The purpose of the present post hoc analysis was to assess the incidence of Δ ALDs 5 years after surgery in patients who participated in a multicenter randomized controlled trial comparing TDR using ProDisc-L and circumferential fusion for single-level DDD of the lumbar spine.

Methods

Study Design

Under an FDA-regulated investigational device exemption clinical trial (Clinical trial registration no. NCT00295009, <http://ClinicalTrials.gov>), patients at 17 investigational sites across the US were enrolled from October 2001 to June 2003. Approval was required from every site's institutional review board, and all patients provided written informed consent prior to treatment. Randomization was weighted in a 2:1 ratio of ProDisc-L (TDR) to circumferential fusion (fusion). Treatment was unblinded to the patient after surgery. Specific inclusion and exclusion criteria for that study have been described elsewhere.²⁴ In general, included patients had single-level DDD between L-3 and S-1, back and/or leg pain, an ODI score $\geq 40\%$, and at least 6 months of failed conservative treatment. Degenerative disc disease was clinically assessed with radiographic confirmation via CT, MRI, discography, plain film radiography, myelography, and/or flexion and extension radiography. Investigators typically relied on negative discography at the adjacent level if there was any question of that level's involvement.

Clinical Outcomes

Preoperatively and 5 years after surgery, patient assessments included the ODI and the SF-36. A 10-cm VAS was provided for patients to rate their pain (VAS pain) and treatment satisfaction (VAS satisfaction). Subsequent surgical intervention at adjacent levels was also documented.

Radiographic Analysis

All radiographic analysis was performed via digitized radiographic review by independent radiologists (Medical Metrics, Inc.). Adjacent-level degeneration was assessed at levels immediately adjacent to the treated index level based on neutral and lateral standing radiographs obtained prior to TDR and fusion surgery as well as 5 years after surgery. For patients with an index level at L3-4 or L4-5, both the superior and inferior adjacent levels were evaluated. For patients whose index level was L5-S1, only the superior adjacent level was evaluated. The presence of any preoperative initial ALD was as-

sessed, and 5-year postoperative Δ ALD was categorized as changes that occurred subsequent to that preoperative assessment.

To characterize ALD, Medical Metrics, Inc., developed an objective composite measure that was a semiquantitative adaptation of a published grading system^{14,20,23} that included 4 characteristics: disc height loss, endplate sclerosis, osteophytes, and spondylolisthesis. Medical Metrics, Inc., assessed disc height and spondylolisthesis measurements with its quantitative motion analysis system, a previously validated software system. Adjacent-level disc height loss was calculated relative to the disc with the greatest height, which was assumed to be normal for the patient. Two independent radiologists graded endplate sclerosis and osteophytes, and a third independent radiologist participated to resolve any grading discrepancies. An atlas of images was used for reference. The radiologists were blinded to clinical outcomes. The adjusted percent agreement between radiologists in assessing endplate sclerosis was 87% and in assessing osteophytes was 85%, indicating good reproducibility.

Each of the 4 ALD characteristics was assigned a grade that could be applied to both preoperative and 5-year findings (Table 1). To establish a grade of preoperative disc degeneration at each adjacent level, the following formula was applied: $[(\text{disc height loss grade} \times 10) + (\text{endplate sclerosis grade} \times 5) + (\text{osteophyte grade} \times 5) + (\text{spondylolisthesis grade} \times 5)]/10$. Disc height loss received a higher weighting than other components, as it is the most severe consequence of disc degeneration, with the potential developments of loss in foraminal height, annular bulging, and increased segmental stress. Degeneration grade was rounded to the nearest integer, and the highest grade was set at 3; that is, any computed grades more than 3 were assigned a grade of 3. A grade of 0 indicated no initial disc degeneration, and a grade of 1, 2, or 3 represented mild, moderate, or severe ALD, respectively. Adjacent-level degeneration for a patient was scored based on the worst-case findings of adjacent-level grades.

