TWO-LEVEL TOTAL DISC REPLACEMENT WITH MOBI-C® OVER 3-YEARS

ARTROPLASTIA TOTAL DE DISCO COM MOBI-C® DEPOIS DE TRÊS ANOS

ARTROPLASTÍA TOTAL DE DISCO CON MOBI-C® DESPUÉS DE TRES AÑOS

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ABSTRACT

Objective: To evaluate the safety and effectiveness of two-level total disc replacement (TDR) using a Mobi-C® Cervical Artificial Disc at the 36 month follow-up. Methods: a Prospective, randomized, controlled, multicenter clinical trial of an artificial cervical disc (Mobi-C® Cervical Artificial Disc) was conducted under the Investigational Device Exemptions (IDE) and the U.S. Food & Drug Administration (FDA) regulations. A total of 339 patients with degenerative disc disease were enrolled to receive either two-level treatment with TDR, or a two-level anterior cervical discectomy and fusion (ACDF) as control. The 234 TDR patients and 105 ACDF patients were followed up at regular time points for three years after surgery. Results: At 36 months, both groups demonstrated an improvement in clinical outcome measures and a comparable safety profile. NDI scores, SF-12 PCS scores, patient satisfaction, and overall success indicated greater statistically significant improvement from baseline for the TDR group, in comparison to the ACDF group. The TDR patients experienced lower subsequent surgery rates and a lower rate of adjacent segment degeneration. On average, the TDR patients maintained segmental range of motion through 36 months with no device failure. Conclusion: Results at three-years support TDR as a safe, effective and statistically superior alternative to ACDF for the treatment of degenerative disc disease at two contiguous cervical levels.

Keywords: Arthroplasty; Discectomy; Intervertebral disc degeneration; Cervical vertebrae; Spinal fusion.

RESUMO

Objetivo: Avaliar a segurança e a eficácia da artroplastia total de disco (ATD) em dois níveis, usando o disco cervical artificial Mobi-C® aos 36 meses de acompanhamento. Métodos: Realizou-se estudo clínico prospectivo, randomizado, controlado e multicêntrico de disco cervical artificial (Mobi-C®) regido pelas regulamentações de Investigational Device Exemptions (IDE, isenção do dispositivo em investigação) e da Food & Drug Administration (FDA) dos Estados Unidos. Um total de 339 pacientes com doença degenerativa de disco foi inscrito para receber tratamento com ATD em dois níveis ou discectomia cervical anterior e fusão em dois níveis (DCAF) que constituíram o grupo controle. Os 234 pacientes tratados com ATD e os 105 tratados com DCAF tiveram acompanhamento em pontos do tempo regulares durante três anos após a cirurgia. Resultados: Aos 36 meses, ambos os grupos apresentaram melhora das medidas de desfecho clínico e perfil de segurança comparável. Os escores NDI, SF-12 e PCS, a satisfação dos pacientes e o êxito geral indicaram melhora com maior significância estatística desde o início do estudo no grupo ATD, em comparação com o grupo DCAF. Os pacientes do grupo ATD tiveram percentuais menores de cirurgia subsequente e taxas inferiores de degeneração do segmento adjacente. Em média, os pacientes do grupo ATD mantiveram a amplitude de movimento segmentar nos 36 meses, sem falhas do dispositivo. Conclusão: Os resultados aos três anos corroboram que a ATD é uma alternativa segura, eficaz e estatisticamente superior à DCAF no tratamento de doenças degenerativas de disco em dois níveis cervicais contíguos.

Descritores: Artroplastia; Discotomia; Degeneração do disco intervertebral; Vértebras cervicais; Fusão vertebral.

RESUMEN

Objetivo: Evaluar la seguridad y la eficacia de la artroplastía total de disco (ATD) en dos niveles, usando el disco cervical artificial Mobi-C® a los 36 meses de acompañamiento. Métodos: Se realizó estudio clínico prospectivo, aleatorio, controlado y multicéntrico de disco cervical artificial (Mobi-C®) regido por las reglamentaciones de Investigational Device Exemptions (IDE, exención del dispositivo en investigación) y de la Food & Drug Administration (FDA) de los Estados Unidos. Un total de 339 pacientes con enfermedad degenerativa de disco fue inscripto para recibir tratamiento con ATD en dos niveles o discectomía cervical anterior y fusión en dos niveles (DCAF) que constituyeron el grupo control. Los 234 pacientes tratados con ATD y los 105 tratados con DCAF tuvieron acompañamiento en puntos de tiempo regulares durante tres años después de la cirugía. Resultados: A los 36 meses, ambos grupos presentaron mejora de las medidas de resultado clínico y perfil de seguridad comparable. Los registros NDI, SF-12 y PCS, la satisfacción de los pacientes y el éxito general indicaron mejora con mayor significado estadístico desde el inicio del estudio en el grupo ATD, en comparación con el grupo DCAF. Los pacientes del grupo ATD tuvieron porcentuales menores de cirugía subsiguiente y tasas inferiores de degeneración del segmento adyacente. Como promedio, los pacientes del grupo ATD mantuvieron la amplitud de movimiento segmentar en los 36 meses, sin fallas del dispositivo. Conclusión: Los resultados a los tres años corroboran que la ATD es una alternativa segura, eficaz y estadísticamente superior a DCAF en el tratamiento de enfermedades degenerativas de disco en dos niveles cervicales contiguos.

