Multiple-Level Lumbar Total Disk Replacement

A Prospective Clinical and Radiographic Analysis of Motion Preservation at 24–72 Months

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Background: Recent studies demonstrate the efficacy of lumbar arthroplasty using the ProDisc-L. Patients frequently present with multilevel pathology and may be candidates for multilevel disk replacement.

Purpose: To evaluate clinical outcomes and sagittal range of motion of operated levels and adjacent lumbar motion segments in multiple-level ProDisc-L constructs after 2–6 years follow-up.

Patient Sample: A total of 159 patients underwent adjacent 2-level (n = 114), 3-level (n = 41), or 4-level (n = 4) lumbar total disk replacement (TDR).

Study-Design: This is a prospective cohort.

Outcome Measures: Clinical measures: Oswestry Disability Index and Visual Analog Score of patient satisfaction (VAS-S) and pain (VAS-P) data were collected. Radiographic measures: sagittal motion on preoperative and postoperative lumbar radiographs at each operative segment and adjacent segment.

Methods: Patients were evaluated with radiographic and clinical outcomes measures preoperatively, at 6 weeks, 3 months, 6 months, and annually for 24–72 months postoperatively.

Results: Radiographic: at the motion segment adjacent to the TDR, mean preoperative range of motion (ROM) was 8.20 ± 2.88 degrees, compared with 8.40 ± 2.4 degrees postoperatively at last follow-up ($P > 0.05$). Between the 3 TDR groups, there were no significant differences in ROM at any time point except at L5–S1. Across both groups for TDR motion segments, the mean preoperative ROM was 10.15 ± 2.71 versus 12.30 ± 2.25 degrees postoperatively ($P = 0.011$) at last follow-up. At L5–S1 mean preoperative motion was 7.60 ± 3.90 versus 5.81 ± 3.1 degrees postoperatively ($P = 0.60$). Clinical: at 24–72 months postoperatively, all patients had significant reductions in Oswestry Disability Index, VAS-P, and VAS-S scores ($P < 0.05$). At up to 72 months of follow-up, no patient underwent adjacent-level surgery but there were 3 cases of index-level revision surgery.

Conclusions: Multilevel TDR preserves ROM at the individual TDR levels. Most significantly, the nonoperative adjacent level maintains its preoperative ROM at 2–6 years postoperatively. At up to 6 years of follow-up, there has been no need for revision or adjacent-segment surgery. Patients also demonstrate significant improvement in pain and disability at latest follow-up.

Key Words: lumbar total disk replacement, total disk arthroplasty, artificial disk replacement, lumbar spine, back pain, multilevel disk replacement

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Low back pain is an exceedingly common cause of disability in the United States. Although most cases are self limited, ∼5% of patients will have symptoms that are persistent and disabling enough to merit medical attention.[1] The treatment of these patients has been challenging. Some cases of low back pain, especially those caused by degenerative disk disease (DDD), are particularly resistant to even intensive nonoperative modalities. DDD of the lumbar intervertebral disk involves varying degrees of disk bulging, herniation, annular tearing, desiccation (as seen on T2-weighted magnetic resonance imaging), and mechanical instability.[2] The clinical result is axial back pain with or without radiculopathy. The patients with DDD who fail conservative treatment have traditionally had recourse to lumbar fusion.

The clinical efficacy of lumbar fusion for low back pain is a subject of polarizing debate, and evidence-based guidelines remain equivocal to this day.[3] Less debatable, however, are the long-term adverse effects of lumbar fusion: loss of motion, adjacent segment degeneration, sagittal imbalance, and painful pseudarthrosis.[4,5] Lumbar DDD often affects more than one motion segment. In these patients in whom fusion is used to treat multilevel disk disease, the long-term problems are amplified. Pseudarthrosis rates are higher, adjacent level disk height is decreased, and biomechanical burden on the adjacent-level facet/disk complexes is increased.[5,6] The clinical and radiographic results of fusion for multilevel disease are therefore less reliable than and potentially suboptimal to single level fusion.[7–9]

Lumbar total disk replacement (TDR) has been proposed as an alternative to fusion in the surgical management of intractable low back pain from lumbar DDD. Lumbar TDR theoretically simulates physiological motion-segment biomechanics and thus has the theoretical advantage of minimizing the incidence of adjacent segment disease.[9] Five prospective randomized multicenter Food and Drug Administration Investigational Device

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Exemption (FDA IDE) investigations and a Cochrane review have demonstrated the clinical equivalency and/or superiority of lumbar TDR to fusion in the treatment of single level discogenic back pain.[3,10–16] At 24 months, patients with lumbar TDR had better outcomes in the areas of physical function, pain, return-to-work, and overall satisfaction. These results are maintained at 5 years according to the most recent analyses.