To characterize Δ ALDs between preoperative and 5-year images, the same formula and rounding process used to assign an ALD grade were applied, except that disc height loss, endplate sclerosis, and osteophyte formation were entered into the algorithm as the difference relative to the preoperative grade. For example, if a level had mild osteophytes preoperatively (Grade 1) and there was no change in the osteophyte grade at 5 years (Grade 1), then the osteophyte grade used in calculating the Δ ALD was 0. Grades for the Δ ALD at each adjacent level (rounded to the nearest integer) ranged from 0 to 3, with 0 indicating no Δ ALD, and a grade of 1, 2, or 3 representing mild, moderate, or severe changes, respectively. The Δ ALD for each patient was assigned based on the worst-case findings of adjacent-level grades.

In addition to the ALD assessments, angular ROM and AP translation at the index and adjacent levels were measured as the difference between the inferior endplate of the superior vertebral body and the superior endplate of the inferior vertebral body based on flexion and extension radiographs. Measurements were made using quantitative motion analysis software.

TABLE 1: Radiographic scoring of ALD*

Parameter	Reference	Grade			
		0, None	1, Mild	2, Moderate	3, Severe
disc height†	disc w/ greatest height assumed to represent "normal" disc height for patient	w/in 25% of normal	>25% to 50% less than normal	>50% to 75% less than normal	>75% less than normal
endplate sclerosis‡	images representing different grades of sclerosis were selected & agreed on by 2 radiologists	none	modest loss of definition of 1 or both endplates compared w/ adjacent levels, &/or mild localized densification of bone adjacent to endplate	loss of definition of 1 or both endplates &/or definitive densification of adjacent bone that involves at least half of endplate width	NA
osteophytes‡	images representing different grades of sclerosis were selected & agreed on by 2 radiologists	none	at least 1 mm of osteophyte protrusion but not more than 3 mm	1 or more osteophytes protruded more than 3 mm but less than 6 mm	1 or more osteophytes protruded over 6 mm or seemed likely to restrict intervertebral motion
spondylolisthesis†	position of posterior-inferior corner of superior vertebra relative to posterior-superior corner of inferior vertebra, measured parallel to superior endplate of inferior vertebra	≤5 mm	>5 to ≤10 mm	>10 mm	NA

* NA = not applicable.

† Quantitative Motion Analysis (QMA®) software.

‡ Two radiologists and a third for ties.

Statistical Methods

The frequency of patients with initial ALD and 5-year Δ ALDs was compared in TDR versus fusion groups by using a 2-sided Fisher exact test. Nominal logistic regression was used to determine whether Δ ALDs at any adjacent level correlated with treatment (fusion or TDR), the presence of baseline ALD, level of index surgery, or interactions. Stepwise regression was applied to identify prognostic factors for Δ ALDs, and these factors were included in the regression when $p < 0.15$.

By applying a 2-way ANOVA, clinical outcomes (ODI, VAS pain, SF-36 PCS, VAS satisfaction) at 5 years after treatment were evaluated to determine whether any were correlated with treatment (fusion or TDR), Δ ALDs, or interactions. In addition, an ANCOVA was used to determine whether outcome was related to patient scores at baseline, Δ ALDs at 5 years after treatment, or interactions. The ROM, AP translation, and disc height at superior and inferior adjacent levels were compared in TDR versus fusion patients by using Wilcoxon tests. The JMP statistical discovery software, version 8.0.2.2 (SAS Institute, Inc.), and an alpha of 0.05 were used for all statistical analyses.

As the sponsor of this investigational device exemption study, Synthes Spine, Inc., managed the overall database and provided technical assistance with the data analysis. We, the authors, independently interpreted the data, developed the manuscript, and established our conclusions.

Results

Clinical and Radiographic Follow-up

The prospective, randomized, multicenter study population consisted of 161 TDR and 75 fusion patients. All patients with complete radiographic data at 5 years were included in the present post hoc analysis; no patient with complete radiographic data was excluded. Incomplete data sets due to missed follow-up visits, missing films, or poor film exposure were the primary reasons for incomplete radiographic data in patients excluded from the database. Five-year radiographic data were available for 123 of the TDR patients (76.4%) and 43 of the fusion patients (57.3%) based on a total of 163 TDR levels and 54 fusion levels.

