

# A systematic review of risk factors and adverse outcomes associated with anterior cervical discectomy and fusion surgery over the past decade

## ABSTRACT

**Background:** Anterior cervical discectomy and fusion (ACDF) is one of the most frequently performed cervical surgeries in the world, yet there have been several reported complications.

**Objective:** To determine the actual incidence of complications related to ACDF as well as any risk variables that may have been identified in earlier research.

**Methods:** To evaluate the origin, presentation, natural history, and management of the risks and the complications, we conducted a thorough assessment of the pertinent literature. An evaluation of clinical trials and case studies of patients who experienced one or more complications following ACDF surgery was done using a PubMed, Cochrane Library, and Google Scholar search. Studies involving adult human subjects that were written in the English language and published between 2012 and 2022 were included in the search. The search yielded 79 studies meeting our criteria.

**Results:** The overall rates of complications were as follows: Dysphagia 7.9%, psudarthrosis 5.8%, adjacent segment disease (ASD) 8.8%, esophageal perforations (EPs) 0.5%, graft or hardware failure 2.2%, infection 0.3%, recurrent laryngeal nerve palsy 1.7%, cerebrospinal fluid leak 0.8%, Horner syndrome 0.5%, hematoma 0.8%, and C5 palsy 1.9%.

**Conclusion:** Results showed that dysphagia was a common postoperative sequelae with bone morphogenetic protein use and a higher number of surgical levels being the major risk factors. Pseudarthrosis rates varied depending on the factors such as asymptomatic radiographic graft sinking, neck pain, or radiculopathy necessitating revision surgery. The incidence of ASD indicated no data to support anterior cervical plating as more effective than standalone ACDF. EP was rare but frequently fatal, with no correlation found between patient age, sex, body mass index, operation time, or number of levels.

**Keywords:** Anterior cervical fusion, anterior plate, cervical spine disease, cervical spine, discectomy, stand-alone cage

## INTRODUCTION

The anterior cervical discectomy and fusion (ACDF) procedure was developed in 1958 by Smith and Robinson<sup>[1]</sup> and has since gained widespread acceptance as the preferred way to treat symptomatic myelopathy and/or radiculopathy owing to cervical spondylosis. The complex anatomy of the neck region makes the anterior approach associated with a wide range of unique potential risks and complications.<sup>[2]</sup> In addition, if not addressed immediately, many of these complications can be fatal. The goal of the current study

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was to shed light on the prognosis and management of complications following anterior cervical surgery rather than to determine the incidence. Thus, we set out to present this systematic review through the qualitative assessment of the incidence, causes, risk factors, treatment options, and results of surgical complications following anterior cervical spine surgery in adults.

The use of Anterior plating (AP) has historically been employed to boost fusion rates, lessen subsidence, and prevent postoperative kyphosis.<sup>[3]</sup> The prolonged operating time, screw loosening, screw pullout, dysphagia, plate malposition, and hastened adjacent segment degeneration are some of the potential drawbacks and consequences of AP.<sup>[4]</sup> Although using additional posterior instrumentation is beneficial, it requires a second procedure with longer recovery times and more blood loss.<sup>[5]</sup> As cage technology continues to advance, spine surgeons are increasingly using standalone cervical cages in single- and multilevel ACDF procedures to prevent any issues that could arise from the use of added instrumentation. However, more research is needed on this argument in relation to its application at 3- and 4-levels as data are insufficient.

The current literature of complications associated with the anterior approach to the cervical spine is largely comprised of retrospective studies and case reports. Out of the two most recent review of complications of ACDF,<sup>[2,5]</sup> one was a comparative study of ACDF with anterior plate (AP) versus standalone cage and included limited studies and few parameters only, whereas the other systematic review was predominantly based on the retrospective studies and case reports with limited prospective studies. The present study is the only study reporting the analysis of most recent data of the last one decade (2012–2022) on ACDF risks and complications. Prospective and retrospective studies have been considered for most of the complications, while case reports have been included in some classes of complications where sufficient prospective data were lacking.

## METHODS

A systematic search was conducted from July 2022 to December 2022 following the guidelines of the Preferred Reporting Items for Systematic Review and Meta-analysis to identify the relevant studies through PubMed, Google Scholar, and Cochrane database. We used the Medical Subject Headings (MeSH) terms: “anterior cervical discectomy and fusion and “outcome” and/or “complications” and/or “anterior cervical.” Studies were limited to those involving adult human subjects, written in the English

language, and published over the past 10 years (January 2012–December 2022). For the majority of frequently occurring surgical complications, such as esophageal perforations (EPs), recurrent laryngeal nerve palsy (RLNP), and subdural hematomas, case reports were included as there were not enough evidence to draw conclusions from prospective or retrospective investigations. Excluded were studies using cadavers, single-stage combined anterior and posterior techniques, abstracts, letters to the editor, existing systematic reviews, meta-analyses, and nonhuman studies. The authors first screened all the titles and abstracts and then jointly assessed that the patients underwent anterior-only cervical spine surgery and suffered a surgical complication that was not present preoperatively. Studies with a follow-up period of at least 12 months were included. Details on the onset, origin, treatment, and results of complications were abstracted. Only the more recent study was used for providing pooled occurrences in the presence of overlapping patient populations across trials. The aggregate of all the patients at risk is reflected in the presented “*n*” numbers. There was little room for comparative study due to the diversity of patient demographics. Hence, qualitative analysis was carried out.