The most recent FDA IDE study of the ProDisc-L lumbar TDR specifically investigated its use in 2-level DDD. As had the previous single-level studies, the 2-level ProDisc study demonstrated superior results in terms of physical function, pain, narcotic use, return-to-work, and quality of life over circumferential 2-level fusion at 24 months. The results of the FDA study have provided the impetus to consider lumbar TDR as an alternative to fusion for multilevel DDD (≥ 2 levels). The use of lumbar TDR at more than 2 consecutive levels has been formally investigated by very few studies[17], and an analysis comparing the motion of the treated versus the adjacent levels by subgroup has to the best of our knowledge not yet been reported. In the present study, we seek to demonstrate the clinical efficacy and biomechanical performance of multilevel lumbar TDR (2–4 levels) at up to 72 months of follow-up.

MATERIALS AND METHODS

Patient Selection

This study was a prospective cohort of patients at a single center who underwent lumbar TDR with the ProDisc-L (Synthes Spine, Westchester, PA) at 2 (TDR-2), 3 (TDR-3), or 4 (TDR-4) adjacent levels as part of either the 2-level ProDisc-L FDA IDE trial, or under continued access or compassionate use (for cases involving more than 2 level replacement). The patients had to have DDD at 2 or more contiguous levels of the lumbar spine from L1–S1, to have failed 6 months of conservative treatment according to American Pain Society guidelines, to have radicular or nonradicular back pain, and to have demonstrated a minimum Oswestry Disability Index (ODI) low back pain questionnaire score of $>40\%$ (40/100) impairment. All patients had a minimum of 24 months of follow-up, with complete radiographs and clinical questionnaires for each follow-up time-point.

Surgical Technique for Multilevel ProDisc-L

The design and surgical technique for the single level ProDisc-L TDR has been described previously, and with the exception of a more extensile approach, the technique for multilevel replacement is identical.[16] The primary surgeon in all cases was the senior author (R.D.). Patients were positioned in a supine, neutral position and either a mini-open (for 2 levels) or standard (for 3 or 4 levels) retroperitoneal approach was used. A complete discectomy, denudation of cartilaginous endplates, and meticulous release of the posterior longitudinal ligament at each level were undertaken. With adequate mobilization of the intervertebral space and under fluoroscopic control, an implant trial was advanced to the posterior margin of the vertebral bodies and a chisel advanced into the bodies until fully seated against the trial. The prosthetic endplates were then inserted in collapsed manner with the keels following the chiseled troughs. Finally, the polyethylene insert was then placed with minimal distraction.

Outcome Measures

Clinical Measures

To determine clinical outcomes, patients were given the standardized ODI and Visual Analog Score for Pain and for Satisfaction (VAS-P and VAS-S) preoperatively and during all postoperative visits: at 6 weeks, 3 months, 6 months, and annually for up to 72 months. With each postoperative survey, patients were also asked whether they would undergo the surgery again. At each visit, standardized physical and neurological examinations were conducted by the senior author and included straight-leg test, sensation to light touch, motor strength, and reflexes. Neurological success was defined as the preservation of or improvement in all 4 of the neurological criteria tested: straight-leg test, sensation to light touch, motor strength, and reflexes.

Biometric Measures

Range of motion (ROM) analysis was based on lateral active flexion-extension films of the lumbar spine, obtained preoperatively and at each postoperative visit. Films were obtained at maximum flexion and extension. Segmental ROM was obtained by calculating the difference between segmental lordosis at flexion and extension using the validated "spike method" previously described.[5] The method was chosen for its high interobserver and intraobserver reliability. Values were obtained for each operative motion segment as well for the segment adjacent to the entire prosthetic construct. Measurements were performed using a precision digital goniometer with resolution of 0.1 degree (Macklanburg-Duncan Electronic Digital Protractor, Oklahoma City, OK). Every film was analyzed independently by 3 experienced spine surgeons. Each radiograph was measured twice by the same observer, yielding 6 measurements per radiograph.