Descriptores: Artroplastia; Discectomía; Degeneración del disco intervertebral; Vértebras cervicales; Fusión vertebral.

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INTRODUCTION

In cases of symptomatic radiculopathy and myelopathy caused by degenerative disc disease, anterior cervical discectomy and fusion (ACDF) surgery is a standard treatment.[1-5] However, ACDF has demonstrated prompting of hypermobility and heightened intradiscal pressures at adjacent levels due to the elimination of natural motion at treated segments.[6-9] In ACDF patients, the altered stress and motion profiles are considered a primary cause for adjacent segment degeneration.[10-12] Total disc replacement (TDR) maintains natural motion of treated segments and overall cervical spine biomechanics, thus TDR may avoid heightened adjacent segment degeneration and its symptoms while still providing necessary mechanical stability after neural decompression.[13,14] In comparing TDR and ACDF treatment at two contiguous levels, clinical data is minimally available. This prospectively controlled clinical study presents the largest known cohort of randomized patients treated at two contiguous levels with TDR in comparison to ACDF.

The Mobi-C® Cervical Artificial Disc (LDR Medical; Troyes, France) is a semi-constrained, mobile bearing, bone sparing TDR evaluated in a prospective, randomized, controlled FDA investigational device exemptions (IDE) trial. (Figure 1) Previous two-year follow-up results[15] have demonstrated specific clinical advantages of TDR as a safe and effective alternative to ACDF for indicated patients. Two-year results have also shown statistically improved pain and functional outcomes for two-level TDR.[15] These clinical advantages are also supported by extensive Outside the United States (OUS) experience with TDR.[16] Here, we test the hypothesis that the enhanced clinical outcomes for two-level TDR at two years will be sustained through three years. Clinical Trial Registration no: NCT00389597 (ClinicalTrials.gov).

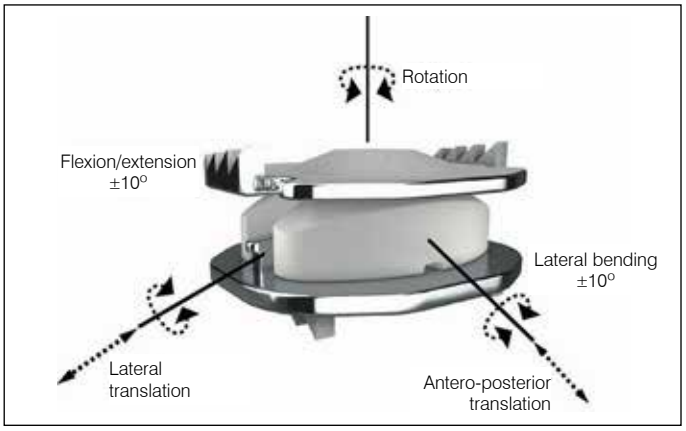

Figure 1. Mobi-C® Cervical Artificial Disc with two Cobalt Chrome Molybdenum alloy endplates and an Ultra High Molecular Weight Polyethylene mobile insert facilitating five independent degrees of freedom.

MATERIALS AND METHODS

Subjects and Study Design

A complete description of the study design and surgical technique was previously reported.[15] As part of the FDA IDE randomized and controlled clinical trial, patient surgeries occurred between April 2006 and March 2008 at 24 clinical sites in the U.S. Requirements for the study included a diagnosis of DDD with radiculopathy or myeloradiculopathy at two contiguous levels from C3 to C7 that was unresponsive to non-operative treatment for at least six weeks or demonstrated progressive symptoms calling for immediate surgery. (Table 1) Prior cervical spine surgery was an exclusion criterion. (Table 2) Patients gave informed consent and were randomized in a 2:1 ratio (TDR: ACDF); 225 patients received treatment with a Mobi-C® Cervical Artificial Disc and 105 patients received corticocancellous allograft and an anterior cervical plate using the standard ACDF technique. The Primary Analysis Population includes the TDR and ACDF randomized population for a total

Table 1. Study inclusion criteria.

