

Clinical Study

Maintaining range of motion after cervical discectomy does not prevent adjacent segment degeneration

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Abstract

BACKGROUND: Motion preservation prostheses were introduced to prevent adjacent disc degeneration (ASD) and to diminish neck disability in the postsurgical follow-up. However, it is still a controversial issue, and the relationship between range of motion (ROM) and ASD has not been studied.

PURPOSE: To compare the correlation between ROM of the cervical spine and the presence of radiological ASD after anterior discectomy. Clinical outcome was also correlated to ROM and ASD.

STUDY DESIGN: Retrospective cohort study.

METHODS: In all, 253 patients who underwent anterior discectomy for cervical radiculopathy due to a herniated disc were analyzed for segmental and global cervical ROM and the presence of ASD both preoperatively, and 12 and 24 months postoperatively. Patients who were included in two randomized, double-blinded trials comparing anterior cervical discectomy with arthroplasty, anterior cervical discectomy with intervertebral cage, or anterior cervical discectomy without intervertebral cage for one level disc herniation were analyzed. ROM was defined by a custom-developed image analysis tool. ASD was defined by decrease in disc height and anterior osteophyte formation on X-rays. Clinical outcome was evaluated by means of the Neck Disability Index (NDI).

RESULTS: Two years postoperatively, no correlation was demonstrated between ROM and ASD. The incidence of ASD was comparable in the three groups, being 34% at baseline, and 58% at 2-year follow-up. Likewise, ASD progression was comparable in the three treatment arms. No correlation was demonstrated between ROM and NDI or ASD and NDI.

FDA device/drug status: Not applicable.

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Europe and Netherlands Neurosurgical Society (NNvN), faculty for EANS, CSRS, Eurospine and webinar for AO spine (F).

Trial Registration: NECK trial, Dutch Trial Register Number: NTR1289. PROCON trial, Trial Register Number: ISRCTN41681847.

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CONCLUSIONS: Since ROM is not correlated to ASD, and clinical outcome is not correlated to ROM either, the relevance of continued ROM at the target level seems absent. © 2019 Elsevier Inc. All rights reserved.

Keywords: Adjacent segment degeneration; Arthroplasty; Anterior cervical discectomy; Cervical spine; Neck disability; Range of motion

Introduction

It was reported that cervical arthrodesis of a motion segment caused by fusion leads to increased mechanical load at the adjacent levels [1]. Hypothetically, this can contribute to degeneration of the cervical discs at the adjacent levels (ASD), which may cause neck pain and disability in follow-up years [2,3]. Some researchers reported that patients treated with anterior cervical discectomy with fusion (ACDF) have higher rates of ASD than those who underwent cervical arthroplasty (ACDA) during follow-up [4–8].

A variety of studies demonstrate that ACDA is able to maintain range of motion (ROM) at the index level [9–13]. Only a limited number of articles reported on the ROM of the whole cervical spine (C2–C7) and examined whether ACDA affected this differently in comparison to ACDF. Sala et al. [14] and Wang et al. [15] demonstrated similar cervical ROM in both ACDF and ACDA groups at the end of follow-up, but Li et al. [16] and Grasso et al. [17] reported the global cervical ROM in the ACDA group to be larger than that in the ACDF. Although meta-analyses reported that the incidence of ASD was lower in the ACDA than ACDF [18,19], a recent study disputed this and demonstrated that the presence of ASD was similar in the ACDA and ACDF at 5-year follow-up, both clinically and radiologically [20]. Additionally, the problem with the vast majority of studies is that the level of evidence is low to very low, since risk of bias is high, methods to assess ROM are insufficiently precise, and results are contradictory [21].

The objective of the current study is to study ROM in patients who were included in two randomized double-blind trials on patients treated by anterior cervical discectomy with or without interbody fusion and arthroplasty for cervical radiculopathy. The correlation between ROM at the index level and the presence of ASD was studied. The ROM at the index level was compared between the surgical methods, as well as the ROM of the total cervical spine. Moreover, ASD and ROM were correlated to neck disability.

