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CLINICAL ARTICLE

Cervical disc arthroplasty with the Prestige LP disc versus anterior cervical discectomy and fusion, at 2 levels: results of a prospective, multicenter randomized controlled clinical trial at 24 months

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OBJECTIVE The authors compared the efficacy and safety of arthroplasty using the Prestige LP cervical disc with those of anterior cervical discectomy and fusion (ACDF) for the treatment of degenerative disc disease (DDD) at 2 adjacent levels.

METHODS Patients from 30 investigational sites were randomized to 1 of 2 groups: investigational patients (209) underwent arthroplasty using a Prestige LP artificial disc, and control patients (188) underwent ACDF with a cortical ring allograft and anterior cervical plate. Patients were evaluated preoperatively, intraoperatively, and at 1.5, 3, 6, 12, and 24 months postoperatively. Efficacy and safety outcomes were measured according to the Neck Disability Index (NDI), Numeric Rating Scales for neck and arm pain, 36-Item Short-Form Health Survey (SF-36), gait abnormality, disc height, range of motion (investigational) or fusion (control), adverse events (AEs), additional surgeries, and neurological status. Treatment was considered an overall success when all 4 of the following criteria were met: 1) NDI score improvement of ≥ 15 points over the preoperative score, 2) maintenance or improvement in neurological status compared with preoperatively, 3) no serious AE caused by the implant or by the implant and surgical procedure, and 4) no additional surgery (supplemental fixation, revision, or nonelective implant removal). Independent statisticians performed Bayesian statistical analyses.

RESULTS The 24-month rates of overall success were 81.4% for the investigational group and 69.4% for the control group. The posterior mean for overall success in the investigational group exceeded that in the control group by 0.112 (95% highest posterior density interval = 0.023 to 0.201) with a posterior probability of 1 for noninferiority and 0.993 for superiority, demonstrating the superiority of the investigational group for overall success. Noninferiority of the investigational group was demonstrated for all individual components of overall success and individual effectiveness end points, except for the SF-36 Mental Component Summary. The investigational group was superior to the control group for NDI success. The proportion of patients experiencing any AE was 93.3% (195/209) in the investigational group and 92.0% (173/188) in the control group, which were not statistically different. The rate of patients who reported any serious AE (Grade 3 or 4) was significantly higher in the control group (90 [47.9%] of 188) than in the investigational group (72 [34.4%] of 209) with a posterior probability of superiority of 0.996. Radiographic success was achieved in 51.0% (100/196) of the investigational patients (maintenance of motion without evidence of bridging bone) and 82.1% (119/145) of the control patients (fusion). At 24 months, heterotopic ossification was identified in 27.8% (55/198) of the superior levels and 36.4% (72/198) of the inferior levels of investigational patients.

ABBREVIATIONS ACDF = anterior cervical discectomy and fusion; AE = adverse event; ASD = adjacent segment degeneration; CAC = Clinical Adjudication Committee; CDA = cervical disc arthroplasty; DDD = degenerative disc disease; FDA = Food and Drug Administration; FSU = functional spinal unit; HO = heterotopic ossification; HPD = highest posterior density; IDE = investigational device exemption; MCS = Mental Component Summary; NDI = Neck Disability Index; NRS = Numeric Rating Scale; PCS = Physical Component Summary; SF-36 = 36-Item Short-Form Health Survey.

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CONCLUSIONS Arthroplasty with the Prestige LP cervical disc is as effective and safe as ACDF for the treatment of cervical DDD at 2 contiguous levels and is an alternative treatment for intractable radiculopathy or myelopathy at 2 adjacent levels.

Clinical trial registration no.: NCT00637156 (clinicaltrials.gov)

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KEY WORDS cervical disc arthroplasty; anterior cervical discectomy and fusion; artificial cervical disc; adjacent segment disease

Anterior cervical discectomy and fusion (ACDF) has been the standard surgical procedure for cervical degenerative disc disease (DDD) associated with intractable radiculopathy or myelopathy since its inception in the 1950s.[1,3,4,17,46] However, ACDF, which aims to eliminate segmental motion between the fused vertebrae, creates abnormal loads, increasing stress and intradiscal pressures on segments adjacent to the fusion.[7,53] This altered biomechanics of the spine has been reported to increase the incidence of adjacent segment degeneration (ASD) and to cause recurrent radiculopathy in as many as 25% of patients.[16,21,25,45]

Cervical disc arthroplasty (CDA) has become a more commonly used surgical procedure in the treatment of cervical DDD. Several large Food and Drug Administration (FDA) investigational device exemption (IDE) clinical trials have established that CDA and ACDF are at least equally safe and effective in treating symptoms associated with single-level cervical DDD.[13,18,20,22,36,37] However, many patients have multilevel disease, and multilevel CDA may be a desirable alternative to fusion because multilevel ACDF can cause even greater stresses to adjacent discs,[30] thereby potentially hastening ASD. Furthermore, compared with single-level ACDF, multilevel ACDF yields higher rates of pseudarthrosis,[48] complications, revisions, and reoperations.[51] In contrast, CDA at 2 adjacent cervical levels has been found to provide near normal mobility at the 2 implanted levels without affecting the adjacent levels,[19] so that each implanted segment in a multilevel CDA is considered biomechanically independent of the adjacent segments.[42] An IDE study demonstrated that patient outcomes were superior and complications fewer with 2-level CDA than with 2-level ACDF.[14] A recent meta-analysis reported that multilevel CDA is as safe and effective as single-level CDA for the treatment of cervical disc diseases.[56]

The purpose of this study, which is registered with the ClinicalTrials.gov database (http://clinicaltrials.gov; registration no. NCT00637156), is to report the 24-month results of an FDA-regulated IDE clinical trial that compared the safety and effectiveness of 2-level CDA using Prestige LP (Medtronic Inc.) with those of 2-level ACDF to treat cervical DDD at 2 contiguous levels.

Methods

Study Design

Patient enrollment required a diagnosis of DDD at 2 adjacent levels (from C-3 to C-7) involving intractable radiculopathy and/or myelopathy unresponsive to at least 6 weeks of nonoperative treatment. Inclusion and exclusion criteria are listed in Table 1. Patients were evaluated preoperatively, intraoperatively, and postoperatively at 1.5, 3, 6, 12, and 24 months. Data in this paper represent all available 24-month safety and effectiveness data as of April 15, 2015.

Sample Size

Determination was based on the hypothesis of noninferiority in overall success of the investigational device compared with the control treatment. Expected success rates were assumed to be 72% and 70% in the investigational and control groups, respectively. With a noninferiority margin of 10%, an alpha level of 0.05, and a power of 80%, the required sample size was 177 patients for each group. With an adjustment of 15% for potential loss to follow-up, 210 ± 5 patients were needed per group. Given the 1:1 randomization, the enrollment goal for this trial was 420 ± 10 patients. Two hundred nine patients received the investigational device, and 188 patients received the control treatment.

The study was approved by independent institutional review boards at each investigational site. All patients who met inclusion requirements and agreed to participate signed an informed consent form. Patients at 30 participating sites were randomized into treatment groups at a 1:1 ratio stratified by site and by varying block sizes (2, 4, and 6). The randomization schedule was centrally generated by the sponsor's statistician using statistical software (SAS, SAS Institute Inc.). Patients and surgeons were blinded only through the screening and informed consent process.

Investigational Device

The Prestige LP is an unconstrained metal-on-metal device comprising 2 low-profile plates that interface through a ball-and-trough mechanism that allows for 4 independent degrees of freedom. The plates attach to the vertebral bodies through impaction of the dual serrated keels. The device comes in a variety of heights and depths to accommodate individual patient anatomy. The low-profile design of the Prestige LP, which avoids obstruction of adjacent levels, makes it well suited for multilevel implantation. Following an IDE clinical trial (NCT00667459), the Prestige LP artificial disc was approved by the FDA in 2014 to treat intractable radiculopathy or myelopathy at a single level of the cervical spine.

