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CLINICAL ARTICLE

Subsequent surgery rates after cervical total disc replacement using a Mobi-C Cervical Disc Prosthesis versus anterior cervical discectomy and fusion: a prospective randomized clinical trial with 5-year follow-up

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OBJECTIVE Cervical total disc replacement (TDR) has been shown in a number of prospective clinical studies to be a viable treatment alternative to anterior cervical discectomy and fusion (ACDF) for the treatment of symptomatic degenerative disc disease. In addition to preserving motion, evidence suggests that cervical TDR may result in a lower incidence of subsequent surgical intervention than treatment with fusion. The goal of this study was to evaluate subsequent surgery rates up to 5 years in patients treated with TDR or ACDF at 1 or 2 contiguous levels between C-3 and C-7.

METHODS This was a prospective, multicenter, randomized, unblinded clinical trial. Patients with symptomatic degenerative disc disease were enrolled to receive 1- or 2-level treatment with either TDR as the investigational device or ACDF as the control treatment. There were 260 patients in the 1-level study (179 TDR and 81 ACDF patients) and 339 patients in the 2-level study (234 TDR and 105 ACDF patients).

RESULTS At 5 years, the occurrence of subsequent surgical intervention was significantly higher among ACDF patients for 1-level (TDR, 4.5% [8/179]; ACDF, 17.3% [14/81]; p = 0.0012) and 2-level (TDR, 7.3% [17/234]; ACDF, 21.0% [22/105], p = 0.0007) treatment. The TDR group demonstrated significantly fewer index- and adjacent-level subsequent surgeries in both the 1- and 2-level cohorts.

CONCLUSIONS Five-year results showed treatment with cervical TDR to result in a significantly lower rate of subsequent surgical intervention than treatment with ACDF for both 1 and 2 levels of treatment.

Clinical trial registration no.: NCT00389597 (clinicaltrials.gov)

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KEY WORDS Mobi-C Cervical Disc Prosthesis; cervical disc arthroplasty; total disc replacement; reoperation; subsequent surgical intervention; anterior cervical discectomy and fusion; cervical spine; fusion; clinical trial

Anterior cervical discectomy and fusion (ACDF) has been a standard surgical procedure for cervical disc decompression. It functions to decompress affected neural components, provide mechanical stability and lordosis, and preserve intradiscal height.[26] However, investigators have also reported an increase in motion, shear strain, and intradiscal pressure in adjacent vertebrae after treatment.[10,21] The displacement of motion and mechanical stress to adjacent segments is a major concern because force and motion translocation are believed to lead to increased rates of adjacent-segment degeneration in patients treated with ACDF.[6,10,16,17,21] It is also hypothesized that adjacent-segment degeneration is further heightened in multilevel ACDF treatment.[11]

Cervical total disc replacement (TDR) is a treatment option for symptomatic radiculopathy and myelopathy. A

ABBREVIATIONS ACDF = anterior cervical discectomy and fusion; IDE = Investigational Device Exemption; NDI = neck disability index; TDR = total disc replacement.

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number of clinical trials have shown that TDR is a safe and effective alternative to ACDF for 1- and 2-level cervical decompression.[3,5,7,11,15,19,22,27–29] As with ACDF, cervical TDR acts to decompress the affected segment, provide stabilization, and preserve intradiscal height while maintaining mobility.[3,22,28] Investigators have suggested that the preservation of mobility may result in a decreased frequency of adjacent-segment degeneration compared with that observed in patients treated with ACDF.[1,5,31]

The results of multiple independent studies suggest that cervical TDR at 1 level may also result in decreased rates of subsequent operations at the treatment and adjacent levels.[5,9,12,15,22,23,28–30] Long-term studies have shown that treatment with ACDF results in significantly higher subsequent surgery rates than cervical TDR, although few studies have analyzed 2-level subsequent surgery outcomes.[2,9,24] In long-term studies, the ACDF subsequent surgery rate was observed to be as high as 5 times the rate of TDR subsequent surgical intervention.[9] The purpose of this study was to evaluate 5-year subsequent surgery rates at index and adjacent levels in patients treated at 1 or 2 contiguous levels with TDR or with the ACDF control procedure, as part of an FDA Investigational Device Exemption (IDE) clinical trial.

Methods

Study Design

This study elaborates on the results from prospective, multicenter, 2-arm, randomized (2:1), unblinded, concurrently enrolled, noninferiority clinical trials comparing the safety and effectiveness of the Mobi-C Cervical Disc Prosthesis (LDR Medical) at 1 or 2 contiguous levels with an ACDF control.

The study design has been previously described in detail.[7,18] The patient population included a total of 260 1-level and 339 2-level subjects randomized (2:1) to receive either TDR or ACDF treatment at 1 of 24 investigational sites. These 1- and 2-level results include 5 years of patient follow-up data. Institutional review board approval was obtained for all investigational sites. This study was registered with the ClinicalTrials.gov database (http://clinicaltrials.gov), and its registration no. is NCT00389597.

Patient Population

Eligible patients had degenerative disc disease with radiculopathy or myeloradiculopathy symptomatic at 1 or 2 contiguous levels from C-3 to C-7 and had a neck disability index (NDI) score ≥ 15/50. Patients must have been unresponsive or shown progressive symptoms after nonoperative, conservative treatment for at least 6 weeks from symptom onset. See Tables 1 and 2 for complete inclusion and exclusion criteria.

Study Interventions

The investigational device is the Mobi-C Cervical Disc Prosthesis (LDR Medical). The implant is composed of an ultra-high-molecular-weight polyethylene (UHMWPE per ISO 5834–2) mobile insert between 2 endplates (Fig. 1). The control device is ACDF, using either the Slim-Loc Anterior Cervical Plate System (DePuy Spine) or the Sofamor Danek Atlantis or Atlantis Vision Anterior Cervical Plate Systems (Medtronic) with corticocancellous allograft. Postoperative care for both groups was left to the discretion of the treating surgeon.

TABLE 1. Inclusion criteria for 599 patients with symptomatic degenerative disc disease enrolled to receive 1- or 2-level treatment with either TDR or ACDF

Age, 18–69 yrs
Symptomatic cervical degenerative disc disease in 1 or 2 levels btwn C-3 and C-7 w/ any of the following:
Neck and/or arm pain
Decreased muscle strength
Abnormal sensation and/or abnormal reflexes
Deficit confirmed by imaging (CT, MRI, or radiograph)
NDI score ≥30
Unresponsive to nonoperative, conservative treatment for at least 6 wks or presence of progressive symptoms or signs of nerve root/spinal cord compression despite continued nonoperative treatment
No prior surgery at the operative level and no prior cervical fusion procedure at any level
Physically and mentally able and willing to comply w/ the protocol
Signed informed consent
Willingness to discontinue all use of NSAIDs from 1 wk before surgery to 3 mos after surgery

Study Outcomes

The intent of this study was to assess subsequent surgery rates of patients treated at 1 or 2 contiguous levels with a TDR or an ACDF. A subsequent surgery was considered to be any operation that occurred at the initial treatment level or at adjacent levels after the primary operation. Subsequent surgeries were categorized by 4 methods based on the levels involved during the subsequent surgery: only index-level surgeries, only adjacent-level surgeries, index- and adjacent-level surgeries, and index-level surgeries leading to study failure. Subsequent surgical interventions leading to study failure were considered to be any secondary surgery at an index-level segment that was classified as a removal, revision, supplemental fixation, or reoperation according to the FDA IDE study protocol. Index-level surgeries leading to study failure would be duplicated in 1 of the other categories. Index-level surgeries that did not indicate study failure were also included in the analysis. In the instance of multiple subsequent surgeries, only the first subsequent surgery was used to determine the subsequent surgery rates. Operations at C7–T1 were included in the calculation of adjacent-level surgery rates.

