Utilization of the Fragility Index to Assess Randomized Controlled Trials comparing Cervical Total Disc Arthroplasty to Anterior Cervical Discectomy and Fusion

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INTRODUCTION

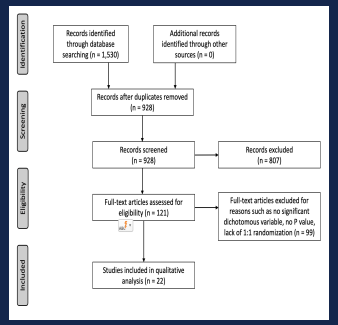
Background Cervical total disc arthroplasty (cTDA) remains an alternative to anterior cervical discectomy and fusion (ACDF) in select patients with cervical radiculopathy or myelopathy secondary to degenerative disc disease. RCTs investigating CTDA often have conflicting conclusions and varying quality.

Rationale The fragility index (FI) is a metric that can be used to assess the robustness of statistically significant, dichotomous outcome variables in RCTs. Spine literature is amongst the least robust, with 75% of RCTs boasting an FI less than 3.[1,2] A review of studies classified as robust by the AAOS suggests a threshold FI of ≥ 2.[3]

Objective To investigate the fragility of RCTs comparing cTDA vs ACDF.

METHODS

A systematic review was performed by searching PubMed, Ovid MEDLINE, Web of Science, and Embase for RCTs with two parallel study arms and 1:1 allocation of subjects to treatment or control groups investigating CTDA vs. ACDF with at least one statistically significant, dichotomous outcome. The FI was calculated by individually shifting one patient from the event group to the non-event group with re-calculation of Fisher's Exact test until the reported P value was no longer statistically significant ($p > 0.05$).



RESULTS

The search identified 934 abstracts for screening with 22 RCTs meeting inclusion criteria. The mean patient sample size was 277.1 (median 209, range 30-541). The number of patients lost to follow-up was 0 in only 1 of the studies and ranged from 0-231 (mean 74.3, median 45). The reported P-value of the significant dichotomous outcomes used for FI calculation ranged from <0.001 to 0.049. The mean FI of all included studies was 2.27 (range 0-7, median 1.5, mode 1) with 3 (13.6%) studies having an associated FI of 0. The FI was <2 in 68.2% (15/22) of studies and ≥2 in 31.8% (7/22) of studies. Three studies had an FI of zero Loss to follow up exceeded the fragility index in all but one of the 22 included studies.