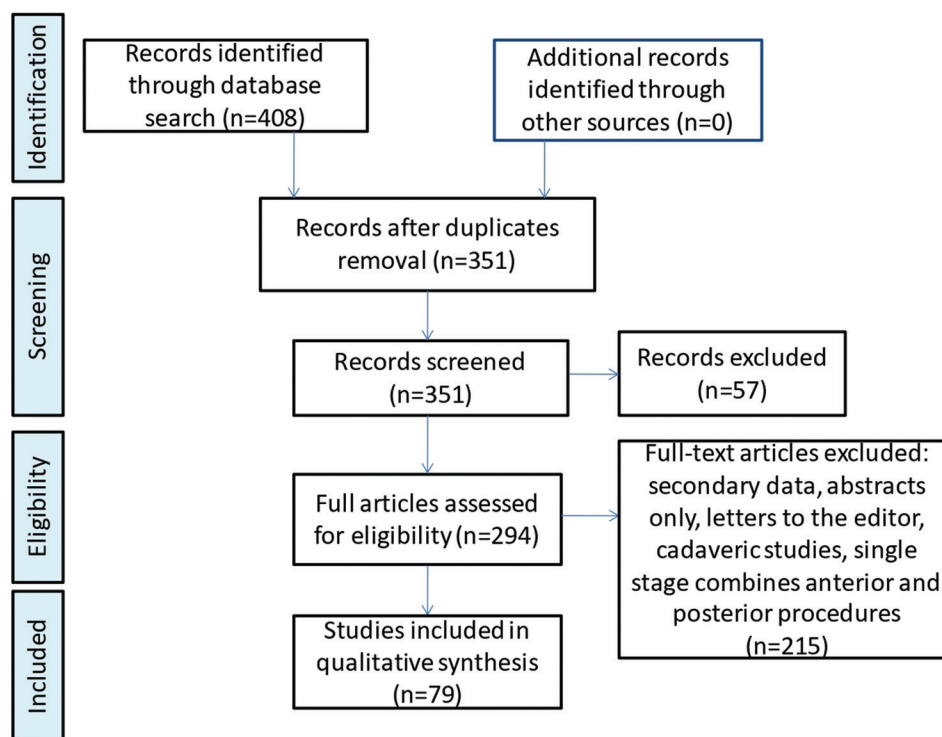
## RESULTS

The initial database search yielded 408 records. After the removal of duplicates, we were left with 351 records. A title and abstract review excluded 57 records resulting in 294 full-text articles to be assessed for eligibility. After excluding 215 full text articles, 79 studies remained for inclusion in the systematic review. A flowchart of this process is illustrated in Figure 1. A summary of pooled complication rates and ranges is displayed in Table 1. The summary of recent prospective and retrospective studies reporting various complications of ACDF surgery is given in Table 2.

**Table 1: Summary of complications rates and ranges across all prospective and retrospective studies conducted between 2012 and 2022**

Complication	Pooled incidence (%)	Range (%)
Dysphagia	7.9	0.5–34.5
Adjacent segment disease	8.8	1.8–24.8
Pseudarthrosis	5.8	0.0–31.0
Graft or hardware failure	2.2	0.0–24.6
C5 palsy	1.9	0.3–5.7
Recurrent laryngeal nerve palsy	1.7	0.0–10.0
Hematoma	0.8	0.1–7.0
Infection	0.3	0.2–5.5
CSF leak	0.7	0.05–6.0
Horner syndrome	0.5	0.06–3.6
Esophageal perforation	0.5	0.1–0.8

CSF - Cerebrospinal fluid leak



**Figure 1: Systematic review flow diagram. The Preferred Reporting Items for Systematic Review and Meta-analysis flow diagram for the systematic review detailing the database searches, the number of abstracts screened and full texts retrieved**

## Dysphagia

We identified 12 prospective cohort studies<sup>[7,8,11-14,16,19-23]</sup> and 16 retrospective cohort studies.<sup>[6,9,10,15,24-35]</sup> Across all studies ( $n = 4270$ ), the rate of postoperative dysphagia at any point of time was 7.9%. Among prospective studies ( $n = 1707$ ), overall rates of postoperative dysphagia ranged from 0.5% to 34.5% with a pooled incidence of 11.1%. Among prospective studies reporting chronic dysphagia (lasting longer than 3 months)<sup>[13,14,16,23]</sup> ( $n = 537$ ), this rate ranged from 1.1% to 32% with overall rate of chronic dysphagia of 13.3%. Among retrospective studies ( $n = 2563$ ), overall rates of postoperative dysphagia ranged from 0.5% to 24.3% with a pooled incidence of 5.8%. Among retrospective studies,<sup>[15,27,29,32,35]</sup> reporting rates of chronic dysphagia ( $n = 741$ ), incidence ranged from 0.6% to 12.6% with a pooled incidence of 2.9%.

Yadav *et al.*<sup>[6]</sup> [Table 2], in a retrospective study of 128 patients, found a significant increase in the incidence of dysphagia in patients undergoing 3-level ACDF as compared to those undergoing 1- or 2-level procedures (75% vs. 14.5%). This finding was further supported by a retrospective study of 1576 patients undergoing ACDF by a single surgeon.<sup>[10]</sup> A retrospective study of 97 patients conducted by De la Garza-Ramos *et al.*<sup>[9]</sup> [Table 2] found a significantly increased risk of dysphagia in patients undergoing 4-versus 3-level ACDF (30.8% vs. 12.7%).

