

Evaluation of Adverse Events in Total Disc Replacement: A Meta-Analysis of FDA Summary of Safety and Effectiveness Data

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Paul A. Anderson, MD¹, Ahmad Nassr, MD², Bradford L. Currier, MD²,
Arjun S. Sebastian, MD², Paul M. Arnold, MD, FACS³, Michael G. Fehlings, MD, PhD⁴,
Thomas E. Mroz, MD⁵, and K. Daniel Riew, MD^{6,7}

Abstract

Study Design: Systematic review and meta-analysis.

Objectives: The safety of new technology such as cervical total disc replacement (TDR) is of paramount importance and is best evaluated in randomized clinical trials (RCT). We compared complication risks of TDR to fusion using data from Investigational Device Exemptions.

Methods: A systematic review of FDA Summary of Safety and Effectiveness reports of the 8 approved cervical TDRs was performed. These were all randomized controlled trials comparing anterior cervical discectomy and fusion (ACDF) to TDR. Important outcome variables were dysphagia, wound infection, neurologic injuries, heterotopic ossification, death, and secondary surgeries. A random effects model was selected a priori. Data on adverse events was abstracted and analyzed by calculating relative risk of ACDF to TDR by meta-analysis techniques.

Results: The study included 3027 patients with 1377 randomized to ACDF and 1652 to TDR. No statistical differences were present between the 2 groups in dysphagia/dysphonia, hardware related, heterotopic ossification, death, and overall neurologic adverse events and incidence of neurologic deterioration. The relative risk of wound-related problems ACDF to TDR was 0.76 (95% confidence interval [CI] = 0.59, 0.98) favoring ACDF, which was statistically significant, but these were minor and never required a second surgical procedure for deep wound infection. The relative risk of ACDF to TDR in surgical-related neurologic events and secondary surgeries was 1.62 (95% CI = 1.04, 2.53) and 1.79 (95% CI = 1.17, 2.74), both favoring TDR.

Conclusions: Cervical TDR appears to be as safe as or safer than ACDF at 2-year follow-up.

Keywords

cervical arthroplasty, cervical total disc replacement, adverse events, randomized controlled trials, meta-analysis

Introduction

Safety is of primary concern when evaluating and implementing new technology such as cervical total disc replacement (TDR). Safety (also called harms) is evaluated by preclinical, animal, and finally randomized clinical trials (RCTs). Outcomes of cervical TDR RCTs in published peer-reviewed journals show equivalency in safety and outcome between TDR and fusion controls.¹⁻³ However, the rates of reported adverse events vary, likely due to differences in definitions, intensity of acquiring, and reporting of adverse events. Furthermore, peer-reviewed publications in general have poor reporting of adverse events in randomized controlled trials.^{4,5} This leads to uncertainty and makes recommendation for their use more difficult.

¹ University of Wisconsin, Madison, WI, USA

² Mayo Clinic, Rochester, MN, USA

³ Kansas University Medical Center, Kansas City, KS, USA

⁴ Toronto Western Hospital, Toronto, Ontario, Canada

⁵ Cleveland Clinic, Cleveland, OH, USA

⁶ Columbia University, New York, NY, USA

⁷ New York-Presbyterian/The Allen Hospital, New York, NY, USA

Corresponding Author:

Paul A. Anderson, Department of Orthopedic Surgery and Rehabilitation, University of Wisconsin, UWMF Centennial Bldg, 1685 Highland Ave, 6th Floor, Madison, WI 53705-2281, USA.
Email: Anderson@ortho.wisc.edu



Table 1. Study Cohorts, FDA Summary Safety and Effectiveness Data Reports.

