Systematic Review and Meta-Analysis

Medicine®

OPEN

Prevalence of adjacent segment disease following cervical spine surgery

A PRISMA-compliant systematic review and meta-analysis

Lingde Kong (MD), Junming Cao (PhD), Linfeng Wang (PhD), Yong Shen (PhD)*

Abstract Prevalence estimates of adjacent segment degeneration (ASD) following cervical spine surgery varied greatly in current studies. We conducted a systematic review and meta-analysis to summarize the point prevalence of ASD after cervical spine surgery.

Methods Comprehensive electronic searches of PubMed, Embase, Web of Knowledge, and Cochrane Library databases were conducted to identify any study published from initial state to January 2016. Those reporting the prevalence of ASD after cervical surgery were included. A random-effects model was used to estimate the prevalence of radiographic ASD, symptomatic ASD, and reoperation ASD. Univariate meta-regression analyses were conducted to explore the potential associations between prevalence and length of follow-up. All analyses were performed using R version 3.2.3 (R Foundation for Statistical Computing).

Results A total of 83 studies were included in the meta-analysis. The prevalence of radiographic ASD, symptomatic ASD, and reoperation ASD after cervical surgery was 28.28% (95% confidence interval [CI], 20.96–36.96), 13.34% (95% CI, 11.06–16.00), and 5.78% (95% CI, 4.99–6.69), respectively, in a general analysis. It was found 2.79%, 1.43%, and 0.24% additions per year of follow-up in the incidence of radiographic ASD, symptomatic ASD, and reoperation ASD, respectively.

Conclusion This meta-analysis provides some details about the prevalence of radiographic ASD, symptomatic ASD, and reoperation ASD after cervical spine surgery. However, the results of this meta-analysis should be interpreted with caution because of the heterogeneity among the studies.

Abbreviations: ACDF = anterior cervical discectomy and fusion, ASD = adjacent segment degeneration, CI = confidence interval, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RR = risk ratio, TDR = total disc replacement.

Keywords: adjacent segment disease, cervical surgery, meta-analysis, prevalence, review

1. Introduction

Cervical degenerative disease is a pathological condition that affects the adult spine and is a common cause of cervical radiculopathy and myelopathy in older patients. Cervical surgery can decompress the neural elements and stabilize the affected segments at the same time. However, adjacent segment degeneration (ASD) is often observed in patients who are followed for a long period.[1,2]

Postoperative degenerative changes include both radiographic ASD and symptomatic ASD. Radiographic ASD could develop into symptomatic ASD, which correlates with some clinical findings, and symptomatic ASD could lead to serious pain, dysfunction or need for additional surgery. Hilibrand et al[3] reported an incidence of 2.9% per year of the development of symptomatic ASD after single-level anterior cervical discectomy and fusion (ACDF) and estimated that about 25.6% of patients would have symptomatic ASD within 10 years after their index surgery. They also found that more than two-thirds of patients developing symptomatic ASD experienced failure of conservative treatment and required surgical procedures.

A reliable estimate of the prevalence of postoperative ASD is important for informing efforts to prevent, treat, and identify causes of ASD. Over the past few years, several meta-analyses have reported on ASD after lumbar or spinal surgery,[4–6] but to the best of our knowledge, no comprehensive meta-analysis of the epidemiological data on ASD following cervical surgery has been published. Thus, we conducted this systematic review and meta-analysis to obtain accurate figures on the prevalence of ASD after cervical surgery.

2. Methods

This study followed the systematic review methodology proposed in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[7] As all the analyses were performed by using data extracted from published trials, it is not necessary to obtain ethical approval for this study.

Editor: Perbinder Grewal.

The authors have no funding and conflicts of interest to disclose.

Department of Orthopedics, The Third Hospital of Hebei Medical University, Shijiazhuang, Hebei, P.R. China.

* Correspondence: Yong Shen, Department of Orthopedics, The Third Hospital of Hebei Medical University, 139 Ziqiang Road, Shijiazhuang, Hebei 050051, P.R. China (e-mail: shenyongspine@126.com).

Medicine (2016) 95:27(e4171)

Received: 19 March 2016 / Received in final form: 1 June 2016 / Accepted: 3 June 2016

http://dx.doi.org/10.1097/MD.0000000000004171

2.1. Literature search strategy

We searched PubMed, Embase, Web of Knowledge, and Cochrane Library databases for articles published up to January 2016, using the following search terms: ("adjacent level" or "adjacent segment") and ("pathology" or "disease") and ("cervical" or "spine" or "spinal"). The references of all publications were also retrieved to obtain further publications.

2.2. Inclusion and exclusion criteria

The following criteria were used for screening the literature. First, the study design included randomized controlled trials, cohort study, case–control study, and cross-sectional study. Second, sample size and point prevalence of ASD were provided or could be calculated. Third, the method of diagnosing ASD was described. Fourth, population was restricted to patients after cervical surgery.

Publications were excluded if they were review articles, case reports, editorials, or letters. Any biomechanical studies or clinical studies investigating cervical tumor, infection, or trauma were also excluded. The number of levels treated with total disc replacement (TDR) or ACDF was not a criterion for exclusion.

2.3. Data extraction and outcome measures

For each included study, the following information was extracted: first author, year of publication, country, sample size, surgical approach, study design, length of follow-up, and number of patients with ASD after surgery. The most comprehensive publication was used when several studies involved the same population.

2.4. Diagnosis of ASD and other criteria

Three main results were investigated in this study: radiographic ASD, symptomatic ASD, and reoperation ASD. Radiographic ASD was defined as radiographic changes at levels adjacent to a previous surgical segment. Symptomatic ASD is 1 type of radiographic ASD that leads to a new development of radiculopathy or myelopathy. Symptomatic ASD that required a further surgical intervention was considered reoperation ASD.

According to the different length of follow-up, <5 years was considered short-term follow-up; any period longer was considered long-term follow-up.

2.5. Assessment of methodological quality

Each included study was chosen independently by 2 authors using a published quality rating system designed especially for articles reporting on prevalence.[8] This 5-point scale system included whether the study design was appropriate for obtaining prevalence estimates; the sample was representative of the general population of patients after cervical surgery; the ASD diagnostic criteria were acceptable; diagnosis of ASD was performed on a consecutive or random sample of subjects; and the final diagnosis was known for 80% of eligible subjects.

2.6. Statistical analysis

We extracted data from each study, calculated the overall prevalence of ASD or risk ratios (RRs) with 95% confidence intervals (CIs), and obtained corresponding forest plots. Subgroup analysis was also conducted to discover the prevalence of different categories (number of operated level, approach, and type of surgery). In addition, we restricted analysis to randomized controlled trials that compared TDR and ACDF to investigate the different prevalence of reoperation ASD better between fusion and nonfusion techniques. Furthermore, univariate meta-regression analyses were conducted to explore the potential associations between prevalence and length of follow-up. Heterogeneity among studies was assessed by I^2 and Q tests. If I^2 value was <50% and *P* value was >0.10, it was considered significant heterogeneity. In this study, random-effects model was used to pool the results. The influence of individual studies on the overall prevalence estimate was explored by serially excluding each study in a sensitivity analysis. Begg test was used to test the publication bias.

All analyses were performed using R version 3.2.3 (R Foundation for Statistical Computing). *P* value of <0.05 was considered statistically significant.

