Motion preservation in cervical prosthesis surgery: Implications for adjacent segment degeneration

Yang, X.

Chapter 2

Radiological Follow-up after Implanting Cervical Disc Prosthesis in Anterior Discectomy: A Systematic Review

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ABSTRACT

Objective

The objective of this study was to review current literature on comparison of radiological outcome of cervical arthroplasty with fusion after anterior discectomy for radiculopathy.

Methods

A literature search was performed in PubMed, Embase, Web of Science, COCHRANE, CENTRAL and CINAHL using a sensitive search string combination. Studies were selected by predefined selection criteria (patients exclusively suffering from cervical radiculopathy) and risk of bias was assessed using a validated Cochrane Checklist adjusted for this purpose. Additionally, an overview of results of articles published in 21 meta-analyses was added, considering a group of myelopathy with or without radiculopathy.

Results

Seven articles that compared intervertebral devices in patients with radiculopathy (excluding patients with myelopathy) were included in the study. Another 31 articles were studied as a mixed group including patients with myelopathy and radiculopathy. Apart from three studies with low risk of bias, all other articles showed intermediate or high risk of bias. Heterotopic ossification was reported to be present in circa 10% of patients, seemingly predominant in patients with radiculopathy, with a very low level of evidence. Radiological signs of adjacent segment degeneration were present at baseline in 50% of patients, and there is low level of evidence that this increased more (10-20%) in the fusion group at long-term follow-up. However, this was only studied in the mixed study population, which is degenerative by diagnosis.

Conclusions

Although the cervical disc prosthesis was introduced to decrease adjacent segment degeneration, convincing radiological evidence for this benefit is lacking. Heterotopic ossification as a complicating factor in the preservation of motion of the device is insufficiently studied. Regarding purely radiological outcomes, currently, no firm conclusion can be drawn for implanting cervical prosthesis versus performing fusion.

INTRODUCTION

Radiculopathy caused by symptomatic cervical disc degenerative disease is a common diagnosis in spine surgery. Usually, cervical radiculopathy is treated by medical interventional methods. If patients are unresponsive to conservative measures, surgical intervention may be considered. Anterior cervical discectomy and fusion (ACDF) has been a common surgical treatment for cervical radiculopathy since it was initially described in the 1950s[1] and became the gold standard procedure in current surgery. Some clinical researchers have demonstrated excellent clinical outcome with low complication rates in long-term follow-up[2-4]. The procedure remained largely unchanged until the 1990s when the use of cages and allograft bone and the addition of anterior cervical locking plates became popular, thereby decreasing iliac crest harvesting complications and minimizing the occurrence of pseudoarthrosis[5-7].

In the last two decades, anterior cervical discectomy with arthroplasty (ACDA), as an alternative procedure to ACDF, gained increasing popularity in the surgical treatment of cervical herniated discs. ACDA is designed to replace the disc with a device that mimics a natural disc by restoring height and maintaining segmental motion. Maintaining the segment mobile has the theoretical advantage that adjacent segment degeneration (ASD) is less in comparison with a device that induces fusion, which may consequently lead to less neck pain and disability. Opponents of this theory claim that degeneration of the cervical spine is a natural process, that will continue to occur, irrespective of patients being subjected to fusion or to a mobile disc device[8].

Quite a number of papers have been published on comparing ACDF with ACDA in the past 10-15 years. Even some reviews and meta-analyses have been published[9]. To the authors' knowledge, there are no studies or reviews yet specifically discussing the radiological findings. The aim of the present study was therefore to present an overview of the currently available literature on the comparison of radiological findings between ACDF with ACDA.

METHODS

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement[10].

Search strategy and study selection

Up to August 2016, the electronic databases PubMed, Embase, Web of Science, Cochrane, CENTRAL, and CINAHL were searched using the search strategies as shown in Figure 1. To maintain inter-rater reliability, two of the authors (XY and TJ) independently evaluated the articles by title, abstract or by full article, when necessary, to select the studies that met the predefined selection criteria. Selection criteria were stated as follows:

- the article was published in English or Dutch;
- the study included patients diagnosed with cervical radiculopathy due to disc degeneration disease;
- the study included patients who underwent one-level anterior discectomy, comparing ACDF to ACDA;
- the study reported the radiological outcome with a follow-up period of at least one year;
- the study reported a minimum of 20 patients in each group; and
- the article was published in a peer-reviewed journal;

Performed 2016.08.02
("Cervical Vertebrae"[mesh] OR "Cervic"[tw] OR "cervical"[tw] OR "neck"[mesh] OR "neck"[tw]) AND ("Intervertebral Disc Displacement"[mesh] OR "Slipped disk"[tw] OR "Slipped disks"[tw] OR "Slipped disc"[tw] OR "Slipped discs"[tw] OR "Prolapsed disk"[tw] OR "Prolapsed disks"[tw] OR "Prolapsed disc"[tw] OR "Prolapsed discs"[tw] OR "Herniated disk"[tw] OR "Herniated disks"[tw] OR "Herniated disc"[tw] OR "Herniated discs"[tw] OR "hernia"[tw] OR "Disc Displacement"[tw] OR "Disc Displacements"[tw] OR "Disk Displacement"[tw] OR "Disk Displacements"[tw]] OR "displaced disk"[tw] OR "displaced disks"[tw] OR "displaced disc"[tw] OR "displaced discs"[tw] OR "Radiculopathy"[Mesh] OR "Radiculopathies"[tw] OR "Radiculopathy, Cervical"[tw] OR "Cervical Radiculopathies"[tw] OR "Cervical Radiculopathy"[tw] OR "Radiculopathies, Cervical"[tw] OR "Radicular pain"[tw])
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AND
(randomized controlled trial OR controlled clinical trial OR randomized controlled trials OR random allocation OR double-blind method OR single-blind method OR clinical trial OR clinical trials OR "clinical trial" OR ((singl* OR doubl* OR trebl* OR tripl*) AND (mask* OR blind*)) OR "latin square" OR placebos OR placebo* OR random* OR "Research Design"[MeSH:noexp] OR comparative study OR evaluation studies OR follow-up studies OR prospective studies OR cross-over studies OR control* OR controlled* OR prospective* OR volunteer* OR randomised controlled trial OR randomised controlled trials OR randomized active control trials OR randomized active control trial OR randomised active control trials OR randomised active control trial OR "RaCT" OR "RaCTs" OR RCT OR RCTs OR control*[tw] OR "latin square" [tw] OR cross-over studies [mh] OR control[tw] OR "Evaluation Studies "[Publication Type] OR "Evaluation Studies as Topic"[Mesh] OR "Pragmatic Clinical Trial" OR "Pragmatic Clinical Trials")

Figure 1 Search strategy

The exclusion criterion included studies in which myelopathy was the primary complaint of the patients.

Any discrepancy in selection between the two reviewers was resolved in open discussion, and if needed, a third reviewer (CVL) could be asked to act as a referee. For study selection, a third reviewer was needed to be a referee two times. For quality appraisal, 11 items were assessed for each paper. Among seven radiculopathy articles, a third reviewer was needed 11

times. For 31 mixed-group studies, a referee was needed 43 times. For the procedure of data extraction, a third reviewer was needed as a referee three times. Reference screening and citation tracking were performed on the identified articles.

Bartels et al.[9] published a study in 2017, concerning 21 meta-analyses that focused on the outcomes of one-level or two-level arthroplasty. It appeared that those meta-analyses included predominantly studies that allowed inclusion of patients suffering from cervical myelopathy. For reasons of completeness, the studies described in the meta-analyses were evaluated additionally.

Quality assessment

The methodological quality of all studies (including those from the mixed population) was assessed by two independent reviewers (XY, TJ), using an adjusted version of the checklist for cohort studies of the Dutch Cochrane Centre[11]. When there was no consensus about the assessment, a third reviewer (CVL) was consulted.

The items reviewed in the assessment were the definition of the patient group, for which a maximum of three points could be attributed; outcome bias, for which three points could be attributed; selection bias, with a maximum of one point; and attribution bias, with a maximum of two points. Studies could be awarded a maximum of total of nine points. Studies were then divided into low (seven to nine points), intermediate (five to six points) or high (four or less points) risk of bias group using a method adapted from Furlan[12].

Data extraction

Data from the studies focusing on cervical radiculopathy were extracted by two independent reviewers (XY and TJ) on the study design, the sample size, the sizes of the intervention group and the control group, the mean age, and sex difference. In addition, the type of prosthesis used in the intervention group and the cage used in the control group were assessed. With regard to outcomes, range of motion (ROM), migration, subsidence, implant loosening, fusion rate, heterotopic ossification (HO), and ASD were extracted.

Level of evidence

The quality of evidence for all outcome parameters was evaluated using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach (according to Atkins et al.[13] and adapted from Furlan et al.[12]).