| Device | Number of Patients | | Clinical Events Committee | Industry Sponsorship | Follow-up at 24 Months (%) |
|--------------------------------|--------------------|------|---------------------------|----------------------|----------------------------|
| | ACDF | TDR | | | |
| Prestige ST ⁷ | 265 | 276 | No | Yes | 46.0 |
| Prodisc C ⁸ | 106 | 103 | No | Yes | 70.8 |
| Bryan ⁹ | 221 | 242 | No | Yes | 63.3 |
| Secure C ¹⁰ | 144 | 148 | Yes | Yes | 86.9 |
| PCM ¹¹ | 190 | 214 | Yes | Yes | 79.5 |
| Mobi C (1 level) ¹² | 81 | 164 | Yes | Yes | 85.2 |
| Mobi C (2 level) ¹³ | 105 | 225 | Yes | Yes | 77.1 |
| Prestige LP ¹⁴ | 265 | 280 | Yes | Yes | 83.0 |
| Overall | 1377 | 1652 | | | 63.0 |

Abbreviations: ACDF, anterior cervical discectomy and fusion; TDR, total disc replacement.

As of 2015, the US Food and Drug Administration (FDA) has approved 8 cervical arthroplasty devices for marketing. At the time of approval, a letter is forwarded to the manufacturer and Summary of Safety and Effectiveness report (SSED) is published on the FDA website. These SSED reports summarize adverse events in greater detail and have far better granularity (including better descriptions of methodology and reporting of results) than peer-review publications.⁶ This study aims to compare rarer adverse events of cervical TDR compared to anterior cervical discectomy and fusion (ACDF) based on data from the SSED reports. We chose to examine the most clinically relevant adverse events that are shared by both ACDF and cervical TDR.

Methods

We initially planned to perform a multicenter retrospective study, utilizing the data from 17 625 patients who underwent cervical spine surgery between January 1, 2005, and December 31, 2011, in 1 of 21 hospitals from the AOSpine North America Clinical Research Network. However, there were no incidences of arthroplasty complications recorded. A priori, if no cases were identified we planned a systematic review and if appropriate a meta-analysis.

Systematic Review

The FDA website (fda.gov) was searched for cervical disc replacement and cervical arthroplasty. In addition, all known approved cervical TDR trade names were used as search criteria. Inclusion criterion was that the report documented a randomized controlled study comparing ACDF to cervical TDR. The SSED reports for each device were downloaded.⁷⁻¹⁴ Data on adverse events were abstracted and tabulated. The variables of interest were the following: number of patients in randomized cohorts having dysphagia/dysphonia, wound issues, surgical-related events, hardware complications, neurologic injuries, heterotopic ossification, and death.

Statistical Methods

The “intention to treat” method was used in this study. Results were analyzed at 24 months unless stated differently.

Three of the studies reported both randomized cohorts and training cases or continuing access cases. Only data from the randomized patients were included in our analyses. Using a conservative approach, in the circumstances where data was not stratified between training and randomized populations, the randomized sample size was selected. The meta-analysis was performed by calculation of relative risk of ACDF to TDR using Comprehensive Meta-Analysis, version 2.2.050 (Biostat, Englewood, NJ) software. A random effects model was chosen a priori. Publication bias was assessed by funnel plots and sensitivity analysis performed by single study deletion and by variation of any assumption used in the statistical analysis. Since no control was physiologically plausible for heterotopic ossification, pooling was done using log event rates. A P value $\leq .05$ was considered as statistically significant. Confidence intervals (CIs) were reported at 95% levels. Heterogeneity was determined based on I^2 . I^2 is a measure of error between studies. An I^2 value less than 25 indicates no heterogeneity (homogeneous), 25 to 50 moderate, and ≥ 50 large heterogeneities. The Q value was used to test the statistical significance of the null hypothesis (that the studies are homogeneous) using χ^2 distribution. A significant result ($P \leq .05$) rejects the null hypothesis and indicates the results have heterogeneity.

Results

Studies

The search of the FDA database identified 8 SSED reports of high-quality, randomized trials of ADCF compared to cervical TDR (see Table 1). The adverse events were collected and documented by trained research nursing personnel. In the latter 5 studies, a clinical events committee (CEC) reviewed the adverse events, graded severity, and made attributions as to seriousness and relatedness to the surgical procedure and device. Five of the studies included a list of definitions of adverse events. All studies were industry-sponsored.

