Effects of smoking on cervical disc arthroplasty

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OBJECTIVE Cigarette smoking can adversely affect bone fusion in patients who undergo anterior cervical discectomy and fusion. However, there is a paucity of data on smoking among patients who have undergone cervical disc arthroplasty (CDA). The present study aimed to compare the clinical and radiological outcomes of smokers to those of nonsmokers following CDA.

METHODS The authors retrospectively reviewed the records of consecutive patients who had undergone 1- or 2-level CDA for cervical disc herniation or spondylosis and had a minimum 2-year follow-up. All patients were grouped into a smoking group, which consisted of those who had consumed cigarettes within 6 months prior to the CDA surgery, or a nonsmoking group, which consisted of those who had not consumed cigarettes at all or within 6 months of the CDA. Clinical outcomes were evaluated according to the visual analog scale for neck and arm pain, Neck Disability Index, Japanese Orthopaedic Association Scale, and Nurick Scale at each time point of evaluation. Radiological outcomes were assessed using radiographs and CT for multiple parameters, including segmental range of motion (ROM), neutral lordotic curve, and presence of heterotopic ossification (HO).

RESULTS A total of 109 patients completed at least 2 years of follow-up and were analyzed (mean follow-up 42.3 months). There were 89 patients in the nonsmoking group and 20 in the smoking group. The latter group was younger and predominantly male (both $p < 0.05$) compared to the nonsmoking group. The two groups had similar improvements in all clinical outcomes after CDA compared to preoperatively. Radiological evaluations were also very similar between the two groups, except for two factors. The smoking group had well-preserved segmental ROM after CDA at an average of 8.1° (both pre- and postoperation). However, while the nonsmoking group remained mobile, segmental ROM decreased significantly (8.2° to 6.9° , $p < 0.05$) after CDA. There was a trend toward more HO development in the nonsmoking group than in the smoking group, but the difference was without significance (59.6% vs 50.0%, $p = 0.43$).

CONCLUSIONS During an average 3.5 years of follow-up after 1- and 2-level CDA, cigarette smokers and nonsmokers had similar improvements in clinical outcomes. Moreover, segmental mobility was slightly better preserved in smokers. Since smoking status did not negatively impact outcomes, CDA may be a reasonable option for selected patients who have smoked.

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KEYWORDS cervical disc arthroplasty; anterior cervical discectomy and fusion; heterotopic ossification; cigarette; smoke

ANTERIOR cervical discectomy and fusion (ACDF) has been the standard surgical treatment for patients with cervical disc herniation or spondylosis causing intractable radiculopathy or myelopathy. Although symptom relief has been highly satisfactory after ACDF,

there has also been adjacent-segment degeneration (ASD) that requires a secondary ACDF or other reoperation.³² These cases of ASD may be attributable to increased load and compensatory motion after arthrodesis in ACDF. Cervical disc arthroplasty (CDA) was therefore designed to

ABBREVIATIONS ACDF = anterior cervical discectomy and fusion; ASD = adjacent-segment degeneration; CDA = cervical disc arthroplasty; FDA = Food and Drug Administration; HO = heterotopic ossification; JOA = Japanese Orthopaedic Association; NDI = Neck Disability Index; ROM = range of motion; VAS = visual analog scale.

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preserve segmental mobility after anterior cervical discectomy and thus ameliorate the development of ASD. During the past decade, data from US Food and Drug Administration (FDA) clinical trials comparing 1- and 2-level CDA to ACDF have demonstrated equal or superior results for CDA in terms of improvement in neurological function and in the reduction of secondary surgery.^{14,15,18} Much of the literature agrees that these CDA devices can successfully maintain segmental mobility at an average of about 7°–8° during flexion and extension. However, it remains questionable if the CDA can ameliorate ASD in the long run.

Common indications for CDA are 1- and 2-level disc herniation or spondylosis causing radiculopathy or myelopathy that was refractory to medical treatment. In the published reports of the FDA clinical trials,^{14,15,18} cigarette smoking was not specifically addressed for any enrolled patient. Although there is plenty of evidence indicating the adverse effects of smoking in spine surgery, including higher complication rates,^{3,7,9} longer hospitalizations,²³ and lower fusion rates,^{2,8,13,16} there has been a paucity of data on how cigarette consumption affects the outcomes of CDA. There have also been studies demonstrating higher rates of pseudarthrosis and infection in smoking patients after anterior cervical fusion.^{17,19} However, none of the literature indicates how smoking will affect surgery aimed at preserving spinal motion rather than inducing fusion.

