Ten-Year Outcomes of 1- and 2-Level Cervical Disc Arthroplasty From the Mobi-C Investigational Device Exemption Clinical Trial

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BACKGROUND: Short- and mid-term studies have shown the effectiveness of cervical disc arthroplasty (CDA) to treat cervical disc degeneration.
OBJECTIVE: To report the 10-yr outcomes of a multicenter experience with cervical arthroplasty for 1- and 2-level pathology.
METHODS: This was a prospective study of patients treated with CDA at 1 or 2 contiguous levels using the Mobi-C® Cervical Disc (Zimmer Biomet). Following completion of the 7-yr Food and Drug Administration postapproval study, follow-up continued to 10 yr for consenting patients at 9 high-enrolling centers. Clinical and radiographic endpoints were collected out to 10 yr.
RESULTS: At 10 yr, patients continued to have significant improvement over baseline Neck Disability Index (NDI), neck and arm pain, neurologic function, and segmental range of motion (ROM). NDI and pain outcomes at 10 yr were significantly improved from 7 yr. Segmental and global ROM and sagittal alignment also were maintained from 7 to 10 yr. Clinically relevant adjacent segment pathology was not significantly different between 7 and 10 yr. The incidence of motion restricting heterotopic ossification at 10 yr was not significantly different from 7 yr for 1-level (30.7% vs 29.6%) or 2-level (41.7% vs 39.2%) patients. Only 2 subsequent surgeries were reported after 7 yr.
CONCLUSION: Our results through 10 yr were comparable to 7-yr outcomes, demonstrating that CDA with Mobi-C continues to be a safe and effective surgical treatment for patients with 1- or 2-level cervical degenerative disc disease.

KEY WORDS: Cervical disc arthroplasty, Total disc replacement, Mobi-C disc, Degenerative disc disease, Adjacent segment pathology, Heterotopic ossification

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Anterior cervical discectomy and fusion (ACDF) has been the standard surgical treatment for symptomatic cervical spondylosis since the mid-20th century. However, ACDF alters spinal biomechanics by affecting segmental motion and placing additional stress on adjacent discs, which may accelerate degeneration.[1-4] Logically, ACDF was thought to lead to higher incidence of symptomatic adjacent segment pathology (ASP) than cervical disc arthroplasty (CDA).[5]

CDA was designed as an alternative to ACDF for treating degenerative disc disease (DDD) at 1 or more levels while preserving motion. By simulating the natural motion of the spine, CDA is believed to reduce degeneration at the adjacent segments compared to ACDF.[4,6-11] CDA has been extensively evaluated in multiple Food and Drug Administration (FDA) randomized controlled trials, and short- to mid-term data

ABBREVIATIONS: **ACDF,** anterior cervical discectomy and fusion; **ANOVA,** analysis of variance; **ASD,** adjacent segment degeneration; **ASP,** adjacent segment pathology; **CDA,** cervical disc arthroplasty; **CI,** confidence interval; **DDD,** degenerative disc disease; **FDA,** Food and Drug Administration; **HO,** heterotopic ossification; **MCS,** mental component score; **NDI,** Neck Disability Index; **PCS,** physical component score; **rASP,** radiographic adjacent segment pathology; **ROM,** range of motion; **SVA,** sagittal vertical axis; **VAS,** Visual Analog Scale