Overall 3027 patients were enrolled, 1377 in the ACDF group and 1652 in the TDR group. The indications for surgery

Table 2. Meta-Analysis Results of Wound, Dysphagia, and Hardware Adverse Events.

| | Wound-Related Adverse Events (%) | | Dysphagia/Dysphonia (%) | | Hardware Adverse Events (%) | |
|------------------|----------------------------------|-------|-------------------------|-------|-----------------------------|-------|
| | ACDF | TDR | ACDF | TDR | ACDF | TDR |
| Prestige ST | 7.55 | 9.78 | 8.30 | 8.33 | 1.13 | 1.45 |
| Prodisc C | 2.83 | 2.91 | 9.43 | 5.83 | 1.89 | 0.00 |
| Bryan | 4.52 | 7.02 | 8.60 | 10.33 | 0.45 | 0.83 |
| Secure | 4.17 | 0.00 | 6.94 | 4.73 | 0.00 | 0.68 |
| PCM | 2.63 | 6.07 | 12.11 | 10.28 | 1.58 | 11.68 |
| Mobi C (1 level) | 4.94 | 4.27 | 20.99 | 12.20 | 3.70 | 3.66 |
| Mobi C (2 level) | 5.71 | 4.89 | 22.86 | 17.33 | 9.52 | 0.89 |
| Prestige LP | 15.09 | 21.07 | 8.30 | 9.29 | 1.89 | 6.43 |
| Overall | 6.83 | 8.29* | 10.68 | 10.17 | 1.96 | 3.51 |
| P value | P = .03 | | P = .16 | | P = .68 | |

Abbreviations: ACDF, anterior cervical discectomy and fusion; TDR, total disc replacement.

*Statistically significant.

Table 3. Pooled Relative Risk and 95% Confidence Intervals of ACDF to TDR.

| | Relative Risk ACDF/TDR | 95% Confidence Interval | | P Value | I ² | Q |
|---------------------|------------------------|-------------------------|-------|---------|----------------|------|
| | | Lower | Upper | | | |
| Wound | 0.76* | 0.59 | 0.98 | .03 | 0.0 | 6.6 |
| Dysphagia/dysphonia | 1.16 | 0.94 | 1.43 | .16 | 0.0 | 5.21 |
| Hardware | 0.79 | 0.27 | 2.35 | .68 | 72 | 25 |
| Neurologic | | | | | | |
| Overall | 0.98 | 0.81 | 1.18 | .82 | 66.4 | 20.9 |
| Surgical-related | 1.62* | 1.04 | 2.53 | .03 | 40.6 | 6.7 |
| Deterioration | 1.33 | 0.92 | 1.93 | .12 | 48.8 | 13.7 |
| Death | 1.85 | 0.49 | 6.92 | .36 | 0.0 | 2.1 |
| Secondary surgeries | 1.79* | 1.17 | 2.74 | .008 | 55.1 | 15.6 |

Abbreviations: ACDF, anterior cervical discectomy and fusion; TDR, total disc replacement; Q, Cochrane statistic.

*Statistically significant.

were similar among investigations: failure of medical management in patients with painful cervical radiculopathy or myelopathy at a single level from C3 to C7 in 7 reports. One investigation included only patients having surgery at 2 levels. Two studies reported devices with similar trade names, Prestige ST and Prestige LP, but these are independent devices with different materials and fixation methods.

Wound

Wound-related adverse events included superficial and deep wound infections and hematoma. These were rare conditions and the majority were superficial wound problems. No study reported an implant infection requiring removal within 2 years of surgery or which required a surgical incision and drainage in either group.

