Clinical Study

Adjacent segment degeneration and disease following cervical arthroplasty: a systematic review and meta-analysis

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Abstract

BACKGROUND CONTEXT: Cervical arthroplasty is an increasingly popular alternative for the treatment of cervical radiculopathy and myelopathy. This technique preserves motion at the index and adjacent disc levels, avoiding the restraints of fusion and potentially minimizing adjacent segment pathology onset during the postoperative period.

PURPOSE: This study aimed to identify all prospective studies reporting adjacent segment pathology rates for cervical arthroplasty.

STUDY DESIGN/SETTING: Systematic review and meta-analysis were carried out.

PATIENT SAMPLE: Studies reporting adjacent segment degeneration (ASDegeneration) and adjacent segment disease (ASDisease) rates in patients who underwent cervical arthroplasty comprised the patient sample.

OUTCOME MEASURES: Outcomes of interest included reported ASDegeneration and ASDisease events after cervical arthroplasty.

METHODS: We conducted a MEDLINE, SCOPUS, and Web of Science search for studies reporting ASDegeneration or ASDisease following cervical arthroplasty. A meta-analysis was performed to calculate effect summary values, 95% confidence intervals (CIs), Q values, and \(I^2\) values. Forest plots were constructed for each analysis group.

RESULTS: Of the 1,891 retrieved articles, 32 met inclusion criteria. The patient incidence of ASDegeneration and ASDisease was 8.3% (95% CI 3.8%–12.7%) and 0.9% (95% CI 0.1%–1.7%), respectively. The rate of ASDegeneration and ASDisease at individual levels was 10.5% (95% CI 6.1%–14.9%) and 0.2% (95% CI –0.1% to 0.5%), respectively. Studies following patients for 12–24 months reported a 5.1% (95% CI 2.1%–8.1%) incidence of ASDegeneration and 0.2% (95% CI 0.1%–0.2%) incidence of ASDisease. Conversely, studies following patients for greater than 24 months reported a 16.6% (5.8%–27.4%) incidence of ASDegeneration and 2.6% (95% CI 1.0%–4.2%) of ASDisease. This identified a statistically significant increase in ASDisease diagnosis with lengthier follow-up. Additionally, 1- and 2-level procedures resulted in a 7.4% (95% CI 3.3%–11.4%) and...
15.6% (95 CI−9.2% to 40.4%) incidence of ASDegeneration, respectively. Although there was an 8.2% increase in ASDegeneration following 2-level operations (relative to 1-level), it did not reach statistical significance. We were unable to analyze ASDisease incidence following 2-level arthroplasty (too few cases), but 1-level operations resulted in an ASDisease incidence of 0.8% (95% CI 0.1%–1.5%).

**CONCLUSIONS:** This review represents a comprehensive estimation of the actual incidence of ASDegeneration and ASDisease across a heterogeneous group of surgeons, patients, and arthroplasty techniques. Our investigation should serve as a framework for individual surgeons to understand the impact of various cervical arthroplasty techniques, follow-up duration, and surgical levels on the incidence of ASDegeneration and ASDisease during the postoperative period. © 2015 Elsevier Inc. All rights reserved.

**Keywords:** Adjacent segment degeneration; Adjacent segment disease; Cervical arthroplasty; Artificial disc replacement; Systematic review; Meta-analysis

### Introduction

Cervical arthroplasty is an increasingly popular alternative for treatment of cervical radiculopathy, myelopathy, and deformity caused by cervical degenerative disease, tumors, infection, or trauma [1–3]. Traditionally, anterior cervical discectomy and fusion (ACDF) has been the gold standard for relief of cervical degenerative disc disease symptoms [1,2,4–6]. Although ACDF provides clinical relief of symptoms, it is associated with a wide array of complications such as pseudoarthrosis, adjacent segment degeneration (ASDegeneration), and adjacent segment disease (ASDisease) [7–9]. Fusion results in cervical immobilization at the index level, consequently producing increased range of motion and intradiscal pressure at adjacent levels [5,6,9,10].

Conversely, cervical arthroplasty preserves motion at the index and adjacent disc levels, avoiding the restraints of fusion and potentially minimizing adjacent segment pathology onset during the postoperative period [5,9,11]. Assessment of disc height, osteophyte formation, end plate sclerosis, calcification of the anterior longitudinal ligament, and narrowing of the disc space may indicate degenerative changes at the adjacent level [12–17]. These radiographic degenerative changes can progress eventually to clinically symptomatic neurologic deficits, which may consequently result in reoperation [8,17–19]. Many cervical arthroplasty devices have been developed in an attempt to reduce these kinematic and clinical concerns following ACDF procedures [10,15,18,20,21].

