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# Cervical Arthroplasty: Long-Term Outcomes of FDA IDE Trials

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## Abstract

**Study Design:** Special Issues MIS/Navigation.

**Objectives:** Over the past decade, cervical total disc replacement has been established in numerous randomized clinical trials as an alternative to anterior cervical discectomy and fusion. The purpose of this review is to evaluate the long-term outcomes after cervical arthroplasty.

**Methods/Results:** Early outcomes (studies with 2-year follow-up) after arthroplasty established the efficacy of total disc replacement and, more recently, long-term studies have shown the durability of these good clinical outcomes. Biomechanical and clinical data have demonstrated that this motion preservation technology decreases adjacent-level stresses compared with fusion. Additionally, long-term outcomes as well as outcomes after multilevel arthroplasty have now established the role of arthroplasty in select patient populations, namely patients with 1- and 2-level spondylosis/stenosis causing radiculopathy from C3-7.

**Conclusions:** Data on adjacent segment deterioration and adjacent segment reoperation remains controversial but suggest a positive effect after arthroplasty. But these are multifactorial issues and we still do not fully understand all the factors affecting adjacent segment pathology and longer-term studies after arthroplasty will continue to address this issue.



## Keywords

cervical, disc replacement, anterior cervical discectomy and fusion (ACDF), radiculopathy


## Introduction

Over the past decade, cervical total disc replacement (TDR) has been established in numerous randomized clinical trials as an alternative to anterior cervical discectomy and fusion (ACDF).[1-7] Early outcomes (studies with 2-year follow-up) after arthroplasty established the efficacy of TDR and, more recently, long-term studies have shown the durability of these good clinical outcomes. Biomechanical and clinical data have demonstrated that this motion preservation technology decreases adjacent-level stresses compared with fusion.[8-10] Additionally, long term outcomes as well as outcomes after multilevel arthroplasty have now established the role of arthroplasty in select patient populations, namely patients with 1- and 2-level spondylosis/stenosis causing radiculopathy from C3-7. Data on adjacent segment deterioration (ASD) and adjacent segment reoperation (ASR) remain controversial but suggest a positive effect after arthroplasty. But these are multifactorial issues and we still do not fully understand all the factors affecting adjacent segment pathology and longer-term studies after arthroplasty will continue to address this issue. We will review the early Food and Drug Administration (FDA) investigational device exemption (IDE), prospective, randomized controlled studies that established cervical arthroplasty as an effective procedure as well as review the long-term outcomes of these studies and systematic reviews/meta-analysis that included these studies.

## Early Outcomes and Adjacent Segment Degeneration

The prospective, randomized and controlled US FDA IDE trials that have led to 8 US FDA–approved cervical artificial discs (CADs) were designed as non-inferiority studies