The overall incidence was greater in TDR than ACDF, averaging 8.3% versus 6.8% but varied from 0% to 21.1% (see Table 2). The variation in rates of infections was likely from inclusion of other infections into a general category of infection but without stratification to indicate they were wound-related. The relative risk of ACDF to TDR was 0.76 (CI = 0.59, 0.98) favoring ACDF, which was statistically

significant, P value = .03 (see Table 3). The studies had perfect homogeneity ($I^2 = 0.0$), and the null hypothesis test indicated homogeneity, $P = .47$.

Dysphagia/Dysphonia

Dysphagia and dysphonia were combined for this analysis. This was a dichotomized variable in all studies. The mean incidence was 10.7 and 10.2 for ACDF and TDR, respectively, and ranged from 6.9% to 22.9% for ACDF and 4.7% to 17.3% for TDR (see Table 2). The relative risk of having dysphagia/dysphonia was 1.16, which was greater for ACDF but this was not statistically significant, $P = .16$ (see Figure 1). The studies had perfect homogeneity ($I^2 = 0.0$), and the null hypothesis test indicated homogeneity, $P = .47$.

Hardware-Related Adverse Events

Hardware-related adverse events included technical difficulties during insertion, malposition, subsidence, and migration. The mean incidence was 1.96 and 3.51 for ACDF and TDR, respectively. Both groups varied from zero to about 10% (see Table 2). The pooled relative risk was 0.79 (CI = 0.27, 2.35) favoring

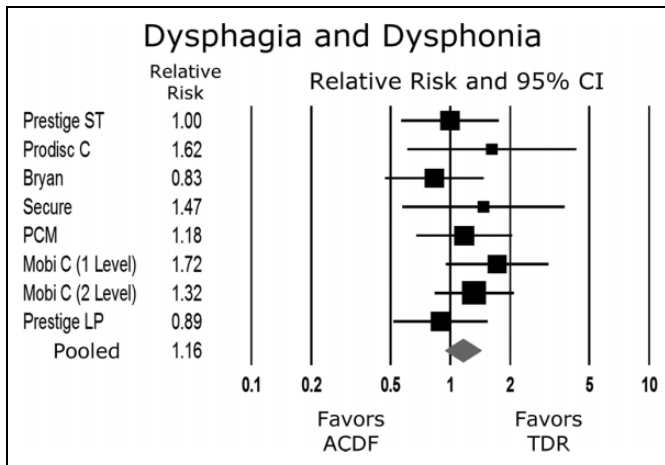


Figure 1. Relative risk of ACDF to TDR of having dysphagia and dysphonia.

ACDF but this was not statistically significant, $P = .68$ (see Table 3). There was large amount of heterogeneity with $I^2 = 72.0$, and the null hypothesis test failed indicating heterogeneity, $P = .0008$.

Neurologic Adverse Events

Neurologic adverse events were difficult to compare among studies. Neurologic events had variable definitions and in many reports included nonsurgical or non-device-related causes. The analysis was performed using 3 methods. We selected the listing of “neurologic” reported in tables of overall adverse events. These were all formatted similarly in the SSED reports. These included neurologic events, many of which were not related to the procedure and those which were transient. There was no ability to assess the neurologic adverse events by severity.

Second, if reported, we analyzed the incidence of neurologic events that were attributed as surgical-related, device-related, or both. This gives the best estimate of the relative risk effect. Finally, all studies reported patients who deteriorated neurologically from baseline. The FDA defines this as a change of motor, sensory, or diminished reflex occurring within 12 months after surgery.

Overall Neurologic Events. The definition and intensity of data collection and reporting was variable as the rates of neurologic adverse events ranged from 2.8% to 73.8% (see Table 4). The relative risk of ACDF to TDR was 0.98 (CI = 0.89, 1.18) favoring TDR but was not statistically significant, $P = .82$ (see Table 3). The heterogeneity was large ($I^2 = 66.4$), and the null hypothesis test failed indicating heterogeneity, $P < .004$.