Patient Demographics and Intraoperative Data

Preoperative characteristics of the 123 TDR and 43 fusion patients were similar. As shown in Table 2, smoking status was the only preoperative characteristic that showed a significant difference between the groups, with a greater percentage of TDR patients characterized as nonsmokers compared with fusion patients ($p = 0.0433$). The index level for 61.0% of the TDR patients and 69.8% of the fusion patients was L5–S1.

The TDR group had significantly decreased intraoperative times, estimated blood loss, and length of hospital stay ($p < 0.0319$) compared with fusion patients.

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TABLE 2: Summary of patient demographics and intraoperative data

Variable	No. (%)		p Value*
	TDR Group	Fusion Group	
no. of patients	123	43	
sex			
M	62 (50.4)	18 (41.9)	0.3780
F	61 (49.6)	25 (58.1)	
mean age in yrs	38.3 ± 7.7	40.5 ± 8.0	0.2064
mean BMI in kg/m ²	26.9 ± 4.3	27.3 ± 4.7	0.7498
smoking status			0.0433
smoker	26 (21.1)	16 (37.2)	1.0000
nonsmoker	97 (78.9)	27 (62.8)	
prior surgery			
no	87 (70.7)	31 (72.1)	0.3602†
yes	36 (29.3)	12 (28.0)	
index level			
L3–4	3 (2.4)	1 (2.3)	0.3602†
L4–5	45 (36.6)	12 (27.9)	
L5–S1	75 (61.0)	30 (69.8)	
mean intraop time in mins‡	123.5 ± 63.1	223.8 ± 75.2	<0.0001
mean estimated blood loss in ml‡	207.0 ± 246.2	425.0 ± 422.5	<0.0001
mean length of hospital stay in days	3.5 ± 1.3	4.3 ± 1.8	0.0319

* Continuous and ordinal variables were analyzed using a Wilcoxon rank-sum test. Categorical variables were analyzed using the Fisher exact test, comparing fusion and TDR patients. Boldface p values indicate significance.

† Vertebral levels L3–4/L4–5 versus L5–S1.

‡ Calculations based on 122 TDR patients and 43 fusion patients. Blood loss estimate for 1 TDR patient was minimal, and thus an estimate was not available. Intraoperative time for another TDR patient was not available.

Preoperative Degeneration and 5-Year Degenerative Changes

Prior to surgery, 73.9% of the TDR patients and 85.7% of the fusion patients had no radiographic evidence of ALD, and no significant differences in the number of levels exhibiting evidence of initial ALD were detected between the treatment groups ($p = 0.1403$; Table 3). At 5 years posttreatment, no evidence of Δ ALD was observed in 108 (90.8%) of 119 TDR patients and 30 (71.4%) of 42 fusion patients. The rate of radiographic Δ ALD at 5 years was statistically significantly greater in the fusion group ($p = 0.0040$, Fisher exact test). The 5-year rate of Δ ALDs (9.2%) refers to “any changing or any worsening of degeneration” and not the baseline presence of ALD as assessed preoperatively. Among patients with no preoperative ALD at any level, postoperative findings of ALD at any level were reported for 8 (6.7%) of 119 TDR patients and 10 (23.8%) of 42 fusion patients ($p = 0.008$). By level, a majority of the Δ ALDs consisted of 1 grade or mild changes as compared with preoperative ALD for both treatment groups. Figures 1–3 feature illustrative preoperative and 5-year radiographs obtained in fusion and TDR patients.

