Systematic Review and Meta-analysis: Anterior Cervical Discectomy and Fusion versus Cervical Disc Replacement in Cervical Disc Herniation

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ABSTRACT

Background:
Cervical disc herniation is a common cause of neck pain in adults. The severity of the disease can range from mild to severe. Anterior cervical discectomy and fusion (ACDF) were considered the "gold standard" for the management of cervical disc herniation. However, in recent years, radiographic and clinical studies have shown that as time passes, the segments adjacent to the fused spinal segments become occasionally degenerated or unstable. Cervical disc replacement differs from ACDF in that rather than fusing the adjacent vertebrae, an artificial disc is inserted to maintain motion between the vertebrae. Some studies show that disc replacement maintains more natural biomechanics within the cervical spine.

Objective:
To perform a systematic review and meta-analysis comparing the total disk replacement (TDR) with ACDF in cervical disk herniation patients with regards to clinical, radiological, biomechanical factors, and patient outcomes.

Patients and Methods:
We included studies that followed the following criteria: (1) Adult patients above 18 years old (2) Double arm designs (3) Studies designs are limited to randomized control trials (RCT) to obtain high-quality evidence (4) English studies (5) Outcomes either clinical or radiological are acceptable. We excluded conference abstracts or unpublished data, studies written in a language other than English, in-vitro studies, and duplicated articles by the same author unless those with longer follow-up studies.

Results:
Ten studies were included qualitatively and nine studies were included quantitatively. We found that the overall symptomatic adjacent level disease requiring surgery (SALDRS) rate of the TDR group was significantly lower than that of the ACDF group after a minimum follow-up period with a P-value of 0.0001. Also, regarding a longer follow-up of 4-5 years in terms of SLDRS rate, we found a significant positive result towards the TDR compared to ACDF (P = 0.006). Longer follow-ups of seven years and nine years postoperatively showed also a significant favorable effect of TDR over ACDF with P-values of 0.01 and 0.02 respectively. postoperative patient satisfaction, subsequent surgical intervention, and the physical component of the SF-36 questionnaire showed a significant difference between TDR and ACDF favoring TDR over ACDF. The pooled analysis of the included studies showed no significant difference between TDR and ACDF regarding Neck Disability Index, dysphagia as an adverse event, major complications and adverse events, postoperative Neck and arm pain VAS score 48 months, and the mental component of the SF-36 questionnaire.

Conclusion:
TDR showed significant positive results regarding postoperative satisfaction as well as reduced risk of adjacent segment disease requiring subsequent surgical intervention. Higher-quality RCTs with longer-term follow-up are required to achieve a better comparative analysis of the SALDRS rate after TDR and ACDF. No trial reported a single outcome at any time point to suggest that ACDF may be superior to TDR.

Keywords:
Cervical Disc replacement; anterior cervical discectomy, and fusion; Cervical Disc Herniation

INTRODUCTION

Cervical disc herniation is a common cause of neck pain in adults. The severity of the disease can range from mild to severe. [(1)].

Anterior cervical discectomy and fusion (ACDF) were considered the "gold standard" for the management of cervical disc herniation. However, in recent years, radiographic and clinical studies have shown that as time passes, the segments adjacent to the fused spinal segments become occasionally degenerated or unstable [(2)].

ACDF involves removing the problematic disc completely and replacing it with a bone graft (or bone graft substitute) to allow the adjacent vertebrae to eventually fuse [(3)].

One of the main limitations of ACDF surgery is that it alters the original mechanical behavior of the spine at the expense of the activity of the fusion segment; and this leads to changes in adjacent vertebral stress distribution and movement patterns, resulting in biomechanical changes including stress concentration of adjacent segments, compensatory increase inactivity, and even instability [(4)].

Nowadays, cervical total disc replacement (CTDR) is a major non-fusion surgical procedure designed to retain as much as possible the intervertebral disc height and segmental activity and to reduce the accelerated adjacent segment degeneration (ASD) that is often caused by ACDF. Its short-term clinical results have been well demonstrated, but the studies reporting long-term curative effects are scarce [(5)].

Cervical disc replacement differs from ACDF in that rather than fusing the adjacent vertebrae, an artificial disc is inserted to maintain motion between the vertebrae. Some studies show that disc replacement maintains more natural biomechanics within the cervical spine and places less stress on the discs above and below the surgical level than ACDF [(6)].