Statistical Analysis

For statistical analysis, patients were placed into a "multilevel group" according to the number of adjacent disk replacements: 2-level, 3-level, or 4-level TDR (TDR-2, TDR-3, or TDR-4). Numerical values from the ODI, VAS-P, and VAS-S were subjected to mean and SD analysis. Statistical significance for differences between final postoperative and original preoperative values, and for differences in outcomes between groups according to numbers of disks replaced, were determined using analysis of variance. Segmental ROM values at a given operative level (eg, L4–L5) within a multilevel class (eg, TDR-3) were averaged and compared with the mean preoperative ROM at that level. The mean postoperative segmental ROM at a given level in a given class was also compared with the ROM of that same level in the other classes

(ROM of L4–L5 in TDR-3 versus that in TDR-2 versus TDR-4). Statistical significance for differences between preoperative and postoperative ROM at a given level, and between ROM of a given level across the various classes, were obtained using the student *t* test. As for the ROM for the adjacent segment (not undergoing TDR), postoperative values in each class were averaged and compared to the mean preoperative ROM values. For all comparisons, *P*-values <0.05 were deemed significant.

RESULTS

A total of 159 consecutive patients who underwent multiple-level lumbar TDR received 367 ProDisc-L TDRs. The average age was 41 years, with a range of 27–66 years. Eighty-nine (56%) patients were males and 70 (44%) were females. The average patient body mass index was 26.0. Twelve patients were smokers. A total of 114 patients were in the TDR-2 group, with 100 receiving TDR at L4–L5/L5–S1 and 14 receiving TDR at L3–L4/L4–L5. A total of 41 patients were in the TDR-3 group, with 38 receiving TDR at L3–L4/L4–L5/L5–S1 and 3 receiving TDR at L2–L3/L3–L4/L4–L5. Four patients were in the TDR-4 group, having received TDR at L2–L3/L3–L4/L4–L5/L5–S1 (Table 1).

Clinical Outcome

Preoperative ODI was 34.2, 33.3, and 34 for the TDR-2, TDR-3, and TDR-4 level groups, respectively ($P > 0.05$).

All groups exhibited statistically significant progressive improvement in ODI relative to preoperative levels. For the TDR-2 patients, the ODI improved from 34.2 at preoperative to 46.7 (36.5%) and 44.8 (31.0%) at 6 weeks and at 72 months postoperatively, respectively ($P < 0.05$). TDR-3 patients had an average improvement from 33.3 preoperative to 40 (20.7%) and 50.7 (52.3%) at 6 weeks and 24 months postoperatively, respectively ($P < 0.05$). For the TDR-4 patients, there was an average improvement from 34 preoperative to 37 (9.0%) and 52.9 (55.6%) at 6 weeks and 24 months postoperatively, respectively ($P < 0.05$).

Although there was greater percent improvement from the preoperative score in the TDR-3 and TDR-4 groups than in the TDR-2 groups at the latest respective follow-up, these between-group differences did not achieve statistical significance ($P > 0.55$ for all 3 comparisons) (Tables 1–3). The improvement in ODI among all groups is consistent with the previously reported improvement of 46.1% at 24 months in TDR patients from the 1-level ProDisc-L IDE study.

The VAS-P scores showed a similar pattern of improvement. There were no significant differences among the groups in preoperative pain scores: 7.7 for TDR-2, 7.7 for TDR-3, and 7.19 for TDR-4 ($P = 0.22$). TDR-2 values improved from 7.7 at preoperative to 4.5 (42.1%) and 3.1 (59.4%) at 6 weeks and 72 months postoperatively, respectively ($P < 0.05$). TDR-3 values improved from 7.7 preoperative to 6.3 (18.0%) and 3.4 (55.4%) at 6 weeks and 24 months postoperatively, respectively ($P < 0.05$); TDR-4 values improved from 7.2 to 2.2 (70%) and 2.2 (70%) at 6 weeks and 24 months, postoperatively, respectively ($P > 0.05$). Within each group, all differences between preoperative and postoperative scores were statistically significant ($P < 0.001$). Between the 3 groups, the differences in final improvement did not reach statistical significance ($P > 0.50$ for each comparison).

The average VAS-S scores improved from 7.62 cm at 6 weeks to 8.63 cm at 72 months in the TDR-2 group ($P < 0.05$), from 7.10 cm at 6 weeks to 8.13 cm at 24 months in the TDR-3 group ($P < 0.05$), and from 8.30 cm at 6 weeks to 9.80 cm at 24 months in the TDR-4 group ($P < 0.05$). The stated improvement in satisfaction at 24–72 months was similar across all three groups ($P > 0.50$ for differences between the groups) and was statistically significant versus the respective 6-week scores ($P < 0.05$ for all 3 comparisons).