Materials and methods

Study design

This is a retrospective cohort study using data from two prospective, randomized double-blind trials: the NECK trial and the PROCON trial.

NECK trial

A prospective, randomized double-blind multicenter trial among patients with cervical radiculopathy due to single-level disc herniation was conducted. Patients were randomly assigned into three groups: anterior cervical discectomy with arthroplasty (ACDA; activC, Aesculap AG, Tuttlingen, Germany), ACDF (Cage stand-alone), and anterior cervical discectomy without fusion (ACD). Patients (age 18–65-year-old) with radicular signs and symptoms in one or both arms for at least 8 weeks, in who conservative therapy failed were eligible for inclusion. All patients were diagnosed with cervical radiculopathy by a neurologist in one of the participating hospitals. If MRI demonstrated a single-level cervical disc herniation and/or osteophyte at one level (C3–C4 to C7–Th1) in accordance with clinical signs and symptoms, patients could be included as surgical candidates for the study by the consulting neurosurgeon. Patients with previous cervical surgery, absence of motion or increased anteroposterior (AP) translation or very narrow (<3 mm) intervertebral space or severe segmental kyphosis (>3°) at the index level on static or dynamic X-rays, neck pain only or symptoms, and signs of chronic myelopathy were excluded. A randomized design with variable block sizes was used, with allocations stratified according to center. The protocol was approved by medical ethics committees, including an approval for randomization after anesthetic induction. All patients gave informed consent.

The design and study protocol were published previously [22]. The 2-year follow-up data revealed no differences in clinical outcomes [23].

PROCON trial

The trial design was a prospective, double-blind, single-center randomized study, with a three-arm parallel group. Patients were randomly allocated into three groups: ACDA (Bryan disc prosthesis, Sofamor Danek, Kerkrade, the Netherlands), ACDF (Cage stand-alone, DePuy Spine, Johnson and Johnson, Amsterfoort, the Netherlands), and ACD. Patients (age 18–55-year-old) were eligible for inclusion with monoradicular syndrome in the arm due to one-level cervical disc degeneration disease and/or an osteophyte at MRI. The radiological findings should be in accordance with the clinical presentation. The patients with myelopathy, previous cervical surgery, psychiatric, or mental disease were excluded. The trial was approved by medical ethics committee. All patients gave informed consent.

Table 1
The classification of ASD (from Goffin et al. [1])

	Disc height	Anterior osteophyte formation
Normal	Same as adjacent disc	No anterior osteophyte
Mild	75%–100% of normal disc	Just detectable anterior osteophyte
Moderate	50%–75% of normal disc	Clear anterior osteophyte <25% of AP diameter of corresponding vertebral body
Severe	<50% of normal disc	Clear anterior osteophyte >25% of AP diameter of corresponding vertebral body

ASD, adjacent segment degeneration; AP, anteroposterior.

The design and study protocol were published previously [24]. The follow-up data up to 8 years postsurgery revealed no differences in clinical outcomes [25].

Clinical outcome measurement

Neck Disability Index (NDI) is a 10-item questionnaire on 3 different aspects: pain intensity, daily work related activities, and nonwork-related activities. Each item is scored from 0 to 5 and the total score ranges from 0 (best score) to 50 (worst score). This 50-point score was converted to a percentage (50 points=100%). The NDI is a modification of the Oswestry Low Back Pain Index and has been shown to be reliable and valid for patients with cervical pathology [26–28].

Radiographic outcomes

Flexion-extension radiographs were obtained preoperatively and at 12 and 24 months postoperatively. The ROM at the index level and of the total cervical spine (C2–C7) was measured. The ROM at index level was defined as the intervertebral sagittal rotation between full flexion and extension. The ROM at index level was measured on dynamic lateral radiographs with a custom-developed image analysis tool (BMGO, KU Leuven, Belgium), which has a measurement error of 0.3° and 0.3 mm and excellent inter-rater and intrarater agreement (intraclass correlation coefficient>0.75) [29]. Fusion was defined as ROM less than 4° [30,31]. The Cobb angle of C2–C7 was measured by the lines drawn parallel to the caudal endplate of C2 and C7.