Both ACDF and artificial cervical disc replacement tend to have favorable clinical outcomes. Successful results from both types of surgery can be expected in more than 70% of eligible patients with degenerative disc disease at a single spinal level. Cervical artificial disc replacement (ADR) has thus far demonstrated at least equivalent results to ACDF in relieving neck pain, arm pain, patient function, and satisfaction, and with no increase in surgical complications [(7)].

There are many important factors when considering disc replacement versus ACDF, depending on the patient's unique situation, one procedure might have benefits over the other [(2)].

AIM OF THE WORK

To evaluate the clinical, radiological, biomechanical factors and patient outcomes comparing ACDF with anterior cervical disc replacement for the treatment of cervical disc herniation.

PATENTS AND METHODS

We followed the PRISMA statement guidelines[(8)] during this systematic review and meta-analysis preparation and performed all steps according to the Cochrane Handbook of Systematic Reviews of Intervention. [(9)]

Search strategy and study selection

We searched PubMed, Scopus, Cochrane, WOS, Embase, and Science Direct on 15 June 2021 and updated the search on 10 July 2021 using relevant keywords. We used the following search strategy for searching different databases: ("Total disc replacement" OR "Replacement, Total Disc" OR "Total Disc Replacements" OR "Arthroplasty, Replacement, Disk" OR "Artificial Disk Replacement" OR "Artificial Disk Replacements" OR "Disk Replacement, Artificial" OR "Disk Replacements, Artificial" OR "Replacement, Artificial Disk" OR "Replacements, Artificial Disk" OR "Total Disc Arthroplasty" OR "Arthroplasties, Total Disc" OR "Arthroplasty, Total Disc" OR "Disc Arthroplasties, Total" OR "Disc Arthroplasty, Total" OR "Total Disc Arthroplasties" OR "Total Disk Arthroplasty" OR "Arthroplasties, Total Disk" OR "Arthroplasty, Total Disk" OR "Total Disk Arthroplasties" OR "Arthroplasty, Replacement, Disc" OR "Artificial Disc Replacement") and (Anterior cervical discectomy and fusion OR ACDF OR Cervical herniation).

Eligibility criteria and study selection

We included studies that followed the following criteria: **(1)** Adult patients above 18 years old **(2)** Double arm designs **(3)** Studies designs are limited to randomized control trials (RCT) to obtain high-quality evidence **(4)** English studies **(5)** Outcomes either clinical or radiological are acceptable. We excluded conference abstracts or unpublished data, studies written in a language other than English, in-vitro studies, and duplicated articles by the same author unless those with longer follow-up studies. All published articles were screened with no restrictions for data search. Titles and abstracts were done in two parts, followed by full-text screening. Reference lists of the included studies were manually screened to find any other eligible studies that may be omitted from previous steps.

Quality assessment

The risk of bias was evaluated by the Cochrane Handbook of Systematic Reviews of Interventions 5.1.0 [(10)], which included the following risks: selection bias "through random sequence generation and allocation concealment," selective reporting, attrition bias, performance bias through blinding of participants, and personnel, detection bias through blinding of outcome assessment. Each bias domain is recorded as one of the following: low risk, high risk, or unclear risk.

Data Sources:

Medline databases (PubMed, Medscape, ScienceDirect. EMF-Portal) and all materials available on the Internet till 2021.

Data Extraction

We obtained data from text, tables (using Graph Grabber version 2.0), and supplementary data. We focused on the following outcome measures:

Overall symptomatic adjacent level disease requiring surgery (SALDRS), SALDRS after 5, 7, and 9 years follow-up postoperatively, postoperative patient satisfaction, Neck Disability Index (NDI), Dysphagia, Major Complication, and overall adverse events, Subsequent Surgical intervention, Postoperative Neck, and arm pain VAS scores 48 months, Mental component of SF-12 questionnaire, and the physical component of the SF-12 questionnaire was assessed and compared.

Statistical Analysis

We conducted this meta-analysis by using Review Manager (RevMan) (Computer program) (Version 5.4. Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2014). Regarding the study outcomes, risk ratio (RR) with 95% confidence interval (CI) was used for dichotomous variables, while the mean difference (MD) and 95% CI were presented for continuous variables. Cochrane's *P* values and I^2 were tested to examine heterogeneity among the studies. High heterogeneity most likely existed due to clinical and methodological factors, so the random effect model was adopted in this meta-analysis even though I^2 was small. Funnel plots and the Egger regression test could not be performed due to the limited number of included trials. (Less than ten studies. Besides, a sensitivity analysis was performed by sequentially deleting trials to check the stability of the primary outcomes.