A prospective randomized control study<sup>[11]</sup> [Table 2] found that the rate of postoperative dysphagia is considerably low with zero profile (ZP) ACDF than with anterior cervical plate (ACP) ACDF (0% for ZP vs. 6% for ACP,  $P = 0.243$ ). Two prospective studies<sup>[8,16]</sup> [Table 2] confirmed that in contrast to ACP, ZP anchored cage systems in ACDF considerably reduced the incidence of postoperative dysphagia. Two prospective studies: one of 108 patients<sup>[12]</sup> [Table 2] and another of 98 patients<sup>[23]</sup> reported that unregulated endotracheal cuff pressure (ETCP) could lead to a significantly higher incidence of hoarseness and dysphagia (22.5% and 20.4%) causing the compression of laryngeal tissue during retraction and intubation. Yagi *et al.* reported that severe prolonged and/or delayed dysphagia and odynophagia were attributable to prevertebral soft-tissue edema.<sup>[32]</sup>

## Pseudarthrosis

We identified 12 prospective studies<sup>[9,11,14,16-19,21,36-39]</sup> and 15 retrospective studies.<sup>[15,24-26,29,30,33-35,39-43]</sup> Across all studies, the rate of pseudarthrosis (radiographic, symptomatic, and those requiring revision) at last follow-up was 5.8%. Among prospective studies, the rate of pseudarthrosis ranged from 0% to 26.8% with a pooled incidence of 9.1% ( $n = 2156$ ). Among retrospective studies, the rate of pseudarthrosis ranged from 0.45% to 31% with a pooled incidence of 3.8% ( $n = 2048$ ). Among studies reporting rates of pseudarthrosis requiring reoperation,<sup>[1-3,6-10,13,16,17,24,28,29,34,35,37,44,45]</sup> the incidence was

**Table 2: Important outcomes and conclusion of different studies on various postoperative complications of anterior cervical discectomy and fusion**

Authors/reference	Study type	Number of patients (n)	Device/graft used	Outcome	Conclusion
Yadav et al., 2017 <sup>[6]</sup>	Retrospective study	128	Tricortical iliac crest autograft/ PEEK cage/artificial disc placement	Dysphagia was the most common complaint (16.4%) followed by neurological dysfunction (7.9%). One patient suffered pharyngeal perforation and presented postoperatively with subcutaneous emphysema and haemoptysis	Postoperative dysphagia and worsening of preexisting myelopathy were the most common complications following ACDF, and multilevel surgery was identified as the most significant risk factor
Hasan et al., 2018 <sup>[7]</sup>	Prospective study	165	PEEK cage for 1-level and 2-level/ plating for 2-level and 3-level	57 patients (34.5%) had transient dysphagia and 2 patients (1.2%) each had a dural tear, surgical site infection, and postoperative hematoma. One patient (0.6%) each had an esophageal injury, slippage of the cage, acute implant extrusion, and Horner syndrome	The incidence of complications is increased with more than 1-level fusion and in multiple comorbid disorders including diabetes mellitus and smoking
Grasso and Landi, 2018 <sup>[8]</sup>	Prospective study	100	Zero profile anchored cage ROI-C cage	Significantly low rate of dysphagia (2%)	No implant related complications were reported. The cage with very low profile avoids an implant contact to the soft tissue in front of the cervical spine. This avoids any mechanical irritation of the esophagus and explains the low dysphagia rates in the patients
De la Garza-Ramos et al., 2016 <sup>[9]</sup>	Retrospective study	97 (n=71 for 3-level; n=26 for 4-level)	Anterior cervical plating	One case (3.9%) of deep wound infection in the 4-level group and one case (1.4%) in the 3-level group. 31% of patients complained of dysphagia in the 4-level group compared with 12.7% in the 3-level group. The fusion rate was 84.6% in 4-level and 94.4% in the 3-level ACDF	Patients who underwent 4-level ACDF had significantly higher rates of dysphagia, postoperative neck pain, and postoperative narcotic usage as compared to those who underwent 3-level ACDF. Psudarthrosis and deep wound infection rates were also higher in the 4-level group
Nanda et al., 2014 <sup>[10]</sup>	Retrospective study	1576	Allograft/PEEK cage/iliac crest autologous bone graft/cadaveric bone graft	Dysphagia was the most common complication at 8.4% (n=133). Dural tear was encountered in 1.2% (n=19), superficial wound infection occurred in 0.2% (n=3). The incidence of postoperative neck hematoma, recurrent laryngeal nerve palsy, esophageal tear were recorded at 0.1% each. Further, graft extrusion was recorded in 0.88% (n=14) cases. There was 0.1% of mortality	Of all the complications, dysphagia was significantly correlated with 3-level ACDF as compared to 1 or 2 level ACDF. Hence, the study concluded that ACDF is a relatively safe procedure with very low morbidity and almost no mortality
He et al., 2018 <sup>[11]</sup>	Prospective study	104	ZP cage/ACP	Pseudarthrosis was the most common complication reported in 2% (n=1) in ZP group and 4% (n=2) in ACP group. Dysphagia was reported in 6% (n=3) in ACP group, nerve injury in 2% (n=1) in ZP group and 4% (n=2) in ACP group, cerebrospinal fluid leak in 1% (n=1) in ZP group and 2% (n=1) in ACP group	ZP used in multilevel ACDF may obtain favourable clinical outcomes and a lower postoperative complication
Gowd et al., 2021 <sup>[12]</sup>	Prospective study	108		20.4% (n=19) patients complained of dysphagia, 1.9% (n=2) complained of aspiration symptoms, and 4.6% (n=5) reported voice hoarseness. RLN remained functional even a month after surgery despite several cases of postoperative dysphagia and voice changes	Endotracheal cough pressure, number of vertebral levels, body mass index, and intubation time were important variables related to postoperative symptoms
Fayed et al., 2021 <sup>[13]</sup>	Retrospective study	321	Allograft cage with plate and screw construct/ standalone cage	4.4% (n=14) total revisions were necessary: 8.7% (n=4) in the standalone group and 3.6% (n=10) in the plated group. There was no significant difference in the incidence of dysphagia (19.6%) and hoarseness (4.4%) in standalone and 3.6% in plated group. surgical site infection (2.2%) was reported in standalone group	Standalone ACDF demonstrates higher, but not statistically significant, revision rates than plate and screw constructs

Contd...

Table 2: Contd...