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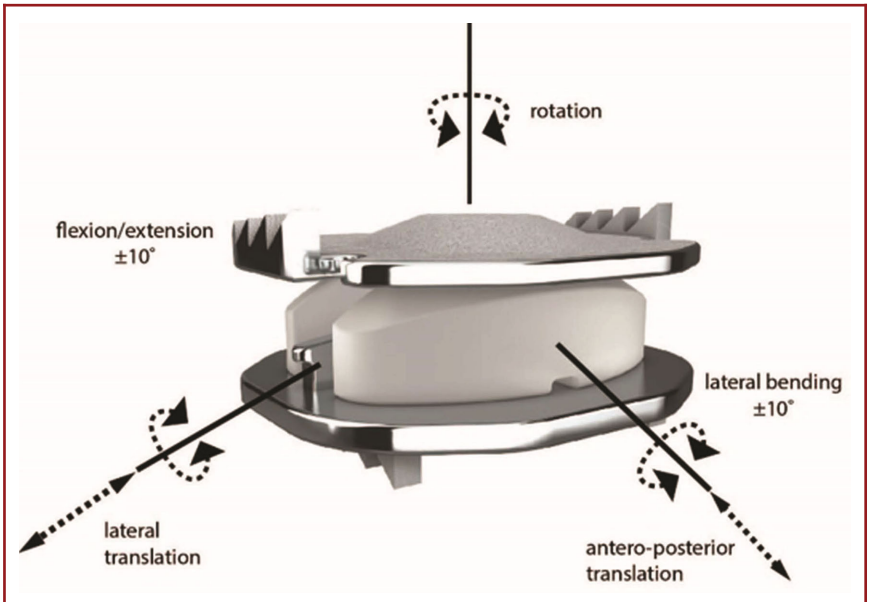

FIGURE 1. *The Mobi-C© Cervical Disc. See* ***Supplemental Digital Content****, for a detailed description of the Mobi-C device. © Zimmer Biomet, used with permission.*

indicate it is a safe and effective treatment for both 1- and 2-level cervical DDD.

The safety and effectiveness of the Mobi-C® Cervical Disc (Mobi-C, Zimmer Biomet, Westminster, Colorado) has been reported at 2 to 7 yr, and at most time points, the Mobi-C has shown statistically superior results to ACDF in terms of composite measures of overall success.[12-16] The purpose of this post market study is to report the 10-yr outcomes of a multicenter experience with a subset of patients treated with Mobi-C for 1- and 2-level pathology.

METHODS

Study Design

This was a prospective cohort study of patients previously treated with CDA at 1- or 2 contiguous levels using the Mobi-C (Zimmer Biomet; Figure 1). Patients were enrolled in the prospective, randomized multicenter Investigational Device Exemption (IDE) clinical trial (ClinicalTrials.gov registration no. NCT00389597). Institutional review board approval and patient informed consent were obtained at all investigational sites. Enrollment criteria included a diagnosis of DDD with radiculopathy or myeloradiculopathy at either 1 or 2 contiguous levels from C3 to C7 with no prior cervical operations. Details of the study protocol, inclusion and exclusion criteria, and patient characteristics have been reported previously.[16]

Patient Selection

Between April 2006 and March 2008, 413 patients were treated with 1- or 2-level CDA. The FDA approved the Mobi-C in 2013 and required a postapproval study to collect data out to 7 yr. The safety and effectiveness outcomes of these CDA patients were compared with the ACDF control patients out to 7 yr postoperatively.[16] Following completion of the 7-yr FDA postapproval study, consenting CDA patients at 9 high-enrolling centers were followed at 10 yr.

Outcomes

Outcomes were defined in the original IDE study and included the Neck Disability Index (NDI), Visual Analog Scale (VAS) neck and arm pain, SF-12 physical component score (PCS) and mental component score (MCS), patient satisfaction, neurologic function, secondary surgical procedures (removals, revisions, reoperations, or additional fixation), and adverse events (AEs). Neurological function was assessed with tests of sensory, reflex, and motor function. Neurological success was defined as maintained or improved motor, sensory, and reflex assessment compared to preoperative baseline. Radiographic endpoints included segmental and global range of motion (ROM), sagittal balance (C2-C6 angle), ASP and heterotopic ossification (HO). Radiographic adjacent segment pathology (rASP) was defined with the Kellgren-Lawrence scale.[17] HO was graded by the system adapted from McAfee and Mehren.[18,19] During the 10-yr postmarket study, sagittal vertical axis (SVA; C2-C7), the horizontal distance between the C2 and C7 plumb lines, was obtained from neutral lateral X-rays at preoperative, early postoperative, and 10 yr. Independent radiologists (Medical Metrics, Inc., Houston, Texas) conducted radiographic evaluations.