RESULTS

Literature search results

The initial search resulted in 2693 articles from six databases: 551 articles from PubMed, 56 articles from Cochrane, 958 articles from Scopus, 215 articles from WOS, 659 articles from Embase, and 254 from ScienceDirect. In addition to 98 records from other different databases. Of these 2791 articles. We excluded 856 articles due to duplication. 1935 articles underwent title and abstract screening, and 1870 were excluded because they did not meet the inclusion criteria. The remaining 65 articles underwent full-text screening. A total of ten studies were finally included in the final qualitative analysis, and nine studies were included in the quantitative analysis.

Characteristics of the included studies

We identified ten studies comparing TDR with ACDF with a total number of 2004 patients who underwent TDR and 1510 patients who underwent ACDF. The age range of patients across the studies ranged between 60 and 90 years. All study designs were limited to randomized controlled trials (RCTs) from 2015 to 2021 to obtain high-quality evidence. The summary and baseline characteristics of the included studies are described in **Table 1**.

Table (1): Summary and baseline characteristics of the included studies

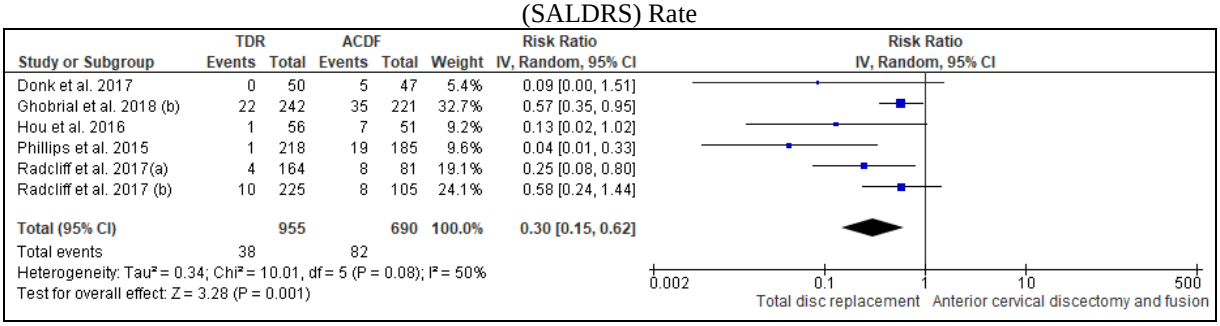
Study ID	Design	Sample size		Age, mean (SD)		Male gender, N (%)		Follow-up duration	Prosthesis	Follow-up rate	
		TDR	ACDF	TDR	ACDF	TDR	ACDF			TDR	ACDF
Phillips, et al. [12]	RCT single-center study	218	185	-	-	-	-	84 months	PCM	31.2%	22.7%
Hou, et al. [15]	RCT single-center study	56	51	46.3 (7.8)	48.5 (8.3)	30 (54%)	28 (55%)	61 months	Mobi-C	91.1%	94.1%
Hisey, et al. [2]	RCT single-center study	164	81	-	-	-	-	60 months	Mobi-C	85.5%	78.9%
Donk, et al. [14]	RCT single-center study	50	47	44.3 (5.6)	43.1 (7.5)	23 (46%)	22 (49%)	9 months	Bryan	98.0%	97.9%
Radcliff, et al. [13]	RCT multi-center study	164	81	43.3 (9.2)	44.0 (8.2)	78 (47.6%)	36 (44.4%)	84 months	Mobi-C	80.1%	74.3%
		225	105	45.3 (8.1)	46.2 (8.0)	113 (50.2%)	45 (42.9%)	84 months	Mobi-C	84.4%	75.0%
Ghobrial, et al. [11]	RCT multicenter study	518	486	-	-	-	-	84 months	Bryan/ Prestige ST	Not specified	Not specified
		242	221	-	-	-	-	120 months	Bryan	53.7%	46.6%
Janssen, et al. [19]	RCT single-center study	103	106	42.1 (8.42)	43.5 (7.15)	48 (47%)	52 (49%)	7 months	ProDisc-C	92%	92%
Sasso, et al. [20]	RCT single-center study	22	25	-	-	-	-	10 months	Bryan	86.40%	92%
Davis, et al. [17]	RCT single-center study	225	105	45.3 (8.1)	46.2 (8)	113 (50.2%)	45 (42.9%)	48 months	Mobi-C	89.0%	81.2%
Pandey, et al. [18]	RCT single-center study	17	17	39.7 (29-57)	39.7 (31-55)	14	13	18 months	-	Not specified	Not specified