Statistical Analysis

Fisher's exact tests were used to assess subsequent surgery rates. Statistical significance was determined by a p value > 0.05.

Results

For both the 1- and 2-level arms, a total of 599 patients were treated with the investigational or control device. For the 1-level arm, 179 patients received TDR and 81 re-

TABLE 2. Exclusion criteria for 599 patients with symptomatic degenerative disc disease enrolled to receive 1- or 2-level treatment with either TDR or ACDF

>2 vertebral levels requiring treatment/immobile levels btwn C-1 & C-7 from any cause
Any prior spine surgery at operative level or any prior cervical fusion at any level
Disc height <3 mm
T score < −1.5 (osteoporosis evaluation)
Paget's disease, osteomalacia, or any metabolic bone disease other than osteoporosis
Active systemic infection of surgical site or history of/anticipated treatment for systemic infection including HIV & hepatitis C
Active malignancy, i.e., a history of any invasive malignancy (except nonmelanoma skin cancer), unless treated w/ curative intent and w/o any clinical signs or symptoms of the malignancy for >5 yrs
Marked cervical instability on resting lateral or flexion-extension radiographs
Known allergy to cobalt, chromium, molybdenum, or polyethylene
Segmental angulation >11° at treatment or adjacent levels
Rheumatoid arthritis, lupus, or other autoimmune disease
Any diseases or conditions that would preclude accurate clinical evaluation
Daily, high-dose oral and/or inhaled steroids or a history of chronic use of high-dose steroids
Body mass index >40
Use of any other investigational drug or medical device w/in 30 days prior to surgery
Pending personal litigation relating to spinal injury (workers' compensation not included)
Smoking >1 pack of cigarettes per day
Reported to have mental illness or belong to a vulnerable population

ceived ACDF treatment. For the 2-level arm, 234 patients received TDR and 105 received ACDF treatment. No significant differences were found between the demographic profiles of the investigational and control groups. The 60-month follow-up rate was 85.5% (TDR) and 78.9% (ACDF) for the 1-level group and 90.7% (TDR) and 86.7% (ACDF) for the 2-level group.

A subsequent surgery was considered to be any operation that occurred at the initial treatment level or at adjacent levels after the primary operation. All TDR and ACDF subsequent surgery cases are listed in Tables 3 and 4.

For the 1-level ACDF group, 14 of 81 patients underwent subsequent surgeries and 1 patient required multiple subsequent surgeries. In the 1-level TDR group, 8 of 179 patients underwent subsequent surgeries and 2 patients required multiple subsequent surgeries. The number of 1-level patients receiving subsequent surgeries was significantly higher for ACDF at 60 months (TDR 4.5% vs ACDF 17.3%; p = 0.0012).

For the 2-level ACDF group, 22 of 105 patients underwent subsequent surgeries and 3 patients required multiple subsequent surgeries. In the 2-level TDR group, 17 of 234 patients underwent subsequent surgeries and 2 patients required multiple subsequent surgeries at the 60-month follow-up point. The percentage of 2-level ACDF patients receiving subsequent surgery was significantly higher

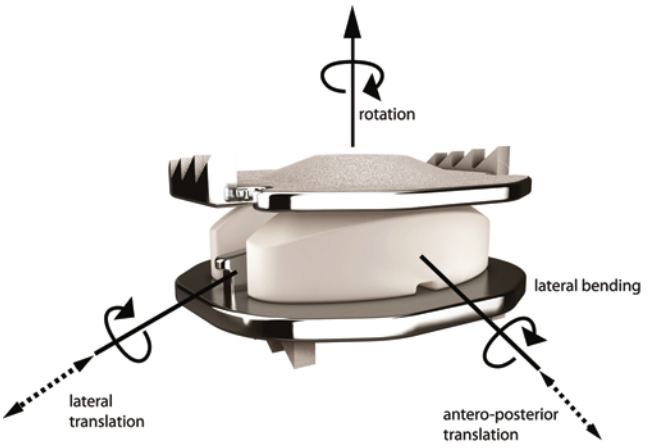

FIG. 1. Mobi-C Cervical Disc Prosthesis (LDR Medical). Copyright LDR Holding Corporation. Published with permission. Figure is available in color online only.

than that of 2-level TDR patients at 60 months (TDR 7.3% vs ACDF 21.0%; p = 0.0007).

Subsequent surgeries were classified by operative level as an index- and/or adjacent-level surgery (Fig. 2). For the 1-level arm at 60 months, there were a total of 8 TDR (4 index, 2 adjacent, 2 index and adjacent) and 14 ACDF (5 index, 4 adjacent, 5 index and adjacent) subsequent surgeries classified by operative level. For the 2-level arm, there were a total of 17 TDR (9 index, 6 adjacent, 2 index and adjacent) and 22 ACDF (10 index, 3 adjacent, 9 index and adjacent) subsequent surgeries classified by operative level at the 60-month follow-up.

Surgeries Involving an Index Level

At 60 months, the rate of subsequent surgeries that involved the index level for the 1-level arm was significantly different at 3.4% (6/179) for TDR and 12.3% (10/81) for ACDF (p = 0.0097). Of the 10 1-level ACDF surgeries involving an index level, 7 ACDF surgeries were a result of index-level indications and 3 surgeries resulted from removal of the anterior plate when treating adjacent-level disease. When censoring patients undergoing plate removal due to adjacent-level indications only, the ACDF group retained a substantially higher subsequent surgery rate, although this difference lost significance (3.4% vs 8.6%; p = 0.1194). The difference in index-level subsequent surgeries was also significant in the 2-level arm, at 4.7% (11/234) for TDR and 18.1% (19/105) for ACDF. Of the 19 2-level ACDF surgeries involving an index level, 13 surgeries were due to index-level indications and 6 surgeries were due to hardware removal for adjacent-level disease. When censoring patients undergoing plate removal due to adjacent-level indications only, the ACDF group maintained a higher rate of subsequent surgeries (4.7% vs 12.4%; p = 0.0197).