Statistical Analysis

All CDA patients and follow-up from 9 sites were included in the analysis. Repeated measures, mixed effects analysis of variance (ANOVA) was used to compare 10-yr outcomes with preoperative and 7-yr outcomes within the CDA group. The analysis was designed to assess whether a statistically significant improvement from baseline observed at 7 yr was maintained out to 10 yr. The ANOVA model also included number of treated levels to evaluate whether results differed between

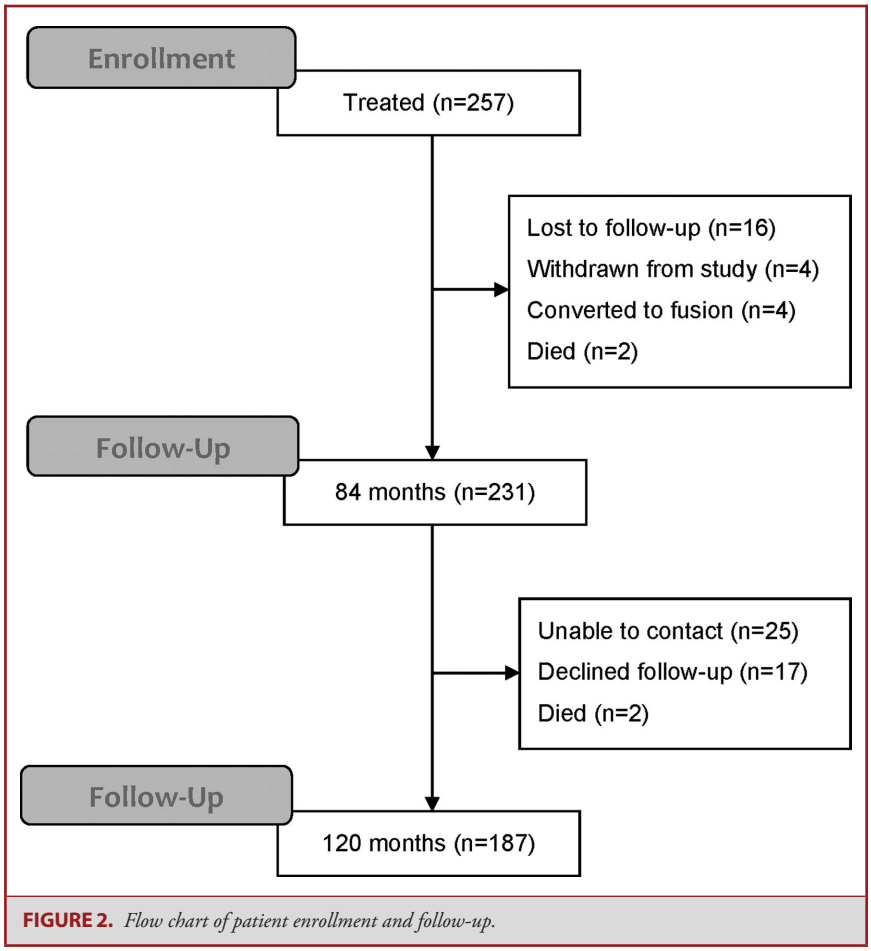

FIGURE 2. *Flow chart of patient enrollment and follow-up.*

1- and 2-level CDA. *P*-values were adjusted for multiplicity using a Monte Carlo simulation-based method to compute adjusted *P*-values and confidence limits. Because follow-up of the control group was completed at 7 yr, data for the CDA patients at 10 yr are assessed without any between-group statistical comparisons with ACDF. Survival function estimates for secondary surgery and serious device-related adverse events were generated using the Kaplan-Meier method, with the log-rank test to compare survival functions. All patients that were withdrawn or lost-to-follow-up were censored at their last visit prior to study withdrawal. CDA patients undergoing a device removal and conversion to fusion were censored after the surgery. Categorical proportions were compared using a 2-sided McNemar's test for comparing dependent samples or Fisher's exact test for independent samples. Confidence intervals for proportions were calculated with the Clopper-Pearson exact binomial method. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Study Cohort