Outcomes

Overall postoperative symptomatic adjacent level disease requiring surgery (SALDRS) Rate

The pooled analysis of the included studies showed a significant difference between TDR versus ACDF favoring TDR over ACDF (RR = 0.30; 95% CI: [0.15, 0.62]; *P* = 0.001). [11-15] The pooled studies were heterogeneous (I2 = 50%, P = 0.08) and the heterogeneity was best resolved by excluding Philips et al.[12] (I2 = 17%, P = 0.3). Table 2

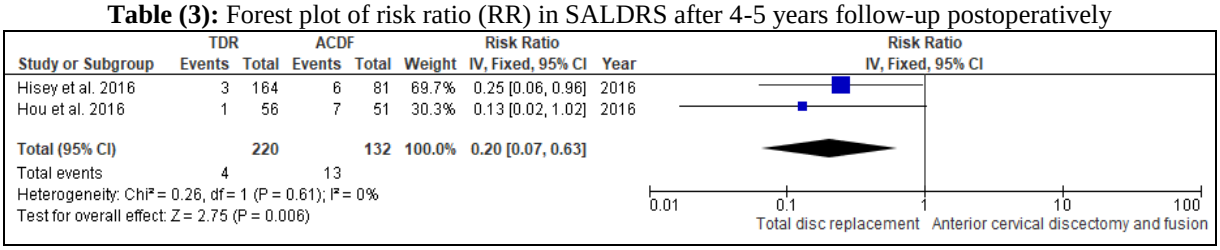
Table (2): Forest Plot of Risk Ratio (RR) in Overall postoperative symptomatic adjacent level disease requiring surgery (SALDRS) Rate



SALDRS after 4-5 years follow-up

The pooled analysis of the included studies showed a significant difference between TDR and ACDF favoring TDR over ACDF (RR = 0.20; 95% CI: [0.07, 0.63]; P = 0.006). [15,16] The pooled studies were homogenous (I2 = 0%, P = 0.61). Table 3

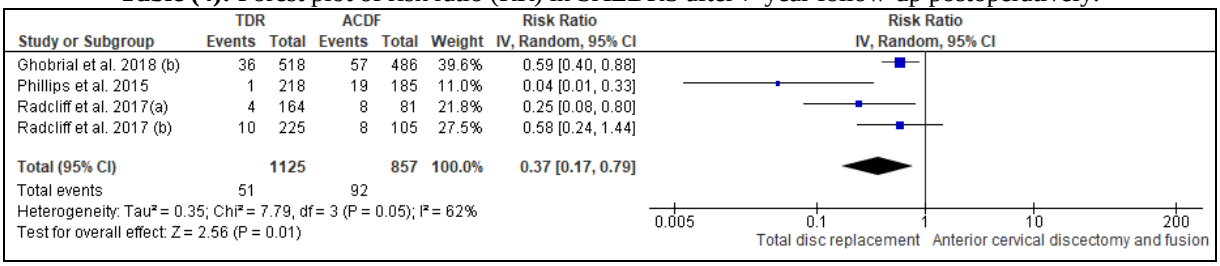
Table (3): Forest plot of risk ratio (RR) in SALDRS after 4-5 years follow-up postoperatively



SALDRS after 7 years follow-up

The pooled analysis of the included studies showed a significant difference between TDR and ACDF favoring TDR over ACDF (RR = 0.37; 95% CI: [0.17, 0.79]; *P* = 0.01). [11-13] The pooled studies were heterogeneous (I2 = 62%, P = 2.56) and the heterogeneity was best resolved by excluding Philips et al.[12] (I2 = 0%, P = 0.38). Table 4

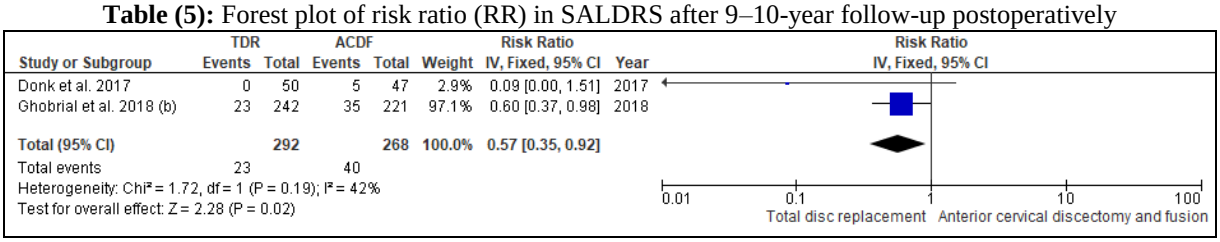
Table (4): Forest plot of risk ratio (RR) in SALDRS after 7-year follow-up postoperatively.