Authors/reference	Study type	Number of patients (n)	Device/graft used	Outcome	Conclusion
Charalampidis et al., 2022 <sup>[14]</sup>	Prospective study	28	Standalone cage	9 patients (32%) complained of dysphagia, 4 (14%) reported hoarseness, 1 (3.6%) each reported Cs palsy and C7 nerve root injury, wound infection, and Horner syndrome. Graft extrusion and hardware failure was reported in 2 patients (7%) for which the patients had to be reoperated. There was 14% incidence of pseudarthrosis	Patients who undergo 4-level ACDF have a significant improvement in clinical outcomes at median 24 months followup
Zhu et al., 2019 <sup>[15]</sup>	Retrospective study	62	Standalone cage/cage -with-plate fixation	Patients in the cage-with-plate group were more likely to have neck pain at last followup. The loss of the cervical lordosis and fusion segment height were higher in the standalone group	Use of standalone cages is safe and effective in treating multilevel cervical spondylotic myelopathy, but for patients who require strong postoperative stabilization and maintaining the cervical alignment better, the cage-with-plate fixations may work better
Lonjon et al., 2019 <sup>[16]</sup>	Prospective study	90	Cage with integrated fixation	One case of dysphagia which resolved within 12 months, and one reoperation for symptomatic pseudarthrosis was reported. 4% subsidence with no clinical consequence or reoperation was reported for the implanted cages	The ACDF using cages with an integrated fixation system demonstrated reliable clinical or radiological outcomes and a high interbody fusion
Shin, 2019 <sup>[17]</sup>	Retrospective study	165	Cage/iliac bone graft	ASD occurred in 41 of 165 patients who underwent ACDF (15.38% at 1-level, 28.57% at 2-level, and 39.4% at 3-level)	ASD occurred predominantly in multilevel cervical fusion, more frequently in the upper segment of the prior fusion and as the number of fusion levels increased
Zigler et al., 2016 <sup>[18]</sup>	Prospective study	186 1-level=81 2-level=105	Anterior plating	Fusion rates were 93.3% in the 1-level group and 86.1% in the 2-level. Adjacent segment degeneration occurred in 54.7% of the patients at superior level and 44.7% at the inferior segment in the 1-level group and 70.8% and 55% respectively in 2-level patients	1-level and 2-level ACDF groups improved significantly and maintained improvement throughout 60 months followup

ZP - Zero profile; ACP - Anterior cervical plate; RLN - Recurrent laryngeal nerve; ASD - Adjacent segment disease; ACDF - Anterior cervical discectomy and fusion; PEEK - Polyetheretherketone

3.9% ( $n = 2741$ ). A prospective study of 107 patients reported no revision surgery for pseudarthrosis and all the patients achieved 100% fusion at 12 months' follow-up.<sup>[19]</sup> However, the study advocated that allograft cage was superior to the polyetheretherketone (PEEK) cage in providing high fusion rate at 3 months' follow-up and fewer complications after 1-and 2-level ACDF procedures. The study reported 91.8% of fusion rate in PEEK cage group at 3 months' follow-up. Three prospective studies<sup>[9,17,18]</sup> [Table 2] and 2 retrospective studies<sup>[26,40]</sup> reported that increase in fused levels is likely to increase the risk of pseudarthrosis. The pseudarthrosis rates were relatively high in 3-and 4-level group as compared to 1-and 2-level group. In contrast, a retrospective study of 25 patients concluded that despite a high nonunion rate (31%), 4-level ACDF was associated with low revision rate as only one revision was due to symptomatic nonunion.<sup>[41]</sup> Another study conducted on 4-level ACDF reported no reoperation for pseudarthrosis with 95% fusion rate at all levels after 12 months' follow-up.<sup>[35]</sup> Chang et al. conducted a prospective

cohort ( $n = 31$ ) using PEEK cages with titanium end plates for cervical arthrodesis and reported good to excellent outcomes with only one patient reporting pseudarthrosis.<sup>[36]</sup>

Lonjon et al. reported only one case of pseudarthrosis ( $n = 90$ ) using a ZP anchored cage system after 24 months' follow-up.<sup>[16]</sup> A retrospective study ( $n = 28$ ) utilized two parallel structured allografts to mitigate the risk of pseudarthrosis at C5–6 and C6–7 levels and reported that this was a safe and effective method to address the higher risk of nonunions at these levels and reported only one case of pseudarthrosis which was clinically asymptomatic and did not require surgical intervention.<sup>[33]</sup>

#### Adjacent segment disease

We identified seven prospective studies<sup>[14,16-18,37,38,46]</sup> and 11 retrospective studies.<sup>[9,15,24,27,30,31,34,39,42,44,47]</sup> Overall, the rates of adjacent segment disease (ASD), inclusive of radiographic cases, symptomatic cases, and those requiring



reoperation, were 8.8%. Among prospective studies, rate of ASD ranged from 3.3% to 24.8%, with a pooled incidence of 12.8% ( $n = 755$ ). Among retrospective studies, rates of ASD ranged from 1.8% to 12.3%, with pooled incidence of 4.5% ( $n = 1325$ ). A retrospective study reported that patients undergoing an anterior revision surgery for ASD after ACDF had higher rates of postoperative radiculopathy and redevelopment of ASD when compared with posteriorly approached patients.<sup>[47]</sup> A study reported radiographic ASD in 20%, 29%, and 15% patients in 1-, 2-, and 3-level surgeries with standalone empty PEEK cages.<sup>[39]</sup> This study further reported that ASD was associated with lower health-related quality of life and older age.