Accurate knowledge of the incidence of ASDegeneration and ASDisease following cervical arthroplasty is essential for both patients and surgeons. An analysis of the overall incidence of adjacent segment pathology would be useful in educating patients and surgeons during the informed consent process and patient follow-up. We conducted a systematic literature review and meta-analysis to estimate the incidence of this potentially serious complication following cervical arthroplasty and to characterize significant differences in the incidence of ASDegeneration and ASDisease across a variety of situations.

### Methods

**Study search**

We conducted MEDLINE, SCOPUS, and Web of Science database searches with the following search algorithm: “cervical” and (“arthroplasty” or “total disc replacement” or “artificial disc replacement”) or (“total disk replacement” or “artificial disk replacement”) and (“adjacent segment” or “adjacent level”) and (“disease” or “degeneration”)) or (“complications” or “outcomes” or “adverse events”). The search returned 1,891 citations (Fig. 1). The search period ended on May 21, 2015.

**Inclusion and exclusion criteria**

Only prospective cohort studies and randomized controlled trials (RCTs) were included in this meta-analysis because of their superior evidence level compared with that of retrospective cohort studies [22]. In particular, we felt that retrospective studies would more often underreport postoperative complications. To create a more homogenous patient cohort, studies only involving the following procedures were excluded: arthrodesis, anterior cervical corpectomy and fusion, and hybrid arthroplasty and arthrodesis techniques. We imposed no restrictions on publication status. Animal, in vitro, biomechanical, and non-English studies were excluded.

**Data collection**

Two reviewers (MFS, AS) independently conducted data extraction from the 32 included articles. The extracted data sets were compared to confirm accuracy. Level of evidence for each of the included articles was assessed using the Oxford Centre for Evidence Based Medicine (or OCEBM) Level of Evidence 2 classification system [22]. From the eligible articles, we obtained the following information: study type, publication year, sample size, number of operated levels, follow-up duration (months), average age of patient cohort, artificial disc type, definition of ASDegeneration or ASDisease, number of levels expressing ASDisease and ASDegeneration, incidence of ASDegeneration and ASDisease, and reoperation rates. We
EVIDENCE & METHODS

Context
The authors sought to perform a systematic review and meta-analysis, reviewing the incidence of adjacent segment degeneration and adjacent segment disease following cervical disc arthroplasty.

Contribution
The authors included 32 articles for review in this meta-analytic study. The overall incidence of adjacent segment degeneration and adjacent segment disease approximated 8% and 1%, respectively. As may be expected, studies with greater lengths of follow-up reported higher rates of adjacent segment disease.

Implications
The strength of a meta-analysis is that patients can be pooled from a number of different studies to enable a higher degree of statistical power. This does not change the fact that selection and indication bias within those individual studies may alter and even confound the results of the meta-analysis itself. In the present work, heterogeneity within the arthroplasty cohort and the way outcomes were evaluated and defined within the original studies included may limit the generalizability of the findings regarding adjacent segment degeneration and adjacent segment disease. There is also the potential for publication bias to play a role, and this does not appear to have been addressed by the authors. Even still, given the size and methodology of this systematic study, findings presented here may represent best available evidence on this topic for the time being.

—The Editors

extracted the number of ASDegeneration and ASDisease events reported in each study, regardless of the study’s method of diagnosis or severity of adjacent level pathology. If a study, or multiple studies, reported ASDegeneration or ASDisease among the same patient population, the incidence was recorded from the latest time point. ASDegeneration and ASDisease incidences were also recorded at every follow-up time reported among the included studies, and these were used to calculate incidence over multiple follow-up durations.

To assess the risk of bias for each study, two reviewers independently investigated the individual studies (MFS, AS) and used The Cochrane Collaboration’s tool for assessing risk of bias [23]. Bias risk assessment was performed at the study level. Inconsistencies in bias risk assessment were reconciled through discussion.

Statistical analysis
We analyzed study data using a random-effects model with inverse variance weighting. Calculations for the meta-analysis and construction of forest plots were completed using an established spreadsheet constructed by Neyeloff et al. [24]. The presence of zero ASDegeneration or ASDisease events in some studies did not permit calculations. To allow for inclusion of these studies, we substituted a value of 0.1 events per study, and calculations were performed using this value. The principal summary measures were the effect summary values and 95% confidence intervals (CIs). We compared results among studies with 95% CIs and forest plots.

We completed meta-analysis calculations for ASDegeneration and ASDisease patient incidence, ASDegeneration and ASDisease levels, less than 24 months follow-up, greater than 24 months follow-up, 1-level and 2-level pathology, superior and inferior disc degeneration, and reoperation rates associated with adjacent level pathology. To calculate the patient incidence, we divided the number of reported ASDegeneration or ASDisease events (absent or present) by the patient cohort size at that follow-up time. We calculated the rate of ASDisease and ASDegeneration levels by dividing the number of reported disc levels displaying or not displaying ASDegeneration or ASDisease by the total number of operated levels among that particular study’s patient cohort.