In the present study, we aimed to investigate the differences between smoking and nonsmoking patients who had undergone 1- and 2-level CDA surgery. All radiological and clinical outcomes of CDA were compared. To date, this is the first study specifically aimed at addressing such an issue. Although smokers did not account for the majority of patients with degenerative spine problems, this study could shed light on technology for spinal motion preservation (e.g., CDA) as an acceptable option for patients who tend to develop pseudarthrosis.

Methods

Patient Population

Consecutive patients who had undergone 1- or 2-level CDA with the Prestige LP disc (Medtronic) at a single medical center (Taipei Veterans General Hospital, Taiwan) in the period from 2009 to 2015 were included in this analysis. Clinical records, radiological examinations, and clinical evaluations were all reviewed retrospectively. The indication for CDA in this series was medically refractory cervical radiculopathy with or without myelopathy that had been caused by 1- or 2-level cervical disc herniation or spondylosis. All patients had received at least 12 weeks of conservative therapy, including medication and physical therapy, prior to the surgery. A patient would not be considered a candidate for CDA if there were any of the following conditions: loss of segmental range of motion (ROM) at the indexed level (< 2°) due to advanced degeneration, ossification of the posterior longitudinal ligament (OPLL), severe facet arthropathy (i.e., elimination of joint space demonstrated on CT), > 50% collapse of the normal disc height, traumatic ligamentous or bony injury, infection, or malignancy. Furthermore, patients who had

undergone prior anterior cervical spine surgery or those with less than or loss to 2 years of follow-up were also excluded from analysis.²⁶ All pre- and postoperative clinical and radiological evaluations were analyzed.

Surgical Technique

General anesthesia was induced in all patients, who were placed supine with the neck maintained in a neutral to slightly lordotic position and with adequate cushioning. A horizontal skin incision was made following one of the skin creases in the right neck. Intraoperative fluoroscopy was always used for confirmation of the surgical level. The standard anterior cervical approach was adapted for exposure of the target disc level with self-retaining retractors. Decompression of the neural elements was performed under the microscope, including removal of the intervertebral disc, resection of the posterior longitudinal ligament, and resection of the bilateral uncovertebral joints. Care was taken to prepare the endplates before implantation of the artificial discs. Proper sizing, accurate midline acquisition, and adequate endplate coverage were the major principles for restoration of disc function. The implant was confirmed by lateral fluoroscopy for optimal positioning intraoperatively. After copious irrigation and hemostasis, all wounds were subsequently closed in layers with a drainage catheter routinely placed to prevent hematoma formation.

Clinical and Radiological Evaluations

Clinical outcomes and radiological evaluations of all patients were reviewed retrospectively. Clinical outcomes according to the visual analog scale (VAS) for neck and arm pain, Japanese Orthopaedic Association (JOA) scale, Neck Disability Index (NDI), and Nurick Scale were measured using a questionnaire completed preoperatively and at approximately 6, 12, 18, and 24 months postoperatively. A special nurse assistant under the supervision of physicians would assist with the entire process during each clinic visit. Pre- and postoperative radiological evaluations included radiography, CT, and MRI (Fig. 1A). Standard anteroposterior, lateral, and flexion and extension radiographs of the cervical spine were obtained preoperatively and at the specified time points in the postoperative follow-up. The neutral lordotic curve was measured using the C2–7 Cobb angle on the standard lateral radiographs in order to assess cervical alignment (Fig. 1B). Segmental ROM at the index level(s) was defined as the difference in the Cobb angle at the index level between flexion and extension radiographs (Fig. 1C). Immobilization (i.e., loss of segmental mobility) at the index level was defined as ROM < 2° on flexion and extension radiographs. Cervical CT scans (Fig. 1D) were acquired annually to assess and identify heterotopic ossification (HO) formation based on the classification published by McAfee et al. in 2003.²⁰ All quantitative measurements were analyzed using the commercial software SmartIris (Taiwan Electronic Data Processing Co.) and were interpreted independently by radiologists and neurosurgeons. If any ambiguity occurred, final determination would be based on a consensus after group discussion.