From the original enrollment of 257 CDA patients at 9 sites, 231 patients were eligible for follow-up after 7 yr (Figure 2). There were no significant differences in preoperative characteristics between these patients and the original FDA cohort. Ten-year follow-up was obtained from 81% (187/231) of patients available at 7 yr, and 75.1% (187/249) of all CDA patients enrolled at these sites, after excluding 8 patients that were converted to fusion or died. Seventeen (17) patients were not available for in-person follow-up and did not have 10-yr radiographs, but patient reported outcomes (NDI, pain, SF-12), adverse events, and reoperation were collected via phone interview and review of medical records. The longest follow-up was 11.2 yr (1897.9 cumulative yr).

Clinical Outcomes

Ten years after CDA, patients continued to have significant improvement ($P < .001$) from baseline NDI, neck and arm pain, and SF-12 PCS and MCS (Table 1). NDI and pain outcomes at 10 yr were significantly improved from 7 yr, but these improvements were less than the minimal clinically important difference for NDI (15/100) and pain (10/100). At 10 yr, 86.3% of CDA patients had maintained or improved neurological function compared to 86% at 7 yr ($P = .60$). Overall patient

TABLE 1. Patient-reported Outcomes*

Outcome	Baseline	7 yr	10 yr	Mean Δ 10 yr vs baseline [95% CI]	*P* value†	Mean Δ 10 vs 7 yr [95% CI]	*P* value‡
NDI	54.4	19.3	15.1	37.3 [33.8–40.8]	<.0001	3.4 [1.5–5.3]	.003
VAS Neck	72.1	20.3	13.3	56.8 [51.7–61.9]	<.0001	6.2 [1.7–10.7]	.002
VAS Arm	69.9	15.5	11.3	57.1 [51.6–62.7]	<.0001	4.7 [0.2–9.2]	.037
SF12 PCS	32.9	45.7	47.5	14.1 [12.0–16.3]	<.0001	1.6 [−0.3–3.5]	.13
SF12 MCS	41.6	51.0	51.5	9.4 [7.1–11.8]	<.0001	0.7 [−1.2–2.5]	.91

*Least squares means and confidence intervals adjusted for other covariates in the model.
†10 yr vs baseline. ‡ 10 yr vs 7 yr.
P-values are adjusted for multiple comparisons. All analyses of patient-reported outcomes included the comparison of outcomes between levels treated. For each outcome, there was no significant difference ($P > .05$) between 1- and 2-level CDA across all time points. Therefore, results for clinical outcomes by visit are reported for all CDA patients combined.

TABLE 2. Subsequent Surgery at the Index or Adjacent Level After CDA Through 10 yr (n = 257)

Subsequent surgery[a]	Patients (%)	95% CI[b]
Surgery at index level	13 (5.1%)	2.7%-8.5%
Removal	6 (2.3%)	–
Reoperation	4 (1.6%)	–
Supplemental fixation	2 (0.8%)	–
Revision	1 (0.4%)	–
Surgery involving adjacent level(s)	11 (4.3%)	2.2%-7.5%
Any subsequent surgery	20 (7.8%)	4.8%-11.8%

[a]Some secondary surgeries involved both index and adjacent levels. Some patients had more than 1 secondary surgery.
[b]Clopper-Pearson exact binomial confidence intervals.

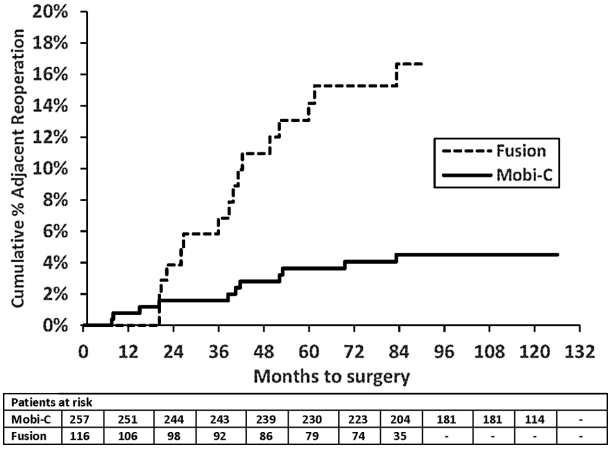

FIGURE 3. *Kaplan-Meier cumulative risk of subsequent surgery at an adjacent level in CDA and fusion patients. Fusion patients are from the same study centers, but were not followed beyond 7 yr. Log rank test; P = .0002.*

satisfaction remained very high, with the majority of CDA patients reporting "very satisfied" (10 yr: 88.8% vs 7 yr: 88.0%; $P = .26$).