Surgical-Related Neurologic Adverse Events. Neurologic adverse events related to the surgical procedure or device is of great interest to surgeons and patients. In 3 studies these were not reported. Two studies reported device-related neurologic adverse events and 3 studies reported both surgical procedure and device-related adverse events. The overall incidence was

4.9% and 3.9% for ACDF and TDR, respectively (see Table 4). Over half of the neurologic procedure-related neurologic events occurred after 12 weeks. The relative risk of ACDF to TDR was 1.62 (CI = 1.04, 2.53) favoring TDR, which was statistically significant, $P = .03$ (see Figure 2). There was moderate heterogeneity ($I^2 = 40.6$), and the null hypothesis test indicated homogeneity, $P = .15$. Only one spinal cord injury related to the cervical spine surgery occurred and this was in a control fusion patient.

Maintenance of Baseline Neurologic Function. Maintenance of baseline neurologic function was a primary outcome criteria used in all studies to determine overall clinical results. The mean incidence of deterioration from baseline was 10.4 and 8.13 for ACDF and TDR, respectively (see Table 4). The incidence ranged from 6.12% to 14.5% for ACDF and 4.41% to 17.20% for TDR. The relative risk of ACDF to TDR was 1.33 (CI = 0.92, 1.93) favoring TDR, but was not statistically significant, $P = .12$ (see Table 3). The I^2 was 48.8 indicating moderate heterogeneity and the test for heterogeneity was negative, $P = .06$.

Heterotopic Ossification

Heterotopic ossification (HO) was reported in 5 studies, 2 of which used the McAfee severity scale.¹⁵ The scale ranges 0 to 4, with grade 4 being the most severe. We dichotomized this variable with grade 0 and 1 into “no” and grades 2 to 4 into “yes.” The control group was not used in this analysis because in fusion HO is not a relevant adverse event and was rarely reported. The mean incidence of HO was 9.5%, ranging from 1.8% to 47.3% (see Table 5). There was significant heterogeneity, $I^2 = 96.1$, and the null hypothesis test failed indicating heterogeneity, $P < .0001$.

The FDA defines radiologic success as having greater than 2 degrees of motion in flexion-extension. Physiologically this reflects spontaneous fusion from heterotopic ossification as well as other conditions. Overall, 13.6% of patients had ≤ 2 degrees of motion (see Table 5). Unlike HO, there was consistency of results with $I^2 = 0.0$, and the null hypothesis test indicated homogeneity, $P = .46$.

Deaths

Overall, 9 deaths occurred within 2 years of enrollment in the studies, 6 deaths in the ACDF group and 3 in the TDR group. No deaths were deemed to be related to the surgical procedure or device. The relative risk of ACDF to TDR was 1.85 (CI = 0.49, 6.92), favoring TDR, which was not statistically significant, $P = .36$ (see Table 3). The studies were homogenous as the I^2 was 0.0, and the null hypothesis test indicated homogeneity, $P = .72$.

Secondary Surgeries

Secondary surgeries were classified as revisions, removals, supplementary fixation, and reoperations. Analysis of

Table 4. Neurologic-Related Adverse Events.

| | Overall Incidence (%) | | Surgical and Device Related (%) | | Neurologic Deterioration (%) | |
|------------------|-----------------------|------|---------------------------------|------|------------------------------|------|
| | ACDF | TDR | ACDF | TDR | ACDF | TDR |
| Prestige ST | 20.8 | 23.9 | 1.5 | 0.4 | 13.4 | 6.4 |
| Prodisc C | 9.4 | 14.6 | — | — | 12.0 | 9.1 |
| Bryan | 20.8 | 19.8 | — | — | 6.1 | 6.00 |
| Secure | 2.8 | 3.0 | — | — | 8.9 | 4.4 |
| PCM | 19.5 | 17.0 | 5.3 | 4.2 | 10.7 | 17.2 |
| Mobi C (1 level) | 64.2 | 73.8 | 32.1 | 13.4 | 14.5 | 8.6 |
| Mobi C (2 level) | 74.3 | 55.1 | 19.1 | 10.7 | 8.2 | 8.9 |
| Prestige LP | 40.8 | 48.6 | 2.6 | 3.9 | 12.1 | 5.4 |
| Pooled | 28.3 | 31.8 | 4.9 | 3.9 | 10.4 | 8.1 |
| P value | P = .82 | | P = .03* | | P = .12 | |

Abbreviations: ACDF, anterior cervical discectomy and fusion; TDR, total disc replacement.