FIG. 1. A patient underwent CDA that addressed a herniated disc at C3–4. Preoperative sagittal T2-weighted MR image demonstrating marked spinal cord compression at the C3–4 level (arrowhead, **A**). After surgery, the Prestige LP artificial disc was positioned with good alignment and reasonable size (**B**). At the 43-month postoperative follow-up, lateral dynamic radiographs demonstrated good preservation of the segmental mobility (**C**). A small HO was demonstrated on the lateral radiographs (arrowhead, **C**). Interestingly, when scrutinized using CT, there were small HOs both anterior and posterior to the artificial disc (arrowheads, **D**). Despite HO formation, the indexed level remained mobile throughout the follow-up.

Study Groups and Statistical Analysis

All patients were placed into two groups according to their history of cigarette consumption before surgery. The patients who had consumed cigarettes within 6 months before surgery were defined as the smoking group, and those who had not smoked at all or within 6 months of CDA were categorized as the nonsmoking group. Demographic data and clinical and radiological outcomes were compared between the two groups.

All statistical tests were two-tailed. Statistical significance was defined by a p value < 0.05 using an (un)paired t -test for continuous variables or chi-square test for categorical variables and was analyzed with MATLAB (MathWorks).

Results

Demographics

During the study period, a total of 197 patients underwent 1- or 2-level CDA (133 vs 64 patients, respectively) for disc herniation or spondylosis. One hundred nine of them met our study inclusion criteria and had completed a follow-up of 2 or more years. In the final analysis, there were 20 patients in the smoking group and 89 in the nonsmoking group, and there was a mean follow-up of 42.3 months (Table 1).

The smoking group was composed of more males and was significantly younger than the nonsmoking group. The average age of the patients who smoked before the CDA surgery was 8 years younger than the average age of those who had not smoked (41.0 ± 10.7 vs 49.0 ± 10.3 , respectively, $p = 0.005$). Male predominance was significantly higher in the smoking group than the nonsmoking group (95% vs 41.6%, $p < 0.001$). Other medical comorbidities were similar between the two groups. For example, the prevalence of diabetes mellitus or essential hypertension was not statistically different between the two groups ($p = 0.89$ and 0.17 , respectively). Moreover, other patient data

such as distribution of operated level(s), estimated intraoperative blood loss, and length of follow-up were not significantly different ($p = 0.73$, 0.82 , and 0.51 , respectively) between the two groups (Table 1).

Radiological Outcomes

During the follow-up, the C2–7 neutral lordotic curve and ROM at the indexed levels remained similar for all patients after the CDA surgery. Furthermore, there were no differences between the smoking and nonsmoking patients in terms of pre- and postoperative C2–7 neutral lordotic curve and ROM at the indexed levels (Table 2). The pre- and postoperative neutral lordotic curve in the smoking group was not statistically different from that in the nonsmoking group (18.0 ± 8.6 vs 15.1 ± 10.7 , $p = 0.20$; and 15.4 ± 10.2 vs 16.1 ± 10.1 , $p = 0.78$, respectively). Further-

TABLE 1. Summary of data for smoker and nonsmoker groups

Characteristic	Group		p Value
	Smoking	Nonsmoking	
No. of patients	20	89	
Age in yrs*	41.0 ± 10.7	49.0 ± 10.3	0.005
Sex: F/M	1/19	52/37	<0.001
Diabetes mellitus	1	8	0.89
Hypertension	2	29	0.17
Operated level			
1 level	12	57	0.73
2 levels	8	32	
Mean surgical blood loss in ml	91.1	87.5	0.82
Mean FU in mos	42.1	39.1	0.51

FU = follow-up.

Boldface type indicates statistical significance.

* Values are presented as the mean $\pm$ standard deviation.