3. Results

3.1. Literature search results

The first searches give a total of 849 records, and 295 records were duplicates. After review of the titles and abstracts, 438 were excluded. We retrieved full articles for further assessment, and 33 records were further excluded. Finally, 83 studies were included in the meta-analysis.[1–3,9–88]Figure 1 shows the details of the screening process.

3.2. Study characteristics

Of the 83 studies, 35 reported radiographic ASD, 24 reported symptomatic ASD, and 52 reported reoperation ASD. There were 4050, 4475, and 13,116 patients involved in the 3 types of ASD, respectively. The studies were from 14 countries. Among them, 36 took place in North America, 29 in Asia, 17 in Europe, and 1 in Oceania. The surgical procedures included ACDF, TDR, laminectomy, laminoplasty, posterior foraminotomy, and posterior cervical fusion. The quality score of the included studies ranged from 3 to 5 points. Detailed information on all included studies is shown in Table 1.

3.3. Prevalence of ASD

Thirty-five studies reported the prevalence of radiographic ASD after cervical surgery and revealed that the occurrence of

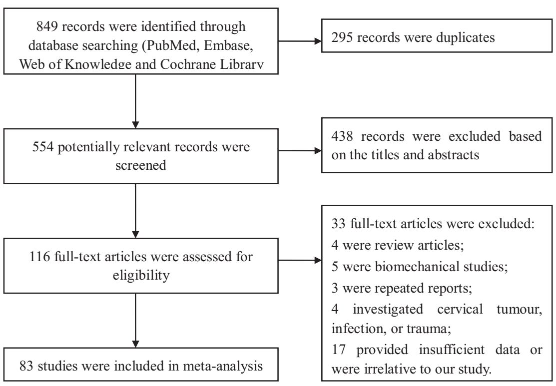

Figure 1. Flow diagram of the study selection process in the meta-analysis.

Table 1

Basic characteristics of included studies.

First author	Publication year	Country	Area	Period	Mean follow-up time, mo	Approach	Surgery	Total number	Score
Hilibrand	1999	United States	Europe	1973–1992	120	Anterior	Fusion	374	5
Bolesta	2002	United States	North America	1990–1997	51	Anterior	Fusion	40	4
Goffin	2004	Belgium	Europe	—	100.6	Anterior	Fusion	180	5
Ishihara	2004	Japan	Asia	1981–1997	112.8	Anterior	Fusion	112	4
Deutsch	2005	United States	North America	1997–2001	36	Posterior	Fusion	58	4
Ikenaga	2005	Japan	Asia	1989–1998	102	Anterior	Fusion	100	5
Robertson	2005	United States	North America	1997–1998, 2000–2004	24	Anterior	Fusion, arthroplasty	232	4
Yue	2005	United States	North America	1992–1997	34.6	Anterior	Fusion	71	4
Papadopoulos	2006	United States	North America	1996–2002	17.6	Anterior	Fusion	46	3
Sekhon	2006	United States	North America	—	30.1	Posterior	Fusion	50	4
Clarke	2007	United States	North America	1972–1992	96	Posterior	Foraminotomy	303	4
Mummaneni	2007	United States	North America	2002–2004	24	Anterior	Fusion, arthroplasty	421	5
Sasso	2007	United States	North America	—	24	Anterior	Fusion, arthroplasty	115	5
Pickett	2008	United States	North America	—	43.2	Anterior	Fusion	76	4
Elsawaf	2009	Italy	Europe	2003–2005	—	Anterior	Fusion	20	4
Ozer	2009	Turkey	Europe	1997–2000	92	Anterior	Fusion	15	3
Yi	2009	Korea	Asia	2003–2006	23	Anterior	Arthroplasty	78	4
Acikbas	2010	Turkey	Europe	1986–2006	89	Anterior, posterior	Fusion	79	5
Burkus	2010	United States	North America	2002–2004	—	Anterior	Fusion, arthroplasty	541	5
Chang	2010	United States	North America	1997–2006	20.8	Anterior	Fusion	27	4
Coric	2010	United States	North America	—	38	Anterior	Fusion, arthroplasty	90	5
Jawahar	2010	United States	North America	—	36.4 (median)	Anterior	Fusion, arthroplasty	93	5
Joo	2010	Korea	Asia	2004–2009	15.9	Anterior	Fusion	42	5
Walraevens	2010	Belgium	Europe	—	—	Anterior	Arthroplasty	89	4
Bisson	2011	United States	North America	1985–2007	26	Anterior	Fusion	17	4
Coric	2011	United States	North America	—	24 (minimum)	Anterior	Fusion, arthroplasty	234	5
Faldini	2011	Italy	Europe	1985–1995	120 (minimum)	Anterior	Fusion	107	4
Hamilton	2011	United States	North America	2003–2008	40	Posterior	Fusion	53	4
Maldonado	2011	Spain	Europe	2004–2006	36 (minimum)	Anterior	Fusion, arthroplasty	190	3
Marotta	2011	Italy	Europe	2001–2003	77	Anterior	Fusion	132	4
Nagata	2011	Japan	Asia	1976–1997	255.6	Anterior	Fusion	22	4
Quan	2011	France	Europe	2000–2001	96 (minimum)	Anterior	Arthroplasty	21	4
Song[40]	2011	Korea	Asia	1999–2004	84.8	Anterior	Fusion	174	5
Song[41]	2011	Korea	Asia	2001–2007	34.1	Anterior	Fusion	21	4
Vedantam	2011	India	Asia	2001–2007	48.5	Anterior	Fusion	36	3
Yao	2011	China	Asia	2000–2004	60 (minimum)	Anterior	Fusion	67	4
Andaluz	2012	United States	North America	1993–2008	180 (minimum)	Anterior	Fusion	130	4
Gao	2012	China	Asia	1996–2006	102.1	Anterior	Fusion	145	4
Komura	2012	Japan	Asia	1997–2006	61.4	Anterior	Fusion	102	5
Nakashima	2012	Japan	Asia	—	49.2	Posterior	Fusion	84	4
Nunley	2012	United States	North America	2005–2007	38 (median)	Anterior	Arthroplasty	170	5
Rollinghoff	2012	Germany	Europe	2006–2009	17.5	Anterior	Fusion	23	4
Singh	2012	United States	North America	2002–2004	42	Anterior	Fusion, arthroplasty	207	4
Upadhyaya	2012	United States	North America	—	24 (minimum)	Anterior	Fusion, arthroplasty	1098	5
Blumenthal	2013	United States	North America	—	55.1	Anterior	Fusion, arthroplasty	136	5
Chen	2013	China	Asia	1996–2005	—	Anterior	Fusion	1241	4
Coric	2013	United States	North America	—	72	Anterior	Fusion, arthroplasty	74	5
Delamarter	2013	United States	North America	—	60 (minimum)	Anterior	Fusion, arthroplasty	133	5
Eubanks	2013	United States	North America	1978–2003	36.2	Anterior	Fusion	364	5
Li	2013	China	Asia	2000–2007	79.6	Anterior	Fusion	89	4
Noriega	2013	Spain	Europe	1989–1995	264	Anterior	Fusion	28	3
Jeong Y Park	2013	Korea	Asia	2005–2006	62.2	Anterior	Fusion, arthroplasty	43	4
Youn-Kwan Park	2013	Korea	Asia	1999–2005	105.6	Anterior	Fusion	44	4
Sung Bae Park	2013	Korea	Asia	2004–2010	29.5	Anterior	Fusion	28	4
Pereira	2013	United Kingdom	Europe	2003–2009	—	Anterior	Fusion	30	4
Saarinen	2013	Finland	Europe	1998–1999	132	Anterior	Fusion	327	4
Burkus	2014	United States	North America	2002–2004	84 (minimum)	Anterior	Fusion, arthroplasty	395	5
Bydon[2]	2014	United States	North America	1990–2010	92.4	Anterior	Fusion	888	4
Bydon[65]	2014	United States	North America	1990–2013	49.8	Posterior	Foraminotomy	151	4
Chung	2014	Korea	Asia	1984–2002	194.4	Anterior	Fusion	177	5
Kan	2014	China	Asia	2002–2012	36 (median)	Anterior	Fusion, arthroplasty	63	5
Lee	2014	United States	North America	1999–2010	48	Anterior, posterior	Fusion, arthroplasty	1358	4
Li	2014	China	Asia	2009–2011	31.2	Anterior	Fusion, arthroplasty	81	4