To assess heterogeneity between individual studies, a Q statistic and I² value were calculated within each group’s meta-analysis. Delong et al. [25] established an I²<25% as low heterogeneity, 25%–75% as moderate heterogeneity, and >75% as severe heterogeneity. These same values were used to assess heterogeneity in our meta-analysis.

Results

Study selection (Fig. 1)

The initial 1,891 retrieved citations were reviewed. After removing 966 duplicates, the titles and abstracts of 925 publications were screened [26]. At this stage, studies that did not mention arthroplasty, total disc replacement or artificial disc replacement and associated complications, or that did not fulfill the inclusion criteria in any manner were excluded. After excluding 764 citations, the full text was assessed in the resulting 161 articles for eligibility criteria. Full-text assessment resulted in 32 eligible articles included in the final analysis. The definition and diagnostic criteria for ASDegeneration and ASDisease varied among the studies and in some studies were not specified (Table 1).

Study characteristics (Table 2)

Of the 32 studies evaluated in this review, the year of publication ranged from 2005 to 2015. Of the included studies, 22 were RCTs, and 10 were prospective cohort studies. Cohorts ranged in size from 14 to 314 patients. Follow-up time ranged from 12 to 96 months, producing a mean 34.8 months of follow-up across all studies. Eighteen studies performed solely single-level arthroplasty, whereas all other studies performed a combination of 1- and 2-level procedures. Unfortunately, most studies did not report ASDegeneration
or ASDisease incidences based on the specific anatomic level or total number of surgical levels. As a result, we were limited in our ability to correlate adjacent level pathology with anatomic or number of operated levels. A variety of artificial disc types were used. The Bryan cervical disc was employed by 12 studies, the most in our review. Mobi-C, dynamic cervical implants or DCI, PCM, Discover, Prestige, and Kineflex-C were also used. Many of these studies reported clinical data from the same RCT at different time points, which prevented us from analyzing differences in ASDegeneration and ASDisease incidence across these artificial discs owing to limited data. Bias risk assessment of the included studies identified a marked difference between RCTs and prospective cohort studies, with no studies demonstrating a high risk of incomplete outcome data or selective reporting of outcomes (Table 3).

**ASDegeneration and ASDisease patient incidence (Fig. 2)**

Across the combined inter-study population of 913 patients, studies reported ASDegeneration at latest follow-up in 183 patients [5,6,13,14,16,17,19,27–33]. Meta-analysis, calculated using a random-effects model with inverse variance weighting, of all included studies produced an overall ASDegeneration incidence of 8.3% (95% CI 3.8%–12.7%). Heterogeneity analysis indicated moderate heterogeneity [25]. Seven of the 14 studies did not include the effect summary value within their respective 95% CIs [6,14,16,19,27,32,33]. Five studies reported zero ASDegeneration events among their patient cohorts [6,14,27,32,33]. Bae et al. [5] reported an ASDegeneration incidence of 42.7%, the highest of all included studies.

A total of 16 individuals out of a combined inter-study population of 765 patients developed ASDisease, producing an
The incidence of ASDisease was 7.4% lower than reported adjacent level pathology, a total of 304 discs following 1,399
27,34,35
21,27,29–33,36
Phillips et al. [2015] ASDegeneration: Independently graded based on observed disc height loss (compared with adjacent normal discs), presence
and size of osteophytes, end plate sclerosis (thickening and density compared to normal)
Skeppholm et al. [2015] ASDisease: New symptoms assessed at adjacent segment, reoperation (converted to fusions at index and adjacent level)
Davis et al. [2014] ASDegeneration: Kellgren-Lawrence Scale: increase of at least one grade of degeneration at either adjacent level
Hisey et al. [2014] ASDegeneration: Kellgren-Lawrence Scale: increase of at least one grade of degeneration at either adjacent level
Karabag et al. [2014] ASDisease: Upper-level or level of disc disorder established clinically within 2 years; ASDegeneration: Upper-level or level of
doctor disorder established radiologically within 2 years
Li et al. [2014] ASDegeneration: Miyazaki five-point scale using MRI grading
Qi zhi et al. [2014] ASDegeneration: New or enlarging osteophyte formation or narrowing of disc space increased by >10% or calcification of the
ALL
Tian et al. [2014] ASDegeneration: Miyazaki five-point scale using MRI grading, cervical degeneration scoring using X-ray or CT
Zhang et al. [2014] ASDegeneration: Kellgren-Lawrence Scale
Davis et al. [2013] ASDegeneration: Kellgren-Lawrence Scale: increase of at least one grade of degeneration at either adjacent level
Delamarter et al. [2013] ASDisease: Symptomatic adjacent level degeneration (persistent pain), requiring surgery
Zhang et al. [2012] ASDegeneration: Reoperation needed at adjacent level owing to adjacent radiculopathy
Coric et al. [2011] ASDegeneration: Quantitative analysis of disc height and subjective assessment of osteophytes and end plate sclerosis
Maldonado et al. [2011] ASDegeneration: Robertson Criteria*
Quan et al. [2011] ASDegeneration: Formation of radial osteophytes and disc space narrowing
Wang et al. [2011] ASDegeneration: Kellgren-Lawrence Scale
Burkus et al. [2010] ASDisease: Reoperation for adjacent segment disease
Coric et al. [2010] ASDisease: Clinically symptomatic adjacent level degeneration, requiring reoperation
Garrido et al. [2010] ASDisease: Symptomatic adjacent level degeneration, requiring reoperation
Beaurain et al. [2009] ASDegeneration: Kellgren-Lawrence Scale: increase of at least one grade of degeneration at either adjacent level
Yang et al. [2009] ASDegeneration: Spinal cord or nerve root compression on CT or MRI
Murrey et al. [2008] ASDisease: Symptomatic adjacent segment disease
Mummaneni et al. [2007] ASDisease: Reoperation at adjacent level
Nabhan et al. [2007] Not defined
Sasso et al. [2007] ASDisease: Symptomatic pathology refractory to non-operative means at adjacent levels
Pickett et al. [2006] ASDegeneration: New herniation, asymptomatic
Hacker [2005] ASDisease: Spondylosis and radiculopathy at adjacent levels, requiring reoperation
Robertson et al. [2005] ASDisease: Symptomatic adjacent level disease; ASDegeneration: New osteophyte formation, enlargement of osteophyte, new
adjacent degenerative disc disease or new or increased calcification of the ALL