Study	Journal	Study Comparison	Primary Outcome	Significant Dichotomous Outcome	Total. No. Patients	Number Lost to Follow-up	P-Value	FI
Anderson et al. 2008	Spine	cTDA vs ACDF (Single Level)	2-year Adverse Events	Adverse Medical Events (6 wks - 3 years)	463	46	0.049	0
Burkus et al. 2014	Journal of Neurosurgery	cTDA vs ACDF (Single Level)	2-year Clinical Outcomes (NDI, neurological status) and Segmental Motion	Maintenance of Neurologic al Status	541	146	0.017	1
Cheng et al. 2011	Clinical Orthopaedics and Related Research	cTDA vs ACDF (1, 2 and 3 Level)	3 year Clinical and Radiographic Efficacy and Safety Modified Odom's Criteria, JOA, SF-36, NDI, ROM, Stability, Subsidence)	Dysphagia	83	2	<0.001	1
Coric et al. 2010	Journal of Neurosurgery: Spine	cTDA vs ACDF (Single Level)	5-year Clinical Outcomes and Efficacy (NDI, NPI, VAS, Composite Success)	Composite Clinical Success	98	8	0.035	0
Coric et al. 2011	Journal of Neurosurgery: Spine	cTDA vs ACDF (Single Level)	2-year Clinical Outcomes and Efficacy (NDI, NPI, VAS, Composite Success)	Composite Overall Success	269	35	0.05	7
Delamarter et al. 2010	SAS Journal	cTDA vs ACDF (Single Level)	4 year Clinical and Radiographic Efficacy (NDI, VAS, Neurological exam, Reoperations)	48-month Rates of Re-operation	209	95	0.0292	1
Delamarter et al. 2013	Spine	cTDA vs ACDF (Single Level)	5-year Reasons/Rates Secondary Surgical Interventions	5 Year Rates of Re-operation	209	76	0.0079	6
Heller et al. 2009	Spine	cTDA vs ACDF (Single Level)	2-year Clinical Outcomes (NDI, Composite Neurological Success)	Composite Neurologic al Success	463	39	0.01	4
Hou et al. 2016	The Bone & Joint Journal	cTDA vs ACDF (Single Level)	5-year Safety and Efficacy (JOA, VAS, NDI, ROM, secondary surgeries)	Rate of Secondary Surgery	108	8	0.49	1
Howell et al. 2015	Spine Journal	cTDA vs ACDF (Single Level)	7 year Clinical and Radiographic Safety and Efficacy (NDI, PI satisfaction, Disc Height, ROM, Secondary surgeries, Adjacent segment Disease)	Maintenance of Normal Disc Height	404	225	<0.001	5
Janssen et al. 2014	Global Spine Journal	cTDA vs ACDF (Single Level)	2-year Safety and Efficacy (VAS, NDI, MOS-SF36, Neurological Success, Adverse Events, Secondary Surgeries)	Number of Secondary Procedures	209	44	0.0099	2
Janssen et al. 2015	Journal of Bone and Joint Surgery	cTDA vs ACDF (Single Level)	7 year Safety and Efficacy (VAS, NDI, SF-36, Neurological Parameters, Secondary Surgeries, Adverse Events, Neck/Arm Pain, Satisfaction Scores)	Number of Secondary Procedures	165	13	0.0099	2
Lavelle et al. 2019	Spine	cTDA vs ACDF (Single Level)	10 year Overall Composite Success (NDI, Neurologic Status, Adverse Events, Reoperation, Failures)	Overall Success Rate	463	231	0.005	4
Leduc et al. 2021	Spine Journal	cTDA vs ACDF (Single Level)	10-year Adverse Events	Cumulative Rate of All Adverse Events	463	229	0.012	2
Murrey et al. 2009	Spine Journal	cTDA vs ACDF (Single Level)	2-year Clinical Safety and Efficacy (NDI, SF-36, VAS, Composite Neurologic Success)	Neurologic al Success	209	7	0.046	1
Phillips et al. 2013	Spine	cTDA vs ACDF (Single Level)	2-year Safety and Efficacy (NDI, VAS, Neurological Status, Composite Overall Success)	No deterioratio n of myelopathy	403	65	0.018	2
Phillips et al. 2015	Spine	cTDA vs ACDF (Single Level)	5-year Safety and Efficacy (NDI, VAS, Neurological Status, Adverse Events, Reoperation, Fusion, Adjacent Segment Disease)	NDI Success	403	115	0.026	2
Quirk et al. 2016	Clinical Spine Surgery	cTDA vs ACDF (2 Non-contiguous Levels)	2.5 year Clinical and Radiographic Safety and Efficacy (JOA, NDI, Lordosis, Complications)	Rate of Adjacent Segment Disease	30	0	0.04	0
Sasso et al. 2011	Journal of Bone and Joint Surgery	cTDA vs ACDF (Single Level)	4-year Composite Overall Success	Composite Overall Success	463	144	0.004	6
Sasselli et al. 2017	European Spine Journal	cTDA vs ACDF (Single Level)	2-year NDI	Frequency of Reoperatio n	136	16	0.029	1
Yang et al. 2018	Orthopedics	cTDA vs ACDF (2 Contiguous Levels)	5 Year Safety and Efficacy (NDI, JOA, VAS)	Rate of Adjacent Segment Disease	96	16	<.05	3
Zigler et al. 2013	Spine	cTDA vs ACDF (Single Level)	5-year Safety and Efficacy (NDI, VAS, SF-36, Neurological Exam, Device Success, Adverse Events, Satisfaction)	Rate of Secondary Surgery	209	76	0.0292	1

DISCUSSION

Overall, comparison suggests that the data regarding cTDA vs ACDF (median 1.5) is inherently more fragile than the totality of spine literature (median 2.0), despite the fact that cTDA vs ACDF studies comprise a substantial component (n=7, 17.5%) of this volume.[1,3] This could indicate that there is only a very slight difference in outcome between ACDF and cTDA, leading the outcomes to appear fragile.

Indeed, the notion that ASD is higher in ACDF was refuted by a meta-analysis by Verma et al., which included many of the same trials as the current study, demonstrating no difference in rates of ASD.[21] A powerful clinical argument to this point is that intervention is often strongly dictated by surgeon preference as it is universally agreed upon that patients do quite well with either option

Additionally, the loss of follow-up amounting to substantially greater than the >20% threshold suggested by Dettori et al. suggests that serious concerns are warranted with regards to study validity for cTDA vs ACDF literature.[6] Said bias and study fragility likely contribute to discrepancies in outcomes between similar cTDA vs ACDF studies.

CONCLUSION

The FI of CDA vs. ACDF literature is quite low and, therefore, fragile. The high average loss to follow-up raises concerns for significant result bias. Discordant outcomes between studies are likely be attributed to the low FIs and high losses to follow-up.

Sources Cited:

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