Of these subsequent surgeries involving the index level at 1 level, 2.8% (5/179) TDR and 11.1% (9/81) ACDF patients (p = 0.014) failed to meet the primary end point criteria due to subsequent surgical intervention. Similarly,

TABLE 3. Subsequent surgical procedures in 1-level arm (in ascending order by time to surgery)

Case No.	Index Level	Device	Time to Surgery	Reason	Description	Treated Segments	Study Failure
1	C3–4	ACDF	5 days	Hematoma	Evacuation of hematoma	C3–4	No
2	C4–5	TDR	3 mos	Radiculopathy	Cervical laminectomy at index level (C4–5)	C4–5	Yes
3	C5–6	ACDF	5 mos	1) Neck pain; 2) radiculopathy; 3) foraminal stenosis; 4) pseudarthrosis	Posterior fusion (C5–6) w/ instrumentation	C5–6	Yes
4	C4–5	TDR	5 mos	1) Radiculopathy; 2) spondylosis	Removal of Mobi-C, fusion of index level (C4–5)	C4–5	Yes
5	C5–6	ACDF	11.5 mos	1) Radiculopathy; 2) pseudarthrosis	Removal of instrumentation, redo C5–6 fusion w/ iliac crest bone graft	C5–6	Yes
6	C4–5	ACDF	12.5 mos	1) Neck pain; 2) muscle spasms; 3) numbness; 4) malpositioned screws	Removal of instrumentation, fusion of inferior adjacent level (C5–6)	C4–6	Yes
4*	C4–5	TDR	13 mos	1) Neck pain; 2) spondylosis	Fusion of C3–4, C5–6, & C6–7	C3–4, C5–6, C6–7	NA
7	C5–6	ACDF	14 mos	1) Neck pain; 2) radiculopathy; 3) herniated disc at adjacent level; 4) pseudarthrosis (1 & 2 resulted from trauma after rock climbing fall)	Removal of instrumentation, fusion of index & superior adjacent level, & extended superiorly (C3–6)	C3–6	Yes
8	C5–6	ACDF	15.5 mos	1) Radiculopathy; 2) pseudarthrosis	Posterior fusion (C5–6) w/ instrumentation	C5–6	Yes
9	C5–6	TDR	19 mos	1) Neck pain; 2) radiculopathy; 3) herniated disc at superior adjacent level	Fusion of superior adjacent level (C4–5)	C4–5	No
10	C5–6	ACDF	20 mos	1) Neck pain; 2) herniated disc at inferior adjacent level	Fusion of inferior adjacent level (C6–7)	C6–7	No
11	C5–6	TDR	25 mos	1) Neck pain; 2) headache; 3) numbness w/ loss of motion	Removal of Mobi-C, fusion of index level (C5–6)	C5–6	Yes
8*	C5–6	ACDF	26 mos	1) Radiculopathy; 2) cervical stenosis	Removal of previous posterior fusion instrumentation (C5–6), posterior fusion (C3–6)	C3–6	NA
12	C6–7	ACDF	27 mos	1) Neck pain; 2) radiculopathy; 3) pseudarthrosis	Posterior fusion (C6–7) w/ instrumentation	C6–7	Yes
13	C5–6	TDR	32 mos	1) Radiculopathy; 2) cervicalgia; 3) device malpositioning causing kyphosis	Removal of Mobi-C, fusion of index level (C5–6)	C5–6	Yes
14	C3–4	ACDF	34 mos	1) Numbness; 2) herniated discs at both adjacent levels	Removal of instrumentation, fusion of inferior adjacent level C4–5 through C-7	C3–7	Yes
15	C5–6	TDR	38 mos	1) Neck pain; 2) radiculopathy; 3) adjacent-level disease	Removal of Mobi-C, fusion of index & inferior adjacent level (C5–7)	C5–7	Yes
16	C6–7	ACDF	42 mos	1) Neck pain; 2) radiculopathy; 3) cervical stenosis	Removal of instrumentation, fusion of index & superior adjacent level (C5–7)	C5–7	Yes
17	C6–7	ACDF	49.5 mos	1) Neck pain; 2) radiculopathy; 3) herniated disc at inferior adjacent level	Decompression & discectomy at inferior adjacent level (C7–T1)	C7–T1	No
18	C6–7	TDR	52 mos	1) Neck pain; 2) headaches; 3) radiculopathy; 4) cervical spondylosis at superior adjacent level	Fusion of superior adjacent level (C5–6)	C5–6	No
19	C5–6	ACDF	52 mos	1) Neck pain; 2) radiculopathy; 3) herniated disc at inferior adjacent level	Fusion of inferior adjacent level (C6–7)	C6–7	No
20	C4–5	TDR	52 mos	1) Radiculopathy; 2) herniated disc at inferior adjacent level	Removal of anterior osteophytes at index level, fusion of inferior adjacent level (C5–6)	C4–6	No
15*	C5–6	TDR	55 mos	1) Neck pain; 2) radiculopathy; 3) pseudarthrosis	Redo fusion at index level, fusion of inferior adjacent level (C5–7) (was previously replaced as a fusion)	C5–7	NA

(*continued*)

TABLE 3. Subsequent surgical procedures in 1-level arm (in ascending order by time to surgery) (*continued*)

Case No.	Index Level	Device	Time to Surgery	Reason	Description	Treated Segments	Study Failure
21	C6–7	ACDF	57 mos	1) Neck pain; 2) adjacent-level degeneration at superior level, w/ posterior annular tear	Removal of instrumentation, ProDisc-C implanted at superior adjacent level (C5–6)	C5–7	Yes
22	C5–6	ACDF	59 mos	1) Radiculopathy; 2) herniated disc at adjacent level	Fusion of inferior adjacent level (C6–7)	C6–7	No

NA = not applicable.
* Indicates a third surgical intervention.

at 2 levels, 3.8% (9/234) TDR and 16.2% (17/105) ACDF patients (p = 0.0002) did not meet the study's primary end point criteria (Fig. 3). There was no statistically significant difference within treatment types between 1- and 2-level rates. The most prevalent reasons for subsequent surgeries at the index level for 1- and 2-level ACDF were radiculopathy, neck pain, and pseudarthrosis. Radiculopathy was the most common indication for subsequent surgery among TDR patients.

Surgeries Involving an Adjacent Level

The rate of subsequent surgeries involving an adjacent level was calculated at 60 months for both 1- and 2-level arms (Fig. 4). The involvement of adjacent level could overlap with a subsequent surgery at the index level. For the 1-level arm at 60 months, the rate of adjacent-level subsequent surgery was significantly higher for ACDF patients, at 11.1% (9/81), than for TDR patients, at 2.2% (4/179) (p = 0.0043). For the 2-level arm at 60 months, the ACDF group also demonstrated a significantly higher rate of adjacent-level subsequent surgical intervention (TDR 3.4% [8/234] vs ACDF 11.4% [12/105]; p = 0.0059). There was no statistically significant difference observed within treatment groups between 1- and 2-level treatments.

The most common reasons for adjacent-level ACDF surgeries were adjacent-level disease and neck pain. Radiculopathy and adjacent-level disease were the most frequent indications for subsequent surgery among TDR patients. Adjacent-level disease was an indication for surgical intervention for 8 of 9 ACDF and 4 of 4 TDR 1-level patients. For 2-level patients, adjacent-level surgery was initiated by adjacent-level disease for 11 of 12 ACDF and 5 of 8 TDR surgeries. The average time from diagnosis of adjacent-level disease to surgery was 35.8 months for ACDF patients and 32.1 months for TDR patients.

Multiple Surgeries

Several patients underwent more than 1 subsequent surgery. In the 1-level TDR group, 1 patient initially had the TDR device removed (C4–5) and replaced with an ACDF at 5 months postsurgery due to worsening radiculopathy and spondylosis, possibly due to an oversized implant. Eight months later, the patient underwent surgery again, with an ACDF at 3 adjacent levels (C3–4, C5–7) due to symptomatic adjacent-level disease. Another patient in the 1-level TDR group had the device removed 38 months postsurgery and underwent fusion at the index level (C5–6) and the inferior adjacent level (C6–7) after experiencing neck pain, radiculopathy, and adjacent-level disease following an injury. Seventeen months later, the patient underwent a revision fusion with supplemental fixation due to pseudarthrosis at C5–6 and foraminal stenosis at C6–7.