TABLE 2. Pre- and postoperative clinical characteristics

Characteristic	Group		p Value
	Smoking	Nonsmoking	
C2–7 neutral lordotic curve (°)*			
Preop	18.0 ± 8.6	15.1 ± 10.7	0.20
Postop	15.4 ± 10.2	16.1 ± 10.1	0.78
ROM at index level(s) (°)*			
Preop	8.1 ± 5.3	8.2 ± 5.2	0.94
Postop	8.1 ± 6.2	6.9 ± 4.7	0.40
HO, % (no.)	50.0 (10/20)	59.6 (53/89)	0.43
Postop immobilization, % (no.)	5.0 (1/20)	5.6 (5/89)	0.67
Preop functional evaluation*			
VAS neck pain	4.5 ± 3.2	4.7 ± 3.4	0.85
VAS arm pain	5.1 ± 3.5	4.3 ± 3.4	0.38
JOA	12.5 ± 1.6	13.1 ± 3.2	0.22
NDI	15.3 ± 7.3	15.8 ± 11.9	0.81
Nurick score	0.8 ± 0.8	1.0 ± 1.2	0.53
Postop functional evaluations*			
VAS neck pain	2.2 ± 2.4	2.6 ± 2.7	0.59
VAS arm pain	1.6 ± 2.6	2.1 ± 2.5	0.59
JOA	14.8 ± 2.0	14.7 ± 2.3	0.86
NDI	5.2 ± 5.1	7.8 ± 7.0	0.19
Nurick score	0.6 ± 0.5	0.5 ± 0.6	0.86
Total periop complications, % (no.)	15 (3/20)	10.1 (9/89)	0.81
Periop complication, no.			
Neurological deficit	1†	0	0.41
Transient C5 palsy	0	1	0.41
Transient hoarseness	1†	1	0.81
Transient dysphagia	1	4	0.62
Wound infection	1	2	0.93
CSF leakage	0	1	0.41
Secondary surgery (%)	0	0	

* Values are presented as the mean ± standard deviation.

† The patient with postoperative neurological deficit in the smoker group also had transient hoarseness after surgery.

more, there were no differences in the preoperative and postoperative ROM at the level of the CDA between the smoking and nonsmoking groups (8.1 ± 5.3 vs 8.2 ± 5.2 , $p = 0.94$; and 8.1 ± 6.2 vs 6.9 ± 4.7 , $p = 0.40$, respectively).

Under the strict detection criteria for the development of HO after CDA, scrutinized on postoperative CT, the incidence of HO formation was lower in the smoking group (50%) than in the nonsmoking group (59.6%), but the difference did not reach statistical significance ($p = 0.43$; Table 2).

The nonsmoking CDA patients had a slightly decreased mean segmental ROM after surgery (approximately 1°). After CDA, patients in the smoking group had a mean ROM at the index level very similar to that preoperatively (8.1 ± 5.3 vs 8.1 ± 6.2 , $p = 0.91$). In contrast, for patients in the nonsmoking group, the mean postoperative ROM was statistically lower than that preoperatively (6.9 ± 4.7 vs 8.2 ± 5.2 , $p = 0.03$; Fig. 2). However, the incidence of

FIG. 2. Comparison of pre- and postoperative segmental ROM at the index level (plotted as mean ± standard error) between smoking and nonsmoking groups. There was no difference between pre- and postoperative ROM in the smokers, whereas a decreased ROM was demonstrated in the nonsmokers. * $p < 0.05$.

immobile segments ($< 2^\circ$) after CDA was not significantly different between the smokers and nonsmokers (5.0% vs 5.6%, $p = 0.67$).

Clinical Outcomes and Complications

All patients in both groups had significantly improved clinical outcomes after CDA. There were no differences between the smoking and nonsmoking groups on any clinical outcome parameter, including VAS neck and arm pain, JOA, NDI, and Nurick scores, comparing them pre- and postoperatively (all $p > 0.05$; Table 2). During the follow-up, there was no patient who underwent a secondary surgery for ASD.

Complication rates were similar in the two groups (15% vs 10.1%, $p = 0.81$). However, there was one serious neurological complication after CDA in the smoking group. One patient developed paraparesis immediately after surgery and was found to have thoracic anterior spinal cord syndrome. He gradually recovered an ability to ambulate with little assistance and had no issues of daily living or body balance after rehabilitation. The same patient also had transient hoarseness, and another patient in the smoking group had transient dysphagia; both patients recovered well. Moreover, three patients (one in the smoking group, two in the nonsmoking group) had superficial wound infections, none of which required surgical intervention. In the nonsmoking group, there was 1 case of transient C5 palsy, 1 of transient hoarseness, and 4 of transient dysphagia, as well as 1 incidental durotomy during the operation and subsequent cerebrospinal fluid leakage that resolved spontaneously. There has been no need for any reoperation in the entire series so far.