• Age 1869 years.
• Symptomatic cervical degenerative disc disease in two contiguous levels between C3-C7 with:
- Neck and/or arm pain and/or
- Decreased muscle strength and/or
- Abnormal sensation and/or abnormal reflexes.
• Deficit confirmed by imaging (CT, MRI, or X-ray).
• NDI Score of ≥ 30
• Unresponsive to non-operative, conservative treatment for at least 6 weeks or presence of progressive symptoms or signs of nerve root/spinal cord compression despite continued non-operative 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 with the protocol.
• Signed informed consent.
• Willingness to discontinue all use of nonsteroidal antiinflammatory drugs (NSAIDs) from one week before surgery until 3 months after surgery.

Table 2. Study exclusion criteria.

• More than one vertebral level requiring treatment/immobile level between C1 and C7 from any cause.
• Any prior spine surgery at operative level of any prior cervical fusion at any level.
• Disc height less than 3 mm.
• Tscore less than 1.5 (osteoporosis evaluation).
• Paget's disease, osteomalacia, or any other metabolic bone disease other than osteoporosis.
• Active systemic infection of surgical site or history of or anticipated treatment for systemic infection including HIV/Hepatitis C.
• Active malignancy: a history of any invasive malignancy (except nonmelanoma skin cancer), unless treated with curative intent and there had been no clinical signs or symptoms of the malignancy > 5 years.
• Marked cervical instability on resting lateral or flexionextension radiographs.
• Known allergy to cobalt, chromium, molybdenum, or polyethylene.
• Segmental angulation of greater than 11° at treatment or adjacent levels.
• Rheumatoid arthritis, lupus, or other autoimmune disease.
• Any diseases or conditions that would preclude accurate clinical evaluation.
• Daily, highdose oral and/or inhaled steroids or a history of chronic use of high dose steroids.
• BMI > 40.
• Use of any other investigational drug or medical device within 30 days prior to surgery.
• Pending personal litigation relating to spinal injury (worker's compensation not included).
• Smoking more than one pack of cigarettes per day.
• Reported to have mental illness or belonged to a vulnerable population.

of 330 patients. In addition, 9 patients were used for training cases and treated with the TDR device. The Safety Population includes the 330 randomized patients and 9 TDR training patients for a total of 339 patients. While surgeons could not be blind to the treatment, patients were blinded until after surgery.

The treating surgeon possessed discretion over post-operative care and each patient went through a rehabilitation program intended to help the patient return to normal activity as soon as possible. Patients were evaluated pre-operatively and at 6 weeks, 3 months, 6 months, 12 months, 18 months, 24 months, and 36 months post-operatively. From one week before surgery to 3 months post-surgery, groups were asked to refrain from taking non-steroidal anti-inflammatory drugs (NSAIDs) with the exception of TDR patients diagnosed with heterotopic ossification (HO) after surgery.

Clinical Outcomes

Measures used to evaluate pain, function, patient satisfaction, and overall clinical success outcomes included: neck disability index (NDI), visual analogue scale (VAS) neck and arm pain, SF-12 Mental Component Score (MCS) and SF-12 Physical Component Score (PCS), subsequent surgical intervention, complications, neurologic function, return to work, radiographic success, patient satisfaction, range of motion (ROM), HO, and adjacent segment degeneration. All radiographic evaluations were conducted by independent radiologists and validated software through Medical Metrics, Inc. (MMI, Houston, TX).[17] Adjacent segment degeneration was evaluated on the Kellgren-Lawrence scale of disc degeneration.[18,19] All adverse effects (AEs) were measured and classified by the clinical events committee (CEC), composed of a neurosurgeon and two orthopedic surgeons. AEs were defined as any clinically adverse sign, symptom, syndrome, or illness that occurred or worsened during or after the initial surgery, regardless of cause.

Neurologic function was evaluated by the investigator through: reflex assessments at the treated levels, motor assessments, pin prick and light touch sensory function assessments. Neurologic success was defined as the absence of significant neurologic deterioration.

Patient satisfaction was determined by a questionnaire asking patients if they were very satisfied, somewhat satisfied, somewhat dissatisfied, or very dissatisfied with their treatment. In addition, patients were asked if they would definitely, probably, probably not or definitely not recommend the same treatment to a friend with the same symptoms and indications.

Subsequent surgical intervention was considered to be any secondary surgery of removal, revision, supplemental fixation or reoperation at an index level segment. Adjacent level subsequent surgeries not involving a treated level were recorded for further investigation but did not indicate a study failure. Radiographic success for the ACDF group was characterized as fusion of both treated levels; less than 2° of angular motion in flexion/extension and indication of bridging bone across the disc space and radiolucent lines at no more than 50% of the graft vertebral interfaces. Radiographic success for the TDR group was characterized as at least 2° angular motion in flexion/extension or no indication of bridging trabecular bone across the disc space. ROM was evaluated by lateral flexion/extension and AP right/left lateral bending radiographs at treated levels.

