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Lumbar Total Disc Arthroplasty Utilizing the ProDisc Prosthesis in Smokers *Versus* Nonsmokers

A Prospective Study With 2-Year Minimum Follow-up

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Study Design. Prospective nonrandomized clinical series.

Objectives. To evaluate the efficacy of ProDisc lumbar artificial disc replacement (ADR) in smokers *versus* nonsmokers.

Summary of Background Data. Smoking is a negative predictor in fusion surgery. To date, a prospective study of the treatment of incapacitating discogenic low back pain using ADR in smokers *versus* nonsmokers has not been described.

Methods. A prospective analysis was performed on 104 patients with disabling discogenic low back pain treated with single-level lumbar ProDisc total disc arthroplasty. Smokers and nonsmokers were assessed before surgery and after surgery using patient satisfaction, Oswestry, and Visual Analog Scores. Additionally, preoperative and postoperative neurologic, radiographic, and pain medication assessments were performed at similar postoperative intervals.

Results. Oswestry, Visual Analog Scores, and patient satisfaction scores revealed statistical improvement beginning 3 months after surgery and were maintained at minimum 2-year follow-up. Patient satisfaction scores were higher in smokers (94%) than in nonsmokers (87%) at 2-year follow-up ($P = 0.07$). Radiographic analysis revealed an affected disc height increase from 4 mm to 13 mm ($P < 0.05$) and an affected disc motion from 3° to 7° ($P < 0.05$). No cases of loosening, dislodgment, mechanical failure, infection, or fusion of the affected segment occurred.

Conclusions. The results of our study indicate that smokers do equally well compared with nonsmokers when ProDisc ADR is used in the treatment of debilitating lumbar spondylosis. Patient outcome and radiographic scores showed significant improvement compared with preoperative levels. Although not evident in our series, additional surveillance for intraoperative and postoperative vascular spasm and occlusion may be warranted in smokers.

Key words: low back pain, discogenic pain, artificial disc replacement, smokers, ProDisc ADR. **Spine 2006;31: 992–997**

The results of lumbar spinal surgery, in particular, lumbar spinal fusion surgery, have been noted to vary with respect to age, smoking status, litigation and Workers' Compensation cases, and others.[1] Smoking has been defined as a detrimental factor in obtaining lumbar spinal fusion.[2–6] Artificial disc replacement has been proposed as a substitute for spinal fusion with the aim of treating back pain while preserving vertebral motion at the operated levels.

Few prospective studies have been published on the results of lumbar disc prosthesis.[7,8] Furthermore, there are no studies that we are aware of that control for the factors known to complicate results with spine fusion performed for degenerative disc disease, specifically tobacco use. The goal of the present prospective study is to evaluate changes in functional and disability outcomes in a prospective cohort of patients, smokers *versus* nonsmokers, that have received the ProDisc lumbar disc replacement for single-level degenerative disc disease with minimum follow-up of 2 years. Our hypothesis is that smoking may have a detrimental effect on lumbar artificial disc replacement (ADR).

Methods

Patient Evaluation. Prospective data were compiled for single-level ProDisc procedures from March 2000 to April 2002. Patients 18 to 60 years of age with disabling and recalcitrant discogenic low back pain and minimal radicular pain secondary to single-level lumbar spondylosis from L4 to S1 were included. Only patients with complete 2-year follow-up data were included for analysis. Sixty percent of our patients had only discogenic low back pain without radicular and/or neurogenic symptoms. Forty percent of our patients had both severe low back pain as well as radicular pain. In these latter patients, the radicular component of the pain was limited to less than 50% of the total (back and leg) pain component. The smoking status of each patient was noted before surgery through a questionnaire. Serum nicotine levels were not obtained. Exclusion-

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ary criteria included: patients with spinal stenosis, osteoporosis, prior fusion surgery, chronic infections, metal allergies, facet arthrosis, inadequate vertebral endplate size, more than one level of spondylosis, neuromuscular disease, pregnancy, Workers' Compensation, spinal litigation, body mass index greater than 35, and/or any isthmic or degenerative spondylolisthesis greater than Grade 1.