Safety Outcomes

Two subsequent surgeries were reported after 7 yr. A patient with 2-level CDA presented with debilitating neck and radicular pain and underwent bilateral posterior instrumented fusion of the index levels 9.5 yr after surgery, with the original Mobi-C implants (Zimmer Biomet) left in place. In the second case, a patient with single level CDA at C5-6 presented with cervical spondylosis at a nonadjacent level and underwent ACDF at the C3-4 level, 7.4 yr after CDA. There were no adjacent level surgeries reported after 7 yr. Of the 13 secondary surgeries at the index level, 6 were device removals, with 4 patients fully converted to fusion and 2 2-level patients converted to hybrid constructs with 1 Mobi-C left in place. Total incidence of subsequent surgery after 10 yr was 5.1% (13/257) at the index level and 4.3% (11/257) at an adjacent level (Table 2). The Kaplan-Meier curves illustrate the consistently low rate of adjacent level secondary surgery (4.5%) in the CDA group at 7 yr and beyond (Figure 3).

The survival function for serious device-related AEs at 7 yr was 96.4% [95% CI: 94.1%-98.7%]. Between 7 and 10 yr, 7 device-related AEs were reported in 5 patients (HO – 5; subsidence-2), but none were classified as serious (ie, required hospitalization or reoperation).

Radiographic Outcomes

CDA patients maintained segmental and global ROM with no statistically significant changes between 7 and 10 yr (Figure 4; Table 3). Similar to ROM, sagittal balance (C2-C6 angle) was maintained from 7 to 10 yr ($P > .05$; Table 4). Both preoperatively and postoperatively, over 80% of patients were lordotic (SVA 0-30 mm). There was a small increase in SVA from preoperative to postoperative, but SVA at 10 yr was not significantly changed from initial postoperative alignment ($P > .05$).

Clinically relevant (grade 3/4) rASP at 10 yr was not significantly different from the 7-yr incidence ($P > .05$; Table 5). The incidence of motion-restricting (grade 3/4) HO at 10 yr was not significantly different from the 7-yr incidence for 1-level (30.6% vs 28.7%; $P = .99$) or 2-level (41.6% vs 38.5%; $P = .58$)

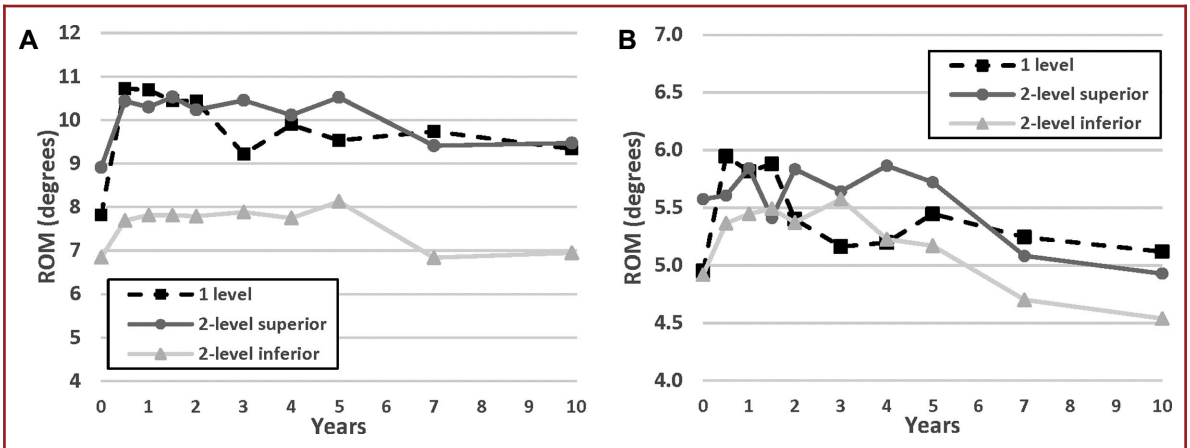

FIGURE 4. *ROM in flexion/extension (left) and lateral bending (right) for CDA patients from preoperative to 10 yr.*

