J Neurosurg Spine 19:527–531, 2013

Does smoking have an impact on fusion rate in single-level anterior cervical discectomy and fusion with allograft and rigid plate fixation?

Clinical article

Myles Luszczyk, D.O.,[1] Justin S. Smith, M.D., Ph.D.,[2] Jeffrey S. Fischgrund, M.D.,[3] Steven C. Ludwig, M.D.,[4] Rick C. Sasso, M.D.,[5] Christopher I. Shaffrey, M.D.,[2] and Alexander R. Vaccaro, M.D., Ph.D.[6]

[1]ORA Orthopedics PC, Bettendorf, Iowa; [2]Department of Neurological Surgery, University of Virginia Health System, Charlottesville, Virginia; [3]Michigan Orthopaedic Institute, West Bloomfield, Michigan; [4]Department of Orthopaedic Surgery, University of Maryland, Baltimore, Maryland; [5]Indiana Spine Group, Indianapolis, Indiana; and [6]Department of Orthopaedic Surgery, Thomas Jefferson University, Philadelphia, Pennsylvania

Object. Although smoking has been shown to negatively affect fusion rates in patients undergoing multilevel fusions of the cervical and lumbar spine, the effect of smoking on fusion rates in patients undergoing single-level anterior cervical discectomy and fusion (ACDF) with allograft and plate fixation has yet to be thoroughly investigated. The objective of the present study was to address the effect of smoking on fusion rates in patients undergoing a 1-level ACDF with allograft and a locked anterior cervical plate.

Methods. This study is composed of patients from the control groups of 5 separate studies evaluating the use of an anterior cervical disc replacement to treat cervical radiculopathy. For each of the 5 studies the control group consisted of patients who underwent a 1-level ACDF with allograft and a locked cervical plate. The authors of the present study reviewed data obtained in a total of 573 patients; 156 patients were smokers and 417 were nonsmokers. A minimum follow-up period of 24 months was required for inclusion in this study. Fusion status was assessed by independent observers using lateral, neutral, and flexion/extension radiographs.

Results. An overall fusion rate of 91.4% was achieved in all 573 patients. A solid fusion was shown in 382 patients (91.6%) who were nonsmokers. Among patients who were smokers, 142 (91.0%) had radiographic evidence of a solid fusion. A 2-tailed Fisher exact test revealed a p value of 0.867, indicating no difference in the union rates between smokers and nonsmokers.

Conclusions. The authors found no statistically significant difference in fusion status between smokers and nonsmokers who underwent a single-level ACDF with allograft and a locked anterior cervical plate. Although the authors do not promote tobacco use, it appears that the use of allograft with a locked cervical plate in single-level ACDF among smokers produces similar fusion rates as it does in their nonsmoking counterparts.
(http://thejns.org/doi/abs/10.3171/2013.7.SPINE13208)

Key Words • **anterior cervical discectomy and fusion** • **cervical spine** • **nicotine** • **smoking** • **surgery**

For over half a century the anterior approach has been used successfully to perform cervical discectomy and fusions in patients with radiculopathy and/or myelopathy. First championed in the 1950s by Robinson and Smith,[32] it has since been widely described in the treatment of cervical disc disease.[1–3,5,7–11,14–20,23–25,27–31,33–36,40–42,44–47]

The early pioneers of the anterior cervical approach first described their procedure using autogenous bone as an interbody graft.[32] Since that time, many authors have proven the efficacy and safety of allogenic bone as an interbody graft, particularly in single-level anterior cervical fusions.[1,8,24,25,33,35,36,45,46] Moreover, the use of allograft has been shown to avoid complications such as persistent donor-site pain, nerve injury, iliac fracture, hernias, and wound hematomas that can occur from autogenous graft harvesting.[2,8,13,20,26,27,37,43,46]