Control Device

The control group received a cortical ring allograft for each of the 2 levels and an Atlantis anterior cervical plate (Medtronic Inc.) as part of ACDF.

TABLE 1. Inclusion and exclusion criteria

Inclusion criteria
Cervical DDD at 2 adjacent levels from C-3 to C-7, requiring surgical treatment & involving intractable radiculopathy, myelopathy, or both
Herniated disc &/or osteophyte formation at each level to be treated, producing symptomatic nerve root &/or spinal cord compression, documented by patient history & radiographic studies
Unresponsive to nonop treatment for at least 6 wks, or progressive symptoms or signs of nerve root/spinal cord compression
No previous surgical intervention at the involved levels
At least 18 yrs old & skeletally mature
Preop NDI score ≥30
Preop NRS neck pain score ≥8
If female, non-pregnant, non-nursing, & agrees not to become pregnant
Willing to comply w/ study plan & sign informed consent
Exclusion criteria
Cervical spinal condition other than symptomatic cervical DDD at the involved levels
Cervical instability relative to adjacent segments at either level, defined as sagittal plane translation >3.5 mm or sagittal plane angulation >20°
More than 2 cervical levels requiring surgical treatment
A fused level adjacent to the levels to be treated
Severe pathology of the facet joints of the involved vertebral bodies
Has previous surgical intervention at either or both of the involved levels or at adjacent levels
Previously diagnosed w/ osteopenia or osteomalacia
If DEXA required, T score of −3.5 or lower, or T score of −2.5 or lower with vertebral crush fracture
Presence of spinal metastases
Overt or active infection
Insulin-dependent diabetes
Tobacco use
Chronic or acute renal failure or history of renal disease
Allergy or intolerance to stainless steel, titanium, or titanium alloy
Prisoner
Pregnant
Alcohol &/or drug abuse
Current or pending litigation regarding a spinal condition
Received drugs that can interfere w/ bone metabolism w/in 2 wks prior to surgery

DEXA = dual-energy x-ray absorptiometry.

Surgical Procedure and Postoperative Care

The surgical procedures in both investigational and control groups were performed via a standard anterior approach. A thorough dissection was performed at both index levels. The anterior annulus, disc, and cartilaginous endplates were removed. Gentle distraction was performed, reestablishing the anatomical disc space height, using either intradiscal distraction or Caspar vertebral body distraction pins. The lateral margins of the disc space were exposed, extending superiorly off of the lateral margins of the inferior vertebral body. The posterior annulus and posterior longitudinal ligament were partially or totally removed based on pathology, and the central spinal canal was exposed and decompressed. The depth of the vertebral body was precisely measured with a caliper. In the investigational group, the endplates were preserved and prepared utilizing a dual keel-cutting device. The size of the Prestige LP implant was selected to approximate the depth and height of the interspace. Care was taken not to overdistract the interspace, and the implant was impacted into the disc space. In the control fusion group, the vertebral endplates were decorticated. An anterior plate was placed over the cortical ring allograft and secured to the adjacent vertebral bodies.

The postoperative care regimen could be modified at the treating physician's discretion to accommodate each patient's needs. The use of nonsteroidal antiinflammatory drugs was recommended to the investigational group for the first 2 postoperative weeks but not thereafter. Postoperative bracing was left to the discretion of the physician, but only a soft collar was recommended for the investigational group.

Clinical Outcome Assessments

Patients completed the following validated questionnaires: the Neck Disability Index (NDI),[52] the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36),[54] and the Numeric Rating Scale (NRS; from 0 to 20 representing intensity and frequency of pain) for neck and arm pain.[32] Gait abnormality was also assessed and graded on a scale of 0–5 using Nurick's classification.[38] Patients were evaluated preoperatively and postoperatively at 1.5, 3, 6, 12, 24 months.

Radiographic Assessment

Two independent radiologists from a core laboratory (Biomedical Systems) performed software-based measurements of digital radiographs. A third independent radiologist adjudicated divergent findings. For the investigational group, radiographic success was determined by the maintenance of motion at both treated levels, defined as 1) angulation > 4° but ≤ 20° of angular motion, and 2) no bridging bone forming a continuous bony connection with adjacent vertebral bodies. For the control group, radiographic success was determined by fusion at both treated levels, defined as 1) angulation ≤ 4°, 2) bridging bone as a continuous bony connection with the vertebral bodies above and below, and 3) no radiolucency covering more than 50% of either the superior or inferior surface of the graft.

Functional Spinal Unit Height Measurement

Functional spinal unit (FSU) height was used as a surrogate measure of subsidence given that disc height is difficult to measure after implantation of the study device. Postoperative anterior and posterior FSU height at both treated levels was compared with the same measurement obtained 6 weeks preoperatively. Subsidence was inferred if the FSU height, anterior or posterior, had decreased by at least 2 mm.

Heterotopic Ossification

In the investigational group, heterotopic ossification (HO) was assessed on radiographs and graded according to the classification by Mehren et al.:[33] 0 = no HO pres-

ent, I = HO detectable in front of the vertebral body but not in the anatomical interdiscal space, II = HO growing in the disc space and possibly affecting the function of the prosthesis, III = bridging ossifications that still allow movement of the prosthesis, or IV = complete fusion of treated segment without movement in flexion or extension.

Safety Assessment

Neurological function was assessed by physician-conducted tests of motor, sensory, and reflex functions. Neurological success was achieved if the preoperative status was maintained or improved. An adverse event (AE) was defined as any adverse clinical sign, symptom, syndrome, or illness that occurred or worsened during the operative and postoperative periods but did not necessarily include the predictable postoperative reactions, such as chills or vomiting. Adverse event categorization followed the FDA suggestion for the single-level Prestige LP IDE trial,[18] which was based, in part, on the study sponsor's internal AE process and in part on the Medical Dictionary for Regulatory Activities (MedDRA) coding system. This hybrid system places each of 20 classifications of AEs under a broad body system (for example, neurological, cardiac disorders), incident (for example, trauma, infection), or other (associated conditions or systems with small numerical incidence). The severity of each AE (Grades 1–4: mild, moderate, severe, or life threatening, respectively, according to WHO criteria) and the association with the implant or surgical procedure were assessed by 2 members of an independent Clinical Adjudication Committee (CAC). A third CAC member adjudicated in cases of disagreement. Secondary surgical interventions were classified as revision, removal, supplemental fixation, or reoperation.

Primary Trial End Point

The primary end point, as required by the FDA, was a composite measure of overall success. Overall success was achieved when all 4 of the following criteria were met: 1) NDI score improvement of ≥ 15 points over the preoperative score, 2) maintenance or improvement in neurological status compared with preoperatively, 3) no serious AE caused by the implant or by both the implant and surgical procedure, and 4) no additional surgery classified as supplemental fixation, revision, or nonelective implant removal.

Other Effectiveness Measurements

Foraminal encroachment was assessed using the foraminal compression test. Foraminal encroachment was deemed present when pain was provoked by applying downward pressure on a patient's head in the neutral position and rotating the head left and right. Patients were asked postoperatively to respond to 3 statements regarding satisfaction with their surgery: 1) I am satisfied with the results of my surgery; 2) I was helped as much as I thought I would be with my surgery; and 3) All things considered, I would have the surgery again for the same condition. The possible answers ranged from "definitely true" to "definitely false." Patients were asked about the perceived effect of treatment. The 7 possible answers ranged from "completely recovered" to "vastly worsened." Patient work status was recorded preoperatively and at all postoperative evaluations. Work status and time to return to work were compared between treatment groups.