CT, computed tomography; MRI, magnetic resonance imaging; ALL, anterior longitudinal ligament.
* New anterior osteophyte formation, enlargement of existing osteophytes, increased or new narrowing of disc space (>30%), new or increased calcification of the ALL or formation of radial osteophytes.

Overall incidence of 0.9% (95% CI 0.1%–1.7%) [6,9,16–20, 27,34,35]. Heterogeneity analysis indicated no apparent heterogeneity [25]. All studies contained the effect summary value within their respective 95% CIs, and the highest reported incidence of ASDisease (3.6%) was identified by Sasso et al. [9] The incidence of ASDisease was 7.4% lower than ASDegeneration (p = .03).

ASDegeneration and ASDisease levels (Fig. 3)

For studies reporting the number of disc levels with adjacent level pathology, a total of 304 discs following 1,399 operated levels exhibited ASDegeneration [5,6,13–17,19, 21,27,29–33,36]. Meta-analysis calculations resulted in an effect summary value of 10.5% (95% CI 6.1%–14.9%). Analysis of the studies indicated moderate heterogeneity [25]. The highest rate of levels with ASDegeneration was 73.1%, reported by Phillips et al. [15].

Eight studies reported the number of levels exhibiting ASDisease [6,9,16–19,27,37]. A total of eight adjacent discs presented with ASDisease following a total of 666 operative levels. Meta-analysis produced a random effects rate of 0.2% (95% CI –0.1% to 0.5%). All studies contained the effect summary within their respective 95% CIs. Heterogeneity analysis identified low heterogeneity [25]. The rate of levels with ASDegeneration was 10.3% greater than the rate of ASDisease during the follow-up period (p = .02).

ASDegeneration incidence during follow-up (Fig. 4, Top)

Ten studies followed patients for 12–24 months [2,11,16,17,27,28,30,32,33,38]. The mean follow-up time for these studies was 20.4 months. Seven studies reported ASDegeneration at 24 months, the most common follow-up time within our review. Davis et al. [2] reported ASDegeneration incidences at both 12- and 24-month
follow-up. Robertson et al. [17] and Davis et al. [2] reported the highest incidences of ASDegeneration (17.6% and 16.0%, respectively) during this follow-up period. The calculated effect summary value was 5.1% (95% CI 2.1%–8.1%). Heterogeneity analysis indicated moderate heterogeneity [25].

Conversely, eight studies followed patients for a duration of greater than 24 months, with a mean follow-up of 50.7 months [5,6,13,14,19,29,31,38]. Two studies, by Davis et al. [38] and Bae et al. [5] reported the highest incidences of ASDegeneration (42.1% and 42.7%, respectively). Both of these studies used a Mobi-C disc and followed patients for 36 and 48 months, respectively. The study reporting ASDegeneration incidences at the longest follow-up was Quan et al. [13], reporting an incidence of 19.0% at 96 months. Meta-analysis calculations resulted in an overall ASDegeneration incidence of 16.6% (95% CI 5.8%–27.4%). Heterogeneity analysis indicated low heterogeneity [25]. There was an 11.5% increase in ASDegeneration identification with follow-up durations greater than 24 months, but this difference was not statistically significant (p=.13).