A composite endpoint was established with multiple conditions including: 1) ≥30 point improvement for patients with baseline NDI ≥ 60 or 50% improvement for patients with baseline NDI <60; 2) no subsequent surgical intervention at either treated level; 3) AEs assessed by the CEC as major complications; 4) maintenance or improvement in neurologic function; 5) radiographic success. These outcome metrics determined overall success rates for both treatments. For this study, patient failure was considered as not meeting one or more of these five outcome metrics. The overall success component has been previously specified in greater detail.[15]

Statistical Methods

A non-inferiority hypothesis was presented in this study to compare the overall success rates of the investigational and control procedures. An exact 95% one-sided confidence bound was used to determine non-inferiority. A post-hoc test assessed superiority in the event of non-inferiority. A 97.5% one-sided confidence bound was used to determine superiority if a 10% non-inferiority margin could be excluded.

Two-sided t-tests were used to assess statistical significance between groups for each continuous outcome measure at each time points. Fisher's exact tests were used to assess success or incident rates. Wilcoxon signed-rank tests were used to evaluate changes from baseline within treatment groups. Statistical significance was determined by a p-value less than 0.05.

RESULTS

Patient Accountability and Baseline Demographics

Three hundred thirty patients were enrolled and randomly assigned to either the TDR or ACDF group.Two hundred twenty five TDR patients and 105 ACDF patients underwent surgery. In addition, 9 patients underwent TDR surgeries as training cases; these patients received a TDR procedure but are not included in the randomized population. Only the randomized population comparisons are presented in the results. There were no significant statistical or clinical differences between baseline demographics of each group. (Table 3) The 36 month follow-up rate was 89.1% for the TDR group and 79.5% for the ACDF group.

Table 3. Patient demographics at baseline.

	Patient Group		
Variable	**TDR**	**ACDF**	**p-value***
Age (years)			0.5657
N	164	81	
Mean (SD)	43.3 (9.2)	44.0 (8.2)	
Gender n (%)			0.6843
Male	78 (47.6%)	36 (44.4%)	
Female	86 (52.4%)	45 (55.6%)	
Ethnicity n (%)			0.6667
Hispanic or Latino	3 (1.8%)	2 (2.5%)	
Not Hispanic or Latino	161 (98.2%)	79 (97.5%)	
Race** n (%)			0.0710
American Indian	2 (1.2%)	1 (1.2%)	
Caucasian	152 (92.7%)	69 (85.2%)	
Asian	3 (1.8%)	1 (1.2%)	
Black or African American	4 (2.4%)	10 (12.3%)	
Native Hawaiian/Other Pacific Islander	1 (0.6%)	0	
Other	2 (1.2%)	0	
BMI			0.8460
N	164	81	
Mean (SD)	27.3 (4.4)	27.4 (4.2)	
Work Status *** n (%)			0.3264
Being able to work	108 (65.9%)	46 (56.8%)	
Not being able to work	37 (22.6%)	22 (27.2%)	
N/A	19 (11.6%)	13 (16.0%)	
Worker's Compensation *** n (%)			0.1586
Receiving	11 (4.9%)	7 (6.7%)	
Not Receiving	214 (95.1%)	98 (93.3%)	
Driving Status *** n (%)			
Being able to drive	155 (94.5%)	79 (97.5%)	0.5035
Not being able to drive	8 (4.9%)	2 (2.5%)	
N/A	1 (0.6%)	0	
Smoking Status *** n (%)			
Less than 1 pack per day	225 (100%)	105 (100%)	>0.9999
More than 1 pack per day	0 (0%)	0 (0%)	

*Using unpaired t-test to compare age and BMI across treatment groups. Using Fisher Exact test to compare gender, ethnicity, race, work status, and driving status. ** Subjects with multiple races are included with the Non-Caucasian subjects. Fisher Exact p-value calculation is based on Caucasian vs. Non-Caucasian subjects. *** Fisher Exact p-value is based on 'Being able to' vs. ' Not being able to'.

NDI

Mean NDI scores were similar at baseline and both TDR and ACDF groups showed significant NDI improvement through 36 months ($p<0.0001$). In comparison to the ACDF group, the TDR group showed significantly greater NDI score improvement at each time point through 36 months. (Figure 2) The mean improvement in NDI score was 37.2 ± 20.7 for the TDR group and 26.9 ± 18.1 for the ACDF group at 36 months ($p = 0.0002$). NDI success rate was also significantly higher for TDR in comparison to ACDF at each time point ($p<0.05$). At 36 months, the TDR success rate was 80.2% while the ACDF success rate was 56.6% ($p<0.0001$).