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comparing arthroplasty to ACDF. These trials have established cervical arthroplasty as a clinically efficacious alternative to fusion for 1- and 2-level cervical radiculopathy. Although statistically designed as noninferiority trials, virtually all the studies demonstrated some element of statistical superiority favoring arthroplasty on individual study parameters. Mummaneni and colleagues[1] published 2-year outcomes for Prestige ST Cervical Disc System (Medtronic Sofamor Danek, Memphis, TN). A total of 276 patients underwent arthroplasty and 265 patients underwent ACDF and were followed for 24 months. Overall composite success rate, as defined in the study as Neck Disability Index (NDI) score improvement >15 points and maintenance or improvement in neurological status, was achieved in 79.3% of arthroplasty patients versus 67.8% of control ACDF ($P = .0053$). Also, the overall reoperation rate was significantly lower in the arthroplasty group (1.1% vs 3.4%, $P = .0492$). Heller reported on 2-year outcomes for BRYAN cervical disc (Medtronic, Sofamor Danek, Memphis, TN) versus ACDF in 463 patients.[2] Similar improvements were seen in arm pain scores in both groups, but the NDI showed statistically greater score improvements in the arthroplasty group at 24 months ($P = .025$). Overall success rates, as defined in the study as primary effectiveness and safety measures, were achieved in 82.6% of artificial disc patients and only 72.7% of ACDF patients ($P = .010$), again statistically significantly superior favoring arthroplasty. Secondary surgery rates at index level were lower in the arthroplasty group but did not reach statistical significance (2.5% vs 3.6%). Murrey *et al*[3] compared the ProDisc-C (Centinel Spine, West Chester, PA) with ACDF and reported statistically significantly fewer secondary surgeries for arthroplasty (1.8%) versus fusion (8.5%). Phillips et al[7] reported the IDE results of the Porous Coated Motion (PCM) cervical disc (NuVasive Inc, San Diego, CA) which demonstrated an overall success rate statistically significantly superior for cTDR group (75%) compared with the ACDF group (65%; $P = .02$) as well as statistically significant lower NDI scores and higher patient satisfaction. Vaccaro et al[5] also reported an overall success rate, which was statistically significantly superior for arthroplasty (Secure-C, Globus Medical; Audobon, PA) compared with ACDF. Likewise, Davis et al[6] demonstrated an overall success rate that was statistically significantly superior for artificial disc (Mobi-C; Zimmer Biomet, Warsaw, IN) compared with ACDF for 1- and 2-level surgery. Gornet et al[11] reported the results of Prestige LP (Medtronic Memphis, TN) versus ACDF at 1-level (280 patients) and 2-level (265 patients) and showed statistically significant superiority in clinical overall success (79% to 67%) and in neurological success (93% to 84%) at 24 months for arthroplasty.

Based on the level 1 data from the IDE trials as well as other studies, the evidence basis for the efficacy of cervical arthroplasty was firmly established. But the effect of motion preservation on adjacent segment pathology, including ASD and ASR remained controversial. Jawahar et al[12] presented results of 3 TDR devices compared with ACDF in 93 patients with minimum 2-year follow-up. Adjacent level degenerative changes at last follow-up were identified in 15% of ACDF patients and 18% of TDR patients, not statistically significant ($P = .885$). Based on the results of this relatively small number of patients with short-term follow-up, the authors concluded that "total disc arthroplasty does not affect the incidence of adjacent segment degeneration in cervical spine." A meta-analysis of single level arthroplasty in 2010 by Bartels *et al*[13] included a total of 1533 patients. Visual analogue scale (VAS) arm/neck scores, Short Form–36 health questionnaire (SF-36) at 12 months, and NDI at 24 months showed statistically significant improvement in arthroplasty versus ACDF. But TDR showed no statistically significant difference at two years, prompting the authors to conclude that "a clinical benefit for cervical disc prosthesis is not proven," and that "these costly devices should not be used in clinical practice." More recently, Vleggert-Lankamp et al[14] evaluated 109 patients with 2-year follow-up and reported "adjacent segment degeneration parameters were comparable" with arthroplasty versus anterior cervical discectomy alone and anterior cervical discectomy with fusion. Unfortunately, given the small annual rate of adjacent level reoperation following ACDF (reported as 0.66% in the seminal study by Hilibrand et al[15] in 1999), these studies are simply not designed or properly powered, in overall patient numbers or length of follow-up, to be able to demonstrate statistically significant differences in ASR rates. Nunley et al[16] reported on 167 patients with 3 artificial disc devices in 4 different FDA IDE trials for with median follow-up of 56 months (range 51-82 months) and included patients with 1 or 2 levels treated. These authors concluded that "degeneration at the adjacent levels is significantly time-dependent and hence cannot be estimated at a short-term follow-up of 24 months or less." Because of the inherently low incidence of adjacent level reoperation (generally <1%), long-term follow-up and/or large patient numbers or meta-analyses are needed to demonstrate statistically significant differences in ASR rates. If artificial disc placement can positively affect the occurrence of ASR, the expectation would be that cervical arthroplasty would result in decreased ASD (radiographic) in the short-term, followed by decreased ASR (clinical) in the longer term. Furthermore, these differences would be expected to become more apparent with longer follow-up as well as with multiple treatment levels.