Standing lateral radiographs of the cervical spine were obtained with the patients in a neutral standing position and instructed to look straight ahead, with hips and knees extended.

ASD was evaluated based on the height of the adjacent level disc and the anterior osteophyte formation on X-rays according to the classification reported by Goffin et al. [1] preoperatively and at 12 and 24 months postoperatively (Table 1). Only if neither the superior nor inferior adjacent level demonstrated loss of disc height or anterior osteophyte formation, the patient was graded as “non-ASD.” Additionally, in a separate analysis, “severe ASD” was defined as in patients with the classification “moderate” or “severe” loss

of disc height or anterior osteophyte formation in either the superior or inferior level. Finally, in order to study progression of adjacent level degeneration, “ASD progression” was marked as positive or negative for patients who did or did not increase in Goffin score during follow-up.

The radiographs were independently evaluated by one senior neurosurgeon dedicated to spine surgery and a junior medical doctor educated for this purpose. The reviewers were not provided with any clinical information of the included patients. Before the evaluation of radiographs, the reviewers met in person to evaluate and refine the definitions.

Correlating ROM to ASD

In order to study the relationship between ROM and ASD, subjects were dichotomized according to the presence of ASD, irrespective of the surgical method. ROM can be studied as ROM at the index level or ROM of the total cervical spine. ASD can be studied as “non-ASD” versus “ASD,” as “mild ASD” versus “severe ASD,” or as “negative progression of ASD” versus “positive progression of ASD.”

Statistical analysis

Patients in the NECK trial and the PROCON trial were subject of this study. All the data were presented as mean± standard deviation. Baseline and follow-up characteristics of the ACD, ACDF, and ACDA treatment group were compared using analysis of variance for continuous data and chi-square test for categorical data. Student *t* test was used to compare continuous data between groups. Logistic regression tests were applied to evaluate correlations between ROM and ASD and ROM and NDI. Chi-square tests or Fisher’s exact test were applied to correlate the dichotomized ROM at the target level to the presence of ASD. Tests were two tailed, and a *p* value of <.05 was considered significant. SPSS software, version 23.0, was used for all statistical analyses (SPSS, Inc., Chicago, IL).

Results

In the NECK trial, 111 patients were included and randomly assigned to ACD (38 patients), ACDF (38 patients),

Table 2
Patient demographics

	ACD	ACDF	ACDA	Total	p Value
Population	83	85	85	253	–
Age (y, mean±SD)	45.3±6.7	45.6±7.6	44.8±7.7	45.2±7.3	.787
BMI (mean±SD)	26.2±3.8	26.6±4.7	26.7±4.1	26.5±4.2	.726
Gender (male)	42	37	43	122	.939
Smoking	33	40	41	118	.305
Alcohol	46	52	55	153	.565
Herniated level					
C4–C5	1	2	0	3	–
C5–C6	46	39	40	125	–
C6–C7	36	43	45	124	–
C7–Th1	0	1	0	1	–

ACD, anterior cervical discectomy; ACDF, anterior cervical discectomy with fusion; ACDA, anterior cervical discectomy with arthroplasty; SD, standard deviation; BMI, body mass index.

or ACDA (35 patients). At baseline, X-ray data were available for 107 patients and for 98 patients at 2-year follow-up.

In the PROCON trial, 142 patients were randomized into ACD (45 patients), ACDF (47 patients), or ACDA (50 patients). At baseline, X-ray data were available for 121 patients and for 70 patients at 2-year follow-up.

Demographics

Baseline characteristics are presented in Table 2. The mean age of the study population was 45.2±7.3 years, ranging from 27 to 70 years. There was no difference regarding baseline characteristics between treatment groups. Surgery was most frequent at levels C5–C6 and C6–C7.

ROM

In Fig. 1, the segmental ROM were not statistically different at baseline (p=.744). At both 1- and 2-year follow-up, the ROM at the index level of patients with ACDA was significantly higher than the ROM in patients with ACD and ACDF (p<.001, Table S1).