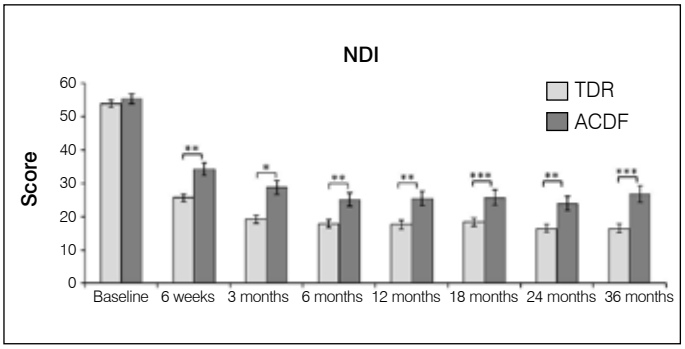

Figure 2. Mean NDI scores at baseline and follow-up time points through 36 months. At all post-operative time points, Mean NDI improvement was significantly greater for the TDR group in comparison to the ACDF group. An unpaired, two-sided t-test was used to determine NDI improvement from baseline between treatments. Asterisks denote statistical significances (*$p<0.05$, **$p<0.01$, ***$p<0.0001$) and error bars represent standard error of the mean.

VAS Neck and Arm Pain

VAS neck and arm pain scores were similar for TDR and ACDF groups at baseline and both groups showed significant improvement in both measures through 36 months ($p<0.0001$). At each post-operative time point, the TDR group had lower VAS neck pain scores. (Figure 3A) Notable statistical significant differences were demonstrated by the TDR group at 3 and 6 month time points. The mean improvement in VAS neck pain score from baseline at 36 months was 54.1 ± 28.9 for the TDR group and 46.5 ± 28.0 for the ACDF group. Mean VAS arm pain scores (Figure 3B) originate from the most symptomatic arm at baseline and continue through the 36 month time point. The mean improvement from baseline in VAS arm pain score was similar between groups with 57.0 ± 32.1 for TDR patients and 54.7 ± 29.7 for ACDF patients.

SF-12 MCS and PCS

Both the TDR and ACDF groups had similar and significant SF-12 MCS improvement from baseline through the 36 month follow-up period ($p<0.0001$). At 36 months, the mean SF-12 MCS score improvement from baseline was 9.3 ± 13.4 for the TDR group and 6.7 ± 14.0 for the ACDF group. (Figure 4A) Also, significant improvements in SF-12 PCS scores were shown in both groups through 36 months ($p<0.0001$) At each time point through the 36 month follow-up, the TDR group showed significantly greater improvement from baseline in SF-12 PCS scores in comparison to the ACDF group. (Figure 4B) At 36 months, the mean improvement from baseline SF-12 PCS scores was 14.1 ± 11.2 for the TDR group and 9.6 ± 12.0 for the ACDF group ($p<0.05$).

Neurologic Success

When evaluating neurologic deterioration, TDR and ACDF groups showed similar scores at baseline and there was no statistical significance at 36 months. At the 36 month follow-up point, 7.1% of TDR and 6.7% of ACDF patients experienced neurologic deterioration.

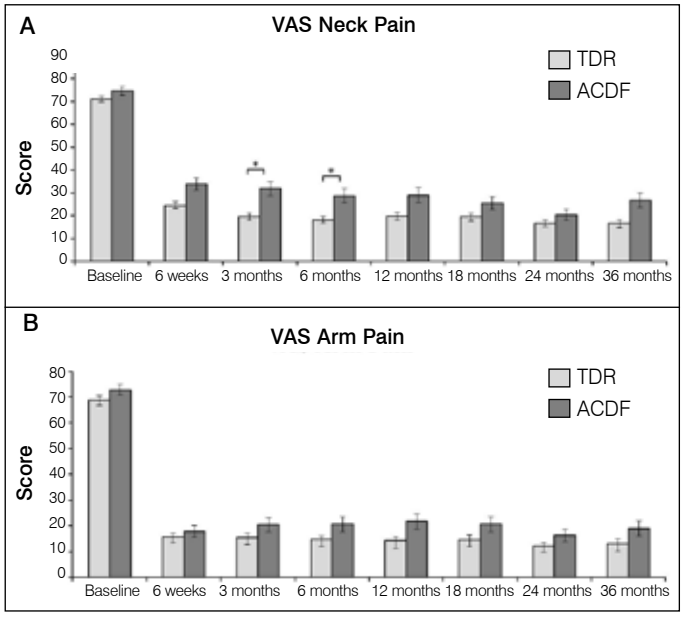

Figure 3. Mean VAS neck pain scores (A) and arm pain scores (B) at baseline and follow-up time points through 36 months. An unpaired, two-sided t-test was used to determine VAS neck pain improvement from baseline between treatments. Asterisks denote statistical significances (*$p<0.05$) and error bars represent standard error of the mean.