In the 1-level ACDF group, 1 patient had a subsequent surgery at 15 months postoperatively for symptomatic pseudarthrosis with radiculopathy, undergoing a posterior foraminotomy and medial facetectomy plus posterior fusion with instrumentation (C5–6). Due to worsening dysesthesia and spinal cord changes, the subject underwent posterior decompression and fusion with allograft at C3–6, as well as removal of the posterior hardware at C5–6 at 26 months postoperatively.

In the 2-level arm, 1 patient with a TDR device continued to experience neck and arm pain following the primary surgery, which was attributed to poor device stability (Fig. 5). The patient underwent removal of both prostheses and received a fusion at both index levels (C4–6) approximately 11 months postsurgery. Nine months later, the patient presented with symptomatic pseudarthrosis at both levels and underwent another anterior and posterior fusion procedure. A second patient in the TDR group had the inferior prosthesis (C5–6) removed after experiencing multiple motor vehicle accidents with concurrent neck pain 23 months postsurgery. The patient had a surgery to remove the superior prosthesis (C4–5) 7 months later at a noninvestigational site and chose not to release their medical records to the investigator.

In the 2-level ACDF group, 3 patients had multiple subsequent surgeries. One patient had a subsequent surgery at 10 months postoperatively due to continuing neck and arm pain (Fig. 6). The patient underwent removal of the index-level (C4–6) hardware and underwent ACDF at an adjacent level (C3–4). A nonunion (C5–6) was detected intraoperatively, and a redo fusion takedown with decompression was performed. One year later, the subject presented with disabling neck pain and was admitted. This patient underwent removal of hardware C3–6 anteriorly; exploration of fusion with a finding of nonunion at C5–6; reinstrumentation of C3–6 with a plate and screw system; and C3–4, C4–5, and C5–6 bilateral posterior-lateral fusion with instrumentation using a posterior cervical fixation system. Seven months later, the patient returned with complaints of recurrent neck pain and underwent removal

TABLE 4. Subsequent surgical procedures in 2-level arm (in ascending order by time to surgery)

Case No.	Index Level	Device	Time to Surgery	Reason	Description	Treated Segments	Study Failure
1	C4–6	TDR	Intraop-erative	Hematoma	Evacuation of hematoma	C4–6	No
2	C5–7	ACDF	3 days	Hematoma	Evacuation of hematoma	C5–7	No
3	C4–6	ACDF	4 days	Hematoma	Evacuation of hematoma	C4–6	No
4	C5–7	TDR	7 days	Hematoma	Evacuation of hematoma, TDR was repositioned by a tap from the surgeon	C5–7	Yes
5	C4–6	TDR	2.5 mos	Posterior migration of inferior end-plate of the inferior index level	Removal of Mobi-C at inferior index level (C5–6), repeat w/ fusion	C5–6	Yes
6	C4–6	TDR	8 mos	Radiculopathy	Posterior foraminotomy at inferior index level & both adjacent levels	C5–7	Yes
7	C5–7	TDR	8 mos	Cervical pain	Implantation of Medtronic spinal cord stimulator	C3–7	No
8	C5–7	ACDF	9 mos	1) Neck pain; 2) radiculopathy; 3) pseudarthrosis	Bilateral hemilaminectomy & posterior fusion at both index levels (C5–7)	C5–7	Yes
9	C5–7	ACDF	10 mos	1) Neck pain; 2) pseudarthrosis	Posterior fusion at index levels (C5–7) w/ instru-mentation	C5–7	Yes
10	C4–6	ACDF	10 mos	1) Neck pain; 2) radiculopathy; 3) pseudarthrosis	Removal of instrumentation at both index levels, revise fusion at inferior index level (C5–6)	C5–6	Yes
11	C4–6	ACDF	10 mos	1) Neck pain; 2) radiculopathy; 3) pseudarthrosis	Removal of instrumentation at both index levels (C4–6), revise fusion at inferior index level, & discectomy at superior adjacent level (C3–6)	C3–6	Yes
12	C4–6	TDR	11 mos	1) Neck pain; 2) radiculopathy; 3) poor attachment of device	Removal of Mobi-C at both index levels (C4–6), repeat w/ 2-level fusion	C4–6	Yes
13	C5–7	ACDF	14 mos	1) Radiculopathy; 2) cervical spon-dylosis; 3) pseudarthrosis	Posterior foraminotomy & repeat fusion at supe-rior index level (C5–6)	C5–6	Yes
14	C4–6	ACDF	14 mos	1) Neck pain; 2) radiculopathy; 3) pseudarthrosis	Posterior fusion of inferior index level (C5–6)	C5–6	Yes
15	C4–6	TDR	15 mos	1) Radiculopathy; 2) adjacent-level degeneration, inferior adjacent level	TDR at inferior adjacent level (C6–7)	C6–7	No
16	C5–7	ACDF	15 mos	1) Radiculopathy; 2) pseudarthrosis	Posterior fusion of both index levels (C5–7)	C5–6, C6–7	Yes
17	C5–7	ACDF	16 mos	1) Radiculopathy; 2) muscle spasms	Posterior foraminotomy for both index levels (C5–7)	C5–7	Yes
18	C5–7	TDR	16 mos	1) Radiculopathy; 2) herniated disc at superior adjacent level	Fusion at superior adjacent level (C4–5)	C4–5	No
19	C4–6	TDR	19 mos	1) Headaches; 2) radiculopathy	Removal of Mobi-C at both index levels (C4–6), revised to fusion	C4–6	Yes
20	C5–7	ACDF	20 mos	1) Radiculopathy; 2) pseudarthrosis	Bilateral laminal foraminotomy, medial facetec-tomy, & posterior fusion at inferior index level	C6–7	Yes
21	C5–7	TDR	20 mos	Neck pain	Facet rhizotomy at superior adjacent level & nonadjacent superior level	C3–5	No
22	C5–7	ACDF	20 mos	1) Neck pain; 2) headaches; 3) her-niated disc at superior adjacent level	Removal of instrumentation, fusion of superior adjacent level C4–5	C4–5, C5–6, C6–7	Yes
12*	C4–6	TDR	20 mos	1) Neck pain; 2) headaches; 3) pseudarthrosis	360° cervical fusion at both index levels (C4–6)	C4–6	NA
23	C4–6	ACDF	20 mos	1) Neck pain; 2) radiculopathy; 3) pseudarthrosis; 4) subsidence reversing normal lordosis	Removal of instrumentation at index levels (C4–6), revise anterior plating, posterior instru-mentation (C4–7)	C4–7	Yes
24	C3–5	ACDF	22 mos	1) Neck pain; 2) radiculopathy; 3) adjacent-level degeneration, inferior level	Removal of instrumentation at both index levels (C3–5), artificial disc implanted at inferior adjacent level (C5–6)	C3–6	Yes

(*continued*)

TABLE 4. Subsequent surgical procedures in 2-level arm (in ascending order by time to surgery) (*continued*)