First author	Publication year	Country	Area	Period	Mean follow-up time, mo	Approach	Surgery	Total number	Score
Litrico	2014	France	Europe	1996–2000	174	Anterior	Fusion	288	4
Malham	2014	Australia	Oceania	2004–2008	92.4	Anterior	Arthroplasty	24	3
Kyung-Jin Song	2014	Korea	Asia	2002–2010	63.85	Anterior	Fusion	231	4
Ji-Soo Song	2014	Korea	Asia	—	81.5	Anterior	Fusion	242	4
Sun	2014	China	Asia	2009–2011	32.4	Anterior	Fusion, arthroplasty	30	5
Uehara	2014	Japan	Asia	1997–2007	90.2	Posterior	Fusion	19	4
van Eck	2014	United States	North America	2000–2010	31	Anterior	Fusion	672	4
Xu	2014	United States	North America	1990–2010	92.4	Anterior	Fusion	888	4
Hisey	2015	United States	North America	—	48 (minimum)	Anterior	Fusion, arthroplasty	245	5
Janssen	2015	United States	North America	2003–2004	84 (minimum)	Anterior	Fusion, arthroplasty	152	5
Lau	2015	United States	North America	2006–2012	25.7	Anterior	Fusion	44	4
Lee	2015	United States	North America	1999–2010	50	Anterior	Fusion	1038	4
Li	2015	China	Asia	2006–2008	31.2	Anterior	Fusion	116	3
Selvanathan	2015	United Kingdom	Europe	2008–2013	24 (median)	Anterior	Fusion	150	4
Shi	2015	China	Asia	2008–2012	41.11	Anterior	Fusion, arthroplasty	36	4
Zhang[85]	2015	China	Asia	1995–2005	114	Anterior	Fusion	122	5
Zhang[86]	2015	China	Asia	—	116.4	Anterior	Fusion	141	5
Hu	2016	United States	North America	2011–2013	12	Anterior	Fusion	104	4
Lei	2016	China	Asia	2005–2007	—	Anterior	Fusion	35	4
Shiban	2016	Germany	Europe	2007–2010	21	Anterior	Fusion	265	4

radiographic ASD ranged from 4.74% to 92.22%; the pooled prevalence was 28.28% (95% CI, 20.96–36.96) (Fig. 2). There was significant heterogeneity for radiographic ASD ($I^2=95.90\%$; Q=837.75; $P<0.01$).

The prevalence of symptomatic ASD ranged between 0% and 54.55% in 24 populations. The summary prevalence of symptomatic ASD was 13.34% (95% CI, 11.06–16.00) with significant heterogeneity ($I^2=76.90\%$; Q=99.67; $P<0.01$) (Fig. 3).

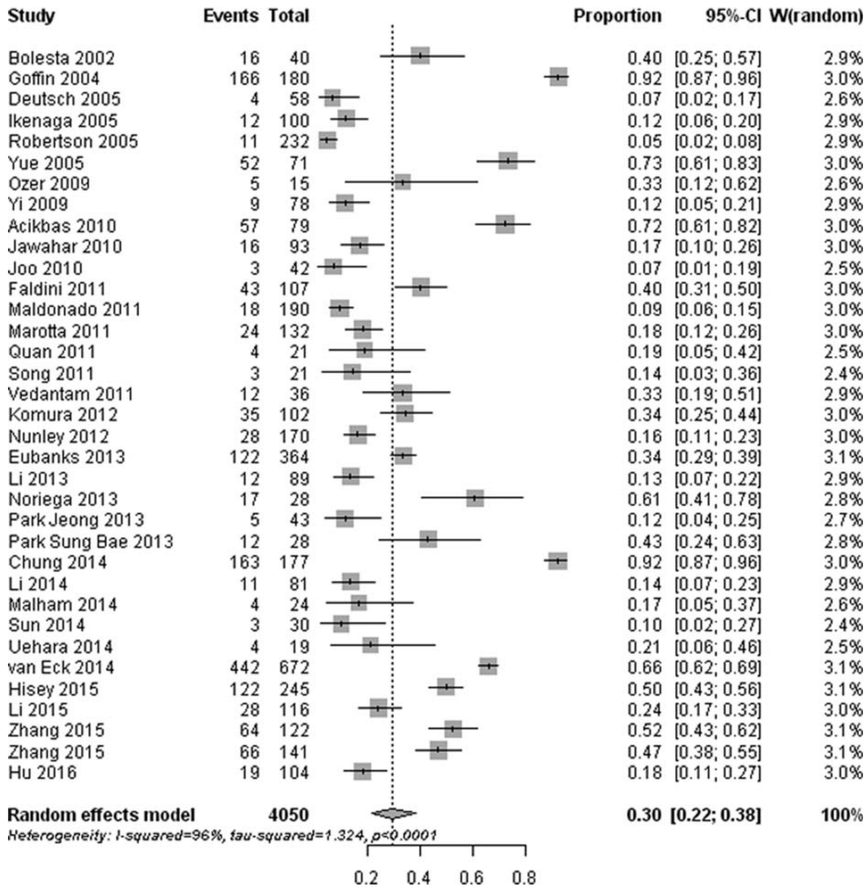

Figure 2. Forest plot of the prevalence of radiographic adjacent segment degeneration after cervical spine surgery.