TABLE 3. Segmental and Global ROM (degrees) in CDA Through 10 yr

	Flexion/extension			Lateral bending			Global ROM (C2-C6 flexion/extension)	
	2-level superior	2-level inferior	1-level	2-level superior	2-level inferior	1-level	2-level	1-level
Preoperative	8.9	6.8	7.8	5.6	4.9	5.0	37.0	38.8
7 yr	9.4	6.8	9.7	5.1	4.7	5.2	37.9	42.7
10 yr	9.5	6.9	9.3	4.9	4.5	5.1	38.2	41.6
P-value[a]	.91	.97	.59	.99	.99	.90	.99	.19

[a]10 yr vs 7 yr.

TABLE 4. Sagittal Balance and Sagittal Vertical Alignment in CDA Patients

	Sagittal balance (C2-C6 angle (°))		Sagittal alignment (C2-C7 SVA (mm))	
Follow-up	2-level	1-level	2-level	1-level
Preoperative	4.3	4.8	16.4	15.7
Postoperative	10.2	7.7	18.5	18.1
7 yr	9.8	8.6	–	–
10 yr	8.6	8.6	20.3	17.4
P values				
10 yr vs preoperative	<.0001	<.0001	<.001	0.69
10 yr vs postoperative	0.78	0.31	0.28	0.82
10 yr vs 7 yr	0.90	0.86	–	–

CDA patients (Table 6). Although segments with grade 3/4 HO had reduced ROM, many retained some motion (Figure 5).

DISCUSSION

The Mobi-C (Zimmer Biomet) received FDA approval in 2013, and the clinical trial was completed after 7 yr of follow-up. This postmarket study evaluated the safety and effectiveness of the Mobi-C implanted at 1 or 2 levels out to 10 yr. At 10 yr, both 1- and 2-level CDA demonstrate sustained improvement of NDI, pain scores, and SF-12. The percentage of patients who maintained their neurological function also remained stable. Progression of rASP and HO from 7 to 10 yr was minimal. One patient underwent secondary surgery at the index level after 7 yr, bringing the cumulative rate to 5.1%. The 10-yr cumulative rate of adjacent surgery was 4.3%.

TABLE 5. Progression of Grade 3/4 rASP

	1-level		2-level	
Years	CDA	ACDF	CDA	ACDF
2	10.1%	11.9%	3.4%	13.9%
5	15.4%	29.0%	8.6%	35.7%
7	22.7%	37.5%	8.4%	45.3%
10	21.3%	–	10.2%	–
P value[a]	.16		<.0001	
P-value[b]	.13		.25	

[a]Mobi-C vs ACDF at 7 yr. Fisher's exact test.
[b]Mobi-C 10 yr vs 7 yr. McNemar's test based on patients with data at both 7 and 10 yr.

ROM and sagittal alignment were maintained at 10 yr compared to early postoperative baseline. Two key advantages of CDA over fusion are preserving segmental ROM, and accommodating flexion/extension with improved global sagittal alignment. The first advantage of CDA has been well established in the literature, but little data exists that illustrates how CDA influences sagittal alignment. In our study, preoperative SVA in CDA patients was similar to normal values reported in the literature for healthy asymptomatic subjects.[20] Patients undergoing CDA would be expected to flex and extend their neck better than the fusion patients. While global ROM improved after CDA, there was little change in sagittal alignment from preoperative to postoperative in the neutral plane (see **Supplemental Digital Content** for a discussion of potential study limitations).