RESULTS

Characteristics of studies

A total of 603 articles were identified, of which 357 original articles were left after removing duplicates. Titles and abstracts were screened, resulting in 42 eligible articles. These articles were read full text, and in total, 14 studies met all criteria to compare cervical disc prosthesis with fusion.

One study was additionally excluded after meticulously investigating the literature. The article of Burkus et al.[14] had to be excluded because it also contained patients suffering from myelopathy. In Burkus et al.'s study, the seven-year results of a study comparing ACDF with prosthesis were reported, describing seemingly a population consisting of patients with radiculopathy. However, we found another paper of this research group, describing the same population, but with two years' follow-up. From that particular article, it was clear that the population was a mixed one, namely, also patients with myelopathy were included. Therefore, this article (with the seven-year follow-up) was excluded.

Thereafter, five more studies were excluded from the review because they concerned the same RCT. Six studies concerning the same RCT comparing ProDisc-C with ACDF (autograft bone and plate) differed in follow up (two on two years' follow-up, one on four years, one on five years, and another two on seven years' post randomization)[15-20]. We decided to include only the article describing the seven-year results (the longest follow-up). It appeared furthermore that one of the studies describing the seven-year follow-up results of this RCT (Loumeau et al.[18]) described the results of only a part of this group of patients (44 patients) plus seven patients who were enrolled in the continued access arm of the study. However, the results of Loumeau et al.[18] are interesting to us, because they concerned not only the clinical but also, in particular, the radiological outcomes and described the occurrence of HO in detail. It is not clear why HO is not described in detail in the group as a whole in the article of Janssen et al.[15]. Likewise, the article of Auerbach et al.[19] is of interest to us, particularly because the ROM of the whole cervical spine in the group of patients who had a complete set of radiological follow-up after two years. Again, it is not clear why this result is not described in the Murrey et al.[16] article. Delamarter et al.[20] reported additionally the results of 136 continued access patients with two-year follow-up.

Additionally one more study was excluded because it described the one-year follow-up results[21], whereas the three-year follow-up study[22] was also available (ProDisc vs ACDF; polyetheretherketone [PEEK] cage). There was one retrospective study (Mobi-C vs PEEK cage)[23] and one prospective non-RCT that compared different prostheses (Prestige ST, Bryan, ProDisc-C)[24] with ACDF (PEEK cage). The remaining three articles described ACDF methods with autograft or plate[25-27] (Figure 2).

Study characteristics are demonstrated in Table 1. The sample size varied from 49 to 209, with a mean follow-up of 4.6 years after surgery.

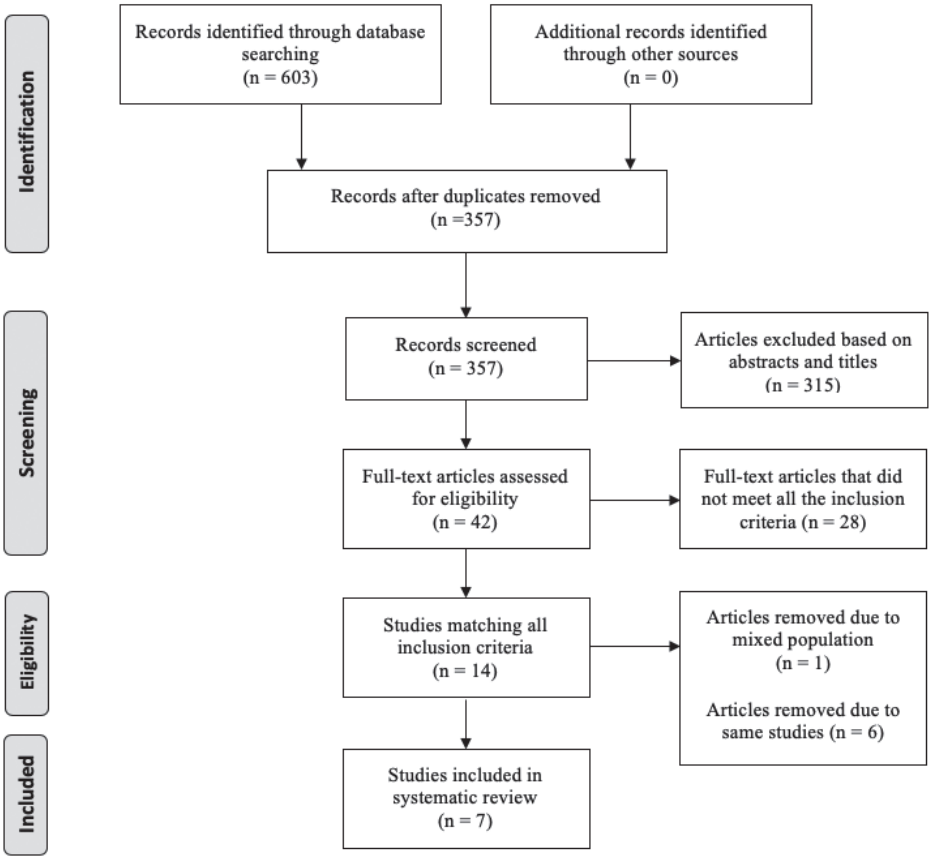

Figure 2 Flow diagram-Studies describing exclusively cervical radiculopathy

Meta-analyses being published already

Twenty-one meta-analyses were identified through the study of Bartels et al.[9]. By means of citation tracking, 206 articles were found on this topic, of which 46 original articles were left after removing duplicates. These articles were read full text and 39 studies were included as they reported radiological outcome on comparison of ACDA and ACDF. Eight of 39 articles concerned same studies; therefore, articles with a longest follow-up were included. In the end, an overview of results of 31 articles was added, considering a group of patients with myelopathy or without radiculopathy (Figure 3). Study characteristics are demonstrated in Table 2.

Table 1 Characteristics of studies describing exclusively cervical radiculopathy

Study (year of publication)	Study design	Prosthetic device	Number of participants		Age (mean ± SD)		Men in %		Follow–up (years)
			ACDA	ACDF	ACDA	ACDF	ACDA	ACDF	
Coric (2013)	Prospective	Bryan, Kineflex	41	43	49.5	49.3	39	42.4	6
Hou (2016)	RCT	Mobi-C	56	51	46.3±7.8	48.5±8.3	58.8	58.3	5
Janssen (2015)	RCT	ProDisc-C	103	106	42.1±8.42	43.5±7.15	45	46	7
Nabhan (2007)	RCT	ProDisc-C	25	24	44#		56.1#		3
Park (2008)	Retrospective	Mobi-C	21	32	45	47	52.4	62.5	20-22 months
Sala (2015)	Prospective non-RCT	Prestige ST, Bryan or Prodisc-C	28	27	41	41	25	33.3	2
Zhang (2014)	RCT	Mobi-C	55	56	44.8	46.7	45.5	46.4	4
Mean			47	48	44.6	45.7	46.0	49.3	4.6

SD: Standard deviation
ACDA: Anterior cervical discectomy with arthroplasty
ACDF: Anterior cervical discectomy and fusion
RCT: Randomly controlled trail
NA: Not available
#: The value of total participants.

Table 2 Characteristics of studies describing myelopathy and cervical radiculopathy

Study (year of publication)	Intervention	Follow-up (years)	Number of participants		Age (mean ± SD)	
			ACDA	ACDF	ACDA	ACDF
Anakwenze (2009)	Prodisc-C	2	89	91	42.2±7.5	41.7±7.9
Burkus (2014)	Prestige ST	7	276#	265#	43.3	43.9
Cheng (2011)	Bryan	3	41	42	47.2±5.7	47.7±5.8
Coric (2006)	Bryan	1.5	17	16	43	43
Coric (2010)	Bryan, Kineflex|C, Discover	2	57	41	46.6	46.3
Coric (2011)	Kinefles|C	2	136	133	43.7±7.76	43.9±7.39
Davis (2015)	Mobi-C	4	225	105	45.3±8.1	46.2±8
Ding (2012)	Prestige LP	1	44	40	46.2±12.3	45.3±11.7
Fay (2014)	Bryan	3	37	40	52.1±9.1	63.0±10.6
Garrido (2010)	Bryan	4	21	26#	40	43.3
Gornet (2016)	Prestige	7	280	265	44.5±8.8	43.9±8.8
Grasso (2015)	Mobi-C or Prodisc-C	2	20	20	47.3	40.5
Hisey (2016)	Mobi-C	5	164	81#	NA	NA
Hou (2014)	Discover	2	149	196	45.8	46.9
Jawahar (2010)	Kineflex-C; Mobi-C; Advent	3	34	59	NA	NA
Kelly (2011)	ProDisc-C	2	100	99	42.1±8.4	43.5±7.1
Kim (2009)	Bryan	1.5	51	54	45.3	50.5
Li (2014)	DCI	2	39#	42#	45.3±8.6	49.5±9.3
Plillips (2015)	PCM	5	218#	185#	45.3±9.0	43.7±8.3
Porchet (2004)	Prestige II	2	27	28	443±8.9	43±6.9
Riina (2008)	Prestige ST	2	10	9	40.8±8.8	38.1±4.9
Robertson (2005)	Bryan	2	74	158	45.7	45.5
Rozankovic (2016)	Discover	2	51	50	41.32±8.8	41.94±9.36
Sasso (2007)	Bryan	2	56#	59#	42.5±7.8	46.1±7.8
Sasso (2011)	Bryan	4	242	221#	NA	NA
Sun (2008)	NA	1	NA	NA	42	
Sun (2012)	Bryan	5	26	24	44.0±6.9	47.5±5.1
Vaccaro (2013)	SECURE-C	2	240	140	43.4 ± 7.50	44.4 ± 7.86
Wang (2008)	Bryan	2	28	31	42	43
Yan (2017)	Bryan	8	39#	54#	48.83±6.70	48.72±7.33
Zhang (2012)	Bryan	2	60	60	44.77±5.60	45.57±5.83