Independent Data Review

As was done in the analysis of the 1-level Prestige LP IDE trial,[18] the study sponsor delivered the entire database of raw data to independent biostatisticians at Vanderbilt University for analysis. This study reports the analyses and results of the independent team, which followed the FDA-approved methods from the original statistical plan and reached the same statistical conclusions as those in the study sponsor analysis. Statisticians for the sponsor used the SAS statistical software (SAS Institute Inc.) to generate the summary tables and WinBUGS (Cambridge Institute of Public Health) to conduct the Bayesian analysis. The independent statisticians at Vanderbilt used R software (R Foundation for Statistical Computing) for the summary tables and JAGS (Cambridge Institute of Public Health) to conduct the Bayesian analysis.

Statistical Analyses

The hypothesis in this trial was that the 24-month overall success rate of the investigational group would be statistically noninferior to that of the control group (with a noninferiority margin of 0.1). If noninferiority were established, we predetermined that superiority would be examined. Bayesian methods were used to compare outcomes between the treatment groups. In addition to the 24-month outcomes, 12-month outcomes were also incorporated into the Bayesian likelihood model, although the focus of the comparison was the 24-month outcomes. Noninformative priors were used.[29] Noninferiority and superiority were established if the posterior probability was at least 95%. Analyses similar to those for the overall success rate were conducted for success in individual effectiveness end points: NDI, FSU height, NRS neck pain, NRS arm pain, Physical Component Summary (PCS), Mental Component Summary (MCS), neurological measure, and gait measure. Success for these individual end points was defined as follows: NDI improvement of at least 15 points; FSU height maintenance within 2 mm; and maintenance or improvement in neck pain, arm pain, SF-36 PCS, SF-36 MCS, neurological status, and gait status, respectively.

Secondary end points included safety measures (AEs and additional surgical procedures or interventions) and surgical and hospitalization information (operative time, blood loss, and number of hospital days). Bayesian methods were also used to examine the difference between the treatment groups for these end points. The null hypothesis (that there was no difference) was rejected if the 95% highest posterior density (HPD) included 0. Superiority was established if the posterior probability of a lower rate or mean in the investigational group than in the control group was at least 97.5%.

Descriptive statistics of demographics, baseline characteristics, and some postoperative measurements were presented using mean and standard deviation for continu-

ous variables and frequencies for categorical variables. Statistical comparisons between groups were made using Fisher's t-test for continuous variables and Fisher's exact test for categorical variables. Preoperative to postoperative changes in NDI, NRS neck pain, NRS arm pain, and SF-36 PCS and MCS scores, as well as radiographic measurements of motion, were assessed using paired t-tests, and gait status and foraminal compression tests were assessed using exact McNemar's test. A p value < 0.05 was considered statistically significant.

To compare return-to-work status between the 2 treatment groups, a Cox proportional-hazards model was fitted with preoperative working status included as covariate.

The primary analysis data set consisted of all patients who received the study treatments. The outcomes of a small number of patients who required an additional procedure (removal, revision, or supplemental fixation) were classified as failures for overall success, and the patients' last observations prior to the additional procedure were carried forward for all subsequent evaluations of the other outcomes.

Results

All surgeries were performed in the period from June 2006 to November 2007. Patient participation is reported in Fig. 1 and patient accountability in Table 2. Data were available to assess overall success for 199 of 209 investigational patients and 160 of 188 control patients for follow-up rates of 95.2% and 85.1%, respectively.

Demographic and Preoperative Characteristics

Except for the fact that more investigational than control patients (69.9% vs 60.1%, p = 0.045) had worked prior to surgery, the 2 treatment groups were similar on all other demographic characteristics. Likewise, there were no significant preoperative differences between the 2 groups in the efficacy end points (NDI, SF-36 PCS and MCS, gait, and neurological function), medical condition, medical history, and medication usage (Table 3).

Surgical Data

All surgical procedures were performed via a standard extrapharyngeal approach. Blood loss and operative time were statistically different between the 2 treatment groups. Mean operative time was 2.1 ± 0.8 hours in the investigational group, compared with 1.7 ± 0.7 hours in the control group (posterior probability of superiority < 0.001). Blood loss was 67.2 ± 64.1 ml in the investigational group and 55.7 ± 46.3 ml in the control group (posterior probability of superiority = 0.019). Length of hospital stay was not different between the 2 groups (1.2 ± 0.5 and 1.3 ± 1.0 days). Proportions of inpatients were similar (75.6% investigational, 73.4% control). The operative levels were most frequently C5–6 and C6–7 (78% investigational, 75% control, for both levels).

Success Rates for Overall Success and Individual Effectiveness End Points

At 24 months after surgery, the observed rates of overall success were 81.4% and 69.4% for the investigational group and control group, respectively. The posterior mean for overall success in the investigational group exceeded that in the control group by 0.112 (95% HPD interval = 0.023 to 0.201) with a posterior probability of essentially 1 for noninferiority and 0.993 for superiority (Table 4), demonstrating the superiority of the investigational group

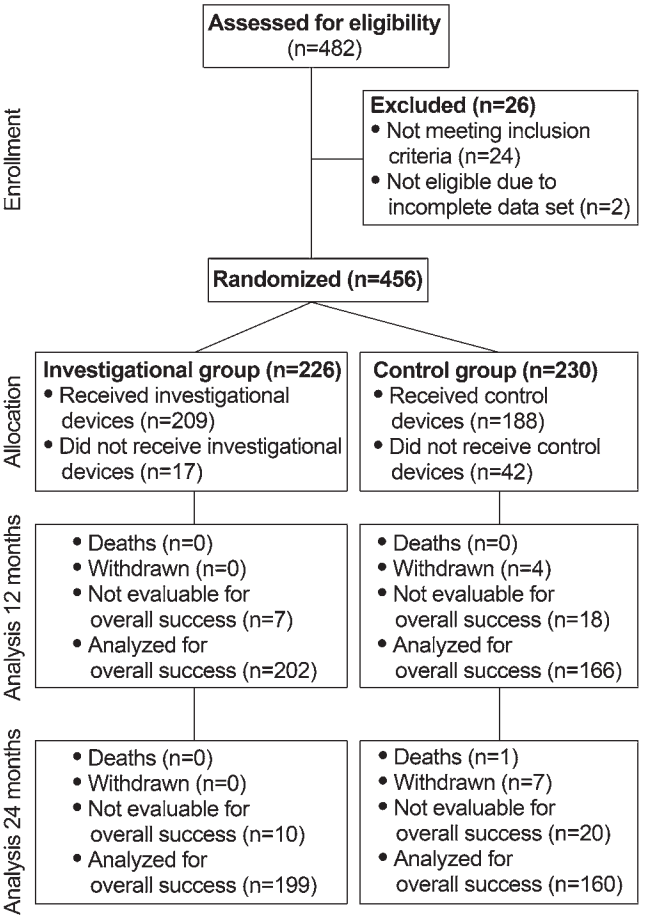

FIG. 1. Patient participation flow diagram.

TABLE 2. Patient accountability

Parameter	No. (%)		
	Investigational Group	Control Group	Total
Time period			
Preop	209 (100)	188 (100)	397 (100)
Postop			
1.5 mos	208/209 (99.5)	185/188 (98.4)	393/397 (99.0)
3 mos	205/209 (98.1)	180/186* (96.8)	385/395* (97.5)
6 mos	204/209 (97.6)	176/186* (94.6)	380/395* (96.2)
12 mos	203/209 (97.1)	168/184* (91.3)	371/393* (94.4)
24 mos	199/209 (95.2)	164/180* (91.1)	363/389* (93.3)
No. w/ data for overall success	199/209 (95.2)	160/180* (88.9)	359/389* (92.3)

* The denominator excludes patients who withdrew from the study or died.