The first cervical fusions were performed without the use of instrumentation.[9,32] Various studies have since demonstrated the efficacy of using locked plate fixation for improving fusion rates in multi- and single-level cervical fusions.[10,25,33,35,40] Proponents of rigid anterior plate fixation cite benefits of the instrumentation in reducing postoperative kyphosis, lowering the rate of graft-related complications, reducing the need for postoperative brac-

Abbreviations used in this paper: ACDF = anterior cervical discectomy and fusion; IDE = investigational device exemption.

ing, and facilitating quicker return to activities of daily living.[25,40]

Despite the widespread use of the anterior cervical approach in treating cervical disc pathology, achieving a solid fusion has always been a concern. Many associated factors can influence the ability of a graft to incorporate and ultimately prevent a fusion mass from forming. In particular, nicotine has been shown to negatively affect bone healing.[4,12,18,21,22,38,39] Studies of the lumbar spine have demonstrated that smokers have lower rates of fusion as well as poorer clinical outcomes.[6,21] These findings have also been documented in smokers undergoing multilevel anterior cervical decompression and fusion.[1,23] Less convincing is the effect of smoking on single-level anterior cervical fusions. Some studies have shown a trend toward an increased rate of pseudarthrosis in smokers who underwent single-level cervical fusions.[2,27,40] However, due to a lack of power, these studies failed to show statistical significance.

The primary purpose of the present study was to evaluate the impact of smoking on the outcome of radiographic fusion in patients who underwent a single-level anterior cervical discectomy and fusion (ACDF) with allograft and rigid plate fixation.

Methods

The study was composed of a review of data obtained in 573 patients who underwent a single-level ACDF with allograft and locked plate fixation. The patient group was composed of the "control" groups from 5 separate prospective randomized FDA investigational device exemption (IDE) studies evaluating the use of an anterior cervical disc replacement device to treat cervical radiculopathy (Bryan [Medtronic Sofamor Danek], Prestige ST [Medtronic Sofamor Danek], ProDisc-C [DePuy Synthes], CerviCore [Stryker Spine], and PCM [Cervitech]). Each of these 5 studies used anterior cervical fusion with allograft and a locked anterior cervical plate as the control group. Data were obtained directly from sponsoring company data sets and not from the published reports.

Of the 573 patients, 156 were smokers and 417 were nonsmokers. Patients were classified as smokers in the study if they were smoking prior to surgery and during the postoperative period. No distinction was made based upon the amount of cigarettes consumed per day. Indications for surgery included radiculopathy- or myelopathy-related progressive symptoms refractory to conservative treatment of greater than 3 months' duration. These symptoms were the result of a herniated nucleus pulposus or a degenerative cervical segment. The clinical diagnoses were confirmed using both radiography and MRI.

Graft types consisted of fibula allograft, iliac crest allograft, or composite material, and they were selected based on surgeon preference. Selection of plate fixation was based on trial study criteria, but all plates used "locked fixation."

Prior to each procedure, patients received preoperative antibiotics. The surgical technique varied according surgeon preference, but a standard ACDF (the Smith-Robinson technique) was performed in all patients.[32]

After surgery, patients were given either a soft or a rigid cervical collar for comfort and were permitted to gradually resume activities of daily living. They were monitored at regular follow-up visits at 6 weeks and 3, 6, 12, 18, and 24 months postoperatively. A minimum follow period of 24 months was required for inclusion in this study. Follow-up anteroposterior and lateral cervical spine radiographs were taken with the patient's neck in neutral, flexion and extension positions to address fusion status. Fusion was considered successful if there was evidence of bony trabecular bridging between the graft and vertebral body, and if motion was absent on postoperative dynamic images. A pseudarthrosis was diagnosed when lucency was visualized between the graft and vertebral endplate or when motion was detected at the operative segment. Radiographically demonstrated fusion was assessed by independent radiologists and/or orthopedic surgeons. Fusion success for the present study was based on the data reported for each FDA IDE trial. Fusion status was compared between smokers and nonsmokers using a 2-tailed Fisher exact test.