ROM

At the motion segment adjacent to the TDR, the mean ± SD preoperative ROM was 8.20 ± 2.88 degrees, compared with 8.40 ± 2.43 degrees postoperatively ($P > 0.50$) at last follow-up. Between the 3 TDR groups (2-level, 3-level, and 4-level replacements), there were no statistically significant

TABLE 1. Summary of TDR Patient Groups

Group	n	Levels Operated (No. Patients)
TDR-2	114	L3–L4 (14) L4–L5 (100)
TDR-3	41	L2–L3/L3–L4/L4–L5 (14) L3–L4/L4–L5/L5–S1 (100)
TDR-4	4	L2–L3/L3–L4/L4–L5/L5–S1 (4)

L indicates lumbar; TDR, total disk replacement.

TABLE 2. Summary of Improvement in Oswestry Disability Index and VAS-P

Outcome Measure	n	Mean Preoperative Score	% Change in Clinical Measurement* 6 wk	24 or 72 mo†	P
ODI					
TDR-2	114	34.2	36.5	31.0	<0.05
TDR-3	41	33.3	20.7	52.3	<0.05
TDR-4	4	34.0	9.0	55.6	<0.05
VAS-P					
TDR-2	114	7.7	42.1	59.4	<0.001
TDR-3	41	7.7	18	55.4	<0.001
TDR-4	4	7.2	70	70	<0.001

*Compared with preoperative score.
†72-month evaluation applies to TDR-2 group.
ODI indicates Oswestry Disability Index; TDR, total disk replacement; VAS-P, Visual Analog Score of Pain.

TABLE 3. Summary of Improvement in VAS-S

	n	Score (cm) 6 wk	24 or 72 mo†	P
TDR-2	114	7.62	8.63	<0.05
TDR-3	41	7.10	8.13	<0.05
TDR-4	4	8.30	9.80	<0.05

†72-month evaluation applies to TDR-2 group.
TDR indicates total disk replacement, VAS, Visual Analog Score.

differences in ROM at a given lumbar level ($P > 0.05$ for all comparisons of a particular level between groups) at any time point, except at L5–S1 ($P < 0.05$ for all comparisons). For all TDR motion segments, excluding L5–S1, the mean preoperative range of motion was 10.15 ± 2.71 versus 12.30 ± 2.25 degrees postoperatively ($P = 0.09$). For L5–S1 the mean preoperative range of motion was 7.60 ± 3.90 versus 5.81 ± 3.1 degrees postoperatively ($P = 0.60$). In the TDR-2 group, 100/114 patients (88.0%) met the criteria for neurological success at 6 months and 102/114 (90.0%) at 72 months. In the TDR-3 group, 37/41 (90.0%) and 38 (93.0%) met neurological success at 6 months and 24 months, respectively. All patients in the TDR-4 group met neurological success at 6 and 24 months, respectively. None of the differences between time points and between groups reached statistical significance (all P-values > 0.5).

COMPLICATIONS

Of the 159 patients, 3 underwent reoperation for various indications. One patient in the TDR-2 group with continued back pain underwent posterior instrumented dynamic stabilization from L4–S1 using the Dynesys system (Zimmer Inc., Warsaw, IN). Another patient in the TDR-2 group underwent removal of prostheses and anterior/posterior fusion from L4–S1 after severe trauma-related vertebral fracture and device dislocation at L5–S1. One patient in the TDR-3 group underwent L2–S1 posterior instrumented fusion for continued back pain. There were no surgeries at adjacent levels in any of the groups. There were 4 cases of postoperative lower extremity radiculopathy, all on the left side, and all were in the TDR-2 group. These were thought to be secondary to the left-sided retroperitoneal approach. All resolved within 6 months of surgery. There were no neurological complications involving loss of motor strength in any of the groups at any time point. There were 4 cases of deep venous thrombosis, all in the TDR-2 group, and all within 3 weeks of surgery. There were no embolic complications from the thrombotic events. There was one superficial infection of the abdominal incisional wound which required operative debridement and oral antibiotics. The deep tissues and implant were not affected and there were no long-term sequelae from the infection (Table 4).

TABLE 4. Summary of Complications (8/159 Patients)

Indication	Group	n	Details of Case
Device dislocation	TDR-2	1	Trauma-related vertebral body fracture and device dislocation at L5–S1. Patient underwent device removal, followed by anterior and posterior fusion of L4–S1
Continued back pain	TDR-2	1	Implantation of posterior dynamic stabilization device (Dynesys, Zimmer Inc.) L4–S1
	TDR-3	1	Posterior instrumented fusion L2–S1
Radiculopathy	TDR-2	4	Self-limited and resolved by 3 wk postoperatively. All on left side. Attributed to left-sided retroperitoneal approach

L indicates lumbar; TDR, total disk replacement.