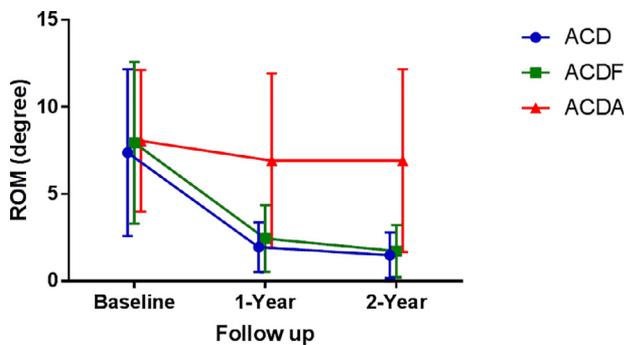


Fig. 1. ROM of index level.

Table 3
Patients with fusion (ROM<4°)

Follow-up	ACD	ACDF	ACDA	Total
1-year follow-up	91.5%	79.6%	33.8%	66.5%
2-year follow-up	95.7%	86.4%	36.8%	70.1%

ROM, range of motion; ACD, anterior cervical discectomy; ACDF, anterior cervical discectomy with fusion; ACDA, anterior cervical discectomy with arthroplasty.

ROM at the target level was not consequently absent (“fused”) in the ACD and ACDF groups, and not consequently maintained (“mobile”) in the ACDA group. If a cut-off value of 4° movement was taken into consideration, it was demonstrated that 96% of patients in the ACD group and 86% of patients in the ACDF group were fused at 2 years’ follow-up, and that 63% of patients in the ACDA group maintained mobile (Table 3). If the 63% of patients in the ACDA group who maintained mobile were considered, the ROM at the target level was 10.1°±3.9°.

In Fig. 2, ROM of the total cervical spine was comparable for all patients at baseline (p=.523). The patients in the ACDA group had a higher global ROM than those in the

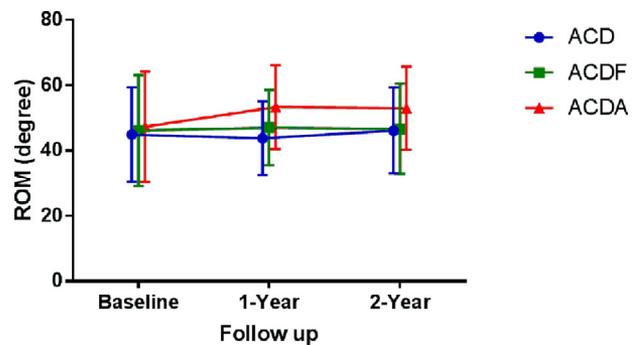


Fig. 2. ROM of total cervical spine.

Table 4
The incidence of ASD

		ACD	ACDF	ACDA	Total	p Value
ASD	Baseline	38.0% (27)	36.3% (29)	28.6% (22)	34.2% (78)	.428
	1-year FU	49.2% (32)	44.3% (27)	46.7% (35)	46.8% (94)	.855
	2-year FU	62.5% (35)	54.9% (28)	55.7% (34)	57.7% (97)	.674
Severe ASD	Baseline	15.5% (11)	13.8% (11)	13.0% (10)	14.0% (32)	.905
	1-year FU	21.5% (14)	23.0% (14)	14.5% (11)	19.3% (39)	.393
	2-year FU	28.6% (16)	25.5% (13)	19.7% (12)	24.4% (41)	.522
Positive ASD progression	1-year FU	24.5% (13)	17.3% (9)	21.0% (13)	21.0% (35)	.662
	2-year FU	32.6% (15)	25.0% (12)	30.9% (17)	29.5% (44)	.693

ASD, adjacent segment degeneration; ACD, anterior cervical discectomy; ACDF, anterior cervical discectomy with fusion; ACDA, anterior cervical discectomy with arthroplasty; FU, follow-up.

ACD group and ACDF group, at both 1- and 2-year follow-up ($p < .001$ and $p = .016$, Table S1).