Individual components of the composite grade for preoperative ALD and 5-year Δ ALD for each of the superior and inferior levels varied. For both treatment groups prior to surgery, superior level ALD (if present) primarily

consisted of endplate sclerosis, osteophytes, and spondylolisthesis, whereas inferior level ALD consisted mostly of disc height loss. At 5 years posttreatment, the predominant change in ALD at the superior level was the presence of, and/or an increase in the scores for, endplate sclerosis and osteophytes in fusion patients as well as the presence of, and/or an increase in the scores for, osteophytes in

TABLE 3: Preoperative ALD and 5-year Δ ALDs*

Variable	No. (%)		p Value†
	TDR Group	Fusion Group	
no. of patients	119	42	
preop ALD			
none	88 (73.9)	36 (85.7)	0.1403
present	31 (26.1)	6 (14.3)	
5-yr Δ ALD			
none	108 (90.8)	30 (71.4)	0.0040
present	11 (9.2)	12 (28.6)	

* Of the 166 patients included in this study, 161 patients (42 fusion and 119 TDR) had complete 5-year and baseline radiographic data needed to assess Δ ALDs.

† Categorical variables were analyzed using the Fisher exact test, comparing fusion and TDR patients. Bolded p values indicate significance.

FIG. 1. Radiographs obtained in a patient with ProDisc-L at L4–5, showing no preoperative evidence of degeneration at adjacent levels (left) and no adjacent-level changes at 5 years after treatment (right).

TDR patients. For both groups at 5 years, any Δ ALD at the inferior level was attributable to retrolisthesis or anterolisthesis.

Nominal logistic regression was used to determine whether the presence of a 5-year Δ ALD at any adjacent level was correlated with treatment, preoperative ALD at the treated or index level, or any interactions. Based on these analyses, TDR patients were significantly more likely to have no Δ ALDs at 5 years than were fusion patients ($p = 0.0088$). The interaction between treatment and index level was also significant ($p = 0.0293$), so that 5-year Δ ALDs were more likely in fusion patients than in TDR patients treated at L5–S1 ($p = 0.0003$) and in TDR patients treated at L4–5 ($p = 0.0158$). The presence of 5-year Δ ALDs was not significantly related to initial degeneration in these patients ($p = 0.6430$). In a stepwise regression model, index ROM, prior surgery, patient sex, smoking, initial degeneration, and treatment groups were evaluated to determine whether there were prognostic factors for Δ ALD. In this analysis, the only significant factor in the final model was treatment group, with the fusion patients having a 4.5

FIG. 2. Radiographs obtained in a patient with ProDisc-L at L4–5, showing no preoperative evidence of degeneration at adjacent levels (left) and adjacent-level changes at 5 years after treatment (right). Lines were drawn parallel to the endplates to make for easier measurement.

FIG. 3. Radiographs obtained in a patient with 360° fusion at L5–S1, showing no preoperative evidence of degeneration at adjacent levels (left) and adjacent-level changes at 5 years after treatment (right).

times greater likelihood of Δ ALDs compared with the TDR group.

Clinical Outcomes

Two-way ANOVA demonstrated that baseline ODI, SF-36 PCS, and VAS pain were not significantly correlated with 5-year Δ ALD, treatment group, or various interactions. In the model with various interactions, TDR patients with Δ ALDs at 5 years had higher ODI scores at 5 years than did other study patients ($p = 0.0299$). There was no significant correlation between 5-year outcomes for SF-36 PCS, VAS pain, or VAS satisfaction and Δ ALD at 5 years.

When correcting for baseline scores with an ANCOVA, 5-year follow-up ODI, SF-36 PCS, VAS pain, and VAS satisfaction scores were not significantly correlated with the development of Δ ALD in either fusion or TDR patients. The overall tendency in both treatment groups was improvement in ODI, VAS pain, and SF-36 PCS scores at 5 years compared with baseline.