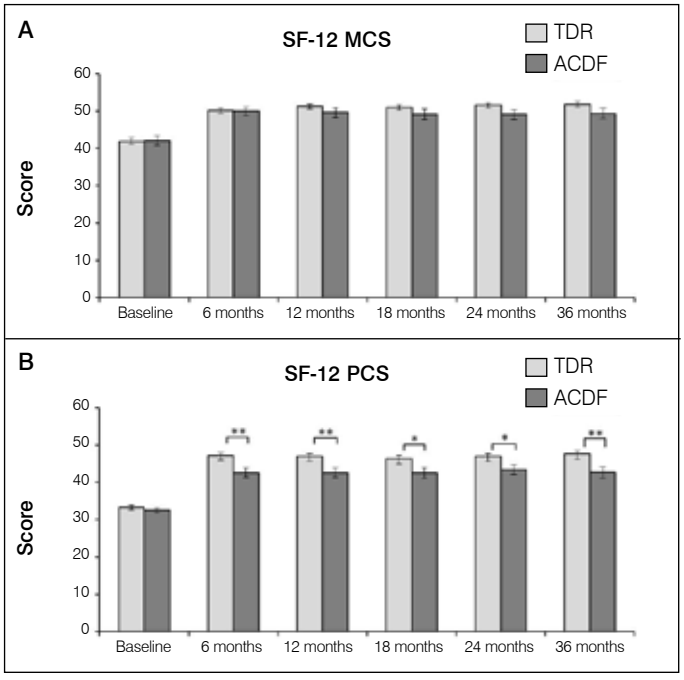

Figure 4. Mean SF-12 MCS scores (A) and PCS scores (B) at baseline through 36 months. The TDR group showed on average a significantly greater improvement in SF-12 PCS scores. An unpaired, two-sided t-test was used to determine SF-12 PCS score improvement from baseline between treatments. Asterisks denote statistical significances (*$p<0.05$, **$p<0.01$) and error bars represent standard error of the mean.

Return to work

For working patients (TDR = 139, ACDF = 60), time to return to work was calculated as the time from the date of surgery until the date the patient started working again. Average return to work time was 46 ± 101 days for TDR patients and 67 ± 113 days for ACDF patients. While this difference is not statistically significant, on average TDR patients return to work 21 days earlier.

Patient Satisfaction

The percentage of patients "very satisfied" or "somewhat satisfied" with their treatment was 94.4% of TDR patients and 93.3% of ACDF patients at 36 months (NS). At 36 months a statistically greater number of TDR patients (96.9%) compared to ACDF patients (88.0%) said they would "definitely recommend" or "probably recommend" the same treatment to a friend ($p < 0.05$).

Major Complications

AE's were major complications in 4.0% of TDR patients and 6.7% of ACDF patients at 36 months, as deemed by the CEC. No statistical significance was found for the difference between groups.

Subsequent Surgical Intervention

Post-operatively, symptomatic pseudarthrosis was the most common reason for subsequent surgery in the ACDF group as was seen in 8.6% of ACDF patients. TDR removal resulted from stenosis, device migration, poor endplate fixation, and persistent neck and/or shoulder pain. The cumulative rate of patients with subsequent surgeries at the index level was statistically lower in the TDR group at the 36 month follow-up point ($p<0.0001$). The subsequent surgery rate was 3.1% for the TDR group (7 patients, 9 surgeries) and 13.3% for the ACDF group (14 patients, 15 surgeries).

Radiographic Outcomes

ROM remained near baseline in flexion/extension (Figure 5A) and lateral bending (Figure 5B) at both segments for the TDR group. The mean ROM at the superior level was 10.1 ± 6.1° in flexion/extension (baseline: 9.1 ± 4.9°) and 5.3 ± 3.5° in lateral bending (baseline: 5.8 ± 3.4°) at 36 months for TDR patients. Also, the mean ROM at the inferior level was 8.2 ± 5.0° in flexion/extension (baseline: 7.4 ± 4.3°) and 5.5 ± 3.6° in right/left lateral bending (baseline: 4.9 ± 3.3) at 36 months for TDR patients.