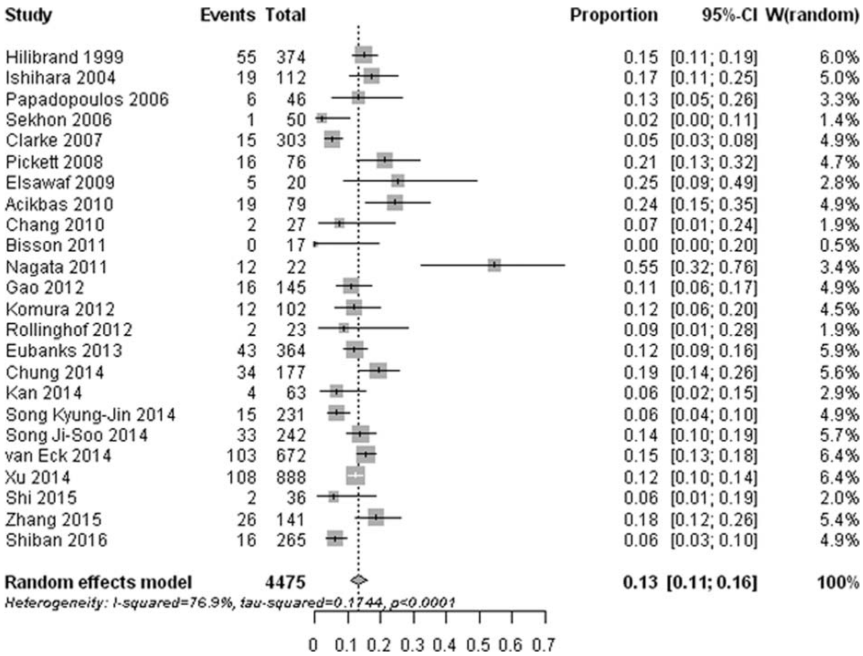

Figure 3. Forest plot of the prevalence of symptomatic adjacent segment degeneration after cervical spine surgery.

Reoperation ASD was reported in 52 studies, and the prevalence of reoperation ASD ranged from 0% to 16.90%; the pooled prevalence was 5.78% (95% CI, 4.99–6.69) (Fig. 4). There was significant heterogeneity ($I^2=69.60\%$; Q=167.58; $P<0.01$) for the reoperation ASD.

3.4. Prevalence of ASD by study-level characteristics

The studies were divided into short-term subgroup and long-term subgroup according to different length of follow-up, and then we summarized the stratified prevalence estimates based on number of level, approach, and surgery types. The pooled prevalence of ASD after single level, anterior approach and fusion surgery was higher than that after multiple level, posterior approach and arthroplasty. All main results of subgroup analyses are shown in Table 2.

3.5. Comparison of ASD between ACDF and TDR

Ten high-quality RCTs compared the prevalence of reoperation ASD after 1- or 2-level TDR with ACDF.[19,20,26,28,33,51,52,55,64,80] The test for heterogeneity was not significant ($I^2=31.3\%$; Q=13.1; $P=0.16$). The prevalence of reoperation ASD was significantly lower in the TDR group compared with the ACDF group (RR, 0.55; 95% CI, 0.35–0.85; $P<0.01$) (Fig. 5).

3.6. Length of follow-up and prevalence of ASD

Because the longitudinal studies reported different prevalence at different follow-up periods, we also investigated the association between length of follow-up and prevalence of ASD. The results of univariate meta-regression analysis found an addition of 2.79% ($P<0.01$), 1.43% ($P<0.01$), and 0.24% ($P=0.03$) per year of follow-up in the development of radiographic ASD, symptomatic ASD, and reoperation ASD, respectively.

3.7. Sensitivity analysis and publication bias

Sensitivity analysis, in which the meta-analyses were serially repeated after exclusion of each study, demonstrated that no individual study affected the overall prevalence estimate of symptomatic ASD or reoperation ASD by more than 1%. Particular individual studies were affecting the overall prevalence estimate of radiographic ASD >1% but <2%.

The funnel plot found an apparent publication bias in the assessment of reoperation ASD ($P=0.02$). No publication bias was found in the assessment of radiographic ASD ($P=0.49$) or symptomatic ASD ($P=0.49$).

4. Discussion

The pooled data of this meta-analysis showed that the prevalence of radiographic ASD, symptomatic ASD, and reoperation ASD after cervical surgery was 28.28%, 13.34%, and 5.78%, respectively. It showed that nearly half of the radiographic ASD patients would develop symptomatic ASD, and less than half of the symptomatic ASD would need additional cervical surgery.

The definition of radiographic ASD varied from 1 study to another, but the 1 proposed by Hilibrand et al[3] was used most: they divided ASD into 4 stages (from 1 to 4) according to plain radiography and magnetic resonance imaging, and stage 2 to stage 4 were considered indicative of radiographic ASD. However, in this meta-analysis, the number of studies using this definition was limited; thus, we cannot draw any convincing conclusions based on this definition. The unclear definition is the main cause of significant heterogeneity among studies in the assessment of radiography ASD. We think it could be better to assess and report radiographic ASD by using a unified classification of severity if possible. The definition of reoperation ASD, on the other hand, was more practical because it is much

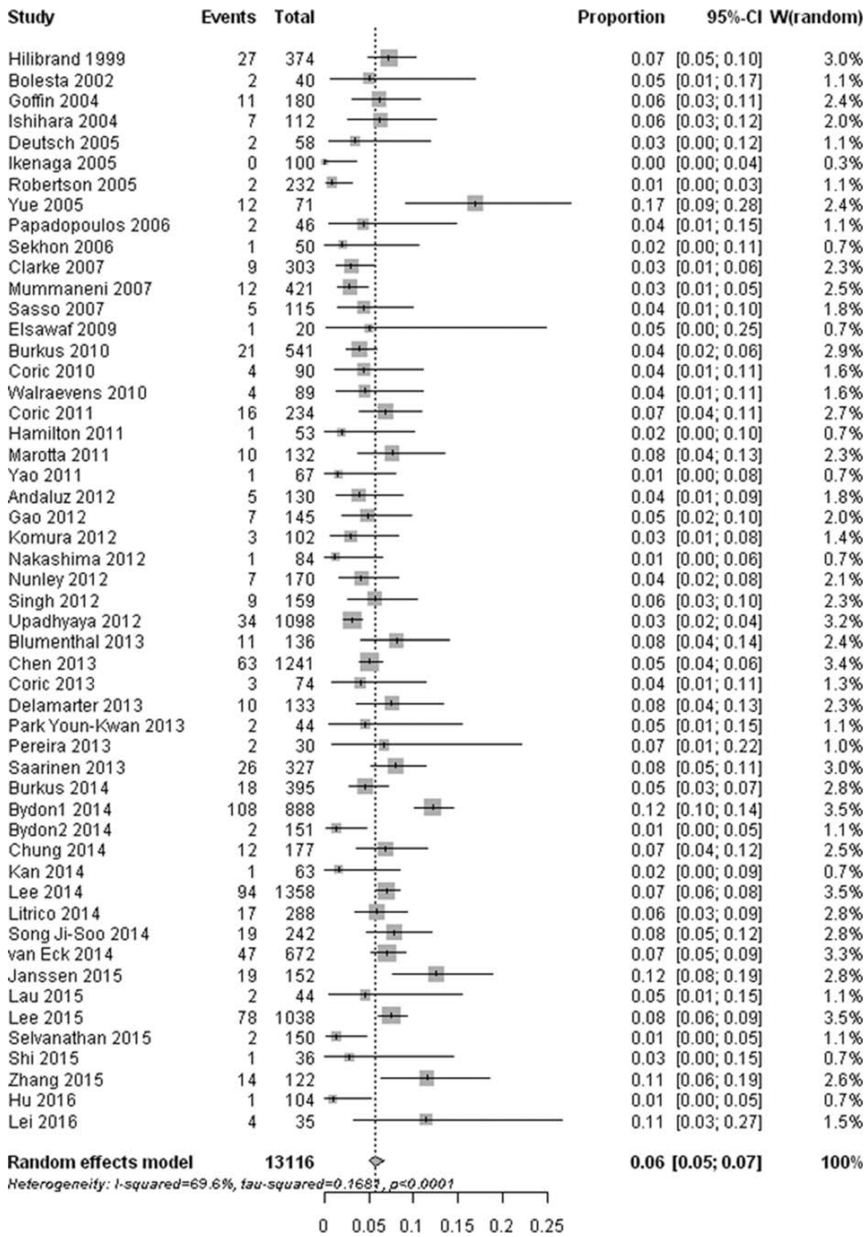

Figure 4. Forest plot of the prevalence of reoperation adjacent segment degeneration after cervical spine surgery.

easier to be unified and thus, could provide more robust results and more precise information to us.