A prospective study reported 21% rate for surgical treatment of ASD at the 10 years follow-up.<sup>[38]</sup> The number of levels fused at the index ACDF was related to secondary adjacent level surgery. 28% of single level cases, 18% of 2-level, and 13% of 3-level cases had adjacent level ACDF. The study also concluded that the adjacent segment surgery was more common in women and had no relation to patient age and smoking status. However, another study conducted by Shin found that ASD occurred predominantly in multilevel cervical fusion, more frequently in the upper segment of the prior fusion and as the number of fusion levels increased.<sup>[17]</sup> A prospective study ( $n = 186$ ) assessed ASD separately at the superior and inferior levels adjacent to the operated segment.<sup>[36]</sup> At 5 years' follow-up, ASD was noted in 54.7% of patients at the superior level and 44.7% at the inferior segment in the 1-level ACDF group and 70.8% and 55.0% respectively, in the 2-level group. There was significant difference at the superior level ( $0.05 < P < 0.10$ ).

The categorization criteria for ASD, period of follow-up, operating technique, number of levels operated, patient population, data collection methods, and possibly other factors are just a few of the numerous variables that could have an impact on the rate of ASD. Although the idea of mixed constructs integrating multilevel ACDF with arthroplasty remains attractive, neither arthroplasty nor anterior cervical plating are superior than standalone ACDF in lowering the likelihood of same segment recurrence or adjacent level degeneration. Rather than surgery, adjacent level degradation is linked to disease progression.<sup>[42]</sup>

### Infection

We identified five prospective studies,<sup>[8,9,11,13,14]</sup> nine retrospective studies,<sup>[6,10,24,27,30,34,40,48]</sup> and one case report.<sup>[49]</sup> While all the prospective cohorts were conducted between 2016 and 2022, the retrospective studies were performed from 2014 to 2021. Across prospective and retrospective

studies ( $n = 12653$ ), the pooled incidence of any infectious complication was 0.3%. Among prospective studies, the incidence of any infectious complication ranged from 1.2% to 4.0% with a pooled incidence of 1.9% ( $n = 315$ ). For retrospective studies, the incidence of any infectious complication ranged from 0.2% to 5.5% with a pooled incidence of 0.3% ( $n = 12274$ ).

A retrospective study reported deep surgical site infection in an elderly patient (70 years old) with diabetes mellitus and chronic kidney disease.<sup>[24]</sup> However, the patient showed complete recovery following debridement and removal of implant. Another prospective study ( $n = 165$ ) also found significantly higher rates of postoperative infection in diabetic patients.<sup>[7]</sup> One patient who presented 30 days after ACDF and titanium cage bone graft fusion at C3–4 and C4–5 with deep cervical abscess growing *Staphylococcus aureus*.<sup>[50]</sup> The abscess was managed through radical neck dissection approach with repeated washing and removal of titanium implant. A prospective study of 321 patients reported that the incidence of surgical site infection was 2.2% in the standalone group and 0.0% in the plated group ( $P = 0.030$ ) [Table 2].<sup>[13]</sup> A multicenter retrospective study of 8887 patients reported very low rate of postoperative infections after ACDF (0.07%). This study confirmed that out of 6 cases of surgical site infection, 50% cases ( $n = 3$ ) were smokers.<sup>[48]</sup>

### Graft and hardware failure

We identified six prospective<sup>[7,13,14,16,17,38]</sup> and 14 retrospective cohort studies.<sup>[6,10,15-24,26,29,34,35,40,43,50,51]</sup> Graft or hardware failure was defined as screw breakage or pullout, screw loosening, cage subsidence, cage slippage, acute implant extrusion, screw malpositioning, or graft fracture. Across prospective and retrospective studies ( $n = 4326$ ), the overall rate of graft or hardware failure was 2.2%. Among prospective studies ( $n = 731$ ), the rate of graft or hardware failure ranged from 1.2% to 7.0% with a pooled incidence of 3.1%. Among retrospective studies ( $n = 3595$ ), the rate of graft or hardware failure ranged from 0% to 24.6% with a pooled incidence of 1.5%. Among studies reporting rates of reoperation,<sup>[6,13,14,16,17,24,29,38,44,51]</sup> ( $n = 1117$ ), the incidence of hardware failure leading to surgical revision ranged from 0.3% to 10.7% with a pooled incidence of 2.2%.

Cage subsidence was found to be associated with numerous factors including bone quality and end plate preparation in addition to cage alone in a retrospective study of 45 patients undergoing ACDF.<sup>[26]</sup> The most feared consequence among patients in the osteoporosis class was screw loosening and cage sinking. Zavras *et al.* performed a prospective study of 24 patients who underwent ACDF at 1- and 2-level with

plate stabilization and compared them to nonplating (cage) cohorts.<sup>[46]</sup> The 2-level cage cohort had an incidental finding of aseptic screw loosening and interbody subsidence leading to C5 vertebral body fracture at 18 months followup. Nonetheless, there were no significant differences between cage and plate groups with regard to subsidence rate. One prospective<sup>[14]</sup> and one retrospective study<sup>[29]</sup> reported cage subsidence with kyphosis. Another retrospective study reported 4.7% ( $n = 211$ ) revision surgeries due to implant failure using standalone cage devices.<sup>[43]</sup> Mechanism of failure included C5 body fracture, fusion in kyphotic alignment after graft subsidence, and acute spondylolisthesis. Four studies reported hardware failure due to screw loosening and interbody subsidence.<sup>[14,24,37,46]</sup> Han *et al.* conducted a retrospective study of ACDF using standalone PEEK cage and PEEK cage with cervical plate.<sup>[51]</sup> The standalone PEEK cage group showed significantly higher incidence rate of segmental subsidence and kyphosis (36.1%) than plate assisted cervical fusion group (15.6%).