TABLE 3. Demographic, preoperative, and surgical characteristics

Variable	Investigational Group	Control Group	p Value
No. of patients	209	188	
Demographics			
Age (yrs)	47.1 ± 8.3	47.3 ± 7.7	0.844
Body mass index (kg/m^2)	28.2 ± 5.6	28.6 ± 4.9	0.481
Male	92/209 (44)	90/188 (47.9)	0.480
Race			0.879
White	195/209 (93.3)	172/188 (91.5)	
Black	8/209 (3.8)	8/188 (4.2)	
Asian	1/209 (0.5)	3/188 (1.6)	
Hispanic	4/209 (1.9)	4/188 (2.1)	
Other	1/209 (0.5)	1/188 (0.5)	
Marital status			0.698
Single	25/209 (12)	29/188 (15.4)	
Married	146/209 (69.8)	133/188 (70.7)	
Divorced	32/209 (15.3)	23/188 (12.2)	
Separated	4/209 (1.9)	2/188 (1.1)	
Widowed	2/209 (1)	1/188 (0.5)	
Education level			0.652
<High school	21/209 (10)	20/188 (10.6)	
High school	63/209 (30.1)	64/188 (34)	
>High school	125/209 (59.8)	104/188 (55.3)	
Workers' compensation	26/209 (12.4)	19/188 (10.1)	0.527
Unresolved spinal litigation case	0/209 (0)	1/188 (0.5)	0.474
Working preoperatively	146/209 (69.9)	113/188 (60.1)	0.045
Medical condition & medicine usage			
Duration of symptoms			0.340
<6 wks	5/209 (2.4)	8/188 (4.2)	
6 wks to 6 mos	56/209 (26.8)	58/188 (30.8)	
>6 mos	148/209 (70.8)	122/188 (64.9)	
Previous neck surgery	0/209 (0)	2/188 (1.1)	0.224
Medications			
Nonnarcotic	138/208 (66.3)	133/185 (71.9)	0.275
Weak narcotic	83/208 (39.9)	78/186 (41.9)	0.758
Strong narcotic	52/207 (25.1)	44/188 (23.4)	0.725
Muscle relaxant	75/208 (36.1)	73/188 (38.8)	0.604
Abnormal status			
Gait	48/209 (23)	56/188 (29.8)	0.138
Neurological motor	112/209 (53.6)	100/188 (53.2)	1.000
Neurological sensory	124/209 (59.3)	122/188 (64.9)	0.257
Neurological reflexes	119/209 (56.9)	113/188 (60.1)	0.542
Neurological overall	167/209 (79.9)	157/188 (83.5)	0.367
Preop clinical end points			
NDI	52.1 ± 13.4	53.2 ± 14.8	0.441
SF-36 PCS	31.8 ± 7.8	30.8 ± 7.4	0.189
SF-36 MCS	43.9 ± 11.8	43.8 ± 12.2	0.930
NRS neck pain score	16.2 ± 2.9	16.3 ± 2.6	0.720
Preop clinical end points (*continued*)			
NRS arm pain score	13.8 ± 5.6	14.4 ± 4.3	0.208

Values expressed as mean ± standard deviation or as number/number with data (percentage).

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for overall success. Noninferiority of the investigational group was demonstrated for all individual end points except for the SF-36 MCS, and superiority was demonstrated for NDI.

Clinical Outcomes

Both the investigational and control groups exhibited significant preoperative to postoperative improvement in scores at all time points for NDI, NRS neck pain, NRS arm pain, SF-36 PCS, SF-36 MCS, gait status, and foraminal compression (Fig. 2). Improvement in NDI and NRS neck pain was greater at all time points for the investigational group. The NDI score improved from 52.1 ± 13.4 preoperatively to 15.0 ± 16.6 at the 24-month follow-up for the investigational group and from 53.2 ± 14.8 to 20.0 ± 20.5 for the control group. The neck pain score improved from 16.2 ± 2.9 to 4.3 ± 4.9 for the investigational group and from 16.3 ± 2.6 to 5.9 ± 5.5 in the control group.

Safety Outcomes

The maintenance or improvement of neurological status at 24 months was attained by 91.5% of investigational patients and 86.2% of controls. As previously mentioned, the rate of neurological success was noninferior in the investigational group (Table 4).

The proportion of patients experiencing any AE (Table 5) was 93.3% (195/209) in the investigational group and 92.0% (173/188) in the control group, which was not statistically different. The rate of patients who reported any serious (Grade 3 or 4) AE was significantly higher in the control group (90 [47.9%] of 188) than in the investigational group (72 [34.4%] of 209) with a posterior probability of superiority of 0.996 (Table 6). The rates of AEs associated with the implant or implant and surgical procedure were similar in the 2 groups: 15.8% (33/209) in the investigational group and 20.7% (39/188) in the control group. The rates of Grade 3 or 4 AEs associated with the implant or implant and surgical procedure were also similar in the 2 groups: 1.9% (4/209) in the investigational group and 5.8% (11/188) in the control group. The 2 groups also had similar rates regarding all specific types of AE (FDA hybrid AE categories) except for nonunion.

Adverse events that required a second surgery at the index levels were considered revisions, removals, supplemental fixations, or reoperations. Revision was a procedure to adjust or in any way modify the original implant configuration. Removal was a procedure to remove one or more components of the original implant configuration

TABLE 4. Comparison of success rates overall and for individual end points at 24 months

Measure	Success Rates		Bayesian Analysis									
					Posterior Mean & 95% HPD							
					p_1 (investigational group)			p_0 (control group)			$p_0 - p_1$	
	Investigational Group	Control Group	Probability of Noninferiority	Probability of Superiority	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
NDI	87.9% (175/199)	79.2% (126/159)	1.000	0.986	0.871	0.822	0.913	0.784	0.720	0.844	−0.086	−0.165	−0.009
Neurological status	91.4% (182/199)	86.2% (137/159)	1.000	0.925	0.902	0.858	0.939	0.853	0.796	0.902	−0.049	−0.117	0.017
FSU	93.5% (159/170)	95.6% (132/138)	0.998	0.275	0.923	0.879	0.957	0.940	0.896	0.972	0.016	−0.039	0.071
NRS neck pain	98.0% (195/199)	95.6% (152/159)	1.000	0.848	0.969	0.941	0.988	0.948	0.910	0.976	−0.021	−0.064	0.019
NRS arm pain	88.9% (177/199)	89.9% (143/159)	0.997	0.390	0.880	0.833	0.920	0.889	0.837	0.932	0.009	−0.057	0.074
SF-36 PCS	90.4% (178/197)	87.8% (137/156)	1.000	0.769	0.896	0.851	0.934	0.872	0.817	0.918	−0.025	−0.091	0.040
SF-36 MCS	69.0% (136/197)	72.4% (113/156)	0.945	0.308	0.687	0.622	0.749	0.712	0.640	0.779	0.024	−0.070	0.118
Gait success	100% (199/199)	98.7% (157/159)	1.000	0.855	0.990	0.973	0.998	0.977	0.949	0.993	−0.013	−0.042	0.010
Overall success	81.4% (162/199)	69.4% (111/160)	1.000	0.993	0.803	0.746	0.855	0.691	0.620	0.758	−0.112	−0.201	−0.023

without replacement with the same type of device. Supplemental fixation was a procedure to add spinal devices not approved as part of the protocol. Reoperation was a procedure that did not remove, modify, or add any component (for instance, decompression or removal of disc material and bone fragments). The observed rates of secondary surgeries at the index levels were 2.4% (5/209) for the investigational group and 8.0% (15/188) for the control group, (Table 7). The investigational group had a statistically lower rate of secondary surgeries than the control group, with a posterior probability of superiority of 0.994. There were no statistical differences between the 2 groups for any subcategory of secondary surgery. Five investigational patients (2.4%) and 6 control patients (3.2%) had secondary surgeries at adjacent levels.