Because there was substantial clinical and statistical heterogeneity, subgroup analyses were performed to explore the sources of heterogeneity and clarify the prevalence of different categories. We found that the prevalence of ASD in multilevel subgroup was lower than that in single-level subgroups, and this result was consistent with the study conducted by Hilibrand et al.[3] This finding may be explained by analysis of the levels that underwent surgery. ASD was more likely to occur at the C5/6 and C6/7 levels than at other levels. In patients with a single-level procedure, the C5/6 or C6/7 was involved most, and the adjacent C6/7 or C5/6 was at high risk to degenerate.[46] ASD was less common after multilevel surgery because these procedures usually included the higher-risk levels and had an end adjacent to segments that were at lower risk for the development of new disease. Our result also showed that anterior-approach subgroups had a higher prevalence of ASD than posterior-approach subgroups. This result could be due to the same reason as already mentioned, because the posterior approach usually was performed on patients with multilevel disc degeneration.

Several biomechanical studies suggested that fusion causes increased stress and strain on neighboring motion segments, which potentially contribute to accelerated degeneration, whereas TDR not only maintains physiologic motion at the operated level but also minimizes changes at the adjacent segments.[89–91] In the clinical trials, ASD was also found in TDR patients after several years of follow-up.[92] In

Table 2

Main results of subgroup analyses.

Types of ASD	Follow-up	Category	Subgroup	No. of studies	Prevalence, %	95% CI	No. of patients	Q	I^2, %	*P*
Radiographic	Short-term	Level	Single level	6	18.06	9.28–32.20	555	43.13	88.4	<0.01
			Multiple level	4	16.22	5.76–38.00	113	12.99	76.9	<0.01
		Approach	Anterior approach	16	23.27	14.25–35.62	2178	425.17	96.5	<0.01
			Posterior approach	1	6.90	2.61–16.98	58	—	—	—
		Surgery	Fusion	15	24.48	15.05–37.23	2178	326.30	95.7	<0.01
			Arthroplasty	6	14.31	9.79–20.45	437	8.29	39.7	0.14
	Long-term	Level	Single level	3	31.32	14.51–55.05	239	18.92	89.4	<0.01
			Multiple level	2	19.44	6.38–46.06	115	4.28	76.6	0.04
		Approach	Anterior approach	12	37.77	20.00–59.58	1063	311.75	96.5	<0.01
			Posterior approach	2	22.75	14.20–34.37	66	0.04	0	0.84
		Surgery	Fusion	13	39.93	23.69–58.73	1205	312.95	96.2	<0.01
			Arthroplasty	2	13.54	6.19–27.08	45	0.57	0	0.45
Symptomatic	Short-term	Level	Single level	1	8.70	2.18–28.88	23	—	—	—
			Multiple level	6	8.28	5.27–12.79	239	4.49	0	0.48
		Approach	Anterior approach	10	11.37	8.46–15.13	1589	23.75	62.1	<0.01
			Posterior approach	1	2.00	0.28–12.88	50	–	–	–
		Surgery	Fusion	9	11.50	8.29–15.74	1540	24.21	67.0	<0.01
			Arthroplasty	0	—	—	—	—	—	—
	Long-term	Level	Single level	2	11.38	2.14–42.96	382	23.37	95.7	<0.01
			Multiple level	0	—	—	—	—	—	—
		Approach	Anterior approach	11	15.53	12.26–19.48	2466	46.14	78.3	<0.01
			Posterior approach	2	11.07	2.15–41.33	350	16.58	94.0	<0.01
		Surgery	Fusion	12	14.50	11.18–18.59	2816	67.91	83.8	<0.01
			Arthroplasty	0	—	—	—	—	—	—
Reoperation	Short-term	Level	Single level	4	6.94	2.39–18.53	788	28.52	89.5	<0.01
			Multiple level	7	4.67	1.20–16.53	312	33.92	82.3	<0.01
		Approach	Anterior approach	17	5.79	4.00–8.31	3635	87.54	81.7	<0.01
			Posterior approach	5	1.91	0.91–3.95	396	1.21	0	0.88
		Surgery	Fusion	19	5.77	3.91–8.43	3113	85.51	79.0	<0.01
			Arthroplasty	7	4.17	2.76–6.25	819	7.53	20.3	0.27
	Long-term	Level	Single level	3	4.62	2.41–8.68	3001	4.44	55.0	<0.01
			Multiple level	1	0	—	100	—	—	—
		Approach	Anterior approach	14	7.07	5.65–8.82	3185	31.85	59.2	<0.01
			Posterior approach	1	2.97	1.55–5.61	303	—	—	—
		Surgery	Fusion	16	6.92	5.50–8.68	3569	43.29	65.4	<0.01
			Arthroplasty	1	4.88	1.22–17.52	41	—	—	—

ASD = adjacent segment degeneration, CI = confidence interval.

our meta-analysis, the prevalence of reoperation ASD after TDR was 44% lower than after ACDF. The prevalence of radiographic ASD and symptomatic ASD was not calculated because the relatively small number of studies reported corresponding data. However, this result gives us some clues that TDR may have the advantage of decreasing the incidence of postoperative ASD.

As we know, the prevalence of ASD increased with the extension of follow-up time.[11] This meta-analysis showed that with the addition of 1 follow-up year, the prevalence of

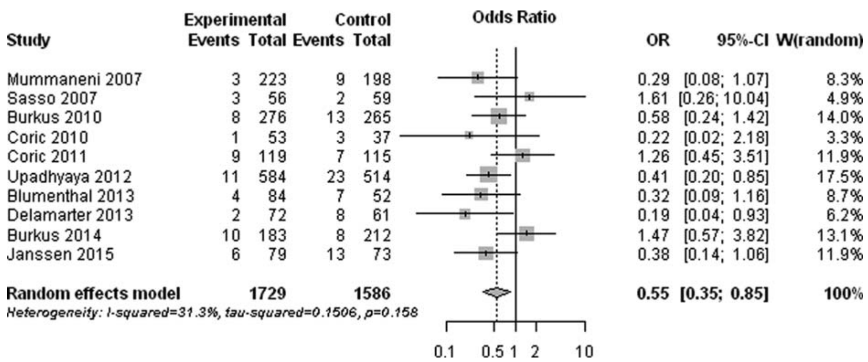

Figure 5. Forest plot showing the risk ratio of reoperation adjacent segment degeneration between the total disc replacement group and the anterior cervical discectomy and fusion group.

radiographic ASD, symptomatic ASD, and reoperation ASD significantly increased by 2.79%, 1.43%, and 0.24%, respectively. Nevertheless, the cervical spine naturally undergoes degenerative changes with increasing age, and this fact poses a notable challenge when establishing ASD resulting from fusion[93] versus that occurring simply as a natural aging process. Herkowitz et al[94] studied patients with cervical radiculopathy after ACDF or posterior foraminotomy without fusion. After a mean of 4.2 follow-up years, 39% of patients developed ASD after fusion, but 50% of patients undergoing posterior foraminotomy also developed ASD at the operated and adjacent levels. Gore[95] studied the natural history of cervical spondylotic disease in 159 asymptomatic patients and found that about 12% developed symptomatic spondylotic disease over a 10-year period. These studies imply that fusion is not the only factor that influences the risk of ASD, and future studies could provide more convincing evidence on this topic.