Long-term Safety and Effectiveness of CDA

At 10 yr, Mobi-C patients maintained statistically significant improvements in NDI, pain, and SF-12 PCS. These results suggest that the Mobi-C continues to be a clinically sound alternative to cervical fusion. The Mobi-C has previously been compared with ACDF for 1- and 2-level cervical disc disease out to 7 yr after surgery in a multicenter, prospective, randomized IDE trial. Postoperative outcomes have demonstrated statistically significant improvement in NDI, VAS arm and neck pain, and SF-12 at 24 to 84 mo in the CDA group compared with ACDF, especially after 2-level treatment.[12-16] In addition, the overall success rate was statistically higher in the 2-level CDA compared to ACDF at 84 mo.

The Mobi-C has also been studied outside of the US in a large single-armed prospective study with outcomes reported through 5 yr.[21] This study included additional indications such as treatment at up to 4 levels, patients with previous spine surgery, even at the index level, and patients with prior cervical fusions. The authors reported favorable outcomes, with no significant difference between the single level and multilevel patients.

Presently, results from 7 to 10 yr have been published on many of the CDA devices that are approved by the FDA for single-level[16,22-26] and 2-level treatment.[16,27,28] These studies consistently demonstrated superiority or noninferiority of CDA compared to ACDF, lower rates of secondary surgeries, low rates of serious AEs, and maintenance of motion.

Adjacent Segment Pathology

One of the major concerns with ACDF is the development of adjacent segment degeneration (ASD) and the resulting need for reoperation to relieve associated symptoms.[29] When motion in treated segments is eliminated through fusion, adjacent segments become hypermobile and adjacent discs experience increased loads and stresses.[6,8,10,11] In turn, these kinematic changes have the potential to initiate or accelerate pathologies in untreated adjacent segments.[30] On the other hand, CDA preserves motion and natural spinal kinematics, provides mechanical stabilization after neural decompression and discectomy, and reduces the incidence of ASP. *In vitro* studies have found that adjacent segment motion, intradiscal pressure, and facet joint loading are unchanged following CDA.[3,31]

CDA has previously been shown to have lower rates of ASD,[16,32-34] and lower rates of adjacent level subsequent surgery,[16,22,23,35-39] compared to ACDF. In this study, the Mobi-C has shown maintenance of motion out to 10 yr, and little or no progression of clinically relevant rASP after 5 yr, suggesting that most progression of rASP after CDA occurs in the first 5 yr postoperatively. In our study, clinically relevant rASP occurred in 10% of 2-level and 21% of 1-level CDA patients. We are only aware of 1 other study that has reported ASD in CDA patients out to 10 yr. Mehren et al[40] reported ASD in 35.7% of patients at 10 yr, but their study used different criteria for defining ASD than that used in our study.

ASP after CDA has been reported sporadically, and sometimes with differing definitions, but long-term studies have reported on

TABLE 6. Progression of Motion-restricting (Grade 3/4) HO in CDA Patients Through 10 yr

	Grade 3-4 HO				
Treated levels	2 yr	5 yr	7 yr	10 yr	*P* value[a]
1-level	11.3% (11/98)	30.0% (27/90)	28.7% (25/87)	30.6% (19/62)	.99
2-level	15.5% (23/148)	26.6% (37/139)	38.5% (50/130)	41.6% (45/108)	.58

[a]Comparison of 10 yr vs 7 yr. McNemar's test based on patients with data at both 7 and 10 yr.