Discussion

This was the first study to address the effect of cigarette consumption in patients who underwent CDA, and it indicated that the clinical outcomes were about the same in patients who smoked and those who had not. Although the sample size was relatively small, our data implied that CDA may be a more reasonable option than ACDF for smoking patients with cervical disc herniation or spondy-

losis requiring discectomy because cigarette consumption can increase the rate of pseudarthrosis in conventional ACDF. In the present study, we retrospectively reviewed the records of consecutive patients who had undergone 1- or 2-level CDA with Prestige LP artificial discs and had a minimum follow-up of 2 years (mean follow-up 42.3 months). All the patients had cervical radiculopathy, myelopathy, or both that had been caused by 1- or 2-level disc herniation or spondylosis and were refractory to medical treatment. According to a medical history of cigarette consumption within 6 months prior to CDA surgery, the patients were categorized into two groups: smoking group ($n = 20$) and nonsmoking group ($n = 89$). In comparing all clinical outcomes (e.g., VAS for neck and arm pain, NDI, JOA, and Nurick scores) and radiological outcomes (e.g., segmental ROM at the index level, neutral lordotic curve of C2–7, and incidence rates of HO formation), we found only minor differences among patients who smoked and those who did not. The smokers who underwent CDA were younger, predominantly male, and had slightly better ROM at the index level. In other words, these smoking patients who underwent CDA had similarly good outcomes compared to those in the nonsmoking patients. In contrast, if these smoking patients had undergone ACDF, they could have had lower fusion rates due to the adverse effects of cigarette consumption. According to previous studies in the literature, the effects of smoking would have disturbed the process of osteogenesis to delay bone healing.²⁴ Although we did not include ACDF patients in the present study for comparison, our indirect evidence could support the application of CDA in smokers. Furthermore, the lower rates of HO formation and higher values for ROM in the smoking group imply the potential advantages of CDA for smokers. The complication rates and secondary surgeries or reoperations were also the same in this series of 1- and 2-level CDA with Prestige LP. However, given the limitations of the present study, the inference to use CDA to treat smoking patients would require a larger sample, longer-term follow-up, and a control group of ACDF patients for comparison for further corroboration.

The actual cause of HO formation after CDA remains elusive. Previous clinical series and finite element studies have demonstrated that the development of HO could be multifactorial. It could be attributed to the mechanical adaption for disc problems that induces bone remodeling for spinal stability and thus similarly induces degeneration and osteophyte formation.^{12,22} One study on the predisposing factors of HO included 170 patients who underwent CDA and found that the occurrence of HO was higher in male patients and could differ according to the type of cervical artificial disc used, although the preexisting degeneration at the index levels was not correlated.³³ There have also been studies demonstrating that surgical levels for CDA could be another cause of HO formation.^{5,10,11,27,30} In these studies, the incidence of HO ranged around 30%–50%, including very small HOs, which were revealed on postoperative CT scans. These studies demonstrated that multilevel spondylosis and more degenerative change (i.e., severe spondylosis) would lead to more HO formation after CDA.^{5,27,30,31} On the other hand, the perioperative prescription of nonsteroidal antiinflammatory drugs,

technically optimal implantation of the device, and soft disc herniation were reportedly correlated with less HO formation.^{26,28} The effect of nicotine or cigarette consumption may interfere with the process of bone formation or fusion. Nevertheless, smoking has not been reported to correlate with HO formation. Patients in the present study also demonstrated little difference in HO, regardless of their smoking history.