Several limitations should be considered when interpreting the findings of this study. First, there was a substantial amount of heterogeneity among the studies. Although potential sources of heterogeneity were explored by subgroup analyses of number of level, approach, and surgery types, none of them could sufficiently explain the heterogeneity. We did not conduct the subgroup analysis by age, gender, study design, or other factors because these data vary greatly. Second, not all of the included studies were designed for the prevalence study. Some of them did not provide detailed characteristics of patients with ASD, and this may have led to the imprecision of the pooled data. Third, the diagnosis criteria of ASD were not uniform among the included studies. Radiographic ASD, for example, could be better assessed and reported using classifications of severity. A multicentre prospective study using a single validated definition of ASD could provide a more accurate estimate of the prevalence of ASD after cervical surgery.

This meta-analysis provides detailed information on the prevalence of radiographic ASD, symptomatic ASD, and reoperation ASD after cervical surgery. This information should be useful to surgeons and patients to gain a better understanding of ASD during follow-up. However, because of the limitations noted earlier, the results of this meta-analysis should be interpreted with caution.

References

[1] Li J, Li Y, Kong F, et al. Adjacent segment degeneration after single-level anterior cervical decompression and fusion: disc space distraction and its impact on clinical outcomes. J Clin Neurosci 2015;22:566–9.

[2] Bydon M, Xu R, De la Garza-Ramos R, et al. Adjacent segment disease after anterior cervical discectomy and fusion: incidence and clinical outcomes of patients requiring anterior versus posterior repeat cervical fusion. Surg Neurol Int 2014;5(suppl 3):S74–8.

[3] Hilibrand AS, Carlson GD, Palumbo MA, et al. Radiculopathy and myelopathy at segments adjacent to the site of a previous anterior cervical arthrodesis. J Bone Joint Surg Am 1999;81:519–28.

[4] Xia XP, Chen HL, Cheng HB. Prevalence of adjacent segment degeneration after spine surgery: a systematic review and meta-analysis. Spine (Phila Pa 1976) 2013;38:597–608.

[5] Ren C, Song Y, Liu L, et al. Adjacent segment degeneration and disease after lumbar fusion compared with motion-preserving procedures: a meta-analysis. Eur J Orthop Surg Traumatol 2014;24(suppl 1): S245–53.

[6] Pan A, Hai Y, Yang J, et al. Adjacent segment degeneration after lumbar spinal fusion compared with motion-preservation procedures: a meta-analysis. Eur Spine J 2016;25:1522–32.

[7] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Open Med 2009;3:e123–30.

[8] Shaikh N, Morone NE, Bost JE, et al. Prevalence of urinary tract infection in childhood: a meta-analysis. Pediatr Infect Dis J 2008;27:302–8.

[9] Bolesta MJ, Rechtine GRN, Chrin AM. One- and two-level anterior cervical discectomy and fusion: the effect of plate fixation. Spine J 2002;2:197–203.

[10] Goffin J, Geusens E, Vantomme N, et al. Long-term follow-up after interbody fusion of the cervical spine. J Spinal Disord Tech 2004;17: 79–85.

[11] Ishihara H, Kanamori M, Kawaguchi Y, et al. Adjacent segment disease after anterior cervical interbody fusion. Spine J 2004;4:624–8.

[12] Deutsch H, Haid RWJr, Rodts GEJr, et al. Occipitocervical fixation: long-term results. Spine (Phila Pa 1976) 2005;30:530–5.

[13] Ikenaga M, Shikata J, Tanaka C. Anterior corpectomy and fusion with fibular strut grafts for multilevel cervical myelopathy. J Neurosurg Spine 2005;3:79–85.

[14] 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.

[15] Yue WM, Brodner W, Highland TR. Long-term results after anterior cervical discectomy and fusion with allograft and plating: a 5- to 11-year radiologic and clinical follow-up study. Spine (Phila Pa 1976) 2005;30: 2138–44.

[16] Papadopoulos EC, Huang RC, Girardi FP, et al. Three-level anterior cervical discectomy and fusion with plate fixation: radiographic and clinical results. Spine (Phila Pa 1976) 2006;31:897–902.

[17] Sekhon LH. Posterior cervical decompression and fusion for circumferential spondylotic cervical stenosis: review of 50 consecutive cases. J Clin Neurosci 2006;13:23–30.

[18] Clarke MJ, Ecker RD, Krauss WE, et al. Same-segment and adjacent-segment disease following posterior cervical foraminotomy. J Neurosurg Spine 2007;6:5–9.

[19] 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.

[20] Sasso RC, Smucker JD, Hacker RJ, et al. Clinical outcomes of BRYAN cervical disc arthroplasty: a prospective, randomized, controlled, multicenter trial with 24-month follow-up. J Spinal Disord Tech 2007;20:481–91.

[21] Pickett GE, Duggal N, Theodore N, et al. Anterior cervical corpectomy and fusion accelerates degenerative disease at adjacent vertebral segments. SAS J 2008;2:23–7.

[22] Elsawaf A, Mastronardi L, Roperto R, et al. Effect of cervical dynamics on adjacent segment degeneration after anterior cervical fusion with cages. Neurosurg Rev 2009;32:215–24. discussion 224.

[23] Ozer AF, Oktenoglu T, Cosar M, et al. Long-term follow-up after open-window corpectomy in patients with advanced cervical spondylosis and/ or ossification of the posterior longitudinal ligament. J Spinal Disord Tech 2009;22:14–20.

[24] Yi S, Lee DY, Ahn PG, et al. Radiologically documented adjacent-segment degeneration after cervical arthroplasty: characteristics and review of cases. Surg Neurol 2009;72:325–9. discussion 329.

[25] Acikbas SC, Ermol C, Akyuz M, et al. Assessment of adjacent segment degeneration in and between patients treated with anterior or posterior cervical simple discectomy. Turk Neurosurg 2010;20:334–40.

[26] Burkus JK, Haid RW, Traynelis VC, et al. Long-term clinical and radiographic outcomes of cervical disc replacement with the Prestige disc: results from a prospective randomized controlled clinical trial. J Neurosurg Spine 2010;13:308–18.

[27] Chang SW, Kakarla UK, Maughan PH, et al. Four-level anterior cervical discectomy and fusion with plate fixation: radiographic and clinical results. Neurosurgery 2010;66:639–46. discussion 646–637.

[28] Coric D, Cassis J, Carew JD, et al. Prospective study of cervical arthroplasty in 98 patients involved in 1 of 3 separate investigational device exemption studies from a single investigational site with a minimum 2-year follow-up. Clinical article. J Neurosurg Spine 2010; 13:715–21.