Radiographic Outcomes

Functional spine unit height was radiographically evaluable in 308 patients and was maintained in 93.5% (159/170) of the investigational patients and 95.6% (132/138) of the control patients (Table 4). Radiographic success was achieved in 51.0% (100/196) of the investigational patients (as maintenance of motion with no evidence of bridging bone) and 82.1% (119/145) of the control patients (as fusion).

Motion at the index (for the investigational group) and adjacent levels was measured by comparing lateral flexion and extension radiographs (Fig. 3). Angular motion at the superior index level was 6.75° ± 4.16° and 6.92° ± 3.96° preoperatively and 24 months postoperatively, respectively. Angular motion at the inferior index level was 5.56° ± 3.89° and 6.85° ± 4.25° preoperatively and 24 months postoperatively, respectively. The change from the preoperative value was not significant for the superior index level but was significant ($p = 0.001$) for the inferior index level. Translatory motion at the superior index level was 1.48 ± 1.08 mm and 1.33 ± 0.78 mm preoperatively and 24 months postoperatively, respectively. Translatory motion at the inferior index level was 1.04 ± 0.74 mm and 1.16 ± 0.71 mm preoperatively and 24 months postoperatively, respectively. The change from the preoperative value was not significant for either the superior or inferior index levels.

For the adjacent level above the treated segments, mean preoperative angular motion was 9.89° ± 4.51° for the investigational group and 10.02° ± 4.41° for the control group. Postoperatively, mean angular motion at the level above the treated segments decreased significantly from baseline then gradually increased to 11.11° ± 4.76° for the investigational group and 11.16° ± 5.13° for the control group at 24 months (a significant increase from baseline for both groups). Mean preoperative angular motion at the adjacent level below the treated segments was consistently less than the angular motion at the level above the treated segments. Preoperative angular motion at the level below the treated segments was 5.02° ± 3.58° for the investigational group and 4.85° ± 3.32° for the control group. At 24 months after surgery, these values were 5.14° ± 3.66° (investigational) and 6.16° ± 3.88° (control), representing a significant increase for the control group.

Translatory motion followed a pattern similar to angu-

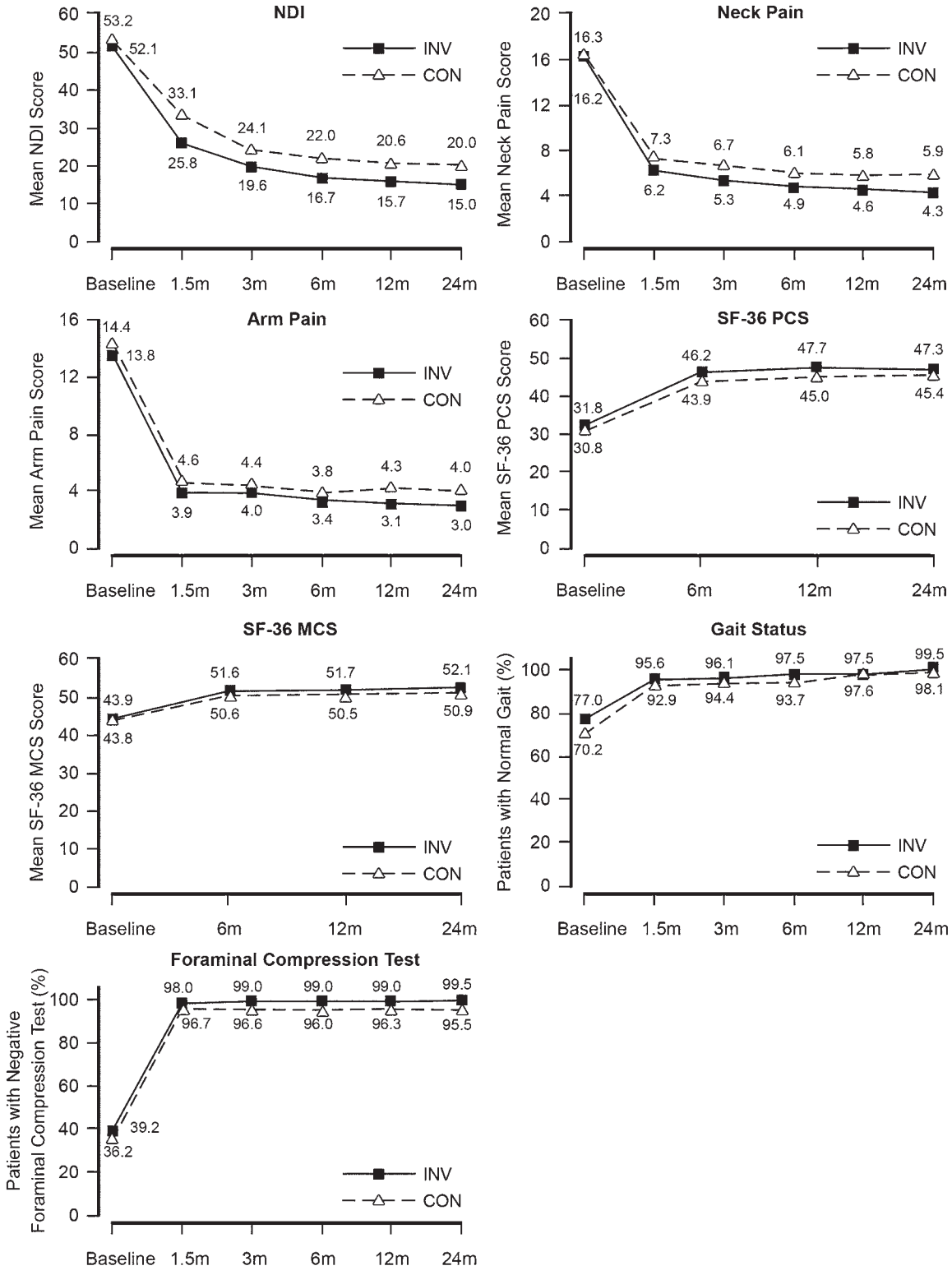

FIG. 2. Preoperative to postoperative improvement at all time points in investigational (INV) and control (CON) groups for NDI, NRS neck pain, NRS arm pain, SF-36 PCS, SF-36 MCS, gait status, and foraminal compression test.

lar motion. Preoperative mean translatory motion at the adjacent level above the treated segments was 2.38 ± 1.35 mm for the investigational group and 2.42 ± 1.21 mm for the control group. It decreased significantly at 1.5 months (to 2.04 mm for the investigational group and 1.92 mm for the control group), then at 24 months it gradually increased to 2.66 ± 1.12 mm for the investigational group and 2.73 ± 1.16 mm for the control group, representing a

