Editorial

Editorial on "Long-term clinical outcomes of cervical disc arthroplasty: a prospective, randomized, controlled trial" by Sasso *et al*.

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In the paper entitled "Long-term clinical outcomes of cervical disc arthroplasty: a prospective, randomized, controlled trial", Sasso *et al*. present seven and ten-year single center data from patients enrolled in the initial FDA Investigational Device Exemption trial of the BRYAN® cervical arthroplasty device. The authors should be commended on the quality of their investigation, as prospective randomized trials with such long term follow-up are a rarity in spine surgery.

The authors present seven and ten-year follow up on 44 and 42 patients, respectively, who underwent anterior cervical discectomy and fusion (ACDF) or cervical disc arthroplasty (CDA) for single level cervical degenerative disease with radiculopathy or myelopathy. Seven years after surgery, the CDA group had lower neck disability index (NDI) scores and VAS neck and arm pain scores. Ten years after surgery, there remained a statistically significant difference in NDI scores favoring CDA, but no difference in VAS arm and neck pain scores. At 10 years, 9% of the CDA group and 32% of the ACDF group had reoperations, which trended towards statistical significance (P=0.55). One of two reoperations in the CDA group and 6 of 8 reoperations in the ACDF group was for adjacent level pathology.

The long-term results presented by Sasso *et al*. suggest an advantage for CDA for single level cervical spondylosis with associated radiculopathy or myelopathy, in agreement with several prior studies reporting shorter follow-up (1-6). Some intermediate follow-up has also echoed similar benefits for CDA, while other studies have suggested convergence of clinical results, with maintained advantage in terms of range of motion and reoperation for CDA (7-12). Indeed, larger registry studies, application of this technology outside of the U.S., and investigations of Worker's Compensation patients have made these conclusions even more generalizable (13-15). Meta-analyses have shown mixed results. A Cochrane Database Review of 2,400 patients showed a statistically significant difference in arm pain, neck pain, neurological outcome and segmental mobility favoring CDA but no difference in reoperation rates (16). However, other studies have suggested lower rates of reoperation at the index and adjacent levels in CDA (17,18).

This newest study has the strength of a prospective, blinded, randomized design with nearly 90% percent follow up at 10 years and use of validated outcome measures. The statistically significant difference in NDI scores meets the threshold of minimal clinically important difference of 5 points. At final follow-up, there were no reoperations at the index level in the CDA group. However, there are aspects of the study that warrant careful scrutiny. Sample size is small, and the study and randomization process was industry-sponsored without explanation regarding up to 15 patients who were deemed ineligible by the sponsor. Comorbidities and social factors (such as socioeconomic status, mental illness, opioid dependence, smoking etc.) that have been shown to affect clinical outcomes following spine surgery were not compared to determine uniformity between the groups (19,20). Finally, the study reports

overall reoperation rate for all causes rather than assessing reoperation rates as it relates to index surgery and adjacent segment disease specifically.

In the current healthcare climate, clinical outcomes of new interventions must be interpreted in the context of cost-effectiveness. Several studies have evaluated this metric in CDA. Multiple studies using advanced statistical modeling have suggested CDA is more cost effective than ACDF (21-23). However, in these models, conclusions only hold true if certain assumed survivorship of implants and rate of reoperation are accurate. Radcliff *et al*. used a database study to evaluate real costs of these interventions and found reduced index and total costs for CDA compared to ACDF (24).

Even with favorable clinical results and cost-effectiveness data, CDA also introduces previously unseen complications to cervical spine surgery. Studies have shown areas of significant osteolysis around CDA implants that may lead to implant malfunction and complicate future surgical interventions (25-27). Case reports have highlighted hypersensitivity to implant metals, implant fracture, and reactions to metal debris (28,29). As the earliest CDA implants now approach 10 years, what other complications may we see? The complications of ACDF are well-documented and catastrophic events are rare. These questions are not yet answered about CDA. Most CDA implants are metal on polyethylene, which can develop wear and may lead to similar immune reactions as seen in hip and knee arthroplasty. The few metal on metal implants form metal debris that can lead to lymphocyte activation and may lead to a pseudotumor-type reaction as seen in metal on metal hip arthroplasty (30,31). If these reactions can lead to problems in large volume areas such as the hip and knee, what can we expect in the small volume area of the cervical spine, near essential structures such as the spinal cord, trachea, and esophagus?