No funding was received in support of the study. Institutional review board approval was obtained for each study prior to patient enrollment and for the present study through the University of Virginia.

Results

A successful arthrodesis was obtained in 524 of the 573 total patients, making the overall fusion rate 91.4%. The rates of nonunion for the IDE trials ranged from 4.0% to 15.5%. In 156 patients who were smokers, 142 had a solid union, resulting in a fusion rate of 91.0%. Similarly, a fusion rate of 91.6% was obtained in the group of patients who did not smoke (382 of 417) (Table 1). The rates of smoking across the 5 IDE trials were similar and ranged from 20.4% to 34.3%. Using a 2-tailed Fisher exact test, a p value of 0.867 was obtained, indicating that there was no significant difference in the union rates between smokers and nonsmokers who had undergone a single-level ACDF with allograft and a fixed locked plate.

Discussion

In single-level fusions in the cervical spine, allograft has been shown to be an efficacious and safe alternative to autogenous bone graft.[1,8,24,25,33,35,36,45,46] In addition, the use of allograft allows for the avoidance of well-known donor-site complications that are associated with the harvesting of autogenous bone.[13,20,26,43] Samartzis et al.[33] reviewed data obtained in 66 patients who underwent single-level ACDF in which rigid plate fixation with allograft or autograft was performed. Their results revealed a 100% fusion rate in the 35 patients in whom allograft was used, whereas a 90.3% fusion rate was documented in the patients in whom autograft was used. In a study by Martin and colleagues of 269 patients who underwent single-level ACDF with freeze-dried fibula allograft, an overall fusion rate of 90% was achieved.[27] The authors' findings supported their belief that the use of allograft is a safe and efficacious alternative to autogenous bone.

TABLE 1: Rates of fusion among 573 patients who underwent ACDF with allograft and rigid plate fixation, stratified by smoking status*

Status	No. of Patients (%)	
	Solid Fusion	Pseudarthrosis
smokers	142 (91.0)	14 (9.0)
nonsmokers	382 (91.6)	35 (8.4)

* p = 0.867, 2-tailed Fisher exact test.

Currently, the vast majority of anterior cervical fusions involve some type of plate system. Kaiser et al.[25] demonstrated a 96% fusion rate in a series of 157 patients who underwent single-level ACDF with allograft and rigid plate fixation. They compared these results to their own previously published study in which they documented a 90% fusion rate in 269 patients who underwent single-level ACDF in which allograft was used without plate fixation. More recently, Fraser and Härtl,[19] in a meta-analysis, showed a statistically significant difference between single-level ACDF performed with plate fixation and single-level ACDF performed without plate fixation (97.1% vs 92.1%, respectively).

Single-level fusions were achieved in the present study using allograft and a locked plating system. In a study of 37 patients who underwent single-level ACDF with allograft and locked plating, Shapiro[35] showed a fusion rate of 100%. Of 28 patients who underwent single-level ACDF with allograft and instrumentation in a study reported by Yue et al.,[45] 96.4% had radiographic and clinical evidence of fusion. Kaiser et al.[25] found a fusion rate of 96% in 157 patients in whom allograft and instrumentation were used in single-level ACDF. In the current study, the overall fusion rate in 573 patients was found to be 91.4%. These results are consistent with those published in previous trials.

The detrimental physiological effects of nicotine on bone healing have been well documented. Nicotine has been shown to decrease cytokines associated with neovascularization and osteoblast differentiation.[12,18,39] Pertaining to the lumbar spine, there is extensive literature demonstrating that smokers have an increased rate of pseudarthrosis.[6,21] Clinical series examining multilevel fusions in the cervical spine have also shown smoking to have a negative impact on fusion rates and clinical outcomes.[1,23] In a series comparing allograft with demineralized bone matrix to autograft in 1-, 2-, and 3-level uninstrumented cervical fusions, An et al.[1] have reported a nonunion rate of 47.1% in smokers and 27.9% in nonsmokers. The data, however, were not extrapolated to isolate the rate of nonunion in smokers versus nonsmokers in single-level cervical fusions. Moreover, Hilibrand and associates[23] reported a 50% nonunion rate in smokers who underwent an uninstrumented multilevel ACDF, further substantiating the negative effects of nicotine on bone healing.