SALDRS after 9-10 years follow up

The pooled analysis of the included studies showed a significant difference between TDR and ACDF favoring TDR over ACDF (RR = 0.57; 95% CI: [0.35, 0.92]; *P* = 0.02). [11,14] The pooled studies were homogenous (I2 = 42%, P = 0.19). Table 5

Table (5): Forest plot of risk ratio (RR) in SALDRS after 9–10-year follow-up postoperatively



Postoperative patient satisfaction.

The pooled analysis of the included studies showed a significant difference between TDR and ACDF regarding postoperative satisfaction of patients undergoing surgery favoring TDR over ACDF (RR = 1.01; 95% CI: [1.04, 1.17]; *P* = 0.0001).[12,15,17] The pooled studies were homogenous (I2 = 0%, P = 0.77).

Neck Disability Index (NDI)

The pooled analysis of the included studies showed no significant difference between TDR and ACDF regarding NDI (MD = 0.68, 95% CI: [-1.74, 13.06]; P = 0.81). [13,15-18] The pooled studies were heterogeneous (I2 = 98%, P < 0.00001). The heterogeneity could not be resolved due to the high variation between the studies' results.

Dysphagia.

The pooled analysis of the included studies showed no significant difference between TDR and ACDF regarding dysphagia as an adverse event (RR = 0.24, 95% CI: [0.04, 1.39]; P = 0.11). [14,19] The pooled studies were homogenous (I2 = 0%, P = 0.90).

Major complications and adverse events.

The pooled analysis of the included studies showed no significant difference between TDR and ACDF regarding postoperative adverse events (RR = 0.81, 95% CI: [0.61, 1.07]; P = 0.13)[4,9,12]. The pooled studies were homogenous (I2 = 0%, P = 0.57).

Subsequent Surgical intervention.

The pooled analysis of the included studies showed a significant difference between TDR and ACDF regarding subsequent surgical intervention favoring TDR over ACDF (RR = 0.26, 95%; CI[0.16, 0.43]; P < 0.00001) [13,17] The pooled studies were homogenous (I2 = 0%, P = 0.99)

Postoperative neck and arm pain VAS scores 48 months.

The pooled analysis of the included studies showed no significant difference between TDR and ACDF regarding postoperative Neck and arm pain VAS scores at 48 months either for neck VAS score (MD = -0.50, 95%; CI[-4.23, 3.23]; P = 0.79) or arm VAS score (MD = 9.88, 95%; CI[-13.09, 32.85]; P = 0.4). In total, there is no significant difference between TDR and ACDF (MD = 4.42, 95%; CI[-3.84, 12.67]; P = 0.29). [13-16,17,19] The pooled studies were heterogeneous (I2 = 100%, P < 0.00001). The heterogeneity could not be resolved due to the high variation between the study's results.

The mental component of the SF-36 questionnaire.

The pooled analysis of the included studies showed no significant difference between TDR and ACDF regarding the mental component of the SF-36 questionnaire (MD = 1.04, 95% CI: [-0.72, 2.79], P = 0.25). [13,17] The pooled studies were homogenous (I2 = 13%, P = 0.32).

The physical component of the SF-36 questionnaire.

The pooled analysis of the included studies showed a significant difference between TDR and ACDF regarding the physical component of the SF-36 questionnaire (MD = 3.07, 95% CI: [1.48, 4.65], P = 0.0002)[13,17] favoring TDR over ACDF. The pooled studies were homogenous (I2 = 0%, P = 0.83).

DISCUSSION

Many clinical results are satisfactory following TDR over ACDF. However, the question of whether TDR can reduce the incidence of cervical disc herniation and adjacent segment disease is uncertain. [21, 22]

Recently, TDR is a major non-fusion surgical procedure, designed to retain as much as possible the intervertebral disc height and segmental activity, to reduce the accelerated ASD that is often caused by ACDF. Its short-term clinical results have been well demonstrated, but the studies reporting long-term curative effects are scarce. [5]

Cervical disc replacement differs from ACDF in that rather than fusing the adjacent vertebrae, an artificial disc is inserted to maintain motion between the vertebrae. Some studies show that

disc replacement maintains more natural biomechanics within the cervical spine and places less stress on the discs above and below the surgical level than ACDF. [23]