### Esophageal perforation

We identified two prospective study,<sup>[7,52]</sup> three retrospective cohort studies,<sup>[6,10,31]</sup> and six case reports.<sup>[53-58]</sup> Among the two prospective studies, one reported 0.6% incidence of EP,<sup>[7]</sup> [Table 2] and the other reported an unusually high incidence of 71.4%.<sup>[52]</sup> This study was excluded from the calculation of pooled incidence of all the studies. The incidence among the retrospective cohorts ranged from 0.1% to 0.8% with a pooled incidence of 0.4% ( $n = 5940$ ). Timing of presentation varied widely from an intraoperative discovery to delayed discovery 25 years postoperatively.<sup>[56]</sup> When not discovered intraoperatively, the most common presentation is with dysphagia alone,<sup>[11,16,32,59-61]</sup> or in combination with delayed onset aspiration pneumonia,<sup>[53]</sup> fever and purulent discharge from the wound,<sup>[54]</sup> retropharyngeal abscess,<sup>[55]</sup> progressive neck pain, neck abscess and cutaneous fistulas, cervical swelling, salivary leakage from cervicotomy, halitosis, and regurgitation.<sup>[57,62]</sup>

Screw loosening and hardware failure are often the causes of delayed EP. Early detection and management could prevent complications in these cases. For cases of large fistulas and systemic infections, partial or total removal of the fixation devices, direct suture of esophageal defect, and coverage with tissue flaps are recommended.<sup>[62]</sup> Park *et al.* reported two delayed EPs occurring 20 and 25 years after ACDF in a patient. EP after 20 years postoperative, healed spontaneously with conservative treatment.<sup>[56]</sup> However, 5 years later, a second perforation developed involving recurrent infection which required surgical intervention. In a case report of EP 15 years after ACDF when spinal hardware had eroded through

the posterior wall of the esophagus creating a traction diverticulum.<sup>[58]</sup> The hardware was removed and the EP was repaired with vascularized tissue from supraclavicular artery island facial flap.

### Recurrent laryngeal nerve palsy

We identified two case reports,<sup>[59,63]</sup> five prospective studies,<sup>[12,22,23,36,60]</sup> and eight retrospective cohort studies.<sup>[6,9,10,27,29,34,37,61]</sup> RLNP was defined as postoperative hoarseness, dysphonia, or vocal cord paralysis. Across retrospective and prospective studies, the pooled incidence of RLNP was 1.7% ( $n = 3261$ ). For prospective studies, the incidence of RLNP ranged from 0% to 10%, with a pooled incidence of 3.0% ( $n = 872$ ). Among retrospective studies, incidence of RLNP ranged from 0.1% to 9.0% with a pooled incidence of 1.4% ( $n = 2389$ ). Within the studies that reported ultimate outcome of postoperative RLNP, 94.7% of patients experienced partial or complete recovery.<sup>[6,10,16,22,32,34,38,39,64-68]</sup>

Neither the level of ACDF surgery nor the application of anterior plate for cervical spine stabilization was associated with any significant difference in the incidence of RLNP in one retrospective study of 128 patients,<sup>[6]</sup> [Table 2]. Staartjes *et al.* reported that RLNP may occur more frequently after secondary ACDF procedures with a clinically relevant effect size.<sup>[22]</sup> Two prospective studies found that ETCP after retractor placement was correlated to postoperative voice hoarseness.<sup>[12,23]</sup> Thus, voice hoarseness does not necessarily indicate RLNP after ACDF but may be caused by compressive forces on laryngeal tissue during retraction or intubation. Thus, laryngoscopy should be performed in cases with high clinical suspicion.

### Cerebrospinal fluid leak

We recognized two prospective studies,<sup>[11,19]</sup> five retrospective studies,<sup>[6,64,65,69,70]</sup> and two case reports.<sup>[71,72]</sup> Across prospective and retrospective studies ( $n = 6444$ ), the rate of cerebrospinal fluid (CSF) leak was 0.7%. Among prospective studies, rates of CSF leak ranged from 0.9% to 2.8%, with a pooled incidence of 1.8% ( $n = 211$ ). For retrospective studies, rates of CSF leak ranged from 0.05% to 6% with a pooled incidence of 0.7% ( $n = 5010$ ). Yeh *et al.* reported a high CSF rate (6%) and found that dural tears occur when parts of the posterior longitudinal ligament were difficult to remove due to severe adhesion to the dura, resulting in CSF leakage.<sup>[70]</sup> Using a blood clot and gelfoam sponge to cover a dural tear site and placing a distant lumbar drain to shunt CSF pressure is an effective and successful method to treat CSF leakage in cervical procedures.

The case reports discussed the following: one patient presented with CSF fistula years after ACDF, the first known

case of delayed CSF leak after ACDF.<sup>[5]</sup> Endoscopic surgery revealed the defect in the oropharynx. A second procedure was performed to remove the spinal hardware and repair the leak. This case highlights the importance of maintaining a broad differential diagnosis to include rare complications and shows that despite dramatic improvements in imaging, locating CSF leaks still presents a challenge. A patient was diagnosed with CSF leak on the second day after ACDF. The indirect repair of CSF leak site was achieved using Surgicel® and fibrin glue without any complications.<sup>[72]</sup>

### Horner syndrome

We identified two prospective studies<sup>[7,14]</sup> [Table 2] and three retrospective studies,<sup>[40,66,67]</sup> that discussed postoperative Horner syndrome (HS). Across all studies, the rate of HS was 0.5% ( $n = 11,319$ ). Across prospective studies ( $n = 1930$ ), the incidence of HS ranged from 0.6% to 3.6% with a pooled incidence of 1.0%. Across retrospective studies ( $n = 11126$ ), the incidence of HS ranged from 0.06% to 0.45% with a pooled incidence of 0.1%. The sympathetic trunk appears to be more vulnerable when operating at C5–C6 levels, according to Traynelis *et al.*<sup>[67]</sup> Maintaining a midline surgical trajectory is preferable, but when lateral exposure is required, especially at caudal cervical levels, meticulous dissection and retraction of the longus colli muscle must be performed. Rarely does HS result in serious functional disability. Two cases of chronic persistent HS in trigeminal autonomic cephalgia subtypes, characterized by a severe headache and accompanying cranial autonomic symptoms that cause full or partial syndrome, were reported by Rozen *et al.*<sup>[73]</sup> Nonetheless, even after months or years of treatment, it is still reversible in some cases.