ASDisease incidence during follow-up (Fig. 4, Bottom)

Eleven studies reported ASDisease during follow-up of 12–24 months, with a mean of 21.8 months [1,9,11,16–18,20,27,34,37,39]. Nine of these studies followed patients for 24 months. Four studies reported zero ASDisease events among their patient cohorts [11,16,17,27]. Hacker [39] reported the highest incidence of ASDisease among these studies, with an incidence of 4.5%. Calculations resulted in an ASDisease incidence of 0.2% (95% CI 0.1%–0.2%). Heterogeneity analysis indicated low heterogeneity [25].

Only four studies reported incidences of ASDisease following patients for greater than 24 months, with a mean follow-up of 43.4 months [6,8,19,35]. Delamarter et al. [19] followed patients for 60 months, the longest among this meta-analysis group, reporting an incidence of 2.8%. Meta-analysis calculations resulted in an effect summary value of 2.6% (95% CI 1.0%–4.2%). Heterogeneity analysis indicated no apparent heterogeneity [25]. There was a 2.0% increase in ASDisease diagnosis among studies following patients for greater than 24 months, reaching statistical significance.
Adjacent segment degeneration incidences following 1-level arthroplasty were reported by 10 studies in our review [6,16,17,19,27,28,30,31,33,40]. Hisey et al. [40] reported the highest incidence of ASDegeneration following 1-level arthroplasty (44.2%). Conversely, four studies reported zero ASDegeneration events among their patient cohorts [6,16,27,33]. Meta-analysis calculations produced an ASDegeneration incidence of 7.4% (95% CI 3.3%–11.4%). Heterogeneity analysis indicated moderate heterogeneity [25]. The incidence of ASDegeneration following 1-level arthroplasty did not exhibit a statistically significant difference relative to the incidence of ASDegeneration reported by all included studies.

Ten studies reported incidences of ASDisease following 1-level arthroplasty [1,6,9,16,17,19,27,32,34,35]. Five studies reported zero ASDisease diagnoses, whereas Sasso et al. [9] reported the highest incidence of ASDisease following 1-level procedures (3.6%) [6,16,17,27,32]. The overall incidence of ASDisease among these studies was 0.8% (95% CI 0.1%–1.5%). Heterogeneity analysis indicated no apparent heterogeneity [25]. We were unable to analyze the incidence of ASDisease following 2-level arthroplasty because the literature was inconsistent in its reporting. There was no statistically significant difference between ASDisease incidences following 1-level arthroplasty and the incidence of ASDisease among all included studies.
**Fig. 2.** Incidence of ASDegeneration and ASDisease, 95% confidence intervals, and forest plots for meta-analysis of studies in our systematic review.

<table>
<thead>
<tr>
<th>Study</th>
<th>Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASD degeneration</strong></td>
<td></td>
</tr>
<tr>
<td>Bae et al., 2015</td>
<td>42.7% (35.4% - 49.9%)</td>
</tr>
<tr>
<td>Karabag et al., 2014</td>
<td>0.0% (−2.7% - 3.8%)</td>
</tr>
<tr>
<td>Li et al., 2014</td>
<td>12.8% (1.6% - 24.1%)</td>
</tr>
<tr>
<td>Qizhi et al., 2014</td>
<td>0.0% (−3.7% - 5.1%)</td>
</tr>
<tr>
<td>Tian et al., 2014</td>
<td>21.4% (4.3% - 38.6%)</td>
</tr>
<tr>
<td>Delamarter et al., 2013</td>
<td>2.8% (−1.1% - 6.6%)</td>
</tr>
<tr>
<td>Coric et al., 2011</td>
<td>9.2% (3.8% - 14.7%)</td>
</tr>
<tr>
<td>Maldonado et al., 2011</td>
<td>8.2% (2.1% - 14.3%)</td>
</tr>
<tr>
<td>Quan et al., 2011</td>
<td>19.0% (0.4% - 37.7%)</td>
</tr>
<tr>
<td>Wang et al., 2011</td>
<td>0.0% (−2.6% - 3.6%)</td>
</tr>
<tr>
<td>Yang et al., 2009</td>
<td>0.0% (−3.5% - 4.8%)</td>
</tr>
<tr>
<td>Nabhan et al., 2007</td>
<td>0.0% (−2.7% - 3.8%)</td>
</tr>
<tr>
<td>Pickett et al., 2006</td>
<td>1.4% (−1.3% - 4.0%)</td>
</tr>
<tr>
<td>Robertson et al., 2005</td>
<td>17.6% (8.0% - 27.1%)</td>
</tr>
<tr>
<td><strong>Effect Summary</strong></td>
<td><strong>8.3% (3.8% - 12.7%)</strong></td>
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<thead>
<tr>
<th>Study</th>
<th>Rate (95% CI)</th>
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<tbody>
<tr>
<td><strong>ASD disease</strong></td>
<td></td>
</tr>
<tr>
<td>Matge et al., 2015</td>
<td>2.1% (−2.0% - 6.3%)</td>
</tr>
<tr>
<td>Skepholm et al., 2015</td>
<td>2.6% (−1.0% - 6.3%)</td>
</tr>
<tr>
<td>Karabag et al., 2014</td>
<td>0.0% (−2.7% - 3.8%)</td>
</tr>
<tr>
<td>Delamarter et al., 2013</td>
<td>2.8% (−1.1% - 6.6%)</td>
</tr>
<tr>
<td>Zhang et al., 2012</td>
<td>1.8% (−1.7% - 5.3%)</td>
</tr>
<tr>
<td>Burkus et al., 2010</td>
<td>2.9% (0.9% - 4.9%)</td>
</tr>
<tr>
<td>Yang et al., 2009</td>
<td>0.0% (−3.5% - 4.8%)</td>
</tr>
<tr>
<td>Sasso et al., 2007</td>
<td>3.6% (−1.4% - 8.5%)</td>
</tr>
<tr>
<td>Pickett et al., 2006</td>
<td>0.0% (−0.7% - 1.0%)</td>
</tr>
<tr>
<td>Robertson et al., 2005</td>
<td>0.0% (−0.7% - 1.0%)</td>
</tr>
<tr>
<td><strong>Effect Summary</strong></td>
<td><strong>0.9% (0.1% - 1.7%)</strong></td>
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</tbody>
</table>
Fig. 3. Rate of levels undergoing ASDegeneration and ASDisease, 95% confidence intervals, and forest plots for meta-analysis of studies in our systematic review.
Fig. 4. (Top) Incidence of ASDegeneration, 95% confidence intervals, and forest plots for studies reporting follow-up durations of 12–24 months and greater than 24 months. (Bottom) Incidence of ASDisease, 95% confidence intervals, and forest plots for studies reporting follow-up durations of 12–24 months and greater than 24 months.
**ASDegeneration: 1-level**