TABLE 5. Time course of all AEs

Event	Operatively		1 Day–4 Wks Postop		1.5 Mos Postop		3 Mos Postop		6 Mos Postop		12 Mos Postop		24 Mos Postop		Total	
	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients
Investigational group																
Any AEs	54	32	166	70	116	50	228	86	245	85	372	102	296	88	1477	195 (93.3)
Cancer	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0 (0.0)
Cardiac disorders	2	1	2	2	3	3	1	1	8	2	8	8	4	4	28	18 (8.6)
Death	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0 (0.0)
Dysphagia/dysphonia	1	1	5	5	2	2	1	1	0	0	4	4	1	1	14	14 (6.7)
Gastrointestinal	5	3	13	8	0	0	12	7	16	7	38	21	17	9	101	43 (20.6)
HO	0	0	1	1	0	0	3	3	3	3	9	8	11	9	27	22 (10.5)
Implant events	4	4	2	1	1	1	0	0	3	2	0	0	5	5	15	13 (6.2)
Infection	0	0	5	5	3	3	3	3	8	7	20	14	9	9	48	36 (17.2)
Neck &/or arm pain	13	6	38	17	36	25	59	37	44	30	52	32	52	32	294	127 (60.8)
Neurological	7	6	23	16	21	14	45	26	37	26	33	21	33	19	199	89 (42.6)
Nonunion	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0 (0.0)
Other	8	6	27	24	13	10	20	14	34	24	52	33	41	28	195	97 (46.4)
Other pain	4	4	26	22	23	16	45	33	44	30	68	44	49	32	259	125 (59.8)
Respiratory	4	3	8	6	1	1	3	3	3	2	14	7	14	7	47	29 (13.9)
Spinal event	2	2	3	2	7	5	20	10	32	18	45	28	40	19	149	74 (35.4)
Trauma	0	0	0	0	5	5	8	8	8	8	15	14	9	8	45	37 (17.7)
Urogenital	1	1	5	4	0	0	6	5	2	2	9	8	8	8	31	25 (12.0)
Vascular	1	1	0	0	0	0	1	1	0	0	3	3	1	1	6	5 (2.4)
Wound (noninfectious)	2	2	8	7	1	1	1	1	3	2	2	2	2	2	19	15 (7.2)
Control group																
Any AEs	38	23	221	68	119	51	266	89	240	68	390	92	319	79	1593	173 (92.0)
Cancer	0	0	0	0	1	1	0	0	0	0	1	1	1	1	3	3 (1.6)
Cardiac disorders	3	2	0	0	0	0	1	1	3	2	8	8	3	3	18	16 (8.5)
Death	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1 (0.5)
Dysphagia/dysphonia	2	1	11	7	4	4	5	4	0	0	3	3	2	2	27	21 (11.2)
Gastrointestinal	2	2	16	7	3	3	7	3	6	5	28	13	17	11	79	38 (20.2)
HO	0	0	2	2	2	2	5	4	5	4	3	3	7	7	24	21 (11.2)
Implant events	0	0	2	2	2	2	2	1	2	2	4	3	0	0	12	10 (5.3)
Infection	1	1	7	7	3	3	7	6	3	3	11	9	9	8	41	32 (17.0)
Neck &/or arm pain	2	1	52	32	28	19	56	33	50	30	58	31	47	29	293	114 (60.6)
Neurological	8	7	25	16	23	14	41	24	22	13	44	29	29	17	192	85 (45.2)
Nonunion	0	0	1	1	1	1	7	7	6	6	2	2	1	1	18	18 (9.6)

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TABLE 5. Time course of all AEs

Event	Operatively		1 Day–4 Wks Postop		1.5 Mos Postop		3 Mos Postop		6 Mos Postop		12 Mos Postop		24 Mos Postop		Total	
	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients	No. of Events	No. of Patients
Other	6	6	24	17	9	6	27	12	22	15	71	35	57	29	216	87 (46.3)
Control group (*continued*)																
Other pain	6	6	36	22	21	19	40	30	57	32	74	40	61	37	295	113 (60.1)
Respiratory	5	4	6	5	2	2	8	6	10	7	13	12	8	6	52	34 (18.1)
Spinal event	0	0	26	13	12	8	45	18	38	18	47	24	29	19	197	80 (42.6)
Trauma	0	0	6	5	2	2	6	6	8	8	14	14	24	16	60	39 (20.7)
Urogenital	1	1	4	4	5	2	3	2	4	2	5	3	14	7	36	19 (10.1)
Vascular	0	0	1	1	1	1	2	2	0	0	1	1	9	3	14	8 (4.3)
Wound (noninfectious)	2	2	2	2	0	0	4	3	4	2	2	1	1	1	15	11 (5.9)

significant increase from baseline for both groups. Preoperative mean translatory motion at the adjacent segment below the treated segments was 1.09 ± 0.64 mm for the investigational group and 1.04 ± 0.74 mm for the control group. At 24 months, these values were 1.25 ± 0.77 mm (investigational) and 1.46 ± 1.03 mm (control), representing a significant increase for the control group.

Heterotopic Ossification

At 24 months, the presence of any HO was identified in 27.8% (55/198) of the superior levels and 36.4% (72/198) of the inferior levels of investigational patients (Table 8). The presence and severity of HO gradually increased over the follow-up period. Severe HO (Grade III and IV) restricts motion of the segment and was evident in 3.5% of the patients at 6 months, 13.4% at 12 months, and 24.2% at 24 months. The incidence of HO did not impact clinical outcomes: the success rates were similar for patients with and without severe HO (Table 9).

Patient Satisfaction and Perception of Treatment Effectiveness

We observed a higher proportion of success in the investigational group than in the control group regarding satisfaction with surgery. Success was defined as responses of "definitely true" or "mostly true" to statements about being satisfied with the results of surgery (94.5% investigational vs 89.3% control), being helped by the surgery (93.9% vs 85.5%), and a willingness to have the surgery again (93.4% vs 88.7%).

Perceived Effect of Treatment

Similar proportions of patients in the 2 treatment groups considered their treatment to be a success. At the 24-month follow-up, 97% of investigational and 93.7% of control patients answered that they were "completely recovered," "much improved," or "slightly improved."

Return to Work

Preoperatively, 69.9% (146/209) of investigational patients and 60.1% (113/188) of control patients reported working. At 24 months, 72.9% (145/199) of investigational and 71.1% (113/159) of control patients reported working. The median return-to-work time after surgery was 49 days for investigational patients and 55 days for control patients. There was no significant difference between the 2 groups ($p = 0.48$ based on Cox proportional-hazards model adjusting for preoperative work status).

Discussion

At 24 months after surgery, overall success rates were 81.4% for the investigational group and 69.4% for the control group. Both the noninferiority and superiority of the investigational treatment were established, thereby demonstrating that arthroplasty with Prestige LP is at least as safe and effective as ACDF for treating DDD at 2 adjacent levels in the cervical spine. Besides overall success, greater improvement in disability and neck pain was attained by the CDA group than the ACDF group. Additionally, the