Despite the knowledge that smoking affects fusion status in multilevel ACDF, less is known about smoking's effect on single-level procedures. In patients who underwent a single-level uninstrumented ACDF with allograft, Martin et al.[27] showed a fusion rate of 85% in 71 smokers compared with one of 92% in 198 nonsmokers. They reported that, although there was a trend toward increased rates of nonunion in smokers, the difference was not statistically significant. Wang et al.[40] reported a nonunion rate of 8.3% in 12 smokers versus a nonunion rate of 5.9% in 68 nonsmokers who underwent a single-level autograft-assisted ACDF with and without plate fixation. These authors did address the lack of statistical significance of their findings and attributed it to the small sample size of smokers in their study. In contrast, Samartzis et al.[33] compared the use of allograft versus autograft in 66 patients who underwent single-level instrumented ACDF, and they noted a 95% fusion rate in 22 individuals who smoked; the fusion in patients who did not smoke was the same (95%). These authors concluded that, in relation to the success of fusion, there was no statistical difference between allograft and autograft or between smoking and nonsmoking status. They suggested that rigid plate fixation may decrease the risk of nonunion in 1-level ACDF in patients who smoke. Furthermore, Hilibrand et al.[23] showed no difference in fusion rates with respect to healing of autogenous iliac crest or fibular strut grafts in corpectomies between nonsmokers and smokers; the rate was 93% in both groups. Although this study did not address single-level cervical fusions, it did provide evidence that when a bony union is required between 2 osseous interfaces, smoking might not influence the fusion rate.

In our study the smokers who underwent a single-level ACDF with allograft and instrumentation had a fusion rate of 91.0%. This is comparable to the fusion rate of 91.6% in patients who were nonsmokers. These findings would suggest that in single-level ACDF involving allograft and instrumentation smoking does not have an impact on fusion status. It seems plausible that in the cervical spine the detrimental effects of nicotine are negated when a bone fusion is required between only 2 osseous interfaces and locked plate fixation is used to stabilize the spine.

Although smoking has been shown to negatively affect fusion rates in multilevel cervical fusions, our study reveals that smoking is less likely to affect fusion status in single-level ACDF. We found that the use of allograft with locked plate fixation in single-level ACDF produces similar fusion rates in patients who smoke and people who do not smoke. We routinely educate our patients on the ill effects of tobacco abuse and strongly recommend smoking cessation. However, if patients are disinclined to stop smoking, it appears that the use of allograft with a locked plate produces acceptable fusion rates in single-level ACDF.

The primary limitation of the present study is the retrospective design. In addition, the definition of "smoker" was not necessarily uniform across studies, and given the study design it cannot be determined whether the degree of smoking (packs per day) is reflective of the public at large. The rates of nonunion varied across the IDE trials, ranging from 4.0% to 15.5%, which may reflect differences in surgeon panels, anterior plate selection, allograft choice, and possible selection bias. It is possible that the method of fusion assessment employed, plain radiographs with dynamic views, may underestimate the rate of non-

union, especially when plates are used, but this would be expected to similarly impact the assessment of fusion for smokers and nonsmokers. Although we cannot directly confirm whether the independent reviewers of the radiographs were blinded to smoking status, we have no indication for any of the IDE studies that this information was specifically provided in the context of imaging review. Furthermore, although each study was conducted as a formal FDA IDE, we cannot independently confirm whether patients were consistently enrolled in a consecutive manner for each of the studies.