<table>
<thead>
<tr>
<th>Study</th>
<th>Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hisey et al., 2015</td>
<td>44.2% (33.1% - 55.3%)</td>
</tr>
<tr>
<td>Karabag et al., 2014</td>
<td>0.0% (-2.7% - 3.8%)</td>
</tr>
<tr>
<td>Li et al., 2014</td>
<td>12.8% (1.6% - 24.1%)</td>
</tr>
<tr>
<td>Delamarter et al., 2013</td>
<td>2.8% (-1.1% - 6.6%)</td>
</tr>
<tr>
<td>Coric et al., 2011</td>
<td>9.2% (3.8% - 14.7%)</td>
</tr>
<tr>
<td>Maldonado et al., 2011</td>
<td>8.2% (2.1% - 14.3%)</td>
</tr>
<tr>
<td>Yang et al., 2009</td>
<td>0.0% (-3.5% - 4.8%)</td>
</tr>
<tr>
<td>Nabhan et al., 2007</td>
<td>0.0% (-2.7% - 3.8%)</td>
</tr>
<tr>
<td>Pickett et al., 2006</td>
<td>0.0% (-1.0% - 1.4%)</td>
</tr>
<tr>
<td>Robertson et al., 2005</td>
<td>17.6% (8.0% - 27.1%)</td>
</tr>
<tr>
<td><strong>Effect Summary</strong> (Q = 29.1, I² = 69.0%)</td>
<td>7.4% (3.3% - 11.4%)</td>
</tr>
</tbody>
</table>

**ASDegeneration: 2-level**

<table>
<thead>
<tr>
<th>Study</th>
<th>Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis et al., 2015</td>
<td>41.5% (32.6% - 50.4%)</td>
</tr>
<tr>
<td>Qizhi et al., 2014</td>
<td>0.0% (-3.7% - 5.1%)</td>
</tr>
<tr>
<td>Pickett et al., 2006</td>
<td>5.0% (-4.8% - 14.8%)</td>
</tr>
<tr>
<td><strong>Effect Summary</strong> (Q = 21.1, I² = 4.0%)</td>
<td>15.6% (-9.2% - 40.4%)</td>
</tr>
</tbody>
</table>