### Hematoma

We identified three prospective studies,<sup>[7,20,37]</sup> 13 retrospective studies,<sup>[10,27-29,32-35,37,40,65,74,75]</sup> and four case reports.<sup>[68,76-78]</sup> The case reports comprised one case of retropharyngeal hematoma 33 h after surgery presented with cervical swelling and dysphagia,<sup>[68]</sup> and one case of postoperative cervical hematoma complicated by ipsilateral carotid thrombosis and aphasia after anterior cervical fusion.<sup>[77]</sup> A case of cervical wound hematoma 6 weeks after 1-level ACDF was associated with instrument settling resulting in neck pain, dysphagia, and shortness of breath.<sup>[78]</sup> All the three patients in the case reports underwent evacuation of the hematoma and ultimately recovered.

The overall rate of postoperative cervical hematoma across all studies ( $n = 7253$ ) was 0.8%. Among prospective studies ( $n = 246$ ), the pooled incidence of postoperative cervical hematoma was 1.2%. For retrospective studies ( $n = 7007$ ), its incidence ranged from 0.1% to 7%, with a pooled incidence of

2.2%. Among studies reporting the rates of reoperation for cervical hematoma<sup>[7,29,33,34,38,41,45,68,75,77-80]</sup> ( $n = 4314$ ), frequency of postoperative hematoma leading to surgical intervention ranged from 0% to 100% with a pooled frequency of 34%. A single retrospective study of 100 patients undergoing single level and 2-level ACDF with standalone titanium cage/bone graft or titanium cage/bone graft with ACP that reported a 7% rate of postoperative hematoma.<sup>[28]</sup> The study reported the use of drain for at least initial 24 h following surgery to avoid this rare but potentially fatal complication. Two retrospective studies reported only 0.1% postoperative hematoma ( $n = 3576$ ) and reported that careful hemostasis combined with close postoperative monitoring for at least 6 h helped to reduce the risk of neck hematoma.<sup>[10,65]</sup>

### C5 palsy

We recognized 11 retrospective studies<sup>[9,15,29,34,35,45,79-83]</sup> and one prospective study,<sup>[14]</sup> that discussed postoperative C5 palsy. Across all the studies ( $n = 23650$ ), the incidence ranged from 0.3% to 5.7% with a pooled incidence of 1.9%. Majority of the patients developed symptoms within 24 h postoperative.<sup>[6,10,50,52]</sup> Thompson *et al.* presented a study which was the largest series of Northern American patients ( $n = 13946$ ) reviewed for C5 palsy across 21 centers.<sup>[79]</sup> The study reported 59 patients experienced postoperative C5 palsy and the incidence rate ranged from 0% to 2.5%. While most of the patients recovered through conservative treatment, physical therapy or no treatment, 3 patients (5.1%) underwent an additional surgical procedure.

Some studies have suggested that extended surgical strategies such as dorsal laminectomies, multilevel corpectomies, and procedures with extensive spinal cord shift were shown to display a high risk of C5 palsy.<sup>[80-82]</sup> The use of extended procedures should therefore be employed cautiously. Combined surgical procedures such as ACDF plus corpectomy can reduce the rate of C5 palsy. The studies have reported that the incidence of C5 nerve root palsy was significantly higher if more levels were involved in the fusion process.<sup>[9,82]</sup> Takase *et al.* reported that older age and foraminal stenosis of C4–5 and C5–6 were the risk factors for postoperative C5 palsy.<sup>[80]</sup> Contrary to this finding, Sinensky *et al.* demonstrated that there were no statistically significant differences in patient age, sex, or number of vertebral levels fused between the groups.<sup>[83]</sup>

## DISCUSSION

We set out to report the prevalence, causes, treatment options, and results of anterior approaches to the cervical spine. One identified prospective study found that



the incidence of dysphagia, one of the most frequent postoperative sequelae, was about 35%. A pooled estimate of <4% indicates that incidence of chronic dysphagia lasting more than 3 months is very low. Bone morphogenetic protein (BMP) use and a higher number of surgical levels were the most frequently occurring risk factors for postoperative dysphagia. Preoperative tracheal traction exercises and intraoperative local steroid administration were both associated with inconsistent benefits in terms of lowered rates of dysphagia. The use of standalone versus cage and plate constructs did not significantly affect the rates of dysphagia. Pseudarthrosis rates might vary greatly depending on whether there is asymptomatic radiographic graft sinking, symptomatic neck pain, or radiculopathy that necessitates revision surgery. At the most recent follow-up, the pooled rate of patients needing a second procedure was still low at 3.9%. In cohorts with plated ACDF, BMP, and fewer operated levels, there were noticeably decreased rates of pseudoarthrosis. One retrospective analysis verified 100% fusion, and no patients required additional surgery for pseudoarthrosis. However, this requires more prospective cohorts to be used in the investigation.

In regard to reporting of radiographic cases, symptomatic cases, recurrence of ASD or those needing reoperation, patient age, and the number of levels operated upon, ASD presented more heterogeneity. The pooled incidence was 17% when taking into account radiographic patients, symptomatic cases, and those needing repeat surgery. The reduced rate of ASD in longer constructs was a finding that was fairly consistent. There is currently no data to support the claim that anterior cervical plating is more effective than standalone ACDF in preventing recurrence of the same segment or adjacent level degeneration. Infectious complications had a low incidence across all investigations, at 0.3%. The majority of the infectious consequences were sepsis or bacterial infections. According to several investigations, diabetes and chronic renal disease are significantly linked to surgical site infections.