[29] Jawahar A, Cavanaugh DA, Kerr EJR, et al. Total disc arthroplasty does not affect the incidence of adjacent segment degeneration in cervical spine: results of 93 patients in three prospective randomized clinical trials. Spine J 2010;10:1043–8.

[30] Joo YH, Lee JW, Kwon KY, et al. Comparison of fusion with cage alone and plate instrumentation in two-level cervical degenerative disease. J Korean Neurosurg Soc 2010;48:342–6.

[31] Walraevens J, Demaerel P, Suetens P, 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 687.

[32] Bisson EF, Samuelson MM, Apfelbaum RI. Intermediate segment degeneration after noncontiguous anterior cervical fusion. Acta Neurochir (Wien) 2011;153:123–7. discussion 128.
[33] Coric D, Nunley PD, Guyer RD, et al. Prospective, randomized, multicenter study of cervical arthroplasty: 269 patients from the Kineflex|C artificial disc investigational device exemption study with a minimum 2-year follow-up: clinical article. J Neurosurg Spine 2011;15: 348–58.
[34] Faldini C, Pagkrati S, Leonetti D, et al. Sagittal segmental alignment as predictor of adjacent-level degeneration after a Cloward procedure. Clin Orthop Relat Res 2011;469:674–81.
[35] Hamilton DK, Smith JS, Reames DL, et al. Safety, efficacy, and dosing of recombinant human bone morphogenetic protein-2 for posterior cervical and cervicothoracic instrumented fusion with a minimum 2-year follow-up. Neurosurgery 2011;69:103–11. discussion 111.
[36] Maldonado CV, Paz RD, Martin CB. Adjacent-level degeneration after cervical disc arthroplasty versus fusion. Eur Spine J 2011;20(suppl 3): 403–7.
[37] Marotta N, Landi A, Tarantino R, et al. Five-year outcome of stand-alone fusion using carbon cages in cervical disc arthrosis. Eur Spine J 2011;20(suppl 1):S8–12.
[38] Nagata T, Takami T, Yamagata T, et al. Significant relationship between local angle at fused segments and C2-7 angle: average duration of longer than 20 years after anterior cervical discectomy and fusion. J Craniovertebr Junction Spine 2011;2:62–6.
[39] Quan GM, Vital JM, Hansen S, et al. Eight-year clinical and radiological follow-up of the Bryan cervical disc arthroplasty. Spine (Phila Pa 1976) 2011;36:639–46.
[40] Song KJ, Choi BW, Jeon TS, et al. Adjacent segment degenerative disease: is it due to disease progression or a fusion-associated phenomenon? Comparison between segments adjacent to the fused and non-fused segments. Eur Spine J 2011;20:1940–5.
[41] Song KJ, Kim GH, Choi BY. Efficacy of PEEK cages and plate augmentation in three-level anterior cervical fusion of elderly patients. Clin Orthop Surg 2011;3:9–15.
[42] Vedantam A, Revanappa KK, Rajshekhar V. Changes in the range of motion of the cervical spine and adjacent segments at ≥24 months after uninstrumented corpectomy for cervical spondylotic myelopathy. Acta Neurochir (Wien) 2011;153:995–1001.
[43] Yao N, Wang C, Wang W, et al. Full-endoscopic technique for anterior cervical discectomy and interbody fusion: 5-year follow-up results of 67 cases. Eur Spine J 2011;20:899–904.
[44] Andaluz N, Zuccarello M, Kuntz C. Long-term follow-up of cervical radiographic sagittal spinal alignment after 1- and 2-level cervical corpectomy for the treatment of spondylosis of the subaxial cervical spine causing radiculomyelopathy or myelopathy: a retrospective study. J Neurosurg Spine 2012;16:2–7.
[45] Gao R, Yang L, Chen H, et al. Long term results of anterior corpectomy and fusion for cervical spondylotic myelopathy. PLoS ONE 2012;7: e34811.
[46] Komura S, Miyamoto K, Hosoe H, et al. Lower incidence of adjacent segment degeneration after anterior cervical fusion found with those fusing C5-6 and C6-7 than those leaving C5-6 or C6-7 as an adjacent level. J Spinal Disord Tech 2012;25:23–9.
[47] Nakashima H, Yukawa Y, Imagama S, et al. Complications of cervical pedicle screw fixation for nontraumatic lesions: a multicenter study of 84 patients. J Neurosurg Spine 2012;16:238–47.
[48] Nunley PD, Jawahar A, Kerr EJR, et al. Factors affecting the incidence of symptomatic adjacent-level disease in cervical spine after total disc arthroplasty: 2- to 4-year follow-up of 3 prospective randomized trials. Spine (Phila Pa 1976) 2012;37:445–51.
[49] Rollinghoff M, Zarghooni K, Hackenberg L, et al. Quality of life and radiological outcome after cervical cage fusion and cervical disc arthroplasty. Acta Orthop Belg 2012;78:369–75.
[50] Singh K, Phillips FM, Park DK, et al. Factors affecting reoperations after anterior cervical discectomy and fusion within and outside of a Federal Drug Administration investigational device exemption cervical disc replacement trial. Spine J 2012;12:372–8.
[51] Upadhyaya CD, Wu JC, Trost G, et al. Analysis of the three United States Food and Drug Administration investigational device exemption cervical arthroplasty trials. J Neurosurg Spine 2012;16:216–28.
[52] Blumenthal SL, Ohnmeiss DD, Guyer RD, et al. Reoperations in cervical total disc replacement compared with anterior cervical fusion: results compiled from multiple prospective food and drug administration investigational device exemption trials conducted at a single site. Spine (Phila Pa 1976) 2013;38:1177–82.
[53] Chen Y, He Z, Yang H, et al. Anterior cervical diskectomy and fusion for adjacent segment disease. Orthopedics 2013;36:e501–8.
[54] Coric D, Kim PK, Clemente JD, et al. 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.
[55] Delamarter RB, Zigler J. Five-year reoperation rates, cervical total disc replacement versus fusion, results of a prospective randomized clinical trial. Spine (Phila Pa 1976) 2013;38:711–7.
[56] Eubanks JD, Belding J, Schnaser E, et al. Congenital stenosis and adjacent segment disease in the cervical spine. Orthopedics 2013;36:e1251–5.
[57] Li J, Zheng Q, Guo X, et al. Anterior surgical options for the treatment of cervical spondylotic myelopathy in a long-term follow-up study. Arch Orthop Trauma Surg 2013;133:745–51.
[58] Noriega DC, Kreuger A, Brotat M, et al. Long-term outcome of the Cloward procedure for single-level cervical degenerative spondylosis. Clinical and radiological assessment after a 22-year mean follow-up. Acta Neurochir (Wien) 2013;155:2339–44.
[59] Park JY, Kim KH, Kuh SU, et al. What are the associative factors of adjacent segment degeneration after anterior cervical spine surgery? Comparative study between anterior cervical fusion and arthroplasty with 5-year follow-up MRI and CT. Eur Spine J 2013;22:1078–89.
[60] Park SB, Chung CK, Lee SH, et al. The impact of menopause on bone fusion after the single-level anterior cervical discectomy and fusion. J Korean Neurosurg Soc 2013;54:496–500.
[61] Park YK, Moon HJ, Kwon TH, et al. Long-term outcomes following anterior foraminotomy for one- or two-level cervical radiculopathy. Eur Spine J 2013;22:1489–96.
[62] Pereira EA, Chari A, Hempenstall J, et al. Anterior cervical discectomy plus intervertebral polyetheretherketone cage fusion over three and four levels without plating is safe and effective long-term. J Clin Neurosci 2013;20:1250–5.
[63] Saarinen T, Niemela M, Kivisaari R, et al. Early and late re-operations after anterior cervical decompression and fusion during an 11-year follow-up. Acta Neurochir (Wien) 2013;155:285–91. discussion 291.
[64] Burkus JK, Traynelis VC, Haid RWJr, et al. Clinical and radiographic analysis of an artificial cervical disc: 7-year follow-up from the Prestige prospective randomized controlled clinical trial: Clinical article. J Neurosurg Spine 2014;21:516–28.
[65] Bydon M, Mathios D, Macki M, et al. Long-term patient outcomes after posterior cervical foraminotomy: an analysis of 151 cases. J Neurosurg Spine 2014;21:727–31.
[66] Chung JY, Kim SK, Jung ST, et al. Clinical adjacent-segment pathology after anterior cervical discectomy and fusion: results after a minimum of 10-year follow-up. Spine J 2014;14:2290–8.
[67] Kan L, Kang J, Gao R, et al. Clinical and radiological results of two hybrid reconstructive techniques in noncontiguous 3-level cervical spondylosis. J Neurosurg Spine 2014;21:944–50.
[68] Lee JC, Lee SH, Peters C, et al. Risk-factor analysis of adjacent-segment pathology requiring surgery following anterior, posterior, fusion, and nonfusion cervical spine operations: survivorship analysis of 1358 patients. J Bone Joint Surg Am 2014;96:1761–7.
[69] Li Z, Yu S, Zhao Y, 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.
[70] Litrico S, Lonjon N, Riouallon G, et al. Adjacent segment disease after anterior cervical interbody fusion: a multicenter retrospective study of 288 patients with long-term follow-up. Orthop Traumatol Surg Res 2014;100(suppl):S305–9.
[71] Malham GM, Parker RM, Ellis NJ, et al. Cervical artificial disc replacement with ProDisc-C: clinical and radiographic outcomes with long-term follow-up. J Clin Neurosci 2014;21:949–53.
[72] Qizhi S, Lei S, Peijia L, et al. A comparison of zero-profile devices and artificial cervical discs in patients with two noncontiguous levels of cervical spondylosis. Clin Spine Surg 2016;29:E61–6.
[73] Song JS, Choi BW, Song KJ. Risk factors for the development of adjacent segment disease following anterior cervical arthrodesis for degenerative cervical disease: comparison between fusion methods. J Clin Neurosci 2014;21:794–8.
[74] Song KJ, Choi BW, Kim JK. Adjacent segment pathology following anterior decompression and fusion using cage and plate for the treatment of degenerative cervical spinal diseases. Asian Spine J 2014;8:720–8.
[75] Uehara M, Takahashi J, Mukaiyama K, et al. Mid-term results of computer-assisted cervical pedicle screw fixation. Asian Spine J 2014;8: 759–67.