ASD

The incidence of ASD was summarized in Table 4. No significant difference could be detected between three treatment arms at both baseline, 1- and 2-year follow-up, neither the incidence of ASD nor the incidence of severe ASD. Similarly, positive progression of ASD was comparable between three groups at 1 year and 2 years after surgery.

Correlation between ROM and ASD

At 2-year follow-up, no correlation between segmental ROM and the presence of ASD was demonstrated ($p = .766$). Neither was there such a correlation if the ROM of the whole cervical spine was considered ($p = .087$). Moreover, neither segmental ROM nor global ROM was correlated with either severe ASD or positive progression of ASD ($p > .05$).

As we stated above, 63% of patients with ACDA had radiographic preserved ROM ($>4^\circ$) versus 37% who did not at 2-year follow-up. In the ACDA group exclusively, no correlation could be demonstrated between preserved ROM and the presence of ASD, severe ASD, nor positive ASD progression (Table 5).

Furthermore, if the patients were studied irrespective of surgical method, no significant correlation could be detected between preserved ROM and ASD, with the

Table 5
ASD and ROM in the ACDA group

	Mobile*	Fused†	p
ASD	31.6% (18)	22.8% (13)	.384
Non-ASD	31.6% (18)	14.0% (8)	
Severe ASD	8.8% (5)	8.8% (5)	.473
Mild ASD	54.4% (31)	28.1% (16)	
Positive ASD progression	17.6% (9)	9.8% (5)	1.0
Negative ASD progression	49.0% (25)	23.5% (12)	

ASD, adjacent segment degeneration; ROM, range of motion; ACDA, anterior cervical discectomy with arthroplasty.

* Range of motion more than 4° .

† Range of motion less than 4° .

exception of the 2-year results, if ASD is dichotomized in “mild ASD” and “severe ASD” ($p = .042$; Table 6).

Correlation between ROM and neck disability

If the 4° cut-off value for ROM at the index level was used to study the correlation between ROM and NDI, no significant correlation could be demonstrated, neither at baseline, 1-year nor 2-year follow-up ($p > .05$).

Correlation between ASD and neck disability

No correlation was found between neck disability with the presence of ASD, mild ASD nor positive ASD progression (Table 7).

Table 6
ASD and ROM

		ASD	Non-ASD	p Value	Severe ASD	Mild ASD	p Value	Positive ASD progression	Negative ASD progression	p Value
1-year FU	Mobile*	14.8% (25)	19.5% (33)	.493	5.3% (9)	29.0% (49)	.493	5.0% (7)	32.4% (45)	.072
	Fused†	32.0% (54)	33.7% (57)		13.0% (22)	52.7% (89)		16.5% (23)	46.0% (64)	
2-year FU	Mobile*	14.4% (21)	15.8% (23)	.115	4.1% (6)	26.0% (38)	.042	8.6% (11)	24.2% (31)	.636
	Fused†	43.2% (63)	26.7% (39)		20.5% (30)	49.3% (72)		20.3% (26)	46.9% (60)	

ASD, adjacent segment degeneration; ROM, range of motion; FU, follow-up.

* Range of motion more than 4° .

† Range of motion less than 4° .

Table 7
ASD and NDI

	ASD	Non-ASD	p Value
Baseline	40.3±15.1	39.2±15.6	.615
1-year FU	14.5±13.8	15.8±16.4	.593
2-year FU	16.0±16.8	16.6±16.3	.837
	Severe ASD	Mild ASD	p Value
Baseline	40.6±12.7	39.4±15.8	.668
1-year FU	13.8±13.7	15.5±15.5	.578
2-year FU	18.2±15.5	15.6±15.5	.438
	Positive ASD progression	Negative ASD progression	p Value
1-year FU	15.4±14.8	14.1±14.0	.704
2-year FU	15.9±15.1	16.5±16.4	.864

ASD, adjacent segment degeneration; NDI, Neck Disability Index; FU, follow-up.