*Statistically significant

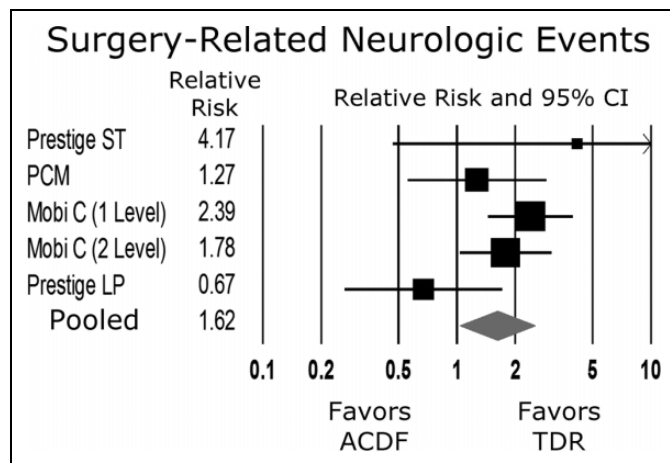


Figure 2. Relative risk of ACDF to TDR of having surgical-related neurologic events.

Table 5. Heterotopic Ossification and Spontaneous Fusion.

| | Heterotopic Ossification (%) | Spontaneous Fusion ^a (%) |
|------------------|------------------------------|-------------------------------------|
| Prestige ST | — | 10.3 |
| Prodisc C | 2.9 | 11.5 |
| Bryan | — | 15.6 |
| Secure | 47.3 | 14.4 |
| PCM | 18.70 | 16.3 |
| Mobi C (1 level) | 5.5 | 10.3 |
| Mobi C (2 level) | 1.8 | 12.7 |
| Prestige LP | 11.1 | 15.2 |
| Pooled | 9.50 | 13.6 |
| I ² | 96.1 | 0.0 |

^aSpontaneous fusion is defined as ≤2 degrees in flexion-extension.

secondary surgeries separately at index and adjacent levels was not possible due to limitations in data reporting; therefore, these results include both index and adjacent levels. Secondary surgeries occurred in 8.8% and 5.2% of ACDF and TDR

Table 6. Secondary Surgeries, FDA Summary Safety and Effectiveness Data.

| Study | ACDF | TDR |
|------------------|----------|------|
| Prestige ST | 9.1 | 3.3 |
| Prodisc C | 9.4 | 1.9 |
| Bryan | 7.7 | 5.8 |
| Secure | 11.8 | 6.8 |
| PCM | 7.4 | 11.7 |
| Mobi C (1 level) | 7.4 | 3.1 |
| Mobi C (2 level) | 11.4 | 4.00 |
| Prestige LP | 7.9 | 4.3 |
| Overall | 8.8 | 5.2 |
| P value | P = .008 | |

Abbreviations: ACDF, anterior cervical discectomy and fusion; TDR, total disc replacement.

*Statistically significant.

patients, respectively (see Table 6). The relative risk of ACDF to TDR was 1.79 (CI = 1.17, 2.74), which was statistically significant, $P = .008$ (see Figure 3). The I^2 was 55.1 indicating large heterogeneity, and the null hypothesis test indicated heterogeneity, $P = .03$.

Publication Bias

Funnel plots of all reported adverse events showed symmetry about the effect size and an absence of publication bias using the “trim and fill” and Orwin’s fail safe N (see Figure 4).