**ASDisease: 1-level**

<table>
<thead>
<tr>
<th>Study</th>
<th>Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karabag et al., 2014</td>
<td>0.0% (-2.7% - 3.8%)</td>
</tr>
<tr>
<td>Delamarter et al., 2013</td>
<td>2.8% (-1.1% - 6.6%)</td>
</tr>
<tr>
<td>Zhang et al., 2012</td>
<td>1.8% (-1.7% - 5.3%)</td>
</tr>
<tr>
<td>Wang et al., 2011</td>
<td>0.0% (-3.1% - 4.2%)</td>
</tr>
<tr>
<td>Burkus et al., 2010</td>
<td>2.9% (0.9% - 4.9%)</td>
</tr>
<tr>
<td>Coric et al., 2010</td>
<td>2.5% (-2.4% - 7.4%)</td>
</tr>
<tr>
<td>Yang et al., 2009</td>
<td>0.0% (-3.5% - 4.8%)</td>
</tr>
<tr>
<td>Sasso et al., 2007</td>
<td>3.6% (-1.4% - 8.5%)</td>
</tr>
<tr>
<td>Pickett et al., 2006</td>
<td>0.0% (-1.0% - 1.4%)</td>
</tr>
<tr>
<td>Robertson et al., 2005</td>
<td>0.0% (-0.7% - 1.0%)</td>
</tr>
<tr>
<td><strong>Effect Summary</strong> (Q = 8.4, I² = 0.0%)</td>
<td>0.8% (0.1% - 1.5%)</td>
</tr>
</tbody>
</table>

Fig. 5. (Top) Incidence of ASDegeneration, 95% confidence intervals, and forest plots following 1- and 2-level arthroplasty procedures. (Bottom) Incidence of ASDisease, 95% confidence intervals, and forest plots following 1-level arthroplasty procedures.
**Superior versus inferior level degeneration**

Adjacent segment degeneration superior to the index operative level was identified by 11 studies [6,10,15,16,21,27,29,32,33,36,40]. Meta-analysis calculations produced an effect summary value of 8.5% (95% CI 4.0%–13.0%). Additionally, 11 studies reported the incidence of inferior ASDegeneration [6,10,15,16,21,27,29,32,33,36,40]. These studies resulted in an ASDegeneration incidence of 7.2% (95% CI 3.5%–10.9%). There was no significant difference between the incidences of superior and inferior ASDegeneration.

**Reoperation rates**

Seventeen studies reported reoperation rates indicated by adjacent segment pathology among their patient cohorts [1,6,9,14–21,27,32,34–36,40]. A total of 0.5% (95% CI 0.1%–0.9%) of patients required reoperation owing to symptomatic adjacent level pathology.

**Discussion**

This study represents a comprehensive systematic literature review and meta-analysis of ASDegeneration and ASDisease incidences associated with cervical arthroplasty. The purpose of this study was to determine the incidence of these two interrelated complications and their association with various factors. Although the 32 included studies represent a small sample of the 925 total studies screened during our systematic review, we solely evaluated prospective studies because of bias and underreported complication rates outlined in retrospective studies. We analyzed reported adjacent segment pathology incidences among the published literature and elucidated differences in the incidence of degeneration versus disease, and their respective incidences following 1- or 2-level surgery and at different time points during follow-up.

**ASDegeneration**

During the early and late postoperative period it is critical that surgeons distinguish ASDegeneration from ASDisease in the clinical setting. A majority of studies within our review classified degeneration at adjacent levels using the Kellgren-Lawrence Scale [5,10,12,38,40,41]. This scaling system permits assessment of degeneration severity at the adjacent disc space [12]. An increase of at least one grade of degeneration at either the superior or inferior adjacent level, relative to the index surgical site, was indicative of ASDegeneration [5,10,36]. Conversely, some studies employed the Robertson criteria to assess degeneration through observation of new or enlarging osteophyte formation, narrowing of the disc space (>30%), calcification of the anterior longitudinal ligament, and formation of radial osteophyte [13,17]. Studies that did not use a previously published outlined scale for investigation of ASDegeneration reported a reduced incidence of degeneration. Pickett et al. [16], Nabhan et al. [33], Yang et al. [6], and Karabag et al. [27] did not use the Kellgren-Lawrence scale or Robertson criteria, and reported rates of levels undergoing ASDegeneration of 1.4%, 0.0%, 0.0%, and 0.0%, respectively [12,17]. These studies showed a statistically significant difference in levels expressing ASDegeneration relative to the calculated effect summary value for all studies reporting levels undergoing ASDegeneration (Fig. 3). This difference highlights the necessity for utilization of a standardized and previously established scale or criteria for the proper radiographic identification of ASDegeneration during the postoperative period.

**ASDisease**

Among the included studies, there was a marked reduction in the incidence of symptomatic disease at the adjacent level relative to degeneration. The incidence of ASDegeneration (8.3%) was significantly higher than ASDisease (0.9%). This emphasizes the point that radiographic elements of degeneration do not always progress to clinically relevant symptomatic manifestations. As well, this may reflect surgeon bias toward avoiding reoperation following disc arthroplasty placement, which may skew the literature and the results of our review. Whereas ASDegeneration was objectively defined and investigated through the use of specific radiographic scales, clinical symptoms and the necessity for reoperation were used for the diagnosis of ASDisease [9,18–20,27,34,35]. Unfortunately, most studies reported either ASDegeneration or ASDisease among their patient cohorts, limiting our ability to analyze the progression of degenerative changes (ASDegeneration) to clinical symptoms (ASDisease). Robertson et al. [17], though, reported a 17.6% incidence of ASDegeneration among their patient cohort, with zero patients showing signs of symptomatic ASDisease at 24 months’ follow-up. Therefore, although progression of degenerative changes to clinically significant neurologic symptomatology is possible, its probability is relatively low [17]. Furthermore, across the included studies, only 0.5% of patients underwent secondary, revision surgery for symptoms or degeneration at the adjacent level, once again elucidating the minimal impact of adjacent level degeneration upon a patient’s clinical status.