Adjacent-Level Surgery

Through 5 years of follow-up, 3 (1.9%) of 161 TDR and 3 (4.0%) of 75 fusion patients underwent surgical procedures at an adjacent level. The rate of adjacent-level surgery did not differ significantly between the treatment groups ($p = 0.6819$). None of the 3 TDR patients and 2 of the 3 fusion patients demonstrated 5-year radiographic Δ ALDs. One year after an L5–S1 index surgery, 1 TDR patient underwent fusion at the L4–5 level and a bilateral laminectomy at L3–4 due to back and leg pain with numbness. One TDR patient underwent fusion at the L4–S1 level 5 years after an L5–S1 index surgery; the TDR was left intact. Five years after L5–S1 surgery, the third TDR patient suffered a herniated nucleus pulposus and underwent a discectomy at L4–5. Among the fusion patients who had reoperations, one underwent bilateral hemilaminectomy at the L4–5 level 6 months after an L5–S1 index surgery, followed 1 year later by fusion at L4–5 as a result of central stenosis and adjacent-segment disease. Three years after an L5–S1 index surgery, the second fusion patient underwent bilateral laminectomy with medial facetectomy and foraminotomy at L3–4 and

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L4–5 because of stenosis. The third fusion patient underwent bilateral laminectomy and discectomy at the L5–S1 level 4 years after an L4–5 index surgery.

While not considered adjacent-level surgery, a spinal cord stimulator was implanted in a fourth L4–5 TDR patient 3 years after the index surgery to address persistent pain at the L5–S1 segment. The index level was not disturbed, with the TDR device left intact.

Other Radiographic Outcomes: Index and Adjacent Levels

Range of motion, AP translation, and disc height measures at the index, superior adjacent, and inferior adjacent levels are displayed in Table 4. The TDR patients had a slight decrease in index level ROM at 5 years (6.0°) compared with baseline (7.3° , $p = 0.0198$). As expected, fusion patients experienced a statistically significant decrease in index level ROM at 5 years compared with preoperatively ($p < 0.0001$). Strict radiographic signs of fusion were reported for all but 2 of the 43 fusion patients. At the superior adjacent level, no significant difference in ROM was seen when comparing 5-year and preoperative results for either treatment group. At the inferior adjacent level, both groups showed an increase in the mean ROM when 5-year results were compared with baseline. The difference was significant only for the TDR patients ($p = 0.0223$).

Preoperative AP translation at the index level or either adjacent level did not differ significantly between the TDR and fusion groups. For translation at the index level, comparing baseline with 5-year data, a significant increase was seen in TDR patients ($p = 0.0280$) and a

significant decrease was seen in the fusion group ($p < 0.0001$). At the 5-year follow-up, no significant changes in translational motion at the superior or inferior adjacent levels were seen from baseline in either treatment group. Anteroposterior translation greater than 4.5 mm at the index or adjacent levels was an atypical finding in either treatment group preoperatively; no fusion patients and only 1 TDR patient (0.7%) exhibited translation greater than 4.5 mm (at the superior adjacent level only). At the 5-year follow-up, translational motion greater than 4.5 mm was observed at the superior adjacent level in 2 of 42 fusion patients (2 of 52 levels, or 3.8%) and in none of the 119 TDR patients (0 of 155 levels).

At 5 years, the average superior level disc height was reduced compared with baseline, and the differences were statistically significant in both the TDR and fusion groups; the mean change was less than 1 mm. At the inferior adjacent level, there were no differences in mean disc height at baseline, 5 years posttreatment, or in the changes from baseline to 5 years.

Discussion

Adjacent-level radiographic degeneration following lumbar spinal surgery has been described by multiple authors.^{5,6,11,12,15,17} Documented rates of ALD vary based on type of surgery performed, imaging modality used for evaluation, and grading scales applied. Park and colleagues¹⁵ review of the literature in 2004 revealed an ALD incidence ranging from 8%–100% in asymptomatic persons and 5%–20% in symptomatic ones. After systematically reviewing the literature, Harrop et al.⁹ found