All patients had failed conservative treatment for a minimum of 9 months. Surgery was performed after a complete radiographic assessment had been performed including anteroposterior (AP)/lateral/flexion/extension radiographs, computerized tomography (CT) in the axial, sagittal, and coronal planes, MRI, and/or discography. As we have seen in our previous studies, there were 2 groups of patients that could be radiographically categorized.[9] The first group included those patients with greater than 50% disc height loss, and the second group included those patients with less than 25% to 50% disc height loss with a concomitant chronic anular tear as exhibited in discography. Patients with evidence of intra-articular facet degeneration, specifically evidence of joint space narrowing with or without cystic changes, were excluded from the study. Patients with minimal extra-articular facet changes (calcifications) were not excluded. Discography was used only in patients with questionable multilevel spondylosis findings on MRI and/or in the setting of minimal disc height loss and a question of a chronically symptomatic anular tear. Positive discography was defined as concordant pain with at least a rating of 6 of 10 and an abnormal postdiscography CT scan contrast pattern (*i.e.*, anular tear, disc extrusion). All procedures were performed by the senior author at a single institution. Bias as to outcome was avoided with the use of primary outcome measurements determined by patient responses to questionnaires. Secondary parameters requiring measurements such as disc height of affected level, adjacent level disc height, and motion were performed by a trained technician blinded to the hypothesis of the primary investigator. The data were collected and compiled by an independent technician, blinded to the hypothesis of the primary investigator. After the above data had been compiled, it was analyzed by an independent examiner who had not had any interaction with the patients or involvement with the surgical procedures.

Surgical Technique. The surgical approach was consistent with the patient in a supine position on a fluoroscopic imaging table with legs and arms abducted with the surgeon working between the patient's legs. Fluoroscopy was obtained in AP and lateral plane to determine level of diseased disc and obliquity of lordosis before incision. A transverse incision for L5–S1, or longitudinal incision for all other levels, was then made at the marked level of diseased disc. A standard right sided median retroperitoneal approach to L5–S1 and left-sided median retroperitoneal approach for all other levels was then performed by the senior author exposing the level of disease.

Trialing was performed to make the assessment of appropriate size with regards to height and AP diameter using assistance of lateral fluoroscopy. Adequate central/midline location of prosthesis was confirmed using AP fluoroscopy before administration of keel cuts. After the midline was determined, keel cuts were made using the keel-cutting chisel guided over the prosthesis trial. The endplates were then distracted and the polyethylene implant was inserted. Following this, AP and lateral fluoroscopy confirmed appropriate prosthesis positioning and size. No other procedures were preformed at that time of the index procedure.

Outcome Measurement. Patients were assessed before surgery and after surgery at 3, 6, 12, and 24 months. The primary functional outcomes assessed before and after surgery were disability and pain scores using the Oswestry Disability Index (ODI)[10] and the Visual Analog Score (VAS). Additional clinical parameters included analysis of preoperative and postoperative patient satisfaction, general back pain, radicular pain, medication usage, and complications. Patient satisfaction was rated as follows: 1 = completely satisfied (pain absent at all times and unimpaired employment and activities of daily living [ADL]); 2 = satisfied (slight pain that requires no medication and that occurs no more than once per day, minimal impairment in employment or ADL); and 3 = unsatisfied (pain that occurs more than one time per day, requires medication, and results in changes in ADL and employment). Back pain, radicular pain, and medication usage were rated none (1), occasional (less than 1 time per day) (2), and regular (greater than 1 time per day) (3).

Radiographic Assessment. Preoperative and postoperative radiographs were obtained in all patients, including standing anteroposterior, lateral, flexion and extension, and lateral bending films. Detailed measurements of intervertebral disc heights of affected and adjacent levels, angular intervertebral disc motion, subsidence, pelvic tilt and incidence, and sacral slope were obtained by using digitized images and appropriate computer software (Medimage Software, Vepro Computersysteme GmbH, Pfungstadl, Germany). Interobserver and intraobserver accuracy measurements of angular motion, migration, and subsidence were performed according to Lim[11] using these digitized images. Heterotopic bone formation and fusion were also noted.

Statistical Analysis. To assess whether there was differential change over time between smokers and nonsmokers, mixed effects models were conducted for the continuous variables (ODI and VAS) and generalized estimating equations were conducted for patient satisfaction. A significant time by smoking interaction would indicate different rates of change between the smoking and nonsmoking groups. If a significant interaction occurred, follow-up analyses were conducted to assess the nature of the interaction. A power analysis was also performed to determine the likelihood of introducing a Type II statistical error.