TABLE 6. Comparison of AE rates between investigational and control groups

Variable	Event Rates (no. of patients [%])		Posterior Mean & 95% HPD									Probability of Superiority	Null Hypothesis
			p_1 (investigational group)			p_0 (control group)			$p_0 - p_1$				
	Investigational Group (209)	Control Group (188)	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper		
AE related to implant/surgical procedure	33 (15.8)	39 (20.7)	0.161	0.112	0.211	0.211	0.156	0.271	0.049	−0.026	0.126	0.899	Accepted
Grade 3 or 4 AE related to implant or implant/surgical procedure	4 (1.9)	11 (5.8)	0.024	0.006	0.045	0.063	0.031	0.098	0.040	−0.000	0.081	0.979	Accepted
Any Grade 3 or 4 AE	72 (34.4)	90 (47.9)	0.346	0.284	0.412	0.479	0.407	0.549	0.133	0.036	0.227	0.996	Rejected
Patients w/ any AE	195 (93.3)	173 (92.0)	0.929	0.891	0.959	0.916	0.872	0.951	−0.013	−0.066	0.039	0.312	Accepted
Cancer	0 (0)	3 (1.6)	0.005	0.000	0.017	0.021	0.006	0.046	0.016	−0.003	0.042	0.953	Accepted
Cardiac disorders	18 (8.6)	16 (8.5)	0.090	0.056	0.132	0.090	0.053	0.134	−0.001	−0.056	0.056	0.491	Accepted
Death	0 (0)	1 (0.5)	0.005	0.000	0.018	0.011	0.001	0.029	0.006	−0.010	0.026	0.775	Accepted
Dysphagia/dysphonia	14 (6.7)	21 (11.2)	0.071	0.041	0.109	0.116	0.075	0.165	0.045	−0.012	0.103	0.941	Accepted
Gastrointestinal AE	43 (20.6)	38 (20.2)	0.208	0.157	0.266	0.205	0.151	0.265	−0.003	−0.082	0.077	0.469	Accepted
HO	22 (10.5)	21 (11.2)	0.109	0.071	0.154	0.116	0.075	0.165	0.007	−0.054	0.069	0.583	Accepted
Implant event	13 (6.2)	10 (5.3)	0.066	0.037	0.103	0.058	0.03	0.095	−0.008	−0.056	0.039	0.361	Accepted
Infection	36 (17.2)	32 (17.0)	0.175	0.127	0.229	0.174	0.123	0.230	−0.002	−0.076	0.073	0.480	Accepted
Neck &/or arm pain	127 (60.8)	114 (60.6)	0.607	0.54	0.671	0.605	0.535	0.674	−0.001	−0.096	0.094	0.490	Accepted
Neurological AE	89 (42.6)	85 (45.2)	0.427	0.361	0.494	0.453	0.383	0.524	0.026	−0.071	0.123	0.701	Accepted
Nonunion	0 (0)	18 (9.6)	0.005	0.000	0.017	0.100	0.061	0.146	0.095	0.056	0.142	1.000	Rejected
Other AE	97 (46.4)	87 (46.3)	0.464	0.397	0.532	0.463	0.393	0.534	−0.001	−0.099	0.096	0.490	Accepted
Other pain	125 (59.8)	113 (60.1)	0.597	0.53	0.662	0.600	0.530	0.669	0.003	−0.093	0.099	0.525	Accepted
Respiratory	29 (13.9)	34 (18.1)	0.142	0.099	0.192	0.184	0.132	0.242	0.042	−0.030	0.115	0.872	Accepted
Spinal event	74 (35.4)	80 (42.6)	0.355	0.293	0.421	0.426	0.357	0.497	0.071	−0.024	0.166	0.928	Accepted
Trauma	37 (17.7)	39 (20.7)	0.180	0.131	0.234	0.211	0.156	0.271	0.030	−0.047	0.109	0.778	Accepted
Urogenital AE	25 (12.0)	19 (10.1)	0.123	0.083	0.171	0.105	0.066	0.152	−0.018	−0.080	0.044	0.281	Accepted
Vascular AE	5 (2.4)	8 (4.2)	0.028	0.011	0.055	0.047	0.022	0.082	0.019	−0.017	0.058	0.846	Accepted
Wound (noninfectious)	15 (7.2)	11 (5.8)	0.076	0.044	0.115	0.063	0.033	0.101	−0.013	−0.063	0.037	0.304	Accepted

Grade 1 (mild), AE is noticeable but does not interfere with routine activity or require removal of the implant(s); Grade 2 (moderate), AE interferes with routine activity but responds to symptomatic therapy or rest and does not require removal of the implant(s); Grade 3 (severe), AE significantly limits the patient's ability to perform routine activities despite symptomatic therapy, may require hospitalization, and may require removal of the implant(s); Grade 4 (life-threatening), AE requires removal of the implant(s), or the patient is at immediate risk of death, even if the AE is not related to the implant(s).

TABLE 7. Rates of secondary surgeries

Surgery	Investigational Group (209 patients)	Control Group (188 patients)	Bayesian Analysis: Posterior Mean & 95% HPD									Probability of Superiority
			p_1 (investigational group)			p_0 (control group)			$p_0 - p_1$			
			Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper	
Any secondary surgery	5 (2.4%)	15 (8.0%)	0.028	0.011	0.055	0.084	0.049	0.128	0.056	0.013	0.103	0.994
Revision	0 (0.0%)	1 (0.5%)	0.005	0	0.017	0.011	0.001	0.029	0.006	−0.01	0.026	0.774
Removal	3 (1.4%)	6 (3.2%)	0.019	0.005	0.041	0.037	0.015	0.068	0.018	0.013	0.052	0.871
Removal, elective	0 (0.0%)	2 (1.1%)	0.005	0	0.017	0.016	0.003	0.038	0.011	0.007	0.034	0.895
Supplemental fixation	1 (0.5%)	3 (1.6%)	0.009	0.001	0.026	0.021	0.006	0.046	0.012	0.011	0.038	0.844
Reoperation	2 (1.0%)	4 (2.1%)	0.014	0.003	0.034	0.026	0.009	0.053	0.012	0.015	0.042	0.816
Any secondary surgery at adjacent level	5 (2.4%)	6 (3.2%)	0.028	0.008	0.051	0.037	0.013	0.064	0.008	0.027	0.044	0.684

CDA group underwent fewer secondary surgeries than the ACDF group. Although early artificial discs were prone to complications,[41] currently available artificial discs are associated with better safety outcomes and fewer AEs and secondary surgeries than ACDF.[15,31,35,50] The results of our study, in accordance with earlier studies, confirm the noninferiority and superiority of multilevel CDA outcomes compared with multilevel ACDF.[9,14,24]

Heterotopic ossification, with its increasing prevalence over time, is a well-known occurrence after CDA. Its prevalence after 2-level CDA has been found to be higher than,[55] lower than,[23] and similar to[10,56] that after single-level CDA. The prevalence of severe HO (Grade III and IV) in the current study was similar to that reported in another 2-level CDA IDE trial,[14] increasing from 3.5% at 6 months to 24.2% at 24 months. In our study, as in