The data collected in the present study are from 5 large, well-designed prospective studies. All studies had similar parameters for fusion success and used independent reviewers to evaluate fusion status. The present study was performed under the auspices of the Cervical Spine Research Society and allowed a unique opportunity for collaboration and cooperation between clinicians and multiple industry partners. This partnership has allowed the Society to produce original research that could not be obtained by a single institution or from a single industry-sponsored study. It is this type of joint effort that demonstrates how clinical and industry partnerships can lead to advances in the clinical arena.

Conclusions

This study revealed no difference in fusion status between smokers and nonsmokers who underwent a single-level ACDF with allograft and a locked anterior cervical plate. Although we do not promote tobacco use, it appears that the use of allograft with locked cervical plate fixation in single-level ACDF among smokers produces similar fusion rates as it does among nonsmokers.

Disclosure

Dr. Shaffrey is a consultant for Medtronic, Biomet, NuVasive, Globus, and Stryker; he receives royalties from and is a patent holder with Biomet and Medtronic. Dr. Smith is a consultant for Biomet, Globus, DePuy, and Medtronic; he receives support for non–study related clinical or research work from DePuy, AOSpine North America, and AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves. Dr. Vaccaro is a consultant for Gerson Lehrman Group, Guidepoint Global, Medacorp, Stout Medical, and Innovative Surgical Design; he is employed by the Rothman Institute; he owns stock in Spine Medica, Computational Biodynamics, Progressive Spinal Technologies, Spinology, Small Bone Innovations, NeuCore, Cross Current, Syndicom, In Vivo, Flagship Surgical, Advanced Spinal Intellectual Properties, Cytonics, Bonovo Orthopaedics, Electrocore, Gamma Spine, Location Based Intelligence, FlowPharma, R.S.I., Replication Medica, Globus, K-2 Medical, Paradigm Spine, Stout Medical, Innovative Surgical Design, Spinicity, and the Rothman Institute and Related Properties; he receives royalty payments from DePuy, Medtronics, Stryker Spine, Biomet Spine, Globus, Aesculap, and NuVasive; he serves on the scientific advisory board/board of directors or serves on committees of AOSpine, Innovative Surgical Design, Association of Collaborative Spine Research, and Spinicity; and he receives institutional/educational grant support from Stryker Spine, NuVasive, and Cerapedics. Dr. Sasso is a patent holder with Medtronic. Dr. Ludwig is a consultant for DePuy Synthes; he has ownership in ASIP/Spinicity/ISD; and he owns stock in Globus. Dr. Fischgrund is a consultant for Stryker, Relievant, and Medtronic; he owns stock in Trans and receives royalties from Stryker.

The authors would like to acknowledge the support and cooperation of Cervitech, Medtronic, Stryker, and Synthes for providing data from their respective cervical disc replacement trials. No industry partner had editorial control or oversight of the data presented in this study or the resulting manuscript.

Author contributions to the study and manuscript preparation include the following. Conception and design: Luszczyk, Fischgrund, Ludwig, Sasso, Vaccaro. Acquisition of data: Luszczyk, Fischgrund, Ludwig, Sasso, Vaccaro. Analysis and interpretation of data: Luszczyk, Fischgrund, Ludwig, Sasso, Vaccaro. Drafting the article: Smith, Luszczyk, Fischgrund, Ludwig, Sasso, Vaccaro. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Smith. Statistical analysis: Luszczyk, Fischgrund. Administrative/technical/material support: Shaffrey, Vaccaro. Study supervision: Vaccaro.

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Manuscript submitted February 27, 2013.
Accepted July 25, 2013.
Please include this information when citing this paper: published online August 30, 2013; DOI: 10.3171/2013.7.SPINE13208.

Address correspondence to: Justin S. Smith, M.D., Ph.D., Department of Neurological Surgery, University of Virginia Health System, P.O. Box 800212, Charlottesville, VA 22908. email: jss7f@virginia.edu.