Discussion

The rationale for cervical motion preserving devices is to reduce accelerated degeneration at adjacent levels. It is thought that this will result in reduction of ASD and better functional outcome in the long term. We demonstrated that ROM, neither at the target level nor of the whole cervical spine, was correlated to ASD 2 years after surgery. Moreover, we demonstrated that there was no difference in ASD in patients who were subjected to cervical anterior discectomy with fusion and patients who received a prosthesis, which is in line with the recent published results of MacDowall et al. [20], who demonstrated that clinical and radiological ASD were comparable between fusion and arthroplasty cohorts. In some patients, accelerated degeneration at the adjacent levels can lead to clinical symptoms, like neck pain, radiculopathy, and disability, which can be represented by the NDI value. In agreement with earlier reports [23] in which the NDI was demonstrated not to differ between the ACD, ACDF, and ACDA treatment arms, ASD did not demonstrate a correlation to NDI.

In the ACDA group, 63% patients with a preserved ROM ($>4^\circ$) did not show a significantly lower incidence of ASD or less positive ASD progression than patients with an immobile cervical segment. Therefore, the rationale for cervical motion preserving devices to reduce accelerated degeneration at the adjacent levels is not confirmed in the present study.

Disc degeneration and osteophyte formation are physiological processes, and therefore some extent of degeneration at the adjacent disc levels is expected to be already present at baseline in a population with a mean age of 45. In accordance, our study documented that this type of degeneration existed in 34% of the patients at baseline. A similar result was reported previously by Coric et al. [4], who demonstrated that ASD was present in more than 50% of patients before undergoing ACDF or ACDA. In the 2-year follow-up period of our patients, the ASD increased to 58%, irrespective of surgical treatment. It is generally presumed that the development of ASD is a slow process,

and that therefore long-term follow-up periods are essential in order to properly judge the occurrence of ASD. Nevertheless, an increase of circa 20% of ASD (or 20% of patients with progression of ASD) in a group of 250 patients, within the first 2 years after surgery, without a difference between the three groups, justifies the conclusion that ASD is not significantly dependent on ROM of the target level. Our results are in contradiction to several studies demonstrating that ACDA results in a lower incidence of ASD [4–8,32] in comparison to ACDF. However, the majority of these studies failed to provide ASD information on baseline, introducing selection bias.

A limitation of the current study may be that determining ROM on X-ray will depend on the ability and willingness of the patients to reach full flexion and extension of the cervical spine. Unfortunately, there is no method to improve it. The quality of X-ray is important as well, because the angles will be influenced by angling of the cervical vertebrae in the coronal plane. Another flaw is the focus on radiological ASD. Clinical ASD would be represented by invalidating radicular symptoms due to a herniated disc at the adjacent level. In ultimo, if these complaints would be significantly invalidating, subsequent surgery would follow. The number of reoperations in the three groups for this diagnosis would therefore be a suitable measure for clinical ASD. In an earlier publication, Donk et al. [33] showed that reoperations were more prevalent in the ACDF group than in the other two groups, but that differences were very small. Likewise, in the NECK trial, reoperation rates were very low. Therefore, numbers are too small to draw meaningful conclusions.

Conclusions

ROM is not correlated to ASD, and clinical outcome is not correlated to ROM following anterior cervical discectomy. Therefore, the relevance of maintaining ROM at the index level seems absent. However, the follow-up of 2 years may be too short to draw firm conclusions.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.spinee.2019.07.011>.