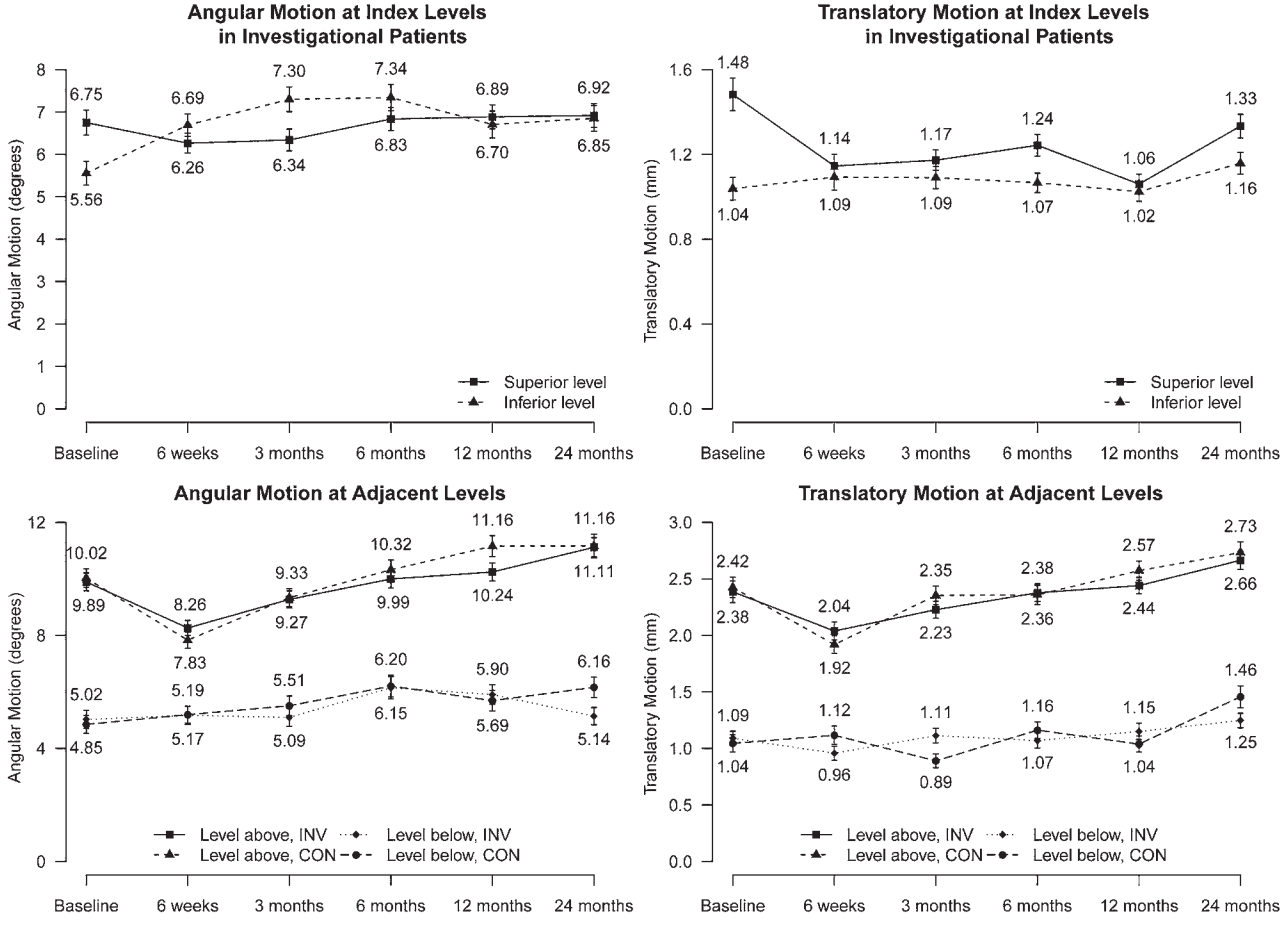

FIG. 3. Comparisons of angular and translation motion at baseline and 24 months in investigational (INV) and control (CON) groups.

TABLE 8. Rates of HO in investigational patients at follow-up intervals

FU Period & HO Grade	No. of Patients (%)	
	Superior Level	Inferior Level
6 mos		
0	185/202 (91.6%)	173/202 (85.6%)
I	5/202 (2.5%)	14/202 (6.9%)
II	10/202 (5.0%)	9/202 (4.4%)
III	2/202 (1.0%)	6/202 (3.0%)
IV	0/202 (0.0%)	0/202 (0.0%)
12 mos		
0	164/202 (81.2%)	151/202 (74.8%)
I	9/202 (4.4%)	11/202 (5.4%)
II	15/202 (7.4%)	18/202 (8.9%)
III	14/202 (6.9%)	21/202 (10.4%)
IV	0/202 (0.0%)	1/202 (0.5%)
24 mos		
0	143/198 (72.2%)	126/198 (63.6%)
I	10/198 (5.1%)	11/198 (5.6%)
II	13/198 (6.6%)	22/198 (11.1%)
III	28/198 (14.1%)	33/198 (16.7%)
IV	4/198 (2.0%)	6/198 (3.0%)

Grade 0 = no HO present, Grade I = HO detectable in front of the vertebral body but not in the anatomic interdiscal space, Grade II = HO growing in the disc space and possibly affects function of the prosthesis, Grade III = bridging ossifications that still allow movement of the prosthesis, or Grade IV = complete fusion of the treated segment without movement in flexion/extension.

TABLE 9. Success rates by severity of HO at 24 months

Measure	Non-Severe HO (Grades 0, I, II)	Severe HO (Grades III, IV)	p Value
No. of patients	150	48	
NDI success	131 (87.3%)	44/48 (91.7%)	0.605
Neurological success	140 (93.3%)	42/48 (87.5%)	0.225
Second surgery failure	3	0	
Associated SAEs	1	0	
Overall success	123 (82.0%)	39/48 (81.3%)	1.000

SAE = serious adverse event.

other studies,[2,8,11,19,26–28,47] HO did not impact patient outcomes. Although the long-term impact of HO is not yet known,[8,11,23,47] it is obviously counter to the goals of CDA, which are the maintenance of motion and the avoidance or reduction of ASD. Despite the HO, the CDA patients in this study underwent fewer adjacent segment surgeries (5 [2.4%] of 209) than the ACDF patients (6 [3.2%] of 188), even though this difference did not reach statistical significance. Other studies have also reported fewer adjacent segment operations after CDA than fusion, up to 7 years after surgery.[6,15,36] Whether the expected ASD decrease will be an "unfulfilled promise"[44] due to the progression of severe HO following CDA remains to be investigated.

The lack of blinding to treatment, a known source of bias, is a limitation of this study. It was not possible to blind the physicians because they had to perform the surgeries. To reduce physician bias, radiographic and safety assessments were conducted by independent reviewers. It was also not possible to blind the patients, who were alerted to their surgeries by processing insurance paperwork. It has been found that, in the absence of a double-blind approach, the investigational treatment is more likely to be judged favorably.[12,34] Indeed, patients in this study reported greater improvement after CDA than ACDF. However, the decompression, which is similar in both control and treatment groups, is the part of each surgical procedure that is responsible for the reduction in pain and disability. Hence, one would expect patients in the 2 groups to report similar improvement.[49] Studies comparing CDA with fusion[15,20,22,36] have generally reported greater reductions in pain and disability following CDA with a variety of devices, but not consistently so.[15,39,43,50] In the face of unexpected patient reports, one cannot rule out the influence of bias favoring the investigational treatment, but one should also expect such bias to wane once "reality sets in." In that regard, some have noted that the patient-reported difference between CDA and ACDF has vanished over time,[22] while, remarkably, other patients have continued to report superior improvement in the long term, even up to 7 years after cervical CDA compared with ACDF.[5,6,14] Although one cannot rule out the existence of a bias favoring CDA in the short term, it seems improbable that bias would remain for so many years. In that respect, longer-term follow-up is underway to ascertain the longevity of the relative benefits of multilevel CDA over ACDF observed in this patient sample.

Another limitation of this study is the potential bias that may stem from conflicts of interest created by the financial relationship between the study sponsor and some investigators. However, several measures were taken to preclude the influence of conflicts of interest: all radiological assessments were made by independent reviewers, all AEs were evaluated by an independent committee, and all reported statistical analyses were performed by independent statisticians. The study sponsor provided the entire raw data set to a team of independent statisticians at Vanderbilt University. Using the statistical analysis plan in the study protocol approved by the FDA, the independent analysis team reached the same statistical conclusions as the study sponsor for all proposed comparisons.

Finally, it should be noted that this clinical trial included patients with intractable radiculopathy or myelopathy or both, at 2 adjacent levels. We report the results of the trial according to the FDA-approved statistical plan, which did not include analyses of pathology subgroups. These analyses and the implications regarding the appropriateness of treatment for the pathology subgroups will be addressed in a separate publication.

Conclusions

Overall, these findings indicate that CDA using Prestige LP is as effective and safe as ACDF for the treatment of cervical DDD at 2 contiguous levels. Hence, it is an alternative treatment for patients with symptoms at 2 adjacent levels of the cervical spine.

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Disclosures

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Conception and design: Gornet. Acquisition of data: Gornet, Lanman, Burkus, Hodges, McConnell, Dryer. Analysis and interpretation of data: Gornet, Copay, Nian, Harrell. Drafting the article: Gornet, Copay. Critically revising the article: Gornet, Lanman, Burkus, McConnell, Dryer, Copay. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Gornet. Statistical analysis: Nian, Harrell.

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