The more widespread adoption of CDA is inevitable as longer term data, such as that reported by Sasso *et al*., continue to support its clinical benefits. With the potential for new and unexpected complications comes the opportunity to learn from our colleagues in the joint replacement community and perhaps develop a central registry where details of optimal implants, techniques, and complications can be collected.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Heller JG, Sasso RC, Papadopoulos SM, et al. Comparison of BRYAN cervical disc arthroplasty with anterior cervical decompression and fusion: clinical and radiographic results of a randomized, controlled, clinical trial. Spine (Phila Pa 1976) 2009;34:101-7.
2. Hisey MS, Bae HW, Davis R, et al. Multi-center, prospective, randomized, controlled investigational device exemption clinical trial comparing Mobi-C Cervical Artificial Disc to anterior discectomy and fusion in the treatment of symptomatic degenerative disc disease in the cervical spine. Int J Spine Surg 2014;8.
3. Phillips FM, Lee JY, Geisler FH, et al. A prospective, randomized, controlled clinical investigation comparing PCM cervical disc arthroplasty with anterior cervical discectomy and fusion. 2-year results from the US FDA IDE clinical trial. Spine (Phila Pa 1976) 2013;38:E907-18.
4. Mummaneni PV, Burkus JK, Haid RW, et al. Clinical and radiographic analysis of cervical disc arthroplasty compared with allograft fusion: a randomized controlled clinical trial. J Neurosurg Spine 2007;6:198-209.
5. Gornet MF, Burkus JK, Shaffrey ME, et al. Cervical disc arthroplasty with PRESTIGE LP disc versus anterior cervical discectomy and fusion: a prospective, multicenter investigational device exemption study. J Neurosurg Spine 2015:1-16.
6. Murrey D, Janssen M, Delamarter R, et al. Results of the prospective, randomized, controlled multicenter Food and Drug Administration investigational device exemption study of the ProDisc-C total disc replacement versus anterior discectomy and fusion for the treatment of 1-level symptomatic cervical disc disease. Spine J 2009;9:275-86.
7. Hisey MS, Bae HW, Davis RJ, et al. Prospective, Randomized Comparison of Cervical Total Disk Replacement Versus Anterior Cervical Fusion: Results at 48 Months Follow-up. J Spinal Disord Tech 2015;28:E237-43.
8. Sasso RC, Anderson PA, Riew KD, et al. Results of cervical arthroplasty compared with anterior discectomy and fusion: four-year clinical outcomes in a prospective,