**Follow-up time**

The incidence of ASDegeneration has been reported to increase with lengthier follow-up [2,38]. The pathogenesis of degeneration at an adjacent level is related to increased cervical immobilization at the index surgery level, ultimately resulting in increased adjacent level range of motion and intradiscal pressure [5,6,9,10]. Although our study identified an 11.5% increase in the incidence of ASDegeneration between studies following patients for 12–24 months and those following patients for greater than 24 months, this difference was not statistically significant (Fig. 4, Top). This may have been limited by the number of studies within our analysis, but does show the potential for increased degenerative
changes with lengthier follow-up. To better understand this phenomenon, it is necessary to follow patients for longer periods postoperatively to assess adjacent segment pathology over time.

Whereas increases in ASDegeneration with longer follow-up time did not reach statistical significance, there was a significant increase in the incidence of diagnosed ASDisease with lengthier follow-up of greater than 24 months. During the early postoperative period of 12–24 months, only 0.2% of patients investigated in the included studies developed neurologic symptoms at the adjacent level [1,9,11,16–18,20,27,34,37,39]. Conversely, 2.6% of patients developed ASDisease with follow-up greater than 2 years. The highest incidence of ASDisease (5.6%) was reported by Garrido et al. [8], reporting adjacent level pathology at 4 years of follow-up. Thus, because patients appear to develop a significant increase in adjacent level symptoms after 2 years of follow-up, this suggests the importance of informing patients of relevant symptoms to monitor even beyond 2 years after the operation.

**Number of operated levels**

Only three studies within our review, which included 234 patients, distinguished reporting of ASDegeneration between 1- and 2-level surgery [10,14,16]. Although 1- and 2-level procedures resulted in ASDegeneration incidences of 7.4% and 15.6%, respectively, this difference was not significant. The lack of significance may have been impacted by the relative small number of patients and studies comparing 1- and 2-level fusion, and therefore, additional studies are needed to compare the relative risks of ASD following single and multilevel procedures.

**Limitations**

Most abstracts and studies screened in this review were retrospective case series, which limited the number of studies we were able to include based on our criteria. In addition, although stratification of ASDegeneration and ASDisease incidences by age and cervical levels would decrease heterogeneity among studies and reveal inherent differences associated with these factors, the primary literature is varied and does not routinely discuss surgical levels in reporting complications. Only three studies separated adjacent level pathology incidence by single and multilevel procedures, which limited that analysis as well. Furthermore, there exists a potential for inherent surgeon bias toward avoiding reoperation following cervical disc arthroplasty placement, which may skew the literature and the results of our review. Additionally, we initially intended to elucidate differences in ASDegeneration and ASDisease by artificial disc type, but because of limited data and overlapping patient cohorts from RCTs, we were unable to perform such an analysis.

**Conclusions**

The resultant ASDegeneration and ASDisease incidences from this systematic review and meta-analysis represent a comprehensive estimation of the actual incidence of adjacent level pathology across a heterogeneous group of surgeons, patients, and arthroplasty techniques. Overall we found that the incidence of ASDegeneration was 8.3% and ASDisease was 0.9%. We identified a statistically significant decrease in ASDisease incidence relative to ASDegeneration, highlighting the limited progression of degenerative changes to clinically relevant neurologic symptomatology. Furthermore, only 0.5% of patients underwent reoperation because of adjacent pathology. Although there was an 11.5% increase in ASDegeneration between follow-up durations of 12–24 months and greater than 24 months, this difference was not statistically significant. ASDisease incidences were significantly higher for studies following patients more than 24 months relative to shorter follow-up periods. Additionally, there was an 8.2% increased incidence of ASDegeneration between 1- and 2-level operations, but this analysis was limited and did not reach statistical significance. To ensure the proper diagnosis of adjacent level pathology, we recommend surgeons use a standardized scale or criteria for the identification of degenerative changes [12,17]. Our investigation should serve as a framework for individual surgeons to understand the impact of various cervical arthroplasty techniques, follow-up duration, and surgical levels on the incidence of ASDegeneration and ASDisease during the postoperative period.

**Appendix: Supplementary material**

Supplementary data to this article can be found online at doi:10.1016/j.spinee.2015.10.032.

**References**