DISCUSSION

The surgical treatment of painful multilevel lumbar DDD that is refractory to conservative management has historically produced mixed results. The results of multilevel fusion are unreliable at both the index and adjacent segments.[7] In the control arm of the recent 2-level ProDisc FDA IDE study, 78.7% of patients with circumferential 2-level constructs fused by 24 months. It should be noted that only one of the cases of pseudarthrosis was clinically significant and required reoperation. Reported fusion rates from smaller studies are more optimistic, with fusion rates of 82%–100%.[7,18] Regardless of the success of fusion, it is clear from both clinical and finite-element studies that multiple level fusion places unnatural burden on the adjacent motion segments.[8] Fusion locks the involved vertebrae into a nonphysiological configuration during ROM, with adjacent nonfused levels undergoing greater excursion stresses than normal.[19] In addition to motion preservation, one of the proposed advantages of the ball-and-socket TDR used in this study is that it allows all involved levels to find their physiological alignment in relation to neighboring levels. It is believed that the putative preservation of motion and protection against adjacent segment loading will lead to better clinical results than fusion.

The goal of this study was to determine the clinical and radiographic characteristics of multilevel (2–4 levels) lumbar ProDisc-L constructs at 24–72 months of follow-up. Aghayev et al[20] have recently reported on both the clinical and ROM effects of multilevel lumbar TDR after the long-term follow-up but the ROM at adjacent untreated levels have not been evaluated by prior studies. The present study demonstrates that even with 3-level and 4-level disk replacements, patients experience the same significant improvement in both ODI and pain scores as originally seen with 1-level and 2-level TDR.[15] These improvements are progressive and sustained, up to the latest follow-up, which for some patients was at 72 months.

Patients in all of the TDR groups experienced clinically and statistically significant improvement in pain relative to the preoperative baselines, as seen with the VAS-P scores and ODI scores. At the most recent follow-up, the ODI had improved an average of 10.6, 17.4, and 18.9 points in the TDR-1, TDR-2, and TDR-3 groups, respectively. Similarly, the VAS-P scores improved 55–70 percentage points. This magnitude of clinical improvement exceeds the minimally clinically important difference of 10 points used in several relevant large clinical trials[17,21] and is similar to the change observed in the 1-level ProDisc IDE trial.[11] The number of levels that were replaced did not appear to affect the amount of pain relief observed, and the addition of more levels certainly did not detract from the results seen with single-level replacement. Similarly, patient satisfaction (VAS-S) was high for all groups regardless of levels replaced.

In terms of biometric performance, the use of lumbar TDR in this study maintained the ROM of every motion segment into which it was implanted. The number of levels undergoing TDR and the particular configuration of the multi-TDR construct (L4–L5/L5–S1 versus L3–L4/L4–L5)

did not influence this segmental motion-sparing effect in any significant way: an L4–L5 TDR in a 2-level construct, for example, demonstrated similar ROM as an L4–L5 TDR in a 3 level construct. The construct-independent behavior of the individual TDR has also never been reported in vivo. Most importantly, the nonoperative level adjacent to the construct maintained its preoperative ROM at up to 72 months of follow-up regardless of the length of the TDR construct. A 3-level TDR had no more, and no less, adjacent segment sparing ability than a 2-level construct.

Although revision surgeries were performed for a limited number of patients, no surgery was necessary at the adjacent motion units in any of the constructs throughout the time-frame of observation (up to 72 mo). This is in contrast to the rate of adjacent segment surgery that has been reported for fusion constructs, which even by conservative figures approaches 20% by 60 months.[7,8] Although various types of complications have been described with the anterior retroperitoneal approach to the lumbar spine[2] the few complications observed in this study (deep venous thrombosis, transient radiculopathy, and superficial infection) were all self-limited and reversible.

Despite its promising results, this observational study has some drawbacks. First, there is no control group (circumferential fusion) against which to compare the results. Therefore, statements can only be made about the clinical feasibility of multilevel TDR as a replacement to fusion. Whether this potential translates into actuality (and before conclusions of noninferiority and superiority can be drawn), the results must withstand the rigors of a prospective, randomized, controlled investigation. This study, although prospective, has a relatively small sample size when considering the TDR-3 and TDR-4 groups. As more of these procedures are performed, more refined observations can be made about the differences between 2-level, 3-level, and 4-level replacements.

The use of the multiple level TDR construct does not inhibit preservation of ROM at the individual TDR levels. Most significantly, the nonoperative level adjacent to the construct maintains its preoperative ROM at 72 months postoperatively. At up to 72 months postoperatively, there has been no need for revision or adjacent-segment surgery. Patients also demonstrate significant improvement in pain and disability at latest follow-up.

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