Case No.	Index Level	Device	Time to Surgery	Reason	Description	Treated Segments	Study Failure
25	C5–7	TDR	22 mos	1) Neck pain; 2) radiculopathy; 3) C5–7 facet spondylosis	Posterior fusion w/ instrumentation at both index levels (C5–7)	C5–7	Yes
11*	C4–6	ACDF	22 mos	1) Pain; 2) adjacent-level disease, superior adjacent level; 3) pseud-arthrosis	Removal of instrumentation, bilateral posterior-lateral fusion w/ instrumentation (C3–6)	C3–6	NA
26	C4–6	TDR	23 mos	1) Neck pain; 2) radiculopathy	Removal of Mobi-C at inferior index level (C5–6), revised to fusion	C5–6	Yes
27	C5–7	ACDF	27 mos	1) Neck pain; 2) radiculopathy; 3) herniated disc at inferior adjacent level	Fusion at inferior adjacent level (C7–T1)	C7–T1	No
11†	C4–6	ACDF	29 mos	Neck pain	Removal of posterior instrumentation at superior adjacent & both index levels (C3–6)	C3–6	NA
26*	C4–6	TDR	30 mos	Neck pain	Removal of Mobi-C at superior index level (C4–5), revised to fusion	C4–5	NA
28	C5–7	ACDF	31 mos	1) Neck pain; 2) facet syndrome; 3) spondylosis	Removal of instrumentation at both index levels (C5–7), fusion at inferior adjacent level (C7–T1)	C5–T1	Yes
9*	C5–7	ACDF	32 mos	1) Neck swelling; 2) cervical spon-dylosis at C3–4	Prestige disc implanted at superior nonadjacent level (C3–4)	C3–4	NA
29	C5–7	ACDF	33 mos	1) Radiculopathy; 2) herniated disc at superior adjacent level	Fusion at superior adjacent level (C4–5)	C4–5	No
30	C4–6	ACDF	36 mos	1) Radiculopathy; 2) herniated disc at inferior adjacent level	Removal of instrumentation, fusion at inferior adjacent level (C6–7)	C6–7	Yes
31	C5–7	TDR	36 mos	1) Neck pain; 2) radiculopathy; 3) headaches; 4) herniated disc at superior adjacent level	Fusion at superior adjacent level (C4–5)	C4–5	No
32	C5–7	ACDF	39 mos	1) Neck pain; 2) radiculopathy; 3) herniated disc at both adjacent levels	Removal of instrumentation, disc replacement at superior adjacent level (C4–5), & fusion at inferior adjacent level (C7–T1)	C4–T1	Yes
33	C5–7	ACDF	40 mos	Trauma (motor vehicle accident)	Decompression & stabilizing fusion at both index levels and inferior adjacent (C5–T1), fusion inferior nonadjacent (T1–2)	C5–T1	Yes
9†	C5–7	ACDF	41 mos	1) Neck pain at cervicothoracic junction; 2) instability of cervical & thoracic spine	Removal of posterior instrumentation, posterior fusion at both index & inferior adjacent level (C5–T2)	C5–T2	NA
34	C5–7	TDR	41 mos	1) Radiculopathy	Foraminotomy at inferior adjacent level (C7–T1)	C7–T1	Yes
35	C4–6	TDR	41 mos	1) Radiculopathy; 2) adjacent-level disease, inferior adjacent level	Fusion at inferior adjacent level (C6–7)	C6–7	Yes
36	C4–6	TDR	46 mos	1) Neck pain; 2) radiculopathy; 3) foraminal stenosis C4–5	Foraminotomy at superior index level (C4–5)	C4–5	Yes
37	C5–7	TDR	52 mos	1) Neck pain following a head injury from fall; 2) cervical stenosis w/ spondylolisthesis	Removal of Mobi-C at inferior index level (C6–7), fusion of inferior index level	C6–7	Yes
24*	C3–5	ACDF	52 mos	1) Neck pain; 2) artificial disc loosening	Removal of artificial disc at inferior adjacent level (C5–6), revised to fusion	C5–6	NA
38	C4–6	ACDF	54 mos	1) Neck pain; 2) radiculopathy; 3) adjacent-level disease; 4) adjacent-level spondylosis	Removal of instrumentation at index levels (C4–6), fusion of both adjacent levels (C3–4, C6–7)	C3–7	Yes
39	C4–6	ACDF	60 mos	1) Neck pain; 2) herniated disc at inferior adjacent level	Fusion at inferior adjacent level (C6–7)	C6–7	No

NA = not applicable.
* Indicates a third surgical intervention.
† Indicates a fourth surgical intervention.

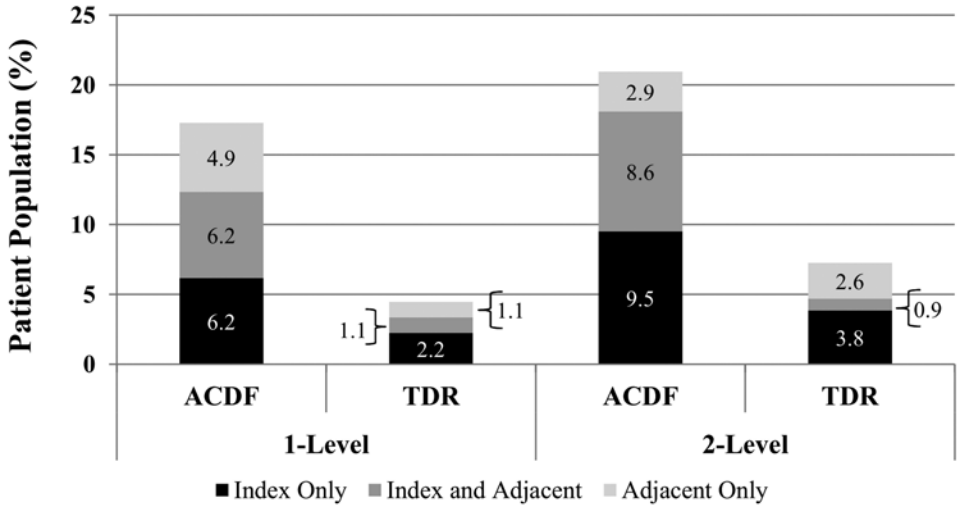

FIG. 2. Subsequent surgery classification by operative levels.

of hardware from C3–6 and exploration of the fusion, which showed solid union.

A second 2-level ACDF subject, who was initially treated at C5–7, developed pseudarthrosis with neck pain 10 months postoperatively. The subject underwent a C5–6 posterior arthrodesis with lateral mass screws and local autologous graft. After the patient reported swelling in her neck 22 months later, it was revealed by MRI that the patient had a large posterior disc protrusion at C3–4 with cord indentation and bilateral foraminal narrowing. The subject underwent anterior cervical discectomy and C3–4 arthroplasty. After presenting with severe cervical and thoracic instability 11 months later, the patient underwent C5–T2 posterior fusion.

A third patient in the 2-level ACDF group treated at C3–5 underwent an additional surgery for adjacent-level disease at C5–6, 22 months after the primary surgery. The patient was treated with discectomy and TDR at C5–6 and removal of the initial hardware at C3–5. Thirty months later, the patient presented with persistent and worsening neck pain, and radiographs showed loosening of the TDR. The subject then underwent removal of the TDR, corpectomy, and anterior cervical fusion.