In the present study, we searched a lot of randomized controlled trials exhaustively and performed a meta-analysis to compare the mid-to-long-term postoperative incidence of SALDRS between ACDF and TDR. We found that the overall SALDRS rate of the TDR group was significantly lower than that of the ACDF group after a minimum follow-up period of 48 months with a P-value of 0.0001. Ren et al. [24] reported that the rate of requiring operation for ASD was not significantly different between patients in the TDR group and the ACDF group; however, the result was derived from only 3 RCTs. Due to the lack of studies reporting on ASD as the indication for operation and the small sample size, Zhang et al. [25] reported that the rate of operations at the adjacent level was not significantly different between the TDR and ACDF groups in their meta-analysis.

Also, regarding longer follow-up durations of 4-5 years in terms of SALDRS rate, we found a significant positive result towards the TDR compared to ACDF (P = 0.006). Seven and nine years postoperatively showed also a significant favorable effect of TDR over ACDF with P-values of 0.01 and 0.02 respectively. Similar results were found by Ghobrial et al. [11]. They reported that symptomatic adjacent-level degeneration did not achieve statistical significance. However, when data from prospective, randomized studies combined to increase the power of the assessment, a significant difference in SADLRS was observed at a 7-year follow-up.

A prospective randomized comparison conducted by Hisey et al. [16] revealed significant improvements in pain and function. Also, TDR patients maintained motion and had significantly lower rates of reoperation and adjacent-segment degeneration compared with ACDF. We agree with the results of Hisey et al. and Ghobrial et al. [11] regarding the significant improvements in TDR patients compared to ACDF.

We also agree with the previous meta-analysis conducted by Findlay et al. [26], they reviewed other outcome measures showing that patients report TDR to be at least as effective as ACDF, and at four to seven years it is superior for most outcomes, including the range of movement, further surgery, satisfaction, and dysphagia.

Regarding dysphagia, we have also found no significant difference between both TDR and ACDF postoperatively with a P-value of 0.11. One trial by Phillips et al. reported dysphagia between four and seven years, with a lower incidence in TDR. [12]

Postoperative major complication showed no significant difference between both TDR and ACDF postoperatively with a P-value of 0.13. However, Hisey et al. [16] supported the safety and efficacy of TDR in appropriately selected patients compared to ACDF.

Some results obtained by Findlay et al. [26] showed that TDR is at least as effective as ACDF for the treatment of degenerative cervical disc herniation, for all patient-reported outcomes. Both treatments provided significant improvement in NDI, neck and arm pain VAS, and SF-36 physical and mental component scores. However, neither TDR nor ACDF resulted in the complete relief of symptoms.

In terms of the neck disability index (NDI), there was no significant difference between either TDR or ACDF postoperatively (P = 0.81). However, Hisey et al. [16] mean Neck Disability Index, visual analog scale, and SF-12 scores were significantly improved in early follow-up in both groups with improvements maintained throughout 48 months. On some measures, TDR had significantly greater improvement during early follow-up.

Regarding the pain score of the neck and the arm _ assessed by VAS score_, there was no significant difference between both groups of TDR and ACDF in either arm or neck pain with P- values of 0.79, and 0.40 respectively. Five of seven trials reporting neck pain also showed significantly lower scores after TDR [27-29] However, arm pain was the only outcome at three months for which most studies did not show TDR to be superior to ACDF. [29,30]

The analysis of our study regarding the SF-36 questionnaire showed a significant difference in physical functioning (P = 0.0002). However, no significant difference was detected regarding the mental component of SF-36 (P = 32). One study reporting SF-36 physical scores at three months found TDR to be superior. [29] Between four and seven years, the number of trials reporting significant superiority of TDR increased compared with the results at two years. Of those reporting NDI, 50% favored TDR, as did 50% of those reporting SF-36 physical component scores. [19]

CONCLUSION

SALDRS rates of the TDR group were significantly lower than those of the ACDF group at 48–120 months' follow-up and different follow-up periods, and the SALDRS rate of the TDR group with unrestricted prosthesis was significantly lower than that of the ACDF group. TDR showed significant positive results regarding

postoperative satisfaction as well as reduced risk of adjacent segment disease requiring subsequent surgical intervention. Physical functioning in SF-36 showed favored results of TDR over ACDF. Higher-quality RCTs with longer-term follow-up are required to achieve a better comparative analysis of the SALDRS rate after TDR and ACDF. No trial reported a single outcome at any time point to suggest that ACDF may be superior to TDR.

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