randomized controlled trial. J Bone Joint Surg Am 2011;93:1684-92.
9. Delamarter RB, Murrey D, Janssen ME, et al. Results at 24 months from the prospective, randomized, multicenter Investigational Device Exemption trial of ProDisc-C versus anterior cervical discectomy and fusion with 4-year follow-up and continued access patients. SAS J 2010;4:122-8.
10. Zigler JE, Delamarter R, Murrey D, et al. ProDisc-C and anterior cervical discectomy and fusion as surgical treatment for single-level cervical symptomatic degenerative disc disease: five-year results of a Food and Drug Administration study. Spine (Phila Pa 1976) 2013;38:203-9.
11. Janssen ME, Zigler JE, Spivak JM, et al. ProDisc-C Total Disc Replacement Versus Anterior Cervical Discectomy and Fusion for Single-Level Symptomatic Cervical Disc Disease: Seven-Year Follow-up of the Prospective Randomized U.S. Food and Drug Administration Investigational Device Exemption Study. J Bone Joint Surg Am 2015;97:1738-47.
12. Hisey MS, Zigler JE, Jackson R, et al. Prospective, Randomized Comparison of One-level Mobi-C Cervical Total Disc Replacement vs. Anterior Cervical Discectomy and Fusion: Results at 5-year Follow-up. Int J Spine Surg 2016;10:10.
13. Staub LP, Ryser C, Röder C, et al. Total disc arthroplasty versus anterior cervical interbody fusion: use of the Spine Tango registry to supplement the evidence from randomized control trials. Spine J 2016;16:136-45.
14. Zhang X, Zhang X, Chen C, et al. Randomized, controlled, multicenter, clinical trial comparing BRYAN cervical disc arthroplasty with anterior cervical decompression and fusion in China. Spine (Phila Pa 1976) 2012;37:433-8.
15. Gornet MF, Schranck FW, Copay AG, et al. The Effect of Workers' Compensation Status on Outcomes of Cervical Disc Arthroplasty: A Prospective, Comparative, Observational Study. J Bone Joint Surg Am 2016;98:93-9.
16. Boselie TF, Willems PC, van Mameren H, et al. Arthroplasty versus fusion in single-level cervical degenerative disc disease. Cochrane Database Syst Rev 2012;(9):CD009173.
17. Zhu Y, Zhang B, Liu H, et al. Cervical Disc Arthroplasty Versus Anterior Cervical Discectomy and Fusion for Incidence of Symptomatic Adjacent Segment Disease: A Meta-Analysis of Prospective Randomized Controlled Trials. Spine (Phila Pa 1976) 2016;41:1493-502.
18. Zhong ZM, Zhu SY, Zhuang JS, et al. Reoperation After Cervical Disc Arthroplasty Versus Anterior Cervical Discectomy and Fusion: A Meta-analysis. Clin Orthop Relat Res 2016;474:1307-16.
19. Armaghani SJ, Lee DS, Bible JE, et al. Preoperative narcotic use and its relation to depression and anxiety in patients undergoing spine surgery. Spine (Phila Pa 1976) 2013;38:2196-200.
20. Lee D, Armaghani S, Archer KR, et al. Preoperative Opioid Use as a Predictor of Adverse Postoperative Self-Reported Outcomes in Patients Undergoing Spine Surgery. J Bone Joint Surg Am 2014;96:e89.
21. McAnany SJ, Overley S, Baird EO, et al. The 5-year cost-effectiveness of anterior cervical discectomy and fusion and cervical disc replacement: a Markov analysis. Spine (Phila Pa 1976) 2014;39:1924-33.
22. Ament JD, Yang Z, Nunley P, et al. Cost-effectiveness of cervical total disc replacement vs fusion for the treatment of 2-level symptomatic degenerative disc disease. JAMA Surg 2014;149:1231-9.
23. Ghori A, Konopka JF, Makanji H, et al. Long Term Societal Costs of Anterior Discectomy and Fusion (ACDF) versus Cervical Disc Arthroplasty (CDA) for Treatment of Cervical Radiculopathy. Int J Spine Surg 2016;10:1.
24. Radcliff K, Zigler J, Zigler J. Costs of cervical disc replacement versus anterior cervical discectomy and fusion for treatment of single-level cervical disc disease: an analysis of the Blue Health Intelligence database for acute and long-term costs and complications. Spine (Phila Pa 1976) 2015;40:521-9.
25. Hacker FM, Babcock RM, Hacker RJ. Very late complications of cervical arthroplasty: results of 2 controlled randomized prospective studies from a single investigator site. Spine (Phila Pa 1976) 2013;38:2223-6.
26. Kim SH, Chung YS, Ropper AE, et al. Bone loss of the superior adjacent vertebral body immediately posterior to the anterior flange of Bryan cervical disc. Eur Spine J 2015;24:2872-9.
27. Tumialán LM, Gluf WM. Progressive vertebral body osteolysis after cervical disc arthroplasty. Spine (Phila Pa 1976) 2011;36:E973-8.
28. Cavanaugh DA, Nunley PD, Kerr EJ 3rd, et al. Delayed hyper-reactivity to metal ions after cervical disc arthroplasty: a case report and literature review. Spine (Phila Pa 1976) 2009;34:E262-5.
29. Fan H, Wu S, Wu Z, et al. Implant failure of Bryan

cervical disc due to broken polyurethane sheath: a case report. Spine (Phila Pa 1976) 2012;37:E814-6.
30. Veruva SY, Steinbeck MJ, Toth J, et al. Which design and biomaterial factors affect clinical wear performance of total disc replacements? A systematic review. Clin Orthop Relat Res 2014;472:3759-69.
31. Staudt MD, Das K, Duggal N. Does design matter? Cervical disc replacements under review. Neurosurg Rev 2016. [Epub ahead of print].

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