SD: Standard deviation
ACDA: Anterior cervical discectomy with arthroplasty
ACDF: Anterior cervical discectomy and fusion
NA: Not available
#: Follow-up rate less than 80%

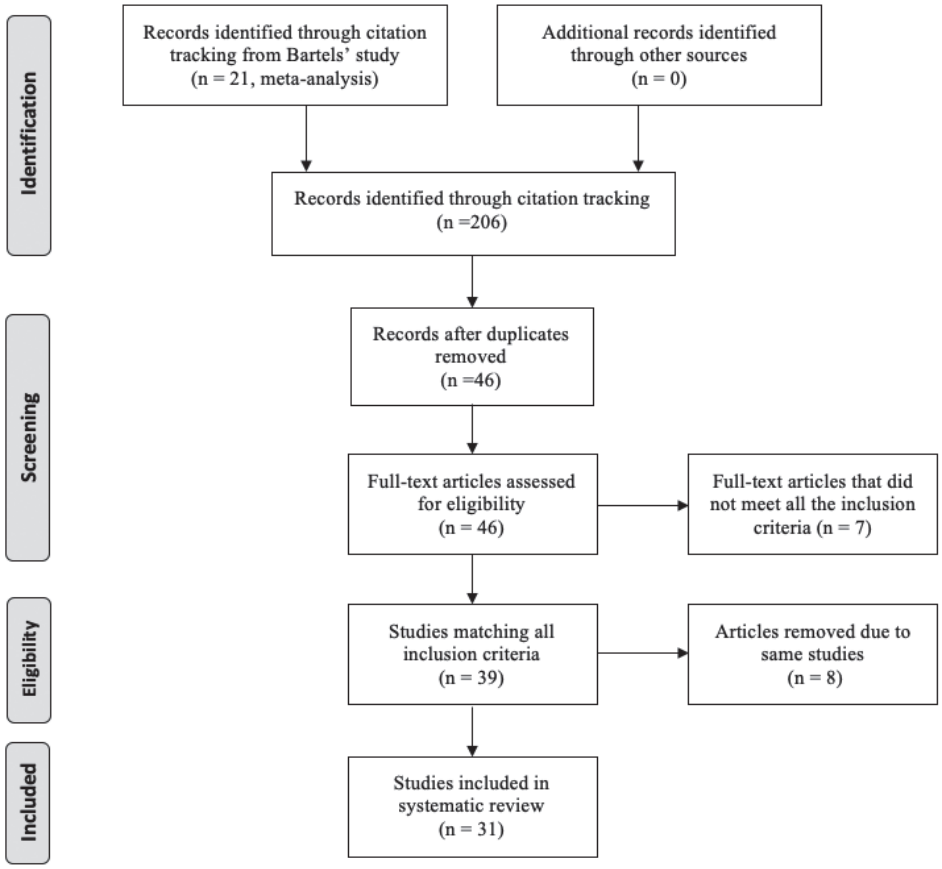

Figure 3 Flow diagram-Studies describing myelopathy and cervical radiculopathy

Quality assessment in radiculopathy studies

None of the studies showed low risk of bias. Three articles[15,25,27] scored five points, indicating intermediate risk of bias. One article[24] scored four points and the other three articles[22,23,26] scored three points, indicating high risk of bias (Table 3).

Quality assessment in mixed studies

Subsequently, risk of bias analysis was performed for the 31 studies on the mixed population (Table 4). Likewise, a maximum of nine points was to be awarded. There were three studies[28-30] with low risk of bias, seven studies with intermediate risk of bias, and 21 studies had high risk of bias.

Table 3 Risk of bias analysis of studies describing exclusively cervical radiculopathy

Study (year of publication)	Total risk of bias score (9)	Patient group and study goal (3)	Outcome properly examined (3)	Absence of selection bias (1)	Absence of attribution bias (2)
Coric (2013)	5*	**	*	-	**
Hou (2016)	5*	**	*	*	*
Janssen (2015)	5*	**	*	*	*
Nabhan (2007)	3*	*	-	*	*
Park (2008)	3*	**	*	-	-
Sala (2015)	4*	**	-	*	*
Zhang (2014)	3*	**	*	-	-

Table 4 Risk of bias analysis of studies describing myelopathy and cervical radiculopathy.

Study (year of publication)	Total risk of bias score (9)	Patient group and study goal (3)	Outcome properly examined (3)	Absence of selection bias (1)	Absence of attribution bias (2)
Anakwenze (2009)	4*	***	-	-	*
Burkus (2014)	4*	***	*	-	-
Cheng (2011)	5*	**	**	*	-
Coric (2006)	4*	**	*	-	*
Coric (2010)	3*	**	*	-	-
Coric (2011)	4*	***	*	-	-
Davis (2015)	7*	***	***	-	*
Ding (2012)	4*	**	*	-	*
Fay (2014)	7*	***	**	*	*
Garrido (2010)	2*	**	-	-	-
Gornet (2016)	4*	***	*	-	-
Grasso (2015)	5*	***	*	-	*
Hisey (2016)	4*	**	*	-	*
Hou (2014)	7*	***	**	-	**
Jawahar (2014)	5*	**	*	*	*
Kelly (2011)	4*	***	-	-	*
Kim (2009)	5*	**	**	-	*
Li (2014)	6*	**	**	-	**
Phillips (2015)	4*	***	*	-	-
Porchet (2004)	6*	***	*	*	*
Riina (2008)	4*	**	*	-	*
Robertson (2005)	4*	***	*	-	-
Rozankovic (2016)	4*	**	*	*	-
Sasso (2007)	3*	**	*	-	-
Sasso (2011)	2*	**	-	-	-
Sun (2008)	2*	-	*	-	*
Sun (2012)	4*	**	*	-	*
Vaccaro (2013)	4*	***	-	-	*
Wang (2008)	4*	**	*	-	*
Yan (2017)	3*	**	*	-	-
Zhang (2012)	5*	***	**	-	-

Range of motion

Definition of range of motion

Two methods to determine the ROM were described: one method described the degrees change in angle measured as a Cobb angle per segment being defined as 'the difference in treated segment angle between full flexion and extension in lateral radiographs'[23,25,26]. Other studies obtained total cervical ROM from flexion and extension radiographs[19,24,27]. The majority of studies failed to give a definition of range of motion[15-18,24].

ROM in studies describing patients with exclusively cervical radiculopathy

Five[15,23,25-27] of seven studies gave data for ROM on the level of the prosthesis, one study[24] reported on ROM of the whole cervical spine and one study[22] did not mention data concerning ROM (Table 5). The average ROM at the index level for ACDA was 9.0 degrees with a range of 5.4 to 15.2 degrees[15,23,25-27]. In four of seven studies, the average ROM for the ACDF group was also measured, and this resulted in an average motion of 0.4 degrees[15,25-27].

Sala et al.[24] reported on the ROM of the whole cervical spine and demonstrated similar cervical ROM in both ACDF and ACDA groups at two years' follow-up. Although Janssen et al.[15] does not describe ROM in the whole cervical spine, Auerbach et al., describing the same patient population at two years' follow-up, additionally give results of the ROM of the whole cervical spine and report in the ACDA group an increase of 5.9 degrees of motion in comparison to baseline motion, whereas a decrease of 0.8 degrees of motion in the ACDF group is reported[19]. However, this is focussing on the change in relation to baseline data.