Discussion

The safety and effectiveness of TDR has been validated across a number of studies at many different follow-up periods.[3,5,15,22,23,27–29,33] Overall, TDR has demonstrated an advantage over ACDF with regard to motion preservation. The nature of ACDF eliminates motion at treated levels, whereas TDR has been shown to preserve segment mobility with high success.[3,22,28] Both short- and long-term results have trended toward similar or greater improvements in NDI, neck pain, and arm pain visual analog scale scores in TDR populations when compared with ACDF, although the significance of these results remains controversial.[5,11,12,14,22,24,27–29]

The results of many single-level TDR clinical trials suggest that TDR may also result in a lower incidence of secondary operations.[5,7,9,12,15,22,23,28,29] Sasso et al. reported

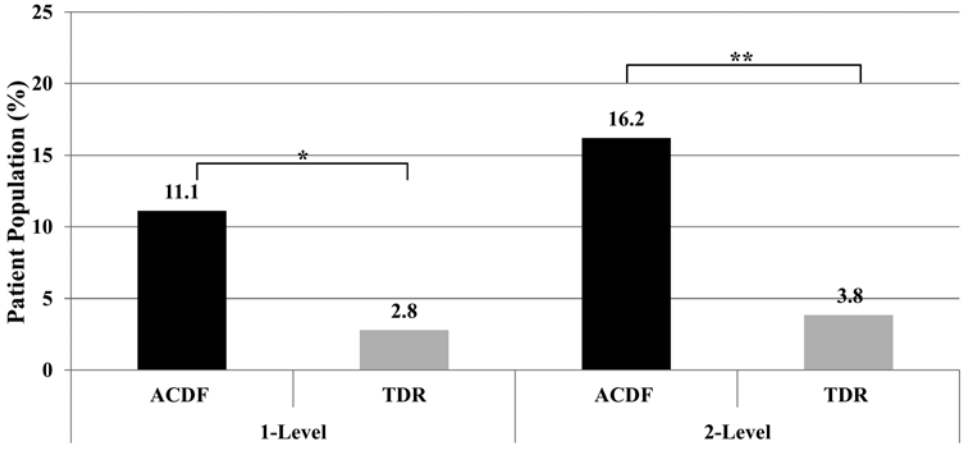

FIG. 3. Subsequent surgery at index level leading to study failure. *p= 0.014; **p = 0.0002.

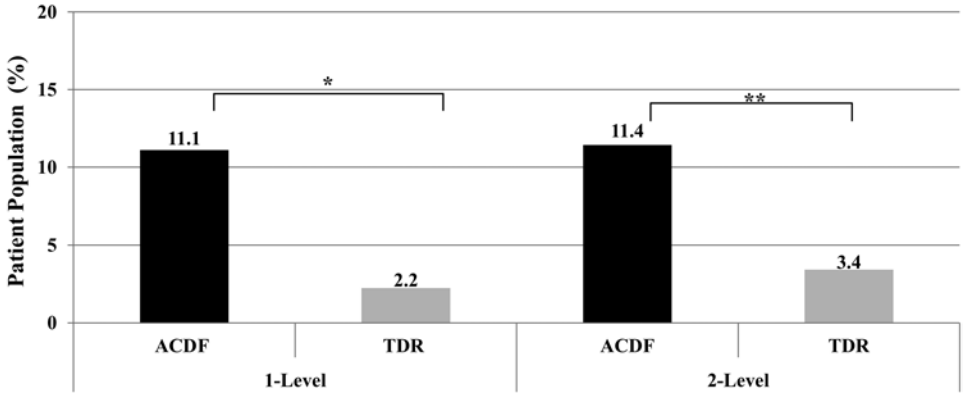

FIG. 4. Subsequent surgery at adjacent level. *p = 0.0043; **p = 0.0059.

a 2-fold increase in secondary surgery rates in patients with 1-level ACDF compared with Bryan cervical disc replacement counterparts after 2 years (TDR 2/56 vs ACDF 4/59).[28] Garrido et al. reported a 4-fold increase in subsequent surgical intervention in patients with 1-level ACDF compared with Bryan cervical disc replacement at 4 years (TDR 1/23 vs ACDF 5/26).[12] In a 5-year study on secondary surgery rates, Delamarter and Zigler reported a significant decrease in secondary surgery rates in patients who received a ProDisc-C artificial cervical disc (2.9%) versus ACDF (14.5%).[9]

The intent of this study was to further demonstrate the benefits of TDR in terms of subsequent surgical intervention rates. In agreement with previous studies, we found that patients with 1-level ACDF who received a TDR device had a significantly lower occurrence of subsequent surgical intervention at the treated level compared with ACDF-treated patients (2.8% TDR vs 11.1% ACDF; $p < 0.05$). Patients with 2-level ACDF who received a TDR device also demonstrated significantly fewer index-level surgeries at 60 months (3.8% TDR vs 16.2% ACDF; $p < 0.001$).

Several authors have hypothesized that TDR may reduce the incidence of adjacent-segment degeneration compared with ACDF as a consequence of maintaining segmental motion and stress profiles.[16,20,25,31] For our 1-level arm at 60 months, we found that 4 times fewer TDR patients required a subsequent operation at adjacent levels (2.2% TDR vs 11.1% ACDF; $p < 0.05$). Similar results were shown in the 2-level arm for adjacent-level surgeries (3.4% TDR vs 11.4% ACDF; $p < 0.05$). These results are in agreement with the findings of other investigators and suggest an elevated rate of adjacent-segment degeneration in the ACDF population.

In a retrospective review of anterior cervical decompression and stabilization, patients with a maximum follow-up of 21 years (range 2–21 years), including patients without cervical instrumentation, Hilibrand and Robbins[17]

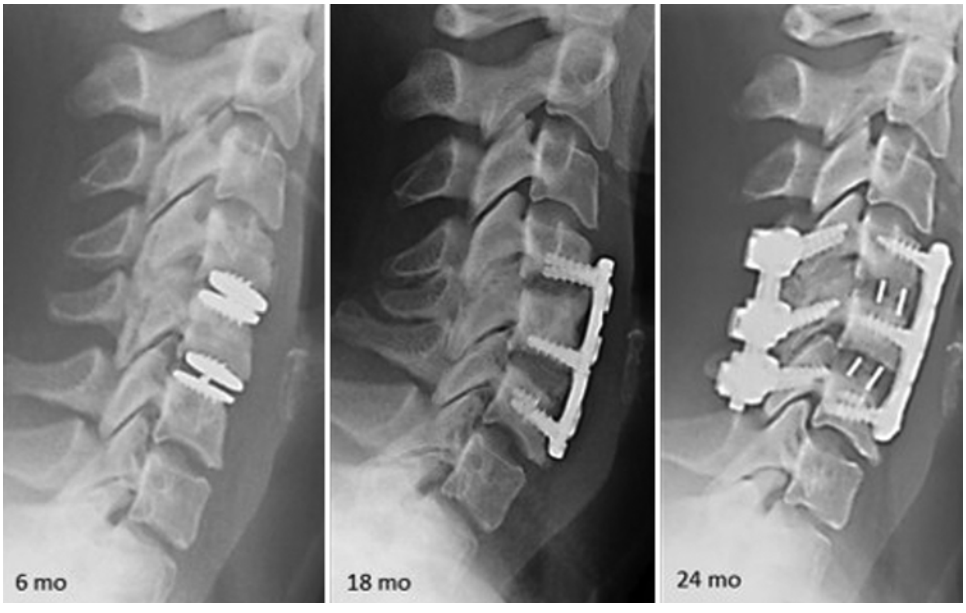

FIG. 5. TDR failure requiring removal and multiple subsequent fusions.