There have been multiple studies on CDA, including large-scale prospective randomized controlled trials by the FDA, which have demonstrated the effectiveness of the preservation of segmental mobility and ROM at the index level after CDA.^{21,29} In selected patients, CDA may even be capable of increasing segmental ROM.⁴ In a study by Chang et al., it was not clear why some of the CDA segments gradually lost motion, but HO seemed to have played a role. Limited segmental ROM at the index level was correlated with HO formation, and vice versa. A retrospective study by Tian et al. included 71 patients who had undergone CDA with a mean follow-up of 79.2 months and demonstrated that high-grade HO at the index level postoperatively could adversely affect postoperative segmental ROM.²⁵ In our study, there was no difference in the rate of loss of mobility between the smoking and nonsmoking groups ($p = 0.67$). Nonetheless, in the nonsmoking group, the postoperative segmental ROM at the index level was lower than that preoperatively by 1.3° (6.9 ± 4.7 vs 8.2 ± 5.2 , $p < 0.05$). Although the majority of the CDA devices in the series remained mobile, the nonsmoking group had a higher trend toward HO formation than the smoking group (59.6% vs 50.0%), but the difference between the two was without significance. Both the lower HO and higher ROM in the smoking group may be attributable to the adverse effect of cigarette smoking on biological bone growth.

There are few data regarding the influence of smoking on HO formation after CDA, though cigarette consumption is commonly accepted to adversely affect bone formation. In an animal model, decreased bone marrow density was found in the femur and lumbar bones of 8-week smoke-exposed rats compared to that in the control groups.¹ Moreover, inhibition of early revascularization by nicotine was observed in a rabbit study, and this mechanism may affect bone healing and osteogenesis.⁶ A number of clinical series have described the phenomenon in human patients. For example, a study included 190 patients who underwent anterior cervical spine surgery, 55 of whom had a history of active cigarette consumption. A significantly higher rate of pseudarthrosis was observed in the smoking group, especially for the patients who underwent multilevel interbody fusion.¹⁷ Apparently, more levels of ACDF leads to higher chances of pseudarthrosis in ACDF patients who smoke. The differences might have been magnified when more levels of cervical discectomy and reconstruction were attempted. The discrepancies demonstrated by the present study might have become more prominent in patients with more than 2-level CDA.

There are several limitations of this study. It was a retrospective nonrandomized cohort study that could only yield a 1:4 comparison of smokers to nonsmokers. There was no addressing the dose relationship of nicotine exposure to the

outcomes. The study only addressed preoperative cigarette consumption and simplified the postoperative exposure, which might have played an even more crucial role in the outcomes and complications of CDA. Furthermore, there were no cases of ACDF, which remains the gold standard surgical treatment for cervical disc herniation, for comparison in the study. The patients who opted to undergo CDA might be inherently healthier and have less degeneration, no deformity, and better bone quality. Furthermore, the disproportionate numbers of patients involved in the study—20 subjects (18.3%) in the smoking group and 89 (81.7%) in the nonsmoking group—could have mitigated the power of statistics. This issue could have been remarkably addressed only if more smokers were enrolled. However, that was a natural limitation of the retrospective cohort. In reality, only a prospective study that aimed to enroll only smokers and randomize them to a CDA or ACDF group could really address this problem. Perhaps future investigations could address this better. Therefore, a larger number of patients, longer-term follow-up, and measurements of the amount of cigarette exposure prior to and after the CDA surgery would provide more information about the effects of smoking on these patients who needed the CDA. This study merits a subsequent clinical study aimed at investigating the effects of smoking. Note that the CDAs were performed by the same group of neurosurgeons (W.C.H. and J.C.W.) and used the same brand of artificial discs.

Conclusions

During an average 3.5 years of follow-up after 1- and 2-level CDA, cigarette smokers had improvements in clinical outcomes similar to those of nonsmokers. Moreover, segmental mobility was slightly better preserved in smokers. Since smoking status did not negatively impact outcomes, CDA may be a reasonable option for selected patients who smoke.