ROM in studies describing patients with myelopathy and cervical radiculopathy

Twenty-four of 31 studies reported data on ROM after anterior discectomy (Table 6). The average ROM in the ACDA group was 9.4 degrees (range 5.2 to 23.5 degrees). The ROM for ACDF was 0.94 degrees on average (range 0 to 1.8 degrees). Coric et al.[31] did not report on a value for the ROM but reported the change in ROM at the index level instead: in the ACDA group, angular motion was improved by 0.91 degrees and reduced by 7.8 degrees in the ACDF group. Instead of ROM at the index level, Davis et al.[29] reported ROM of the superior and inferior levels of the index level, which were 10.0 ± 6.0 degrees and 8.2 ± 5.3 degrees, respectively, in the ACDA group. The ROM in the ACDF group was not provided.

Wang et al.[32] reported a ROM of the whole cervical spine, ranging from C3 to C7, and reported a ROM of 27.6 degrees in the ACDA group, compared to 26.9 degrees in the ACDF group (not statistically different). Similarly, Grasso[33] reported the ROM of the whole cervical spine to be 47.2 (± 6.6) degrees in the ACDA group and 36.5 (± 7.3) degrees in the ACDF group (no statistical information). Likewise, Li et al.[34] and Yan et al.[35] not only reported segmental ROM but also described ROM of the whole cervical spine. Li et al.[34] reported 47.5 (± 19.8) degrees in ACDA group and 35.8 (± 17.6) degrees in ACDF group (statistically different). Yan et al.[35] reported a ROM of 42.8

Table 5 Radiological outcomes of studies describing exclusively cervical radiculopathy

Study (year of publication)	Range of motion		Migration		Subsidence		Implant loosening		Fusion rate	Pseudarthrosis	HO	Bridging bone
	ACDA	ACDF	ACDA	ACDF	ACDA	ACDF	ACDA	ACDF	ACDF	ACDF	ACDA	ACDA
Coric (2013)	8.6°	0.2°	0	0	0	NA	0	1(3%)	97%	NA	NA	7(17%)
Hou (2016)	5.4±0.9°	0.4±0.3°	NA	NA	NA	NA	NA	NA	NA	NA	0	NA
Janssen (2015)	8.12±5.91°	0.66±0.58°	NA	NA	NA	NA	NA	NA	NA	NA	NA	8(11%)
Nabhan (2007)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Park (2008)	15.2°	NA	NA	NA	0	5(15.6%)	NA	NA	NA	NA	0	NA
Sala (2015)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Zhang (2014)	7.9°†	0.2°†	3(5.4%)	NA	0	0	NA	NA	NA	1(1.8%)	18(32.7%) *	NA
Mean	9.0	0.4	-	-	-	-	-	-	-	-	-	-

ACDA: Anterior cervical discectomy with arthroplasty
ACDF: Anterior cervical discectomy and fusion
HO: Heterotopic ossification
NA: Not available
†: The value is estimated from the graph in the study
*: McAfee grading system

Table 6 Radiological outcomes of studies describing myelopathy and cervical radiculopathy

Study (year of publication)	Range of motion		Migration		Subsidence		Implant loosening		Fusion rate	Pseudarthrosis	HO	Bridging bone
	ACDA	ACDF	ACDA	ACDF	ACDA	ACDF	ACDA	ACDF	ACDF	ACDF	ACDA	ACDA
Anakwenze (2009)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Burkus (2014)	6.75°	0.48°	1	0	7 (4.2%)	4 (3.1%)	6 (3.1%)	7 (3.1%)	96.9%	NA	NA	20(10%)
Cheng (2011)	7.4° ± 0.5°	0.6° ± 0.2°	NA	NA	0	NA	0	NA	90.5%	3(7.1%)	1(2.4%)	NA
Coric (2006)	7°	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0
Coric (2010)	+0.91°*	-7.8°*	NA	NA	NA	NA	0	0	97%	NA	3(5.6%)	NA
Coric (2011)	9.8°	0.8°	2	NA	1	NA	NA	0	82%	3(2.6%)	1(1%)	NA
Davis (2015)	S=10.0°±6° I=8.2°±5.3°	NA	1	0	0	0	NA	NA	92.2%%	NA	25.6% (G3+G4)†	NA
Ding (2012)	13.5°	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Fay (2014)	23.5° ±7.8°	1.6°±1°	NA	NA	NA	NA	NA	NA	100%	0	NA	NA
Garrido (2010)	NA	NA	NA	NA	NA	NA	NA	NA	NA	1(3.8%)	NA	NA
Gornet (2016)	6.78°	NA	NA	NA	NA	NA	NA	NA	96%	NA	44(15.7%)	36(13%)
Grasso (2015)	47.2°±6.6°§	36.5°±7.3°§	NA	NA	0	0	0	0	NA	NA	0	NA
Hisey (2016)	10°	<1°	0	0	NA	NA	NA	NA	NA	5	8.5%-G4†	NA
Hou (2014)	Single: 11.6° ±1.1° Double: 11.0° ±1.9°	Single: 2.0° ±0.8° Double: 1.7° ±0.2°	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Jawahar (2010)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Kelly (2011)	9.5°	0.9°	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Table 6 Radiological outcomes of studies describing myelopathy and cervical radiculopathy (continued)

Study (year of publication)	Range of motion		Migration		Subsidence		Implant loosening		Fusion rate	Pseudarthrosis	HO	Bridging bone
	ACDA	ACDF	ACDA	ACDF	ACDA	ACDF	ACDA	ACDF	ACDF	ACDF	ACDA	ACDA
Kim (2009)	Single: 12.1° ±2° Double: 12.3° ±1.9°	Single: 2.3° ±0.8° Double: 1.3° ±0.2°	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Li (2014)	8.9°±4.4°/ 47.5°±19.8°§	0.8°±0.7° 35.8°±17.6°§	1	NA	2	2	NA	NA	94.9%	2	0	NA
Phillips (2015)	5.2°±3.8°	0.5°±0.5°	NA	NA	NA	NA	NA	NA	94.4% (119/126)	NA	6.7%-G3† (10/149) 6.0%-G4† (9/149)	NA
Porchet (2004)	5.9°	1.1°	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Riina (2008)	NA	NA	NA	NA	NA	NA	0	NA	9(100%)	NA	NA	0
Rozankovic (2016)	NA	NA	0	1	NA	NA	NA	NA	98%	1	4	NA
Robertson (2005)	NA	NA	NA	NA	NA	NA	NA	NA	NA	13	NA	NA
Sasso (2007)	7.04° ± 4.29°	0.85° ± 0.71°	NA	NA	NA	NA	0	NA	NA	NA	0	NA
Sasso (2011)	8.5°	1.1°	NA	NA	NA	NA	0	NA	NA	NA	NA	NA
Sun (2008)	11.2° ± 3.9°¶	14.4° ± 4.9°¶	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sun (2012)	NA	NA	NA	NA	NA	NA	NA	NA	100%	NA	11(42.3%): 1-G2†; 8-G3†; 2-G4†	NA
Vaccaro (2013)	9.7°	NA	0	NA	0	NA	0	NA	89.1%	NA	NA	NA
Wang (2008)	27.6° ± 4.7°§	26.9° ± 0.6°§	NA	NA	NA	NA	NA	NA	NA	NA	2	NA

Table 6 Radiological outcomes of studies describing myelopathy and cervical radiculopathy (continued)

Study (year of publication)	Range of motion		Migration		Subsidence		Implant loosening		Fusion rate	Pseudarthrosis	HO	Bridging bone
	ACDA	ACDF	ACDA	ACDF	ACDA	ACDF	ACDA	ACDF	ACDF	ACDF	ACDA	ACDA
Yan (2017)	6.60°±4.1°/ 42.8°±6.9°§	0/ 39.6°±6.5°§	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Zhang (2012)	8.79° ± 0.89°	0.79° ± 0.63°	0	0	0	0	NA	NA	NA	NA	7(12.5%): 3-G1†; 3-G2†; 1-G3†	NA

ACDA: Anterior cervical discectomy with arthroplasty
ACDF: Anterior cervical discectomy and fusion
HO: Heterotopic ossification
NA: Not available
S: Superior level
I: Inferior level
Single: patient group of single level surgery
Double: patient group of double level surgery
*: The degree of angular motion improved
§: Range of motion of global cervical spine
†: McAfee grading system
¶: Range of motion of the adjacent space

degrees from C2 to C7 in the ACDA group and a ROM of 39.6 degrees in the ACDF group (not statistically different).

Level of evidence

The level of evidence for ROM at the index level is only lowered with one level because most of articles have a high or intermediate risk of bias. Therefore, the level of evidence that the segment in which the prosthesis was implanted stays mobile is moderate (considering that a mean value is given, and no data on percentages of patients were given).