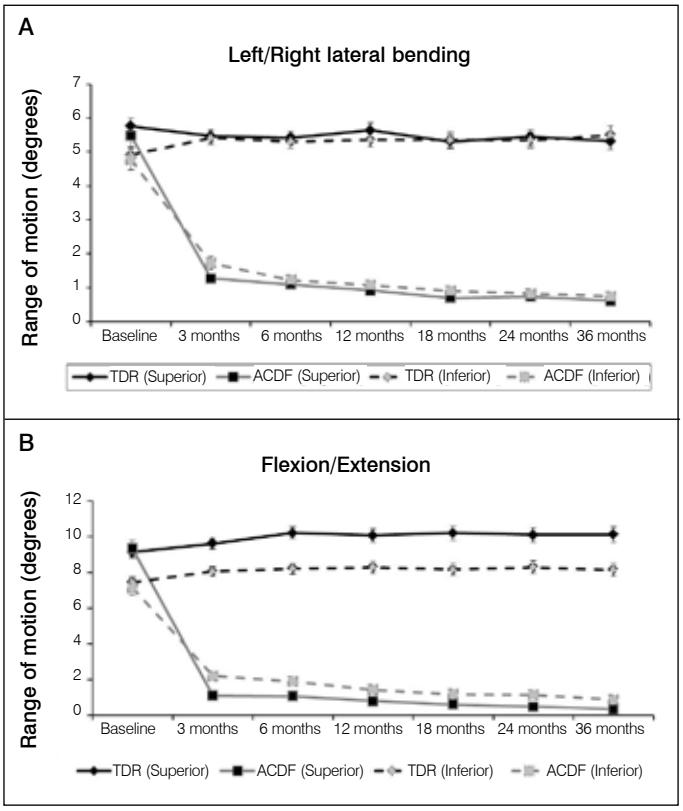

Figure 5. ROM in both flexion/extension (A) and left/right lateral bending (B) through 36 months. Overall, while the ACDF group had large reductions in both flexion/extension and left/right lateral bending, the TDR group maintained baseline ROM in both measures. Error bars represent standard error of the mean.

At the 36 month time point, 12 TDR patients and 11 of ACDF patients failed the criteria for radiographic success. Clinically relevant HO (grades III and IV) was observed in 23.1% of TDR patients with radiographs available at the 36 month time point, with 8.7% of patients with the presence of grade IV HO at either level. TDR patients experienced clinically relevant HO in 15.4% of superior segments and 15.4% of inferior segments, totaling 15.4% (60/390) of treated levels.

In the ACDF cohort, 13.1% of patients with available radiographs failed to achieve fusion status at 36 months. ACDF patients experienced failed fusion in 9.5% of inferior levels and 3.6% of superior levels, totaling 6.5% of treated levels This does not include patients that had corrective surgery for failed fusion at earlier time points.

Adjacent segment degeneration was defined by the Kellgren-Lawrence grading scale as an increase of one or more points compared to the baseline values at either segment. No grade of degeneration or combination of grades led to statistically significant differences in adjacent segment degeneration between groups at baseline. The superior levels indicated a significant difference between 59.2% of ACDF and 26.7% of TDR patients showing degeneration at 36 months ($p < 0.0001$). Inferior level results were similar at 46.8% of ACDF and 15.2% of TDR patients showing degeneration ($p < 0.0001$).

One case of posterior migration was previously reported; no cases of migration or subsidence have been reported since the 24 month results.

Overall Success

Overall success incorporates the success rates of five individual components at this composite endpoint. Based on this predefined criteria, at the 36 month composite endpoint (Figure 6) 66.8% of the TDR group and 41.4% of the ACDF group achieved overall success ($p<0.0001$). TDR demonstrated better outcomes for all five individual components, however only NDI success and secondary surgery assessments showed statistically significant results. In the ACDF group, 43.4% of patients had failing NDI improvement in comparison to only 19.8% of TDR patients; NDI was the leading cause of ACDF group failure.

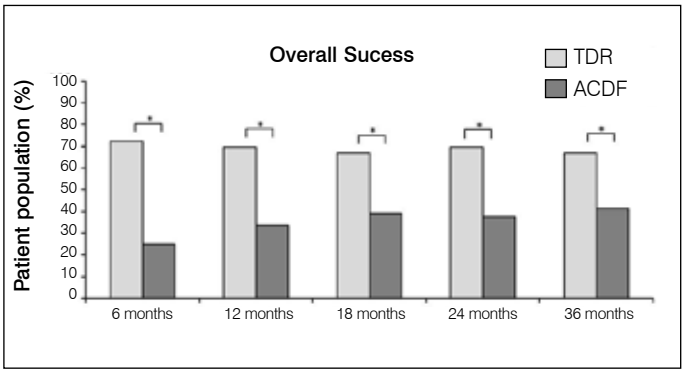

Figure 6. Overall success for the TDR and ACDF groups through 36 months. At each time point, success rates for the TDR group were significantly higher than the ACDF group. Overall success rate between treatments was determined by a Fisher exact test. Asterisks denote statistical significance (*$p<0.0001$).

DISCUSSION

Here, we analyzed two-level TDR using two Mobi-C® Cervical Artificial Discs for safety and efficacy comparisons to ACDF, the standard surgical treatment for degenerative disc disease. Three-year results are part of an ongoing randomized, controlled, clinical trial. Results presented were from the FDA, IDE trial and included the first level one evidence[20] of two-level TDR through 36 months. Regarding the predefined overall success rate, TDR treatment is statistically superior to that of ACDF. While both ACDF and TDR patients experienced significant improvement from baseline, at 36 months

TDR demonstrated statistically better outcomes in NDI scores, SF-12 PCS scores, patient satisfaction, subsequent surgery rates, adjacent segment degeneration, and overall success.