[76] van Eck CF, Regan C, Donaldson WF, et al. The revision rate and occurrence of adjacent segment disease after anterior cervical discectomy and fusion: a study of 672 consecutive patients. Spine (Phila Pa 1976) 2014;39:2143–7.
[77] Xu R, Bydon M, Macki M, et al. Adjacent segment disease after anterior cervical discectomy and fusion: clinical outcomes after first repeat surgery versus second repeat surgery. Spine (Phila Pa 1976) 2014;39: 120–6.
[78] 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.
[79] Hu X, Ohnmeiss DD, Zigler JE, et al. Restoration of cervical alignment is associated with improved clinical outcome after one and two level anterior cervical discectomy and fusion. Int J Spine Surg 2015;9:61.
[80] 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.
[81] Lau D, Chou D, Mummaneni PV. Two-level corpectomy versus three-level discectomy for cervical spondylotic myelopathy: a comparison of perioperative, radiographic, and clinical outcomes. J Neurosurg Spine 2015;23:280–9.
[82] Lee JC, Lee SH, Peters C, et al. Adjacent segment pathology requiring reoperation after anterior cervical arthrodesis: the influence of smoking, sex, and number of operated levels. Spine (Phila Pa 1976) 2015;40: E571–7.
[83] Selvanathan SK, Beagrie C, Thomson S, et al. Anterior cervical discectomy and fusion versus posterior cervical foraminotomy in the treatment of brachialgia: the Leeds spinal unit experience (2008–2013). Acta Neurochir (Wien) 2015;157:1595–600.
[84] Shi JS, Lin B, Xue C, et al. Clinical and radiological outcomes following hybrid surgery in the treatment of multi-level cervical spondylosis: over a 2-year follow-up. J Orthop Surg Res 2015;10:185.
[85] Zhang JT, Cao JM, Meng FT, et al. Cervical canal stenosis and adjacent segment degeneration after anterior cervical arthrodesis. Eur Spine J 2015;24:1590–6.
[86] Zhang JT, Wang LF, Liu YJ, et al. Relationship between developmental canal stenosis and surgical results of anterior decompression and fusion in patients with cervical spondylotic myelopathy. BMC Musculoskelet Disord 2015;16:267.
[87] Lei T, Liu Y, Wang H, et al. Clinical and radiological analysis of Bryan cervical disc arthroplasty: eight-year follow-up results compared with anterior cervical discectomy and fusion. Int Orthop 2016;40: 1197–203.
[88] Shiban E, Gapon K, Wostrack M, et al. Clinical and radiological outcome after anterior cervical discectomy and fusion with stand-alone empty polyetheretherketone (PEEK) cages. Acta Neurochir (Wien) 2016;158:349–55.
[89] Chang UK, Kim DH, Lee MC, et al. Changes in adjacent-level disc pressure and facet joint force after cervical arthroplasty compared with cervical discectomy and fusion. J Neurosurg Spine 2007;7:33–9.
[90] Dmitriev AE, Cunningham BW, Hu N, et al. Adjacent level intradiscal pressure and segmental kinematics following a cervical total disc arthroplasty: an in vitro human cadaveric model. Spine (Phila Pa 1976) 2005;30:1165–72.
[91] McAfee PC, Cunningham BW, Hayes V, et al. Biomechanical analysis of rotational motions after disc arthroplasty: implications for patients with adult deformities. Spine (Phila Pa 1976) 2006;31(suppl): S152–60.
[92] Nunley PD, Jawahar A, Cavanaugh DA, et al. Symptomatic adjacent segment disease after cervical total disc replacement: re-examining the clinical and radiological evidence with established criteria. Spine J 2013;13:5–12.
[93] Matsunaga S, Kabayama S, Yamamoto T, et al. Strain on intervertebral discs after anterior cervical decompression and fusion. Spine (Phila Pa 1976) 1999;24:670–5.
[94] Herkowitz HN. A comparison of anterior cervical fusion, cervical laminectomy, and cervical laminoplasty for the surgical management of multiple level spondylotic radiculopathy. Spine (Phila Pa 1976) 1988;13:774–80.
[95] Gore DR. Roentgenographic findings in the cervical spine in asymptomatic persons: a ten-year follow-up. Spine (Phila Pa 1976) 2001;26: 2463–6.