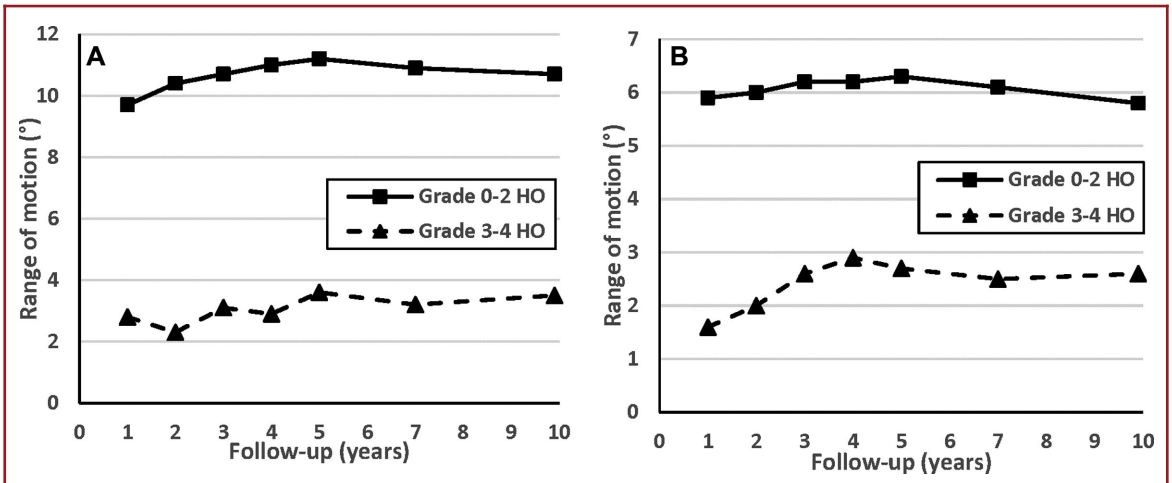

FIGURE 5. *ROM in flexion/extension (left) and lateral bending (right) in CDA patients by follow-up and HO grade. After 5 yr, ROM remained stable regardless of level of HO.*

the incidence of adjacent level subsequent surgery as a proxy for clinically symptomatic ASP. Our rate of adjacent surgery at 10 yr was 4.3% and unchanged from earlier time points. Other long-term studies of CDA reported adjacent level surgery occurring in 4.5% to 13.8% of patients, compared to rates of 16% to 24% in ACDF controls.[25,26,28,41] Long-term studies and meta-analyses estimate a cumulative incidence of adjacent level surgery ranging from 21% to 37% at 10 yr after ACDF.[7,42-45] Recent studies have addressed the need to differentiate radiographic evidence of ASP from clinically symptomatic ASP, as well as identify the factors that lead to ASP and adjacent level surgeries after CDA.[39,46,47]

HO and Effect on ROM

In this study, rates of grade 3/4 HO at 10 yr were 30.6% in 1-level patients and 41.6% in 2-level (highest grade at either level). These rates were not significantly higher than those at 7 yr. Our findings at 7 yr also reflect those reported earlier for grades 3/4 (1-level: 28.7%; 2-levels: 37.4%) with the Mobi-C device.[48] Similarly, Gornet et al[26,28] reported grade 3/4 HO of 28.6% and 39% in 1- and 2-level patients at 10 yr, while Mehren et al[40] reported grade 3/4 HO rates of 58% at 10 yr. Several studies have reported complete HO (grade 4) or solid fusion in approximately 11% of CDA patients at 7 yr.[22,26,28,48] Grade 4 HO in our study at 10 yr was 12.9% and 12.0% in 1- and 2-level patients, respectively. Similarly, Gornet et al[26,28] reported 9% and 13% incidence of grade 4 HO at 10 yr, while Mehren et al[40] reported a rate of 26% at 10 yr. Although significant HO can restrict segmental ROM,[40,48] we show that those patients with grade 3/4 HO and reduced ROM still retain some motion at 10 yr. Although HO can negate the motion-preserving advantage of CDA, it does not appear to negatively affect patient-reported outcomes.[48-50] In those cases, complete loss of motion after CDA would be considered equivalent to a successful ACDF surgery.

CONCLUSION

Our results through 10 yr demonstrate that CDA with Mobi-C (Zimmer Biomet) continues to be a safe and effective surgical treatment for patients with 1- or 2-level cervical DDD. This study provides additional evidence of the long-term durability of CDA out to at least 10 yr.

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Disclosures

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Supplemental Digital Content. Device description, study limitations. The Supplemental Digital Content provides a detailed description of the Mobi-C (Zimmer Biomet) cervical disc and a discussion of potential study limitations.