TABLE 4: Radiographic outcomes*

Component & Level	Preop Assessment			5-Yr Assessment			p Value for Comparison Btwn Preop & 5-Yr Assessments	
	Fusion Group	TDR Group	p Value†	Fusion Group	TDR Group	p Value†	Fusion Group‡	TDR Group‡
no. of patients	59	141		42	115			
no. of index levels	39	120		42	115			
no. of superior levels	59	139		42	115			
no. of inferior levels	18	49		11	41			
ROM ($^\circ$)								
index	6.7 ± 5.1	7.3 ± 4.7	0.3828	0.7 ± 0.8	6.0 ± 4.5	<0.0001	<0.0001	0.0198
superior	6.7 ± 4.6	7.0 ± 4.7	0.6525	8.5 ± 6.0	7.3 ± 5.5	0.2438	0.3557	0.5037
inferior	9.1 ± 5.7	6.9 ± 4.5	0.1030	10.0 ± 4.2	8.8 ± 6.1	0.5257	0.9580	0.0223
AP translation (mm)								
index	0.9 ± 0.9	0.8 ± 1.0	0.6006	0.1 ± 0.3	1.1 ± 1.1	<0.0001	0.0001	0.0280
superior	1.3 ± 1.1	1.3 ± 1.1	0.8133	1.6 ± 1.3	1.3 ± 1.1	0.2821	0.4544	0.8298
inferior	0.6 ± 0.5	0.6 ± 0.7	0.6834	0.9 ± 0.5	0.7 ± 0.6	0.2656	0.1463	0.7956
disc height (mm)								
index	7.4 ± 1.8	7.9 ± 1.9	0.0831	9.7 ± 2.3	12.5 ± 1.6	<0.0001	<0.0001	<0.0001
superior	9.5 ± 1.3	9.9 ± 1.4	0.0178	9.0 ± 2.3	9.6 ± 1.5	0.1466	0.0121	<0.001
inferior	9.1 ± 1.5	9.5 ± 2.1	0.3116	8.7 ± 1.2	9.2 ± 2.2	0.2299	0.9805	0.0694

* Values are expressed as the means $\pm$ standard deviations. Bolded p values indicate significance.

† Wilcoxon test, comparing fusion and TDR patients.

‡ Wilcoxon signed-rank test, comparing 5-year data and preoperative data with hypothesized mean change = 0.

a postfusion incidence of 34% asymptomatic ALD and 14% symptomatic ALD, noting that factors contributing to postfusion ALD included age and preexisting degeneration at the adjacent level. Other postoperative contributors to ALD may include facet joint injury, use of posterior instrumentation, sagittal malalignment, and fusion length. Various authors have attributed the etiology of ALD to increased stiffness, altered biomechanics with changes in the center of rotation, abnormal motion, and increased intradiscal pressure.^{12,15,17}

Cadaveric animal and human spine studies have shown increased mobility at the segment adjacent to a fusion, theoretically because of transferred stresses and compensatory motion between an immobile operated segment and adjacent free segments.^{2,7,13,15} Our study demonstrated no statistically significant difference in the amount of adjacent-level translation in either treatment group at 5 years compared with baseline or between the fusion group and the TDR group at 5 years. At the 5-year follow-up, 96.2% of levels adjacent to fusion and all of the levels adjacent to TDR were within normal vertebral body sagittal plane translation stability limits of less than 4.5 mm, as defined by White and Panjabi.²²

The TDR patients had a mean preoperative index-level ROM (7.3°) that was statistically significantly lower at 5 years posttreatment (6.0°, $p = 0.0198$). This group showed increased ROM at the inferior adjacent level, whereas the fusion group did not. No changes in superior adjacent level ROM were noted at 5 years in either treatment group.

Changes in ALD at 5 years were observed in 9.2% of TDR patients and 28.6% of fusion patients ($p = 0.0040$). No baseline variables, other than treatment group, in the statistical modeling indicated an increased risk for Δ ALDs. Over the 5-year time period, the TDR group showed a progressive rate of ALD averaging 1.8% per year; the fusion group averaged 5.7% per year. Findings for the fusion group are comparable to those in a study by Ghiselli et al.,⁸ who used the criterion of changes adjacent to posterior lumbar fusions in over 200 patients over a 10-year period.