■ Results

Demographic

The demographic results are summarized in Table 1. A total of 104 of a possible 110 patients fulfilled all follow-up criteria. Complete follow-up data were not possible in 6 patients because of distant places of domicile. All attempts were made to obtain clinical and radiographic follow-up in these 6 patients. There were 34 (33%) smokers and 70 nonsmokers. The average smoking history was 23 pack-years. The median follow-up time was 34 months (range, 24–47 months) for nonsmokers and 33 months (range, 24–49 months) for smokers. The median age in the nonsmokers was 49 years (range, 29–60 years), and the median age for smokers was 45 years (range, 30–60 years). The average

Table 1. Demographic and Outcomes Data

	Smokers	Nonsmokers
N	34	70
Age (yr)	45.5	49.5
Prior surgery (%)	61.8	48.6
VAS (preoperative, 3 mo, 24 mo)	7.5, 3.2, 4.5	7.5, 3.0, 3.8
Oswestry (preoperative, 3 mo, 24 mo) (%)	55, 29, 28	52, 31, 32
Patient satisfaction (3 mo, 24 mo) (%)	97, 94	94, 87
Leg pain (preoperative, 24 mo) (%)	50, 16	48.6, 9
Work rates (full- and part-time preoperative) (%)	6, 3	11.6, 4.3
Work rates (full- and part-time 24 mo postoperative) (%)	50, 23.5	30.9, 36.8

duration of pain before surgery was 104 months (median, 70 months; range, 9–400 months). Forty-nine percent of patients who were nonsmokers had prior posterior surgery at the affected levels. Sixty-one percent of patients who were smokers had prior posterior surgery at the affected levels. The predominant level of surgery was L5–S1 in both groups (Table 2).

Clinical Outcomes

Clinical outcomes are summarized in Table 1. Preoperative ODI decreased from 55% to 28% at 2 year follow-up ($F = 27.75$, $P < 0.001$) in smokers and from 52% to 32% in nonsmokers ($F = 26.35$, $P < 0.001$). However, there was no significant differential change between the two groups on ODI scores ($F = 0.80$, $P = 0.53$), and smokers and nonsmokers did not differ on overall ODI scores across all time periods ($F = 0.36$, $P = 0.55$). Similarly, preoperative VAS decreased from 7.5 to 4.5 at the 2-year follow-up ($F = 16.30$, $P < 0.001$) in smokers and from 7.5 to 3.8 in nonsmokers ($F = 16.30$, $P < 0.001$). However, there was no significant differential change between the two groups ($F = 0.62$, $P = 0.65$), and smokers and nonsmokers did not differ on overall VAS scores across all time periods ($F = 0.39$, $P = 0.53$).

Patient satisfaction levels were 97% satisfied or completely satisfied at the 3-month follow-up and 94% satisfied or completely satisfied at the 2-year follow-up in smokers ($P = 0.55$). Patient satisfaction levels were 94% satisfied or completely satisfied at the 3-month follow-up and 87% satisfied or completely satisfied at the 2-year follow-up in nonsmokers ($P = 0.07$). The difference in change in patient satisfaction between smokers and nonsmokers from the 3-month to 2-year follow-up was not significant ($\chi^2 = 0.71$, $P = 0.39$). In addition, smokers and nonsmokers did not differ on overall patient satisfaction across all time periods ($\chi^2 = 2.81$, $P = 0.09$).

Table 2. Levels of Surgery in Smokers and Nonsmokers

Nonsmokers	Level of Surgery	Smokers
4	L3–L4	3
12	L4–L5	5
51	L5–S1	25
3	L5–L6	2

The presence of leg pain was not significantly different in smokers or nonsmokers ($F = 0.53$, $P = 0.47$). Leg pain significantly decreased for both smokers and nonsmokers (all, $P < 0.001$); however, there was no significant differential change in leg pain between smokers and nonsmokers (0.53, $P = 0.47$). Regular usage of nonsteroidal medication decreased significantly in smokers ($\chi^2 = 25.12$, $P < 0.001$) and nonsmokers ($\chi^2 = 15.22$, $P < 0.001$). However, there was no differential change between smokers and nonsmokers ($\chi^2 = 2.92$, $P = 0.09$). In addition, there was no differential change between smokers and nonsmokers on narcotics ($\chi^2 = 0.02$, $P = 0.89$) and morphine derivatives (Tramadol) ($\chi^2 = 0.27$, $P = 0.60$). Smokers and nonsmokers did not significantly change in morphine derivative use ($\chi^2 = 0.31$, $P = 0.58$ for smokers; $\chi^2 = 0.01$, $P = 0.94$ for nonsmokers). However, nonsmokers showed a slight decrease in narcotic use ($\chi^2 = 4.11$, $P < 0.05$), whereas smokers did not significantly decrease their narcotic use ($\chi^2 = 1.85$, $P = 0.17$) (Table 3). Employment patterns following surgery revealed a 3- to 8-fold increase in full-time and/or part-time employment in both smokers and nonsmokers.