Sensitivity Analysis

Single elimination of the Bryan study made dysphagia and Secure C wound complications statistically significant in favor of TDR. The analysis of surgical-related neurologic events was sensitive to elimination of any of the studies since there were only 5 studies included initially. In each case single elimination changed the effect from significant to nonsignificant. Using a fixed rather than random effect model when studies were

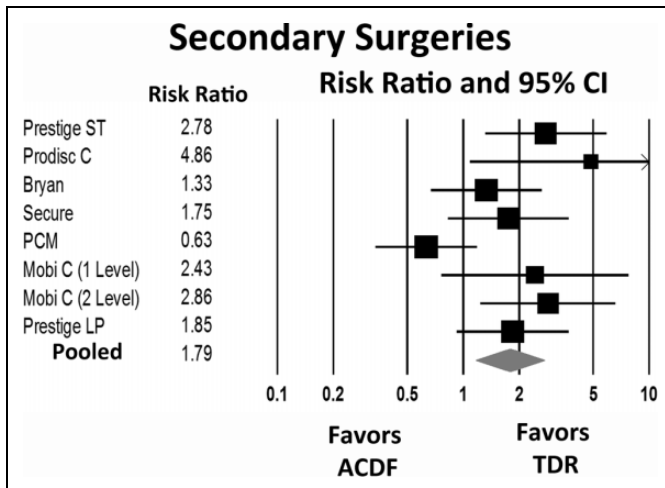


Figure 3. Relative risk of ACDF to TDR of having secondary surgery.

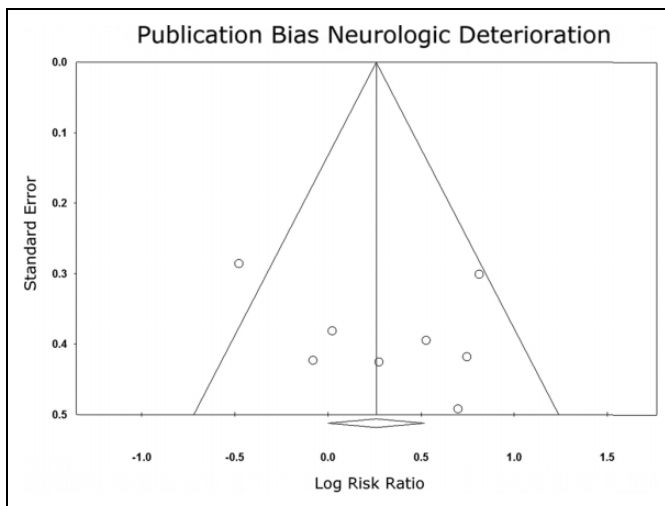


Figure 4. Funnel plot to assess publication bias of neurologic deterioration showing symmetry about relative risk indicating a lack of bias.

homogeneous did not result in a change of statistical significance.

Discussion

The goal of this investigation was to assess the safety of cervical TDR compared to ACDF. We used a meta-analysis technique that allows pooling of data among randomized controlled trials and is useful when evaluating conditions where numbers of events are small such as in rarer complications as investigated in this study. We selected the FDA SSED reports rather than peer-reviewed journal publications as source material, as these had far greater granularity in reporting adverse events of interest.⁶

The results showed that TDR was as safe as and maybe safer than ACDF. Most analyses comparing the 2 groups

failed to show statistical significance with a few exceptions. Although wound-related adverse events were statistically greater for TDR, these were minor and never led to a reoperation, deep wound infection, or explantation within 2 years of surgery. The relative risk of ACDF to TDR for surgical-related neurologic events was significant, although most of these appeared late (therefore not likely directly related to the surgical procedure). Instead, they were more likely due to pseudoarthrosis and adjacent segment degeneration. Similarly, secondary surgeries from pseudoarthrosis occurred only in the ACDF group, which biased results toward higher relative risk for ACDF. Dysphagia and dysphonia are common complications of anterior cervical spine surgery. The TDR group had a lower risk but this was not statistically significant. This analysis would have benefited by assessment of the severity of dysphagia, which was only performed in one study. One esophageal perforation occurred in a control patient.