References

- Ajiro Y, Tokuhashi Y, Matsuzaki H, Nakajima S, Ogawa T: Impact of passive smoking on the bones of rats. **Orthopedics** 33:90–95, 2010
- Andersen T, Christensen FB, Laursen M, Høy K, Hansen ES, Bünger C: Smoking as a predictor of negative outcome in lumbar spinal fusion. **Spine (Phila Pa 1976)** 26:2623–2628, 2001
- Bisson EF, Bowers CA, Hohmann SF, Schmidt MH: Smoking is associated with poorer quality-based outcomes in patients hospitalized with spinal disease. **Front Surg** 2:20, 2015
- Chang HK, Chang CC, Tu TH, Wu JC, Huang WC, Fay LY, et al: Can segmental mobility be increased by cervical arthroplasty? **Neurosurg Focus** 42(2):E3, 2017
- Chang PY, Chang HK, Wu JC, Huang WC, Fay LY, Tu TH, et al: Differences between C3–4 and other subaxial levels of cervical disc arthroplasty: more heterotopic ossification at the 5-year follow-up. **J Neurosurg Spine** 24:752–759, 2016
- Daftari TK, Whitesides TE Jr, Heller JG, Goodrich AC, McCarey BE, Hutton WC: Nicotine on the revascularization of bone graft. An experimental study in rabbits. **Spine (Phila Pa 1976)** 19:904–911, 1994
- De la Garza Ramos R, Goodwin CR, Qadi M, Abu-Bonsrah N, Passias PG, Lafage V, et al: Impact of smoking on 30-day morbidity and mortality in adult spinal deformity surgery. **Spine (Phila Pa 1976)** 42:465–470, 2017
- Dickman CA, Fessler RG, MacMillan M, Haid RW: Transpedicular screw-rod fixation of the lumbar spine: operative technique and outcome in 104 cases. **J Neurosurg** 77:860–870, 1992
- Elsamadicy AA, Adogwa O, Sergesketter A, Vuong VD, Lydon E, Behrens S, et al: Reduced impact of smoking status on 30-day complication and readmission rates after elective spinal fusion (≥ 3 levels) for adult spine deformity: a single institutional study of 839 patients. **World Neurosurg** 107:233–238, 2017
- Fay LY, Huang WC, Tsai TY, Wu JC, Ko CC, Tu TH, et al: Differences between arthroplasty and anterior cervical fusion in two-level cervical degenerative disc disease. **Eur Spine J** 23:627–634, 2014
- Fay LY, Huang WC, Wu JC, Chang HK, Tsai TY, Ko CC, et al: Arthroplasty for cervical spondylotic myelopathy: similar results to patients with only radiculopathy at 3 years' follow-up. **J Neurosurg Spine** 21:400–410, 2014
- Ganbat D, Kim YH, Kim K, Jin YJ, Park WM: Effect of mechanical loading on heterotopic ossification in cervical total disc replacement: a three-dimensional finite element analysis. **Biomech Model Mechanobiol** 15:1191–1199, 2016
- Glassman SD, Anagnost SC, Parker A, Burke D, Johnson JR, Dimar JR: The effect of cigarette smoking and smoking cessation on spinal fusion. **Spine (Phila Pa 1976)** 25:2608–2615, 2000
- Gornet MF, Burkus JK, Shaffrey ME, Argires PJ, Nian H, Harrell FE Jr: Cervical disc arthroplasty with PRESTIGE LP disc versus anterior cervical discectomy and fusion: a prospective, multicenter investigational device exemption study. **J Neurosurg Spine** 23:558–573, 2015
- Gornet MF, Burkus JK, Shaffrey ME, Nian H, Harrell FE Jr: Cervical disc arthroplasty with Prestige LP disc versus anterior cervical discectomy and fusion: seven-year outcomes. **Int J Spine Surg** 10:24, 2016
- Hermann PC, Webler M, Bornemann R, Jansen TR, Rommelspacher Y, Sander K, et al: Influence of smoking on spinal fusion after spondylodesis surgery: a comparative clinical study. **Technol Health Care** 24:737–744, 2016
- Hilibrand AS, Fye MA, Emery SE, Palumbo MA, Bohlman HH: Impact of smoking on the outcome of anterior cervical arthrodesis with interbody or strut-grafting. **J Bone Joint Surg Am** 83-A:668–673, 2001
- Lanman TH, Burkus JK, Dryer RG, Gornet MF, McConnell J, Hodges SD: Long-term clinical and radiographic outcomes of the Prestige LP artificial cervical disc replacement at 2 levels: results from a prospective randomized controlled clinical trial. **J Neurosurg Spine** 27:7–19, 2017
- Lau D, Chou D, Ziewacz JE, Mummaneni PV: The effects of smoking on perioperative outcomes and pseudarthrosis following anterior cervical corpectomy: clinical article. **J Neurosurg Spine** 21:547–558, 2014
- McAfee PC, Cunningham BW, Devine J, Williams E, Yu-Ya-hiro J: Classification of heterotopic ossification (HO) in artificial disk replacement. **J Spinal Disord Tech** 16:384–389, 2003
- Mummaneni PV, Amin BY, Wu JC, Brodt ED, Dettori JR, Sasso RC: Cervical artificial disc replacement versus fusion in the cervical spine: a systematic review comparing long-term follow-up results from two FDA trials. **Evid Based Spine Care J** 3 (S1):59–66, 2012
- Park SB, Jin YJ, Kim KJ: Heterotopic ossification and clinical outcome in nonconstrained cervical arthroplasty. **J Spine Surg** 2:351–352, 2016
- Seicean A, Seicean S, Alan N, Schiltz NK, Rosenbaum BP, Jones PK, et al: Effect of smoking on the perioperative outcomes of patients who undergo elective spine surgery. **Spine (Phila Pa 1976)** 38:1294–1302, 2013
- Sloan A, Hussain I, Maqsood M, Eremin O, El-Sheemy M:

- The effects of smoking on fracture healing. **Surgeon** 8:111–116, 2010
25. Tian W, Fan MX, Liu YJ, Han X, Yan K, Wang H, et al: An analysis of paravertebral ossification in cervical artificial disc replacement: a novel classification based on computed tomography. **Orthop Surg** 8:440–446, 2016
 26. Tu TH, Wu JC, Huang WC, Chang HK, Ko CC, Fay LY, et al: Postoperative nonsteroidal antiinflammatory drugs and the prevention of heterotopic ossification after cervical arthroplasty: analysis using CT and a minimum 2-year follow-up. **J Neurosurg Spine** 22:447–453, 2015
 27. Tu TH, Wu JC, Huang WC, Guo WY, Wu CL, Shih YH, et al: Heterotopic ossification after cervical total disc replacement: determination by CT and effects on clinical outcomes. **J Neurosurg Spine** 14:457–465, 2011
 28. Tu TH, Wu JC, Huang WC, Wu CL, Ko CC, Cheng H: The effects of carpentry on heterotopic ossification and mobility in cervical arthroplasty: determination by computed tomography with a minimum 2-year follow-up: clinical article. **J Neurosurg Spine** 16:601–609, 2012
 29. Upadhyaya CD, Wu JC, Trost G, Haid RW, Traynelis VC, Tay B, et al: Analysis of the three United States Food and Drug Administration investigational device exemption cervical arthroplasty trials. **J Neurosurg Spine** 16:216–228, 2012
 30. Wu JC, Huang WC, Tsai HW, Ko CC, Fay LY, Tu TH, et al: Differences between 1- and 2-level cervical arthroplasty: more heterotopic ossification in 2-level disc replacement: Clinical article. **J Neurosurg Spine** 16:594–600, 2012
 31. Wu JC, Huang WC, Tsai TY, Fay LY, Ko CC, Tu TH, et al: Multilevel arthroplasty for cervical spondylosis: more heterotopic ossification at 3 years of follow-up. **Spine (Phila Pa 1976)** 37:E1251–E1259, 2012
 32. Wu JC, Liu L, Wen-Cheng H, Chen YC, Ko CC, Wu CL, et al: The incidence of adjacent segment disease requiring surgery after anterior cervical discectomy and fusion: estimation using an 11-year comprehensive nationwide database in Taiwan. **Neurosurgery** 70:594–601, 2012
 33. Yi S, Shin DA, Kim KN, Choi G, Shin HC, Kim KS, et al: The predisposing factors for the heterotopic ossification after cervical artificial disc replacement. **Spine J** 13:1048–1054, 2013

Disclosures

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Author Contributions

Conception and design: Wu, Kuo. Acquisition of data: Kuo. Analysis and interpretation of data: Kuo. Drafting the article: Kuo. Critically revising the article: Wu, Tu. Reviewed submitted version of manuscript: Wu, Tu, Kuo. Approved the final version of the manuscript on behalf of all authors: Wu. Statistical analysis: Kuo. Administrative/technical/material support: Tu, Huang, Fay, Cheng. Study supervision: Huang, Cheng.

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