## Adjacent Segment Reoperation: Long-Term Follow-up and Meta-Analyses

Given the findings from early arthroplasty studies, larger studies with longer follow-up were necessary to further clarify the effect of motion preservation on ASD and ASR. Two separate meta-analyses of prospective, randomized studies comparing cervical arthroplasty to ACDF have addressed ASR rates. Upadhyaya et al[17] evaluated 3 randomized US FDA IDE studies with a total of 1098 patients at 24-month follow-up after arthroplasty or ACDF. A significant risk reduction in the ASR favoring arthroplasty was found using a fixed effects model (relative risk of 0.460, $I^2 = 2.9\%$, $P = .030$). A larger meta-analysis by Zhang et al[18] included 19 randomized controlled

trials. A total of 4516 patients were included and cervical arthroplasty had better functional outcomes (NDI, NDI success, NRS [Numeric Rating Scale]/VAS neck pain scores, overall success). Also, short-term studies (2- or 3-year follow-up) showed significantly lower ASR in the artificial disc group (odds ratio, 0.28; 95% CI 0.11-0.72; $P = .008$).

Several studies with long-term follow-up (>5 years) have shown a significantly positive effect of motion preservation on ASR for 1- and 2-level cervical disc disease. Zigler et al[19] reported on 5-year follow-up of Pro-Disc-C. At 5 years, arthroplasty patients had a significantly lower rate of reoperation compared with ACDF patients (2.9% vs 11.3%). Coric et al[20] reported on 5-year follow-up of Kineflex-C artificial disc which showed no difference in reoperation rate compared to ACDF but the ACDF group showed significantly worse ASD. Burkus et al[21] presented 7-year follow-up on Prestige ST versus ACDF in 541 patients with a 73% follow-up rate. At 7-year follow-up, ASR were statistically significantly lower for arthroplasty (4.6% or 0.7%/year) compared to ACDF (11.9% or 1.7%/year), $P = .008$. Furthermore, NDI and overall improvement in neurologic status at 84 months were significantly improved in arthroplasty compared with ACDF. Similar findings were seen by Vaccaro et al[22] for 7-year follow-up of Secure-C of 380 patients with follow-up rate of 83%. ASR for the artificial disc group was 4.2% (0.6%/year) compared with 16% for ACDF (2.2%/year). Long-term clinical results and ASR were shown to be significantly better at 5- and 7-year follow-up after 1- and 2-level arthroplasty by Radcliff et al.[23,24] Lanman et al[25] and Gornet et al[26] have reported on long-term outcomes of 7- and 10-year follow-up of 1- and 2-level cervical disc replacement for Prestige LP. Index level reoperation rates were significantly lower (4.2% vs 14.7%) for arthroplasty group at 7-year follow-up, though ASR did not reach statistical significance (6.5% vs 12.5). Ten-year follow-up data by Gornet et al[26] showed a cumulative operative rate at adjacent levels of 13.8% (1.4%/year). Lavelle et al[27] reported on 10-year outcomes of FDA IDE study of BRYAN cervical disc. At 10-year follow-up, disability and VAS neck and arm scores were significantly improved in the arthroplasty groups and adjacent segment reoperation rates were 9.7% vs. 15.8% for ACDF ($P = .146$). Furthermore, motion preservation was maintained with mean angular motion of 8.69° at index level. These multiple 5- to 10-year IDE follow-up studies have now shown the long-term effect hypothesized from early studies on adjacent segment disease and reoperation rates.

## Conclusion

A growing body of level-1 and -2 evidence now demonstrates that cervical arthroplasty provides sustained, long-term clinical benefits as well as a positive effect on the incidence of adjacent level pathology for select patient populations. Adjacent segment reoperation remains somewhat controversial due to its inherent multifactorial etiology beyond choice of surgical intervention (arthroplasty vs fusion). Some of these disparate factors include natural history of the underlying degenerative process, surgical technique and overall spinal balance. The discussion should focus on objective evidence of adjacent level disease, that is, reoperation (unequivocally clinically relevant), not subjective definitions. Because of the inherently low incidence of ASR (generally <1%/year), long-term follow-up, and/or large patient numbers are needed to demonstrate statistically significant differences. This topic merits ongoing investigation.

### Declaration of Conflicting Interests

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