References

- [1] Goffin J, Geusens E, Vantomme N, Quintens E, Waerzeggers Y, Depreitere B, et al. Long-term follow-up after interbody fusion of the cervical spine. *J Spin Disord Tech* 2004;17:79–85.
- [2] Gore DR. Roentgenographic findings in the cervical spine in asymptomatic persons: a ten-year follow-up. *Spine* 2001;26:2463–6.
- [3] Okada E, Matsumoto M, Ichihara D, Chiba K, Toyama Y, Fujiwara H, et al. Aging of the cervical spine in healthy volunteers: a 10-year longitudinal magnetic resonance imaging study. *Spine (Phila Pa 1976)* 2009;34:706–12.
- [4] Coric D, Nunley PD, Guyer RD, Musante D, Carmody CN, Gordon CR, et al. Prospective, randomized, multicenter study of cervical arthroplasty: 269 patients from the KineflexC artificial disc investigational device exemption study with a minimum 2-year follow-up: clinical article. *J Neurosurg Spine* 2011;15:348–58.
- [5] Phillips FM, Geisler FH, Gilder KM, Reah C, Howell KM, McAfee PC. Long-term outcomes of the US FDA IDE prospective, randomized controlled clinical trial comparing PCM cervical disc arthroplasty with anterior cervical discectomy and fusion. *Spine* 2015;40:674–83.
- [6] Hisey MS, Zigler JE, Jackson R, Nunley PD, Bae HW, Kim KD, 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.
- [7] Sun Y, Zhao YB, Pan SF, Zhou FF, Chen ZQ, Liu ZJ. Comparison of adjacent segment degeneration five years after single level cervical fusion and cervical arthroplasty: a retrospective controlled study. *Chin Med J* 2012;125:3939–41.
- [8] Davis RJ, Nunley PD, Kim KD, Hisey MS, Jackson RJ, Bae HW, et al. Two-level total disc replacement with Mobi-C cervical artificial disc versus anterior discectomy and fusion: a prospective, randomized, controlled multicenter clinical trial with 4-year follow-up results. *J Neurosurg Spine* 2015;22:15–25.
- [9] Janssen ME, Zigler JE, Spivak JM, Delamarter RB, Darden 2nd BV, Kopjar B. 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 Vol* 2015;97:1738–47.
- [10] Park JH, Roh KH, Cho JY, Ra YS, Rhim SC, Noh SW. Comparative analysis of cervical arthroplasty using Mobi-C(r) and anterior cervical discectomy and fusion using the solis(r)-cage. *J Korean Neurosurg Soc* 2008;44:217–21.
- [11] Hou Y, Nie L, Pan X, Si M, Han Y, Li J, et al. Effectiveness and safety of Mobi-C for treatment of single-level cervical disc spondylosis: a randomised control trial with a minimum of five years of follow-up. *Bone Joint J* 2016;98-b:829–33.
- [12] Zhang H-X, Shao Y-D, Chen Y, Hou Y, Cheng L, Si M, et al. A prospective, randomised, controlled multicentre study comparing cervical disc replacement with anterior cervical decompression and fusion. *Int Orthop* 2014;38:2533–41.
- [13] Coric D, Kim PK, Clemente JD, Boltes MO, Nussbaum M, James S. Prospective randomized study of cervical arthroplasty and anterior cervical discectomy and fusion with long-term follow-up: results in 74 patients from a single site. *J Neurosurg Spine* 2013;18:36–42.
- [14] Sala V, Lisi C, Di Natali G, Zanellato S, Dall'Angelo A, Tinelli C, et al. Functional and quality of life evaluation after single level cervical discectomy and fusion or cervical artificial disc replacement. *Giornale italiano di medicina del lavoro ed ergonomia* 2015;37:239–44.
- [15] Wang Y, Cai B, Zhang XS, Xiao SH, Wang Z, Lu N, et al. Clinical outcomes of single level Bryan cervical disc arthroplasty: a prospective controlled study. *Zhonghua wai ke za zhi [Chin J Surg]* 2008;46:328–32.
- [16] Li Z, Yu S, Zhao Y, Hou S, Fu Q, Li F, et al. Clinical and radiologic comparison of dynamic cervical implant arthroplasty versus anterior cervical discectomy and fusion for the treatment of cervical degenerative disc disease. *J Clin Neurosci* 2014;21:942–8.
- [17] Grasso G. Clinical and radiological features of hybrid surgery in multilevel cervical degenerative disc disease. *Eur Spine J* 2015;24(suppl 7):842–8.
- [18] Latka D, Kozłowska K, Miekisiak G, Latka K, Chowaniec J, Olbrycht T, et al. Safety and efficacy of cervical disc arthroplasty in preventing the adjacent segment disease: a meta-analysis of mid- to long-term outcomes in prospective, randomized, controlled multicenter studies. *Ther Clin Risk Manag* 2019;15:531–9.
- [19] Xu S, Liang Y, Zhu Z, Qian Y, Liu H. Adjacent segment degeneration or disease after cervical total disc replacement: a meta-analysis of randomized controlled trials. *J Orthop Surg Res* 2018;13:244.
- [20] MacDowall A, Canto Moreira N, Marques C, Skeppholm M, Lindhagen L, Robinson Y, et al. Artificial disc replacement versus fusion in patients with cervical degenerative disc disease and radiculopathy: a randomized controlled trial with 5-year outcomes. *J Neurosurg Spine* 2019;30:323–31.
- [21] Yang X, Janssen T, Arts MP, Peul WC, Vleggeert-Lankamp CLA. Radiological follow-up after implanting cervical disc prosthesis in anterior discectomy: a systematic review. *Spine J* 2018;18:1678–93.
- [22] Arts MP, Brand R, van den Akker E, Koes BW, Peul WC. The Netherlands Cervical Kinematics (NECK) trial. Cost-effectiveness of anterior cervical discectomy with or without interbody fusion and arthroplasty in the treatment of cervical disc herniation; a double-blind randomised multicenter study. *BMC Musculoskelet Disord* 2010;11:122.
- [23] Vleggeert-Lankamp CLA, Janssen TMH, van Zwet E, Goedmakers CMW, Bosscher L, Peul W, et al. The NECK trial: effectiveness of anterior cervical discectomy with or without interbody fusion and arthroplasty in the treatment of cervical disc herniation; a double-blinded randomized controlled trial. *Spine J* 2019;19:965–75.
- [24] Bartels RH, Donk R, van der Wilt GJ, Grotenhuis JA, Venderink D. Design of the PROCON trial: a prospective, randomized multi-center study comparing cervical anterior discectomy without fusion, with fusion or with arthroplasty. *BMC Musculoskelet Disord* 2006;7:85.
- [25] Donk RD, Verbeek ALM, Verhagen WIM, Groenewoud H, Hosman AJF, Bartels R. What's the best surgical treatment for patients with cervical radiculopathy due to single-level degenerative disease? A randomized controlled trial. *PLoS One* 2017;12:e0183603.
- [26] Vernon H, Mior S. The Neck Disability Index: a study of reliability and validity. *J Manipulative Physiol Ther* 1991;14:409–15.
- [27] Vos CJ, Verhagen AP, Koes BW. Reliability and responsiveness of the Dutch version of the Neck Disability Index in patients with acute neck pain in general practice. *Eur Spine J* 2006;15:1729–36.