The level of evidence for ROM of the whole cervical spine is lowered with three levels. All articles have a high or intermediate risk of bias, findings are inconsistent, and estimates of effect are not sufficiently precise as not all articles state the exact data or statistically significant difference. Therefore, the level of evidence that the ROM of the whole cervical spine is comparable in ACDA and ACDF is very low.

In conclusion, motion at the index level in the ACDA group remained present and disappeared in the ACDF group. The average ROM in the ACDA group is equivalent in patients suffering from exclusively cervical radiculopathy (9.0) in comparison with the mixed population group (9.3). The results on ROM of the whole cervical spine are inconclusive.

Migration

Definition of migration

To grade migration of the implant material, the definition 'more than a 3-mm anteroposterior slip of the implant parallel to the vertebral endplates'[17,18] was used, if any definition was used at all.

Migration in studies describing patients with exclusively cervical radiculopathy

Three of seven studies provided data of disc implant migration (Table 5). Zhang et al.[26] reported that in three patients (5.4%), the prosthesis moved anteriorly over a distance of 2-3 mm without any relevant clinical symptoms. In another two studies[17,27], no migration was detected in ACDA. Coric et al.[27] also reported that no migration of the implanted cage was found.

Migration in studies describing patients with myelopathy and cervical radiculopathy

Eight of 31 studies reported results regarding migration of the device (Table 6). Coric et al.[36] reported only two cases (1.5%) in which the prosthesis migrated. Davis et al.[29], Li et al.[34], and Burkus et al.[14], respectively, reported one case of migration (0.4%, 2.6%, and 0.4%). Rozankovic et al.[37], Zhang et al.[38], Hisey et al.[39], and Vaccaro et al.[40] did not observe migration of a prosthesis. Migration of a cage in ACDF was observed in only one patient in the whole group of studies[37].

Table 7 Adjacent segment degeneration

Study (year of publication)	Adjacent segment degeneration (patients)			Baseline data at adjacent level
	ACDA: N. (rate)	ACDF: N. (rate)	Difference with significance (P-value)	
Studies describing myelopathy and cervical radiculopathy				
Anakwenze (2009)	NA	NA	-	-
Burkus (2014)	11(4.6%)	24(11.9%)	Yes (0.008)	No
Cheng (2011)	NA	NA	-	-
Coric (2006)	NA	NA	-	-
Coric (2010)	1 (2.5%)	3 (8.1%)	NA	No
Coric (2011)	62%	82%	NA	Yes
Davis (2015)	S:27.6% I: 16.4%	S: 64.7% I: 56.2%	Yes (P<0.0001) Yes (P<0.0001)	Yes
Ding (2012)	NA	NA	-	-
Fay (2014)	NA	NA	-	-
Garrido (2010)	1(5.6%)	3(15%)	NA	No
Gornet (2016)	NA	NA	-	-
Grasso (2015)	NA	NA	-	-
Hisey (2016)	S: 38% I: 37%	S: 55% I: 56%	S: Yes (<0.05) I: Yes (<0.05)	Yes
Hou (2014)	NA	NA	-	-
Jawahar (2010)	18%	15%	No (P=0.885)	No
Kelly (2011)	NA	NA	-	-
Kim (2009)	NA	NA	-	No
Li (2014)	12.8% (5/39)	14.3% (6/42)	No (NA)	No
Phillips (2015)	S: 33.1% I: 49.2%	S: 50.9% I: 51.7%	S: Yes (0.006) I: No (0.779)	Yes
Porchet (2004)	NA	NA	-	No
Riina (2008)	NA	NA	-	No
Robertson (2005	13(17.5%) *	54(34.6%) *	0.009	Yes
Rozankovic (2016)	NA	NA	-	No
Sasso (2007)	3(5.4%)	2(3.4%)	NA	No
Sasso (2011)	10 (4.1%)	9 (4.1%)	No (1.000)	No
Sun (2008)	NA	NA	-	-
Sun (2012)	9 segments	29 segments	P<0.001	Yes
Vaccaro (2013)	4 (1.7%)	2 (1.4%)	NA	No
Wang (2008)	NA	1(3.2%)	-	No
Yan (2017)	13(44.83%)	19(48.72%)	No (NA)	No
Zhang (2012)	1(1.7%)	3(5%)	NA	No
Studies describing patients with exclusively cervical radiculopathy				
Coric (2013)	2 (4.9%)	1 (3.0%)	No (NA)	No
Hou (2016)	1(2.0%)	NA	-	No
Janssen (2015)	6(6%)	13(12.6%)	NA	No

Table 7 Adjacent segment degeneration (continued)

Study (year of publication)	Adjacent segment degeneration (patients)			Baseline data at adjacent level
	ACDA: N. (rate)	ACDF: N. (rate)	Difference with significance (P-value)	
Nabhan (2007)	NA	1	-	No
Park (2008)	NA	NA	-	-
Sala (2015)	NA	NA	-	-
Zhang (2014)	NA	4(7.1%)	-	No

ACDA: Anterior cervical discectomy with arthroplasty
ACDF: Anterior cervical discectomy and fusion
N: Number of patients
NA: Not available
S: Superior level
I: Inferior level
*: This number include anterior osteophytes (14 in ACDA and 4 in ACDF), degenerative disc degeneration (10 in ACDA and 11 in ACDF) and calcification (5 in ACDA and 5 in ACDF)

Level of evidence

The level of evidence is lowered with three levels. Most of articles have a high or intermediate risk of bias, findings are inconsistent, and estimates of effect are not sufficiently precise as not all articles state the statistically significant difference. Therefore, the level of evidence is very low.

In conclusion, based on the abovementioned data, migration of the device is only a minor issue but occurs more often with prostheses than with cages.

Subsidence

Definition of subsidence

Subsidence was defined as 'bone penetration of the implant more than 3 mm into the superior and/or inferior endplate of the adjacent vertebral body'[17,18].

Subsidence in studies describing patients with exclusively cervical radiculopathy

Zigler et al.[17] found only one (0.5%) case of prosthesis subsidence at five years' follow-up in 209 patients; no subsidence was observed in the ACDF group (Table 5). Park et al.[23] demonstrated that five of 53 patients (15.6%) underwent insertion of a cage, experiencing subsidence. Coric et al.[27] found no subsidence in prosthesis group without providing information of the fusion group. Zhang et al.[26] reported that no patient can be detected with subsidence. The other three articles do not mention subsidence.

Subsidence in studies describing patients with myelopathy and cervical radiculopathy

Burkus et al.[14] found seven cases (4.2%) of subsidence in the ACDA group and four cases (3.1%) in the ACDF group (Table 6). In Li et al.[34], two subjects in both the ACDA (5.1%)

and the ACDF (4.8%) groups were detected to have subsidence. Coric et al.[36] reported one subsidence case in the ACDA group and none in the ACDF group. Cheng et al.[41] and Vaccaro et al.[40] reported that no prosthesis subsided. Zhang et al.[38], Grasso[33], and Davis et al.[29] claimed subsidence can be detected in neither the ACDA nor the ACDF group. The other 23 articles do not mention subsidence.

Level of evidence

The level of evidence is lowered by two levels. Most of articles have a high or intermediate risk of bias, and estimates of effect are not sufficiently precise as most articles lack statistics on this subject. Therefore, the level of evidence that subsidence occurs equally in prosthesis and in cage is low.

Overall, subsidence is reported only in a small percentage of cases.

Implant loosening

Definition of implant loosening

No definition was given to define implant loosening.

Implant loosening in studies describing patients with exclusively cervical radiculopathy

Nabhan et al.[21] evaluated implant loosening in the one-year follow-up result and reported no occurrence of this in the ACDA group. Coric et al.[27] reported one implant loosening case (3%) in ACDF group but none for ACDA group (Table 5).

Implant loosening in studies describing patients with myelopathy and cervical radiculopathy

Six (3.1%) and seven (3.1%) cases of implant loosening were reported in ACDA and ACDF, respectively, by Burkus et al.[14] (Table 6). Additionally, five articles (Cheng et al.[41], Vaccaro et al.[40], Sasso et al.[42], Sasso et al.[43], Riina et al.[44]) reported no implant loosening without mentioning the result of the ACDF group. Coric et al.[36] found no implant loosening in fusion patients but did not provide the data for patients who underwent arthroplasty. Neither prosthesis nor cage loosening was found throughout follow-up, reported by Coric et al.[31] and Grasso[33].

Level of evidence

The level of evidence is lowered with three levels. All articles have a high or intermediate risk of bias, findings are inconsistent, and estimates of effect are not sufficiently precise as not all articles state the statistically significant difference. Therefore, the level of evidence that implant loosening is comparable in prosthesis and cage is very low.

In conclusion, the majority of authors do not report on implant loosening.