The average reduction in ODI was 10.69, with a standard error of the mean equal to 1.06. For smokers, the average reduction was 12.61, with a standard error of the mean equal to 2.07. The difference in these improvements was not statistically significant (one-sided two-sample t test P value = 0.20). Conditioning on these standard errors, the power of such a test (having significance level = 0.05) is described by the power curve in Figure 1. If, for example, in our study, smokers had a reduced absolute ODI score of 6 compared with nonsmokers (on average), this test would have a power of roughly 0.80 against this alternative. A difference of 20% (absolute number of 10 points) would have a power of roughly 0.95.

Radiographic Analysis

The median preoperative height of the affected discs significantly increased for both smokers and nonsmokers (all, $P < 0.001$). However, there was no significant differential change in height between smokers and nonsmokers ($F = 0.69$, $P = 0.41$), and there was no difference in overall height of the affected discs between smokers and nonsmokers ($F = 2.19$, $P = 0.14$). Motion of the affected discs was increased for both smokers and nonsmokers (all, $P < 0.001$). However, there was no significant differential change in motion between smokers and nonsmokers ($F = 0.11$, $P = 0.74$), and there was no difference in overall motion between smokers and nonsmokers ($F = 2.66$, $P = 0.10$). The heights of the adjacent level discs were not significantly changed. No correlation was determined to exist between clinical outcome and pelvic incidence, tilt, or sacral slope. There were no cases of subsidence, loosening, dislocation, or failure of metallic or polyethylene components. Our accuracy measurement results were similar to the Lim *et al*

Table 3. A Medication Usage Smokers and Nonsmokers (%)

	NSAIDs		Narcotics		Tramadol	
	Preoperative	24 Months	Preoperative	24 Months	Preoperative	24 Months
Smokers						
None	27	80	82	95	74	75
Occasional	15	15	0	0	0	10
Regular	59	5	18	5	27	15
Nonsmokers						
None	28	68	84	96	74	70
Occasional	28	10	1	0	7	14
Regular	44	22	15	4	19	16

findings with an interobserver measurement of 1.7° and an intraobserver measurement of 1.6°.[11]

Complications

Complications in this study were primarily limited to those associated with the operative approach and operative field. There were two retroperitoneal hematomas requiring drainage and an iatrogenic bladder laceration. No cases of implant neurologic impingement or encroachment occurred. There were no implant-associated complications or need for implant revision. No cases of vascular injury, deep venous thrombosis, retrograde ejaculation, ureteral injury, neurologic injury, or infection occurred. A single patient had persistent leg pain following application of an L5–S1 implant that required posterior exploration and decompression. Posterior foraminal exploration revealed posterior subarticular stenosis. The patient continued to be unsatisfied with her outcome at 32 months post index procedure.

■ Discussion

The use of total disc arthroplasty for debilitating discogenic low back pain has been under investigation for over approximately 20 years. A number of studies have investigated the use of other lumbar disc arthroplasty techniques, including an unpublished review of the initial lumbar ProDisc performed in the early 1990s.[7,8,12–19] None of these studies, however, has evaluated the utilization, safety, and/or efficacy of ADR in smokers and the confounding role smoking may have on clinical and/or outcomes.

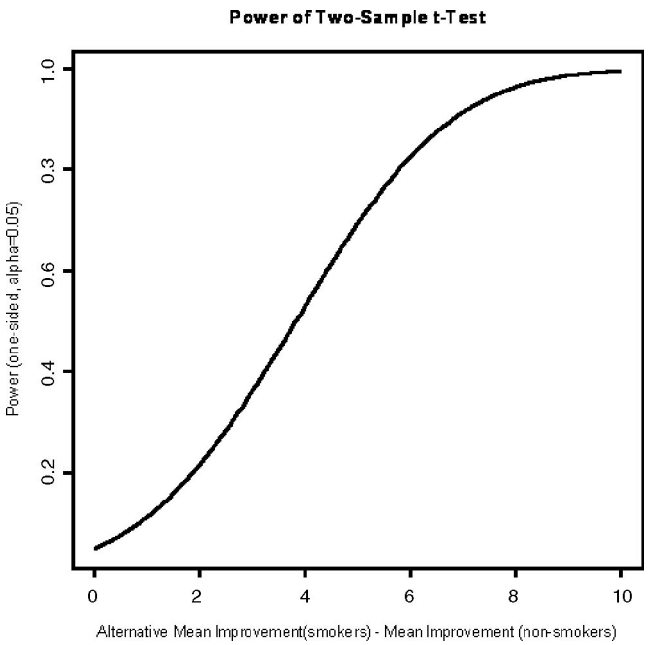

Figure 1. Power analysis curve for Oswestry scores in smokers *versus* nonsmokers.