- [28] Pietrobon R, Coeytaux RR, Carey TS, Richardson WJ, DeVellis RF. Standard scales for measurement of functional outcome for cervical pain or dysfunction: a systematic review. *Spine* 2002;27:515–22.
- [29] Walraevens J, Demaerel P, Suetens P, Van Calenbergh F, van Loon J, Vander Sloten J, et al. Longitudinal prospective long-term radiographic follow-up after treatment of single-level cervical disk disease with the Bryan cervical disc. *Neurosurgery* 2010;67:679–87. discussion 87.
- [30] Baskin DS, Ryan P, Sonntag V, Westmark R, Widmayer MA. A prospective, randomized, controlled cervical fusion study using recombinant human bone morphogenetic protein-2 with the CORNERSTONE-SR allograft ring and the ATLANTIS anterior cervical plate. *Spine (Phila Pa 1976)* 2003;28:1219–24. discussion 25.
- [31] Heller JG, Sasso RC, Papadopoulos SM, Anderson PA, Fessler RG, Hacker RJ, 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.
- [32] Robertson JT, Papadopoulos SM, Traynelis VC. Assessment of adjacent-segment disease in patients treated with cervical fusion or arthroplasty: a prospective 2-year study. *J Neurosurg Spine* 2005;3: 417–23.
- [33] Donk RD, Verhagen WIM, Hosman AJF, Verbeek A, Bartels R. Symptomatic adjacent segment disease after anterior cervical discectomy for single-level degenerative disk disease. *Clin Spine Surg* 2018;31:E50–4.