In our study, 37.2% of the fusion patients were smokers, whereas only 21.1% of the TDR patients were smokers ($p = 0.0433$). The effect of smoking on DDD has been described by several authors. In a Volvo Award paper, Battié et al.¹ showed more lumbar disc degeneration in the spines of identical twins discordant for smoking, "but this effect was small." Vo et al.¹⁹ suggested that both nicotine-mediated vasoconstriction and direct contact of outer annulus cells with blood vessels containing soluble tobacco smoking constituents may alter disc matrix homeostasis. In a regression analysis of our data, smoking was not identified as a significant factor for Δ ALD.

Our intent in this study was to focus on ALD; full clinical outcomes of the ProDisc-L randomized controlled trial at 5 years will be reported separately. The majority of patients in both treatment groups exhibited improvements in clinical outcomes at 5 years, with final outcome scores depending on baseline scores regardless of ALD. Clinical outcomes as assessed using the ODI, SF-36 PCS, and VAS pain were not correlated with

Δ ALD. Five-year Δ ALDs were primarily attributed to an increase in the presence of osteophytes and endplate sclerosis. Other authors have reported that decreases in disc height, and not the presence of osteophytes or endplate sclerosis, were associated with increased pain.^{4,10,16}

While radiographic Δ ALDs were more prevalent in fusion versus TDR patients in our study, the incidence of adjacent-level surgery was not significantly different between the treatment groups. Adjacent-segment disease leading to secondary surgery was reported for 4.0% of fusion patients and 1.9% of TDR patients ($p = 0.6819$). It was beyond the scope of this study to determine whether the need for reoperation for adjacent-segment disease was a result of the surgical intervention or whether symptomatic degenerative disease would have developed as a natural phenomenon in these cases. As the naturally occurring degenerative process continues at adjacent levels, the motion differences between fusion and TDR may show more of a clinical impact over time.

Comparing our results with those of other studies must be done with caution. The present study was a post hoc analysis comparing ALD and Δ ALD in patients treated with ProDisc-L TDR compared with circumferential lumbar fusion and a comparison of adjacent level changes was not described in the original study protocol. These results may not be applicable to all TDR and motion-sparing implants or to other types of fusion procedures. Also note that although the clinical follow-up rate for patients at 5 years posttreatment was over 80% for the combined cohorts, not all radiographs at 5 years were adequate for clear digital analysis, leading to a lower rate of radiographic follow-up in this report.

Conclusions

A majority of the fusion and TDR patients did not have ALD prior to surgery, and there were no differences between treatment groups in the frequency or severity of ALD prior to surgery. At 5 years, no Δ ALDs were observed in 108 (90.8%) of 119 TDR patients and 30 (71.4%) of 42 fusion patients. The rate of radiographic Δ ALD at 5 years was statistically significantly greater in the fusion group ($p = 0.0040$, Fisher exact test). For patients with no preoperative ALD, new findings of ALD 5 years after treatment were reported for 6.7% of TDR patients and 23.8% of fusion patients. At 5 years postoperatively, there was a statistically significant sparing effect on the radiographic appearance of adjacent-level degenerative disease in patients treated with arthroplasty using the ProDisc-L compared with that in patients who had undergone circumferential fusion.

The results of this post hoc analysis of data obtained from a randomized controlled clinical trial provide a baseline reference point in the evolving knowledge database for lumbar TDR and should serve as a benchmark for future study.

Disclosure

Dr. Delamarter receives royalties from Synthes Spine, Inc. Drs. Zigler and Delamarter are consultants for Synthes Spine, Inc. They also serve on the ProDisc-L Publications Committee but have received no direct financial compensation for the writing and editing

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Author contributions to the study and manuscript preparation include the following. Conception and design: all authors. Acquisition of data: Zigler, Glenn. Analysis and interpretation of data: all authors. Drafting the article: Glenn. 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: Zigler. Statistical analysis: Zigler, Delamarter. Administrative/technical/material support: Zigler. Study supervision: Zigler.

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