Fusion rate

Definition of fusion rate

Several definitions of fusion were used and, logically, were applied only to the ACDF patients and not in the prosthesis patients. Janssen et al.[15] did not report fusion in the seven-year evaluation report. Zigler et al.[17], giving the results of the same population at the five-year evaluation point, was very specific and judged fusion to be present only if all of the following were true: 'more than 50% of trabecular bridging on X-ray', 'no motion (≤2 degrees) on dynamic X-ray, and 'no implant loosening'.

Fusion rate in studies describing patients with exclusively cervical radiculopathy

Zhang et al.[26] reported only one patient with 'pseudarthrosis' in the ACDF group (1.8%) (Table 5). Zigler et al.[17] reported a 92.5% fusion rate in their five-year follow-up, and a fusion rate of 97% was reported by Coric et al.[27].

Fusion rate in studies describing patients with myelopathy and cervical radiculopathy

Thirteen studies reported fusion rate in the ACDF group, which ranged from 82%[36] to 100%[28] (Table 6). Alternatively, pseudarthrosis was reported by Garrido et al.[45] (one case), Hisey et al.[39] (five cases) and Robertson et al.[46] (13 cases). The remaining 15 studies did not study fusion nor pseudarthrosis.

Level of evidence

The level of evidence is lowered with two levels because most of articles have a high or intermediate risk of bias and data are insufficiently precise. Therefore, the level of evidence that fusion is present in ACDF is low.

In conclusion, fusion rates are high in ACDF, namely over 90%, but the level of evidence is low.

Heterotopic ossification

Definition of heterotopic ossification

HO can be classified according to the classification system of McAfee et al.[47]. In this classification system, the amount of bone overgrowing the level of interest in which a prosthesis was placed is quantified from grade 0 (no HO present) to grade IV (complete fusion of the treated segment without movement in flexion and extension).

Heterotopic ossification in studies describing patients with exclusively cervical radiculopathy

Four studies reported on data regarding HO in the prosthesis group (Table 5). Only Loumeau et al.[18] and Zhang et al.[26] used the McAfee classification. In Zhang et al.[26] (four-year follow-up), 18 of 55 patients (32.7%) demonstrated HO (McAfee scoring): 11 patients were classi-

fied as grade I, five patients were classified as Grade II, and two patients were classified as Grade III. These results were reported after one year of follow-up, and it was reported that no increase of HO developed in the subsequent three years. However, it was not specified that all radiographs were evaluated for HO again at four years' follow-up. Loumeau et al.[18] reported HO (McAfee grading) to be present in 90% of patients who were fitted with a prosthesis. Six patients (15%) were classified as Grade I, six patients (15%) were classified as Grade II, 17 patients (44%) were classified as Grade III, and six patients (15%) were classified as Grade IV HO. Janssen et al.[15] and Coric et al.[27] used another nomenclature, namely, 'presence of bridging bone', which can be defined as McAfee Grade IV. At seven-year follow-up, 11% of patients with a prosthesis demonstrated bridging bone reported by Janssen et al.[15] and, in another study, 17% by Coric et al.[27] (six-year follow-up). Park et al.[23] and Hou et al.[25] reported the absence of HO but failed to define or classify it.

Heterotopic ossification in studies describing patients with myelopathy and cervical radiculopathy

The presence of HO (or presence of bridging bone) was reported in 17 studies (Table 6). Five studies[29,38,39,48,49] evaluated HO by means of the McAfee classification. Zhang et al.[38] (two-year follow-up) reported that three patients (out of 60) had Grade I, three patients had Grade II, and one patient had Grade III. In Phillips et al.[48] (five-year follow-up), ten patients (6.7%) had Grade III and nine patients (6.0%) had Grade IV HO. Hisey et al.[39] reported 8.5% of patients had Grade IV HO. Davis et al.[29] claimed that Grade III or IV HO was observed in 25.6% of 187 ACDA patients at four years' follow-up. In study of Sun et al.[49], which is a retrospective study, 11 patients (42.3%) were found with HO: one was classified as Grade II, eight were classified as Grade III, and two were classified as Grade IV.

Of the three studies reporting on bridging bone, Burkus et al.[14] reported 20 patients (10%) with a bony bridge at the ACDA index level, and both Coric et al.[50] and Riina et al.[44] observed no case of bridging bone in with a prosthesis. The other studies reported the presence of HO but failed to define or classify it.

Level of evidence

The level of evidence is lowered with three levels. Most of articles have a high or intermediate risk of bias, findings are inconsistent, and data are insufficiently precise. Therefore, the level of evidence that HO is present in 11-90% of patients with radiculopathy and in 1-42% in patients of a mixed population is very low.

In conclusion, HO is only reported in a reliable manner (McAfee classification or bridging bone presence) in a minority of studies. In the radiculopathy studies, the occurrence of HO is higher as is the degree of HO, in comparison with the mixed population group.

Adjacent segment degeneration

Definition of adjacent segment degeneration

To properly judge ASD, defined as degeneration at the level adjacent to the target level, the degeneration at baseline (preoperative) on this adjacent level should be known. Only six articles judged ASD by comparing degeneration with the preoperative situation. Coric et al.[36] evaluated ASD by comparing x-rays from the preoperative period to x-rays produced at the end of follow-up (two-year follow-up) and classified it as none, mild, moderate and severe according to previous literature[51]. The other two articles[46,49] reported whether deterioration of degeneration relative to baseline degeneration was present. Phillips et al.[48] used the same method to determine ASD, while Davis et al.[29] and Hisey et al.[39] evaluated ASD by means of the Kellgren-Lawrence grading scale[52]. All other articles failed to describe a proper radiological measurement of ASD, and reported the rate of second surgery at the level directly adjacent to the treated level instead, which will be disregarded in this review.

Studies describing patients with exclusively cervical radiculopathy

None of the studies reported on radiologically evaluated ASD.

Studies describing patients with myelopathy and cervical radiculopathy

As stated earlier, only six studies reported on radiological ASD in a meaningful way, namely, by comparing to baseline data (Table 7). Of the six studies, only Coric et al.[36] provided baseline information of ASD. At two years' follow-up, Coric et al.[36] reported that ASD increased from 52% preoperatively to 62% postoperatively in ACDA, and increased from 59% preoperatively to 82% postoperatively in ACDF, without mentioning statistics. Presumably, this difference was not statistically different. Phillips et al.[48] reported that worsening of degeneration at the superior adjacent disc level in 33.1% in ACDA patients and in 50.9% in ACDF patients (statistically significant), whereas worsening of ASD in the inferior adjacent level was 49.2% in ACDA versus 51.7% in ACDF patients (not significant). Likewise, at the five-year follow-up, Hisey et al.[39] reported worsening of ASD in ACDA in 38% of patients versus worsening of ASD in ACDF in 55% of patients for the superior level, and worsening of ASD in ACDA in 37% of patients versus worsening of ASD in ACDF in 56% of patients for the inferior level (both significantly different). Additionally, Sun et al.[49] reported that nine segments (17.6%) were detected to have ASD in ACDA, whereas 29 segments (60.4%) were detected to have ASD in ACDF (significantly different). Robertson et al.[46] has a similar result, in which 13 patients (17.5%) had ASD in the ACDA group and 54 patients (34.6%) had ASD in the ACDF group (significantly different). Davis et al.[29] reported worsening of ASD in relation to baseline, and reported worsening of ASD to be higher in the fusion group than in the prosthesis group, for both the level superior and inferior to the index level: superior, 27.6% (ACDA) versus 64.7% (ACDF); inferior, 16.4% (ACDA) versus 56.2% (ACDF), both statistically different.

Level of evidence

The level of evidence is lowered with two levels. Most of the articles have a high or intermediate risk of bias, and estimates of effect are not sufficiently described. Therefore, the level of evidence that ASD occurs more often in ACDF than in ACDA is low.

In conclusion, only limited information is present on ASD. At baseline, ASD is already high, as is to be expected in a population with myelopathy caused by degeneration. The increase in ASD tends to be higher in the fusion group, but it seems that this does not lead to statistically significant differences. Unfortunately, no results on ASD are available in a group of patients with only radiculopathy.

DISCUSSION

The rationale of implanting an artificial disc after anterior discectomy is to preserve motion and to avoid ASD, which can lead to clinical symptoms in due time. The focus in comparing the outcome of implanting a prosthesis with the outcome of implanting a conventional cage should logically be on the signs of ASD. This systematic review revealed that only six[29,36,39,46,48,49] out of 38 studies adequately studied ASD radiologically. None of these studies concerned exclusively patients with radiculopathy, and one study[36] reported baseline presence of degeneration at the adjacent level in a substantial number of included patients, namely, 50%. ASD seemed to deteriorate in a higher percentage of patients (ca. 10-20%) in patients who were subjected to fusion surgery. It is therefore reasonable to state that degeneration of the cervical spine in an ongoing process that progresses irrespective of the immobilization of a segment. However, because data are scarce, the level of evidence is low, and research for radiological ASD was only performed in a population that has degeneration by diagnosis, these data are not convincing.