Individuals who smoke are more likely to have disabling back pain as opposed to those who do not smoke.[4,20] The overall complication rate in smokers in any type of elective orthopedic procedure is also increased.[21–23] The nonunion rate in lumbar fusion in smokers compared with nonsmokers has been demonstrated to be five times higher (40% *vs.* 5%).[3] Gene expression of Type I and II collagen, bone morphogenic protein-2, -4, and -6, basic fibroblast growth factor, and vascular endothelial growth factor are all negatively effected by nicotine.[24] These findings have been corroborated by other similar studies.[2,5,6,25–38]

Similarly, smoking and nicotine have been shown to effect the in-growth of bone into titanium and other implants in animal models.[39–41] Interestingly, smoking appears to have a negative effect on the in-growth of implants in both cortical as well as cancellous bone. In addition, surfaces that have been spray-blasted with titanium, as opposed to machine prepared, are statistically less affected by smoking in terms of bony in-growth. The ProDisc implant is prepared with spray-blasted titanium. The ability of bony in-growth to occur in titanium-sprayed materials may be another explanation for the high success rate of ADR procedures in smokers as opposed to fusion procedures in smokers in which a biologic fusion must occur.

Although it may be intuitive why smokers who receive ADR do better than smokers who undergo fusion due to less than optimum outcomes in fusion patients who smoke,[2–6] it is not immediately intuitive why smokers who receive ADR may do better than nonsmokers who receive ADR. There are several possible explanations for this apparent contradiction. First, chronic exposure to nicotine has been described to cause analgesia.[42] Second, the degree and intensity of both nucleus pulposus and anular fiber cell death have been shown to be greater when

these cells are exposed to nicotine than in those without exposure to nicotine. Lastly, it has been shown in heavy smokers that nicotine induces a phasic blood pressure increase that might have a baroreceptor-dependent pain-dampening effect.[43]

In our current series, the incidence of disabling low back pain and radicular findings was no different at the time of enrollment in smokers as opposed to nonsmokers. At the 2-year follow-up, the incidence of disabling back pain and leg pain was significantly reduced in both smokers and nonsmokers. Significant improvements in VAS and ODI scores were noted in both smokers and nonsmokers, with no difference in the amount of improvement between smokers and nonsmokers. Interestingly, there was a statistical trend toward a higher patient satisfaction rate in smokers ($P = 0.09$). We noted no differences in radiographic outcomes in both groups. These findings suggest that the intervention of disc arthroplasty is not confounded by smoking.

There are limitations in our current series. Our series examines only the results of smokers and nonsmokers who have received the ProDisc arthroplasty for treatment of disabling back pain. We do not have, as part of our series, a nonoperative and/or an arthrodesis treatment group. Thus, direct conclusions of disc arthroplasty as opposed to lumbar arthrodesis are not possible. Although we do not have index study fusion controls in our study, a recent prospective randomized study, which did not control for smoking, comparing circumferential fusion (53 patients) *versus* ProDisc ADR (179 patients), revealed patient satisfaction rates of 62% and 87%, respectively, at an average follow-up of 2.4 years.[44] No statistical differences were noted in ODI and VAS scores in this study. Lastly, our series only examines patients at the 2-year follow-up. The confounding effects of a lifetime of smoking will need to be systematically rereviewed.

Although no increase in vascular complications was noted in our series of both patient groups, a meticulous and mandatory preoperative clinical and radiographic examination is necessary in all patients to ensure satisfactory outcomes. Careful intraoperative and postoperative monitoring of pulses should be performed in all patients.

■ Conclusion

The results of our study indicate that smokers do equally well compared with nonsmokers when ProDisc ADR is used in the treatment of debilitating lumbar spondylosis. Patient outcome and radiographic scores showed significant improvement compared with preoperative levels.

■ Key Points

- ProDisc lumbar disc replacement can improve clinical outcome and pain scores in nonsmokers as well as nonsmokers.
- Stability of implant components and radiographic functional mobility are equal among smokers and nonsmokers.
- No additional complications were exhibited in smokers compared with nonsmokers who received ADR surgery.

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