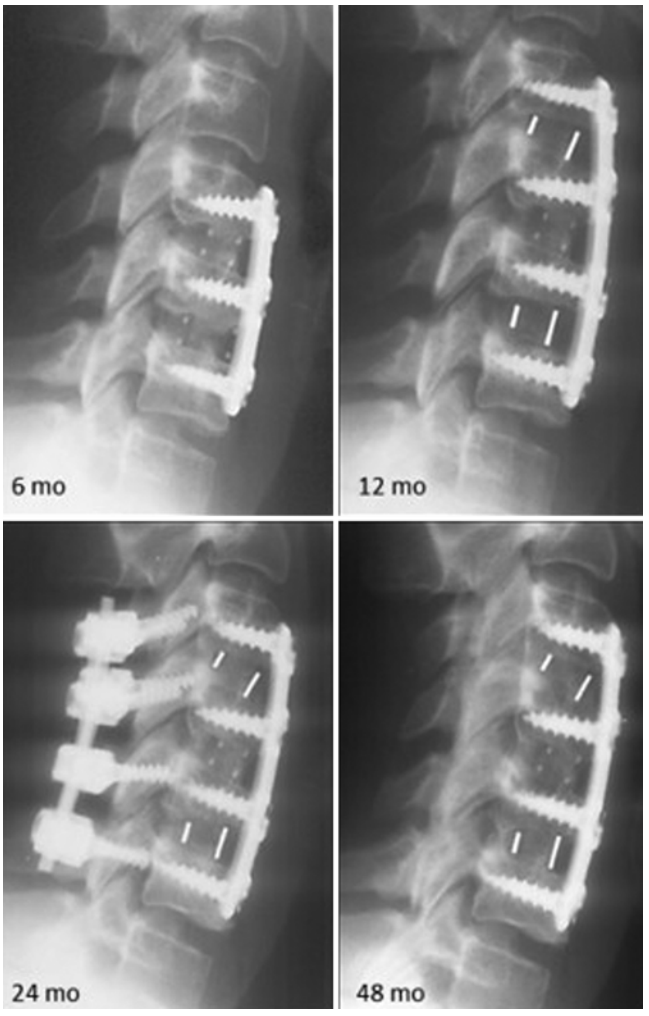

FIG. 6. ACDF nonunion and development of adjacent-level disease leading to subsequent fusion surgeries.

cite studies by Bohlman et al.,[4] Gore and Sepic,[13] and Williams et al.[32] when analyzing rates of adjacent-segment disease among ACDF patients, with an average follow-up of 4.5 years.[17] From these studies, the annual incidence of adjacent-segment disease requiring additional surgery was 1.5%–4%,[17] equating to 7.5%–20% at 5 years. In a long-term TDR study with the Prestige artificial cervical disc, Burkus et al. showed a lower rate of secondary surgeries involving adjacent segments in their TDR population compared with ACDF controls (TDR 2.9% vs ACDF 4.9%).[5] Mummaneni et al. also reported a statistically significant decrease in secondary operations involving adjacent segments in their TDR population (TDR 2/276 vs ACDF 9/265).[22] Davis et al. reported a significantly greater rate of adjacent-segment degeneration at both the inferior and superior index levels for 2-level ACDF compared with TDR at 4 years.[8] Interestingly, the rate of adjacent-level operations was similar between the 1- and 2-level ACDF or TDR groups, and does not reflect the expectation that multilevel ACDF causes a greater amount of adjacent-level disease than single-level ACDF. However, this study was not powered or designed for intratreatment comparisons, and these results are suggestive, not conclusive.

Limitations of this study include the inability to blind surgeons and patients to treatment, which opens the results to the potential of confirmation bias. Although the control group in this study was limited to anterior plating with allograft, other fusion procedures and devices (e.g., standalone devices and the use of autograft) are viable treatment options. The comparative results between the control and investigational groups are limited to anterior plate and allograft and may not be consistent with those of other surgical alternatives for cervical fusion. Additionally, the control group consisted of patients receiving 3 different cervical plate systems, based on surgeon preference. This heterogeneity represents a study limitation because ACDF failures may not have been equally distributed across the 3 fusion systems implanted.

All authors were investigators for the Mobi-C IDE clinical trial, which was sponsored by LDR Spine USA, Inc. Some surgeons received compensation for their participation in the trial or have equity in LDR Spine. To ensure that these potential conflicts of interest have not affected study outcomes, an analysis was performed to compare the subsequent surgery rates between sites with and without financial interests. A site was considered financially interested if an investigator received any payment from the manufacturer or if the investigator held company equity during the study period. At 60 months, the financially interested and nonfinancially interested sites had statistically similar subsequent surgery rates within treatment groups for both treatment arms, with no trend observed. Additionally, 45.9% of patients had subsequent surgeries performed by surgeons not participating in the IDE trial.

Conclusions

The results from this clinical trial suggest that TDR may provide a substantial benefit over ACDF in providing a lower risk for subsequent surgical intervention. Furthermore, a lower rate of subsequent adjacent-level surgical procedures in patients who received TDR devices provides indirect evidence that motion preservation may lead to a lower rate of adjacent-level disease than an anterior fusion approach.

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References

1. Auerbach JD, Anakwenze OA, Milby AH, Lonner BS, Balderston RA: Segmental contribution toward total cervical range of motion: a comparison of cervical disc arthroplasty and fusion. **Spine (Phila Pa 1976) 36:**E1593–E1599, 2011