This literature overview demonstrated that ACDA preserved the mobility at the target level in the cervical spine whereas ACDF resulted in solid fusion in the vast majority of patients. However, ROM was reported as a mean value. It would be more interesting if we could get information about the percentage of patients in which motion persisted. The results on HO and bridging of bone around the prosthesis demonstrated that, on average, 10% of patients who were fitted with a prosthesis developed a bony rim around the prosthesis, preventing it from remaining mobile. This is not represented through the mean ROM. It can even lead to confusing outcome data. For instance, results from Loumeau et al.[18] demonstrated that Grade III and Grade IV HOs were present in nearly 60% of patients, but the mean ROM presented is >7 degrees in the prosthesis group. It would have been better to dichotomise the data in a group with persistent and non-persistent mobility. Unfortunately, no study reported their results in this way.

The results on the ROM of the whole cervical spine are interesting. The ROM of the whole cervical spine was evaluated in six[19,24,32-35] of 38 studies (two radiculopathy + four mixed), and three[24,32,35] of those studies did not demonstrate a difference between the ACDA and ACDF patients. Li et al.[34] reported a significant difference with more motion in the ACDA group, but yielded large standard deviations. Only Grasso[33] has a higher total cervical ROM of the ACDA group compared with the ACDF group with a statistical significance. This interesting result points in the direction of a self-correcting action of the cervical spine to go back to its original motion pattern.

HO has been one of the major complications after undergoing cervical ACDA[53,54]. Prostheses are designed with the purpose of preserving motion at the target level after anterior discectomy, and the occurrence of overgrowth of bone deprives the target level of staying mobile. Regarding the evaluation studies, the presence of HO is, however, evaluated scarcely. Only seven of 38 studies evaluated HO by means of McAfee et al.[47], and five reported bridging bone, which can be defined as Grade IV by McAfee classification. The incidence of HO after undergoing ACDA varied largely, from 17.8 to 94.1%[55]. This large variation may be due to the method used to evaluate overgrowth of bone. In the McAfee classification, it is essential that islands of bone be identified to grade HO. This can be difficult to discern on x-ray or computed tomography. Furthermore, the results available tend to indicate that occurrence of HO occurs more often in patients with radiculopathy than in patients with myelopathy. Because the cervical spine of patients with radiculopathy is likely to be less degenerative in comparison with the patients with myelopathy, and thus more mobile, HO may be related to the presence of a certain minimal mobility of the cervical spine. However, it may also be that the differences that exist between the design in the several types of prosthesis, such as biomechanical characteristics and endplate articulation components, cause this variation. Some researchers propose this to be a predisposing factor for HO, together with variations in surgical procedure[56,57]. However, again, numbers are too low to draw firm conclusions.

Overviewing the results on HO that are available, although scarce and of very low evidence, it seems that HO occurs on average in 10% of cases (very rude estimate). That number is too low to correlate the occurrence of HO to clinical condition, taking into account the relatively low number of patients included in the studies. Therefore, we cannot be sure that overgrowth of bone does not lead to compression of the neural structures, although this does not seem likely.

Only a minority of patients were demonstrated to have implant subsidence. This is a much lower incidence than generally reported in the literature. Subsidence rates were demonstrated to vary from 13% to 67% in previous studies evaluating ACDF[58-64]. Risk factors that were associated with subsidence are cervical malalignment, absence of a plate, old age[65], or an increased number of treatment levels[66]. The patients studied in this review were not of old age (Table 1), and only one level was operated on. This may explain the low percentage of subsidence observed.

There were several limitations at the review level pertaining to the possible incomplete retrieval of identified study and reporting bias. Although we made all attempt to performed search strategies to include research relevant to radiological outcomes after ACDF and ACDA from patients with radiculopathy, we were not able to include all, resulting in a possible incompletion of relevant studies. As we only included studies published in English and Dutch (two in Chinese in mixed group), those articles reported in other languages were possible omissions, which is an additional limitation to the incomplete retrieval of the identified study. Focusing on specific outcomes with regard to one-level anterior discectomy serves as a reporting bias limitation of this review. To reduce reporting bias, we included all studies regarding to radiological outcomes, reporting on the majority of relevant radiological parameters in each study.

CONCLUSIONS

Based on the radiological evidence that is present in literature, the proclaimed advantages of implanting a prosthesis cannot be corroborated, because it is clear that ASD cannot be avoided, but solid evidence that ASD occurs less in comparison to ACDF is lacking. Nor can the proclaimed disadvantages be confirmed. HO studies are scarce, but the results that are available indicate an occurrence of circa 10%. In conclusion, radiologically, no firm conclusion can be drawn on implanting a prosthesis in comparison with performing fusion.

REFERENCES

1. Smith GW, Robinson RA. The treatment of certain cervical-spine disorders by anterior removal of the intervertebral disc and interbody fusion. The Journal of bone and joint surgery American volume 1958;40-a:607-24.
2. Bohlman HH, Emery SE, Goodfellow DB, Jones PK. Robinson anterior cervical discectomy and arthrodesis for cervical radiculopathy. Long-term follow-up of one hundred and twenty-two patients. The Journal of bone and joint surgery American volume 1993;75:1298-307.
3. Gore DR, Sepic SB. Anterior cervical fusion for degenerated or protruded discs. A review of one hundred forty-six patients. Spine 1984;9:667-71.
4. Gore DR, Sepic SB. Anterior discectomy and fusion for painful cervical disc disease. A report of 50 patients with an average follow-up of 21 years. Spine 1998;23:2047-51.
5. Cagli S, Isik HS, Zileli M. Cervical screw missing secondary to delayed esophageal fistula: case report. Turkish neurosurgery 2009;19:437-40.
6. Mummaneni PV SJ, Haid RW , et al. Overview of anterior cervical plating. Spine Surgery 2002;6.
7. Sahjpaul RL. Esophageal perforation from anterior cervical screw migration. Surgical neurology 2007;68:205-9; discussion 9-10.
8. Fekete TF, Porchet F. Overview of disc arthroplasty-past, present and future. Acta neurochirurgica 2010;152:393-404.
9. Bartels R, Donk RD, Verhagen WIM, Hosman AJF, Verbeek ALM. Reporting the results of meta-analyses: a plea for incorporating clinical relevance referring to an example. The spine journal : official journal of the North American Spine Society 2017;17:1625-32.
10. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS medicine 2009;6:e1000097.
11. Formulier III voor het beoordelen van een Cohortonderzoek. Dutch Cochrane Center, 2006. (Accessed 29 March, 2012, at http://dcc.cochrane.org/sites/dcc.cochrane.org/files/uploads/cohort.pdf.)
12. Furlan AD, Pennick V, Bombardier C, van Tulder M. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine 2009;34:1929-41.
13. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. BMJ (Clinical research ed) 2004;328:1490.
14. Burkus JK, Traynelis VC, Haid RW, Jr., Mummaneni PV. Clinical and radiographic analysis of an artificial cervical disc: 7-year follow-up from the Prestige prospective randomized controlled clinical trial: Clinical article. Journal of neurosurgery Spine 2014;21:516-28.
15. Janssen ME, Zigler JE, Spivak JM, Delamarter RB, Darden BV, 2nd, 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. The Journal of bone and joint surgery American volume 2015;97:1738-47.
16. Murrey D, Janssen M, Delamarter R, et al. Results of the prospective, randomized, controlled multicenter Food and Drug Administration investigational device exemption study of the ProDisc-C total disc replacement versus anterior discectomy and fusion for the treatment of 1-level symptomatic cervical disc disease. The spine journal : official journal of the North American Spine Society 2009;9:275-86.
17. Zigler JE, Delamarter R, Murrey D, Spivak J, Janssen M. ProDisc-C and anterior cervical discectomy and fusion as surgical treatment for single-level cervical symptomatic degenerative disc disease: five-year results of a Food and Drug Administration study. Spine 2013;38:203-9.