The hypothesis that the previously reported two-year TDR results will continue through three years was confirmed through this two--level study. Statistical significance in NDI scores, SF-12 PCS scores, patient satisfaction, subsequent surgery rates, adjacent segment degeneration, and overall success was maintained from the 24 to 36 month follow-up points. Also, the two-level TDR results agree with those of one-level TDR IDE study results.[21,22] In a 48 month study, Garrido et al.[21] reported similar or better outcomes for their single level TDR group with respect to NDI, neck pain, arm pain, and secondary surgery rates of the BRYAN Cervical Disc (Medtronic Sofamor Danek, Memphis, TN).

The composite overall success of TDR (66.8%) was statistically superior to ACDF (41.4%) at 36 months ($p<0.0001$). The overall success is mainly due to the statistical significance of NDI success and subsequent surgery components in favor of TDR. The statistically significant differences in NDI success between groups remained from 24 months to 36 months ($p<0.0001$). While the number of TDR patients requiring subsequent surgeries was maintained at 3.1%, the number of ACDF patients requiring subsequent surgeries increased from 11.4% at 24 months to 13.3% at 36 months.

HO is a primary concern for TDR. In the current study, we observed clinically relevant HO (grades III and IV) in 15.4% of segments and 23.1% of patients treated with TDR, which is similar to or less than other reports.[23-25] HO was present in 14.4% of patients and 10.5% of segments as grade III and 8.7% of patients and 4.9% of segments as grade IV. A European study analyzing HO rates in Prodisc-C (Synthes Spine Company, L.P., West Chester, PA) patients at 4 years reported an overall 63% incidence of clinically relevant grade III (45%) and grade IV (18%) HO.[24] Another study analyzing 21 BRYAN Cervical Disc patients at an 8 year follow-up reported an overall 76.2% incidence of grade III (42.9%) and IV (33.3%) HO.[23] The 5-year results of ProDisc-C in the U.S. showed 6 of the 103 patients with grade IV HO present at the index level, however grade III HO was not reported leaving analysis of clinically relevant HO inconclusive in this study.[25] One major difference between the current study and the others mentioned is the use of nonsteroidal anti-inflammatory drugs (NSAIDs). The use of nonsteroidal anti-inflammatory drugs (NSAIDs) has been correlated with a decrease in HO formation. In this study, patients were asked to refrain from NSAID usage before and after surgery. Therefore, since other device trials did not restrict NSAID usage, this difference should be noted in comparisons of the current study and others mentioned. The limited HO rate data available after four or more years also leads to difficult comparisons between TDR devices. Despite these data limitations, concern remains regarding HO in TDR procedures; long-term investigations are needed to analyze the clinical instances and effects of HO.

Another major concern in degenerative disc disease surgery is the possibility of adjacent segment degeneration. Mechanisms leading to the high rates of adjacent segment deterioration in ACDF patients are not clear. While TDR may not eradicate adjacent segment degeneration, radiographic degeneration is reduced with TDR devices. It has been suggested that the preserved biomechanics at the index and adjacent levels maintain the adjacent segments in TDR. However, continued long-term follow-up of TDR patients should further define the mechanism by which radiographic degeneration is correlated to TDR.

Due to recent approval, there is no two-level TDR and ACDF direct comparison data available for treatment of DDD. However, long term data is available for one-level TDR and has proven that this treatment is at least as effective as one-level ACDF in relieving neurologic pain and motor impairment caused by DDD.[26,22] Data up to five years post-surgery show TDR providing safe and effective surgical outcomes.[25] In a recent study, TDR is demonstrated superior to ACDF for one-level treatment.[27] Evidence continues to indicate that at multiple levels, ACDF efficacy decreases and treatment may cause higher stress and hypermobility at adjacent segments.[28,29] It is possible that these observed ACDF effects are primary contributing factors for the increase in rate of adjacent segment degeneration in treated patients. The excess motion and stress at adjacent levels in ACDF patients are avoided in two-level TDR which preserves cervical mobility at treated levels.[15]

CONCLUSIONS

This IDE study through 36 months provides data to demonstrate clinically relevant benefits of TDR over ACDF. Improved clinical outcomes of TDR include pain and function outcomes and superiority in overall primary endpoint success. Occurrences of adjacent segment degeneration and subsequent surgeries were also reduced with TDR. Authors expect both future studies and long-term follow-up of this patient cohort to further establish the superiority of two-level TDR as a surgical option for symptomatic degenerative disc disease.

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