Heterogeneity of the results is as important as the magnitude of the effect size when interpreting meta-analyses. In this study, although the indications, demographic, and surgical technique were nearly all identical, there was either perfect homogeneity or large amounts of heterogeneity. Causes for the heterogeneity are the lack of standardized definitions and variation of intensity of data collection among investigators and studies. In addition, the last 5 studies used a CEC, which individually attributed and graded adverse events that has been shown to be more stringent in the analysis than when performed by surgeons and local research staff.¹⁶ There may have been intrinsic safety differences among implants but this could not be statistically evaluated in a meta-analysis of single studies for each implant type.

Of most interest to surgeons and what is usually included in informed consent are surgical- and device-related complications. Although reported in 5 studies, the surgical-related complications were not stratified by time points making it difficult to know if they were truly related to the surgery. Furthermore, the FDA neurologic criteria are very stringent and not based on sensitivity of the neurologic exam, time dependent variation in mild symptoms such as hand numbness, or any functional tests. Although gait exam was reported in some studies, this was just by gross examination and not quantitatively evaluated.¹⁷ Motor function of key muscle groups and dermatomal sensory examination were graded, but these quantitative data was never reported. Further establishing a threshold that is considered a significant change would be important, as the FDA criteria (any small change of doubtful significance) is too stringent. Reflex change as a criterion is not clinically meaningful and should be dropped from any criteria for meeting clinical success.

The goal of cervical TDR is to maintain intersegmental motion after discectomy; however, this does not always occur. Heterotopic ossification and spontaneous fusion were present frequently, in 9.5% and 13.6% of patients, respectively. Several strategies have been presented to reduce this

tendency, including avoiding TDR in patients with severe spondylosis and limited preoperative motion, use of nonsteroidal anti-inflammatory agents, and limiting immobilization devices. Most of these principles were utilized in the later studies with only a modest reduction of these adverse event outcomes.

These results can be used to inform patients that TDR is as safe as ACDF and at 2 years may result in fewer secondary surgeries. Other recent meta-analysis by Zhou, Ren, and Rao documented efficacy of TDR compared to ACDF, but only analyze overall adverse events and secondary surgeries.¹⁸⁻²⁰ Those results are similar to the current study, but this study analyzes seriousness and individual adverse events as well. Furthermore, this study utilizes a more robust data source regarding adverse events, the SSED reports, than can be found in individual peer-reviewed studies.

The strength of the study is the inclusion of 8 independent RCTs with excellent documentation of adverse events that allow examination of safety. Trained personnel prospectively collected and reported adverse events. Attribution was initially by surgeons and researchers but in the last 5 published studies was by an independent CEC, which is the preferred method. The follow-up at early time points was excellent (>90%), although the studies utilized Bayesian predictive models, which allow early testing for significance before all patients have reached endpoints such as 2-year follow-up. This accounts for the substantially less follow-up as reported. The impact of incomplete follow-up at 2 years is mitigated by the fact that most adverse events of clinical concern related to surgery occur early.

Limitations of this study are lack of standardized definitions among studies, differences in reporting, occasional inclusion of nonrandomized cohorts (training and continuing access) in safety cohorts, and grouping of minor and major adverse events into categories such as wound infections. Important considerations such as severity and attribution as surgical-related were poorly documented in the majority of reports. Follow-up was incomplete: at 2 years was only 63%, which was by design. All studies used Bayesian methods, which applies a predictive model based on accumulated data and does not require all patients having attained desired follow-up. Most of the technically significant complications in this study (except secondary surgeries) occur at the early time points where follow-up was always greater than 90%.

Conclusions

This meta-analysis of 8 RCT comparing ACDF to TDR showed that in the most common adverse events the 2 groups had similar results. Although the most significant difference was secondary surgeries, this was most likely from pseudoarthrosis and adjacent segment degeneration.

Authors' Note

This study did not require institutional ethics committees at any participating site.

Declaration of Conflicting Interests

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