2. Bae HW, Kim KD, Nunley PD, Jackson RJ, Hisey MS, Davis RJ, et al: Comparison of clinical outcomes of 1- and 2-level total disc replacement: four-year results from a prospective, randomized, controlled, multicenter IDE clinical trial. **Spine (Phila Pa 1976) 40:**759–766, 2015
3. Beaurain J, Bernard P, Dufour T, Fuentes JM, Hovorka I, Huppert J, et al: Intermediate clinical and radiological results of cervical TDR (Mobi-C) with up to 2 years of follow-up. **Eur Spine J 18:**841–850, 2009
4. Bohlman HH, Emery SE, Goodfellow DB, Jones PK: Robinson anterior cervical discectomy and arthrodesis for cervical radiculopathy. Long-term follow-up of one hundred and twenty-two patients. **J Bone Joint Surg Am 75:**1298–1307, 1993
5. Burkus JK, Haid RW, Traynelis VC, Mummaneni PV: Long-term clinical and radiographic outcomes of cervical disc replacement with the Prestige disc: results from a prospective randomized controlled clinical trial. **J Neurosurg Spine 13:**308–318, 2010
6. Bydon M, Xu R, Macki M, De la Garza-Ramos R, Sciubba DM, Wolinsky JP, et al: Adjacent segment disease after anterior cervical discectomy and fusion in a large series. **Neurosurgery 74:**139–146, 2014
7. Davis RJ, Kim KD, Hisey MS, Hoffman GA, Bae HW, Gaede SE, et al: Cervical total disc replacement with the Mobi-C cervical artificial disc compared with anterior discectomy and fusion for treatment of 2-level symptomatic degenerative disc disease: a prospective, randomized, controlled multicenter clinical trial: clinical article. **J Neurosurg Spine 19:**532–545, 2013
8. Davis RJ, Nunley PD, Kim KD, Hisey MS, Jackson RJ, Bae HW, et al: Two-level total disc replacement with Mobi-C cervical artificial disc versus anterior discectomy and fusion: a prospective, randomized, controlled multicenter clinical trial with 4-year follow-up results. **J Neurosurg Spine 22:**15–25, 2015
9. Delamarter RB, Zigler J: Five-year reoperation rates, cervical total disc replacement versus fusion, results of a prospective randomized clinical trial. **Spine (Phila Pa 1976) 38:**711–717, 2013
10. Elsawaf A, Mastronardi L, Roperto R, Bozzao A, Caroli M, Ferrante L: Effect of cervical dynamics on adjacent segment degeneration after anterior cervical fusion with cages. **Neurosurg Rev 32:**215–224, 2009
11. Fay LY, Huang WC, Tsai TY, Wu JC, Ko CC, Tu TH, et al: Differences between arthroplasty and anterior cervical fusion in two-level cervical degenerative disc disease. **Eur Spine J 23:**627–634, 2014
12. Garrido BJ, Taha TA, Sasso RC: Clinical outcomes of Bryan cervical disc arthroplasty a prospective, randomized, controlled, single site trial with 48-month follow-up. **J Spinal Disord Tech 23:**367–371, 2010
13. Gore DR, Sepic SB: Anterior cervical fusion for degenerated or protruded discs. A review of one hundred forty-six patients. **Spine (Phila Pa 1976) 9:**667–671, 1984
14. Hacker FM, Babcock RM, Hacker RJ: Very late complications of cervical arthroplasty: results of 2 controlled randomized prospective studies from a single investigator site. **Spine (Phila Pa 1976) 38:**2223–2226, 2013
15. Heller JG, Sasso RC, Papadopoulos SM, Anderson PA, Fessler RG, Hacker RJ, et al: Comparison of BRYAN cervical disc arthroplasty with anterior cervical decompression and fusion: clinical and radiographic results of a randomized, controlled, clinical trial. **Spine (Phila Pa 1976) 34:**101–107, 2009
16. Hilibrand AS, Carlson GD, Palumbo MA, Jones PK, Bohlman HH: Radiculopathy and myelopathy at segments adjacent to the site of a previous anterior cervical arthrodesis. **J Bone Joint Surg Am 81:**519–528, 1999
17. Hilibrand AS, Robbins M: Adjacent segment degeneration and adjacent segment disease: the consequences of spinal fusion? **Spine J 4 (6 Suppl):**190S–194S, 2004
18. Hisey MS, Bae H, Davis R, Gaede S, Hoffman G, Kim K, et al: Multi-center, prospective, randomized, controlled investigational device exemption clinical trial comparing Mobi C Cervical Artificial Disc to anterior discectomy and fusion in the treatment of symptomatic degenerative disc disease in the cervical spine. **Int J Spine Surg 8:**7, 2014
19. Khong P, Bogduk N, Ghahreman A, Davies M: Cervical disc arthroplasty for the treatment of spondylotic myelopathy and radiculopathy. **J Clin Neurosci 20:**1411–1416, 2013
20. Kim SW, Limson MA, Kim SB, Arbatin JJ, Chang KY, Park MS, et al: Comparison of radiographic changes after ACDF versus Bryan disc arthroplasty in single and bi-level cases. **Eur Spine J 18:**218–231, 2009
21. Matsunaga S, Kabayama S, Yamamoto T, Yone K, Sakou T, Nakanishi K: Strain on intervertebral discs after anterior cervical decompression and fusion. **Spine (Phila Pa 1976) 24:**670–675, 1999
22. Mummaneni PV, Burkus JK, Haid RW, Traynelis VC, Zdeblick TA: Clinical and radiographic analysis of cervical disc arthroplasty compared with allograft fusion: a randomized controlled clinical trial. **J Neurosurg Spine 6:**198–209, 2007
23. Murrey D, Janssen M, Delamarter R, Goldstein J, Zigler J, Tay B, et al: Results of the prospective, randomized, controlled multicenter Food and Drug Administration investigational device exemption study of the ProDisc-C total disc replacement versus anterior discectomy and fusion for the treatment of 1-level symptomatic cervical disc disease. **Spine J 9:**275–286, 2009
24. Ren C, Song Y, Xue Y, Yang X: Mid- to long-term outcomes after cervical disc arthroplasty compared with anterior discectomy and fusion: a systematic review and meta-analysis of randomized controlled trials. **Eur Spine J 23:**1115–1123, 2014
25. Robertson JT, Papadopoulos SM, Traynelis VC: Assessment of adjacent-segment disease in patients treated with cervical fusion or arthroplasty: a prospective 2-year study. **J Neurosurg Spine 3:**417–423, 2005
26. Robinson RA, Walker AE, Ferlic DC, Wiecking DK: The results of anterior interbody fusion of the cervical spine. **J Bone Joint Surg Am 44:**1569–1587, 1962
27. Sasso RC, Anderson PA, Riew KD, Heller JG: Results of cervical arthroplasty compared with anterior discectomy and fusion: four-year clinical outcomes in a prospective, randomized controlled trial. **J Bone Joint Surg Am 93:**1684–1692, 2011
28. Sasso RC, Smucker JD, Hacker RJ, Heller JG: Artificial disc versus fusion: a prospective, randomized study with 2-year follow-up on 99 patients. **Spine (Phila Pa 1976) 32:**2933–2942, 2007
29. Upadhyaya CD, Wu J-C, Trost G, Haid RW, Traynelis VC, Tay B, et al: Analysis of the three United States Food and Drug Administration investigational device exemption cervical arthroplasty trials. **J Neurosurg Spine 16:**216–228, 2012
30. Vaccaro A, Beutler W, Peppelman W, Marzluff JM, Highsmith J, Mugglin A, et al: Clinical outcomes with selectively constrained SECURE-C cervical disc arthroplasty: two-year results from a prospective, randomized, controlled, multicenter investigational device exemption study. **Spine (Phila Pa 1976) 38:**2227–2239, 2013
31. Wigfield C, Gill S, Nelson R, Langdon I, Metcalf N, Robertson J: Influence of an artificial cervical joint compared with fusion on adjacent-level motion in the treatment of degenerative cervical disc disease. **J Neurosurg 96 (1 Suppl):**17–21, 2002
32. Williams JL, Allen MB Jr, Harkess JW: Late results of cervical discectomy and interbody fusion: some factors influencing the results. **J Bone Joint Surg Am 50:**277–286, 1968

33. Zhang Z, Gu B, Zhu W, Wang Q, Zhang W: Clinical and radiographic results of Bryan cervical total disc replacement: 4-year outcomes in a prospective study. **Arch Orthop Trauma Surg 133:**1061–1066, 2013

Disclosures

Dr. Nunley has direct stock ownership in Amedica, Paradigm Spine, Safewire, and Spineology; serves as a consultant to Amedica, Vertiflex, LDR, and K2M; and is a patent holder for LDR, K2M, and Osprey. Dr. Hisey is a member of the faculty for LDR clinical courses. Dr. Gaede performed statistical analysis for the study/writing or editorial assistance on the manuscript on behalf of LDR. Dr. Jackson serves as a consultant for LDR. Dr. Bae has direct stock ownership in LDR, serves as a consultant, and receives royalties. Dr. Davis received research support during the trial. Dr. Kim has ownership in Molecular Matrix and Globus, serves as a consultant to FzioMed, and has speaking/teaching arrangements with Precision Spine, LDR, and Globus. Dr. Hoffmann has ownership in Path4/LDR.

Author Contributions

Conception and design: Jackson. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: Jackson, Davis. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Jackson. Administrative/technical/material support: Jackson. Study supervision: Jackson, Bae, Kim, Nunley.

Supplemental Information

Previous Presentations

Portions of this work were presented at the 29th Annual Meeting of North American Spine Society, San Francisco, California, November 12–15, 2014.

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