18. Loumeau TP, Darden BV, Kesman TJ, et al. A RCT comparing 7-year clinical outcomes of one level symptomatic cervical disc disease (SCDD) following ProDisc-C total disc arthroplasty (TDA) versus anterior cervical discectomy and fusion (ACDF). European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 2016;25:2263-70.
19. Auerbach JD, Anakwenze OA, Milby AH, Lonner BS, Balderston RA. Segmental contribution toward total cervical range of motion: a comparison of cervical disc arthroplasty and fusion. Spine 2011;36:E1593-9.
20. Delamarter RB, Murrey D, Janssen ME, et al. Results at 24 months from the prospective, randomized, multicenter Investigational Device Exemption trial of ProDisc-C versus anterior cervical discectomy and fusion with 4-year follow-up and continued access patients. SAS journal 2010;4:122-8.
21. Nabhan A, Ahlhelm F, Shariat K, et al. The ProDisc-C prosthesis: clinical and radiological experience 1 year after surgery. Spine 2007;32:1935-41.
22. Nabhan A, Steudel WI, Nabhan A, Pape D, Ishak B. Segmental kinematics and adjacent level degeneration following disc replacement versus fusion: RCT with three years of follow-up. Journal of long-term effects of medical implants 2007;17:229-36.
23. 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. Journal of Korean Neurosurgical Society 2008;44:217-21.
24. Sala V, Lisi C, Di Natali G, 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.
25. Hou Y, Nie L, Pan X, 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. The bone & joint journal 2016;98-b:829-33.
26. Zhang HX, Shao YD, Chen Y, et al. A prospective, randomised, controlled multicentre study comparing cervical disc replacement with anterior cervical decompression and fusion. International orthopaedics 2014;38:2533-41.
27. 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. Journal of neurosurgery Spine 2013;18:36-42.
28. Fay LY, Huang WC, Tsai TY, et al. Differences between arthroplasty and anterior cervical fusion in two-level cervical degenerative disc disease. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 2014;23:627-34.
29. Davis RJ, Nunley PD, Kim KD, 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. Journal of neurosurgery Spine 2015;22:15-25.
30. Hou Y, Liu Y, Yuan W, et al. Cervical kinematics and radiological changes after Discover artificial disc replacement versus fusion. The spine journal : official journal of the North American Spine Society 2014;14:867-77.
31. Coric D, Cassis J, Carew JD, Boltes MO. 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. Journal of neurosurgery Spine 2010;13:715-21.
32. Wang Y, Cai B, Zhang XS, et al. [Clinical outcomes of single level Bryan cervical disc arthroplasty: a prospective controlled study]. Zhonghua wai ke za zhi [Chinese journal of surgery] 2008;46:328-32.

33. Grasso G. Clinical and radiological features of hybrid surgery in multilevel cervical degenerative disc disease. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 2015;24 Suppl 7:842-8.
34. 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. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia 2014;21:942-8.
35. Yan SZ, Di J, Shen Y. Adjacent Segment Degeneration Following Anterior Cervical Discectomy and Fusion Versus the Bryan Cervical Disc Arthroplasty. Medical science monitor : international medical journal of experimental and clinical research 2017;23:2692-700.
36. 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. Journal of neurosurgery Spine 2011;15:348-58.
37. Rozankovic M, Marasanov SM, Vukic M. Cervical Disc Replacement With Discover Versus Fusion In A Single Level Cervical Disc Disease: A Prospective Single Center Randomized Trial With A Minimum Two-Year Follow - Up. Clinical spine surgery 2016.
38. Zhang X, Zhang X, Chen C, et al. Randomized, controlled, multicenter, clinical trial comparing BRYAN cervical disc arthroplasty with anterior cervical decompression and fusion in China. Spine 2012;37:433-8.
39. Hisey MS, Zigler JE, Jackson R, et al. Prospective, Randomized Comparison of One-level Mobi-C Cervical Total Disc Replacement vs. Anterior Cervical Discectomy and Fusion: Results at 5-year Follow-up. International journal of spine surgery 2016;10:10.
40. Vaccaro A, Beutler W, Peppelman W, et al. Clinical outcomes with selectively constrained SECURE-C cervical disc arthroplasty: two-year results from a prospective, randomized, controlled, multicenter investigational device exemption study. Spine 2013;38:2227-39.
41. Cheng L, Nie L, Li M, Huo Y, Pan X. Superiority of the Bryan((R)) disc prosthesis for cervical myelopathy: a randomized study with 3-year followup. Clinical orthopaedics and related research 2011;469:3408-14.
42. Sasso RC, Smucker JD, Hacker RJ, Heller JG. Clinical outcomes of BRYAN cervical disc arthroplasty: a prospective, randomized, controlled, multicenter trial with 24-month follow-up. Journal of spinal disorders & techniques 2007;20:481-91.
43. Sasso RC, Anderson PA, Riew KD, Heller JG. Results of cervical arthroplasty compared with anterior discectomy and fusion: four-year clinical outcomes in a prospective, randomized controlled trial. The Journal of bone and joint surgery American volume 2011;93:1684-92.
44. Riina J, Patel A, Dietz JW, Hoskins JS, Trammell TR, Schwartz DD. Comparison of single-level cervical fusion and a metal-on-metal cervical disc replacement device. American journal of orthopedics (Belle Mead, NJ) 2008;37:E71-7.
45. Garrido BJ, Taha TA, Sasso RC. Clinical outcomes of Bryan cervical disc arthroplasty a prospective, randomized, controlled, single site trial with 48-month follow-up. Journal of spinal disorders & techniques 2010;23:367-71.
46. Robertson JT, Papadopoulos SM, Traynelis VC. Assessment of adjacent-segment disease in patients treated with cervical fusion or arthroplasty: a prospective 2-year study. Journal of neurosurgery Spine 2005;3:417-23.
47. McAfee PC, Cunningham BW, Devine J, Williams E, Yu-Yahiro J. Classification of heterotopic ossification (HO) in artificial disk replacement. Journal of spinal disorders & techniques 2003;16:384-9.

48. 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.
49. 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. Chinese medical journal 2012;125:3939-41.
50. Coric D, Finger F, Boltes P. Prospective randomized controlled study of the Bryan Cervical Disc: early clinical results from a single investigational site. Journal of neurosurgery Spine 2006;4:31-5.
51. Walraevens J, Liu B, Meersschaert J, et al. Qualitative and quantitative assessment of degeneration of cervical intervertebral discs and facet joints. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 2009;18:358-69.
52. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Annals of the rheumatic diseases 1957;16:494-502.
53. Park JH, Rhim SC, Roh SW. Mid-term follow-up of clinical and radiologic outcomes in cervical total disk replacement (Mobi-C): incidence of heterotopic ossification and risk factors. Journal of spinal disorders & techniques 2013;26:141-5.
54. Kim KS, Heo DH. Do Postoperative Biomechanical Changes Induce Heterotopic Ossification After Cervical Arthroplasty?: A 5-Year Follow-up Study. Clinical spine surgery 2016;29:E309-13.
55. 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. Biomechanics and modeling in mechanobiology 2016;15:1191-9.
56. Alvin MD, Mroz TE. The Mobi-C cervical disc for one-level and two-level cervical disc replacement: a review of the literature. Medical devices (Auckland, NZ) 2014;7:397-403.
57. Yi S, Kim KN, Yang MS, et al. Difference in occurrence of heterotopic ossification according to prosthesis type in the cervical artificial disc replacement. Spine 2010;35:1556-61.
58. Yson SC, Sembrano JN, Santos ER. Comparison of allograft and polyetheretherketone (PEEK) cage subsidence rates in anterior cervical discectomy and fusion (ACDF). Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia 2017;38:118-21.
59. Oh HS, Shim CS, Kim JS, Lee SH. Clinical and radiological comparison of femur and fibular allografts for the treatment of cervical degenerative disc diseases. Journal of Korean Neurosurgical Society 2013;53:6-12.
60. Pinder EM, Sharp DJ. Cage subsidence after anterior cervical discectomy and fusion using a cage alone or combined with anterior plate fixation. Journal of orthopaedic surgery (Hong Kong) 2016;24:97-100.
61. Bartels RH, Donk RD, Feuth T. Subsidence of stand-alone cervical carbon fiber cages. Neurosurgery 2006;58:502-8; discussion -8.
62. Wu WJ, Jiang LS, Liang Y, Dai LY. Cage subsidence does not, but cervical lordosis improvement does affect the long-term results of anterior cervical fusion with stand-alone cage for degenerative cervical disc disease: a retrospective study. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 2012;21:1374-82.
63. Barsa P, Suchomel P. Factors affecting sagittal malalignment due to cage subsidence in standalone cage assisted anterior cervical fusion. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 2007;16:1395-400.

64. Gercek E, Arlet V, Delisle J, Marchesi D. Subsidence of stand-alone cervical cages in anterior interbody fusion: warning. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 2003;12:513-6.
65. Lee YS, Kim YB, Park SW. Risk factors for postoperative subsidence of single-level anterior cervical discectomy and fusion: the significance of the preoperative cervical alignment. Spine 2014;39:1280-7.
66. Kao TH, Wu CH, Chou YC, Chen HT, Chen WH, Tsou HK. Risk factors for subsidence in anterior cervical fusion with stand-alone polyetheretherketone (PEEK) cages: a review of 82 cases and 182 levels. Archives of orthopaedic and trauma surgery 2014;134:1343-51.