The failure of grafts and hardware also exhibited heterogeneity, with symptoms including screw breakage or pullout, screw loosening, case slippage, or graft fracture resulting in spinal cord damage. In comparison to earlier literature assessments, the total incidence rate was substantially lower, at 2.2%, with an estimated reoperation rate of 2.2%. We found that the designs of cage interbody implants have improved year by year with respect to maximization of biocompatibility and osseointegration. EP is incredibly uncommon (pooled incidence of 0.4%) yet frequently fatal (mortality rates between 6% and 34%) with delayed presentations such

new-onset dysphagia, sepsis, spinal abscess, and meningitis. Broad-spectrum antibiotics, debridement, removal of hardware, esophageal repair, and nutritional bypass are nearly the only aggressive treatments used in management. Hence, it is crucial to take follow-up into account for patients whose EP has spontaneously cured, and even years later, they should get a comprehensive evaluation for any potential recurrence.

In all investigations, there was a rate of 1.7% for RLNP, which is characterized by hoarseness and dysphagia, and 90% or more of the patients made partial or full recoveries. There has been no correlation found between postoperative RLNP and patient age, sex, body mass index, operation time, or number of levels. Isolated investigations indicated a higher overall incidence of RLNP after secondary surgeries than in index procedures. This demonstrates that postoperative RLNP may be more dependent on direct mechanical manipulation during surgery than on particular patient or surgical factors. The incidence of cerebral spinal fluid leak was determined to be 0.5%, making it a very uncommon consequence. Substantial correlations between revision versus first procedures and in patients with posterior longitudinal ligament ossification were discovered. When identified in delayed scenario, treatment options varied and included reoperation as well as less invasive techniques such as serial lumbar punctures or cervical epidural blood patches.

With a pooled prevalence of 0.5%, postoperative HS is rare in the literature. By maintaining a midline surgical trajectory and avoiding damage to the sympathetic trunk, the incidence of HS can be considerably decreased. It was discovered that the pooled prevalence of postoperative hematoma requiring reoperation was relatively significant, at 34%. Postoperative hematoma was significantly associated with multilevel ACDF, instrument setup, underweight status, and poor renal function, according to several retrospective studies. In all investigations, the postoperative C5 palsy rate was 1.9%. There was no correlation between the number of operational levels and ACDF. According to the majority of studies, reoperation rates were extremely low and the majority of patients responded satisfactorily to conservative care or physical therapy.

## CONCLUSION

There are few complications after anterior cervical surgery. However, the distinct anatomy of the anterior neck offers a multitude of additional challenges including vascular, aerodigestive, neurological, and osseous components. The effectiveness of locking standalone cages in reducing neck discomfort and overall problems in cervical spondylotic

diseases has not yet been widely agreed upon in the literature. However, true standalone cages may be able to provide a less invasive process and greater results. The elastic modulus of PEEK cages is more similar to that of cancellous bone and hence experience less cage subsidence. ACP is frequently used in multilevel ACDF surgeries since it adds stability and is linked to decreased subsidence rates, but its usage is also associated with the increased rates of dysphagia. Our review was limited by retrospective data and risk of reporting bias.

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### Conflicts of interest

There are no conflicts of interest.

### REFERENCES

- Smith GW, Robinson RA. The treatment of certain cervical-spine disorders by anterior removal of the intervertebral disc and interbody fusion. *J Bone Joint Surg Am* 1958;40-A: 607-24.
- Yee TJ, Swong K, Park P. Complications of anterior cervical spine surgery: A systematic review of the literature. *J Spine Surg* 2020;6:302-22.
- Kasliwal MK, O'Toole JE. Integrated intervertebral device for anterior cervical fusion: An initial experience. *J Craniovertebr Junction Spine* 2012;3:52-7.
- Zhao FD, Yang W, Shan Z, Wang J, Chen HX, Hong ZH, et al. Cage migration after transforaminal lumbar interbody fusion and factors related to it. *Orthop Surg* 2012;4:227-32.
- Cheung JP, Luk KD. Complications of anterior and posterior cervical spine surgery. *Asian Spine J* 2016;10:385-400.
- Yadav R, Chavali S, Chaturvedi A, Rath GP. Post-operative complications in patients undergoing anterior cervical discectomy and fusion: A retrospective review. *J Neuroanaesthesiol Crit Care* 2017;4:170.
- Hasan GA, Raheem HQ, Al-Naser LM, Sheta RA. Early complications of anterior cervical discectomy and fusion: A case series. *J Musculoskelet Surg Res* 2018;2:121-5.
- Grasso G, Landi A. Long-term clinical and radiological outcomes following anterior cervical discectomy and fusion by zero-profile anchored cage. *J Craniovertebr Junction Spine* 2018;9:87-92.
- De la Garza-Ramos R, Xu R, Ramhmdani S, Kosztowski T, Bydon M, Sciubba DM, et al. Long-term clinical outcomes following 3- and 4-level anterior cervical discectomy and fusion. *J Neurosurg Spine* 2016;24:885-91.
- Nanda A, Sharma M, Sonig A, Ambekar S, Bollam P. Surgical complications of anterior cervical discectomy and fusion for cervical degenerative disk disease: A single surgeon's experience of 1,576 patients. *World Neurosurg* 2014;82:1380-7.
- He S, Feng H, Lan Z, Lai J, Sun Z, Wang Y, et al. A randomized trial comparing clinical outcomes between zero-profile and traditional multilevel anterior cervical discectomy and fusion surgery for cervical myelopathy. *Spine (Phila Pa 1976)* 2018;43:E259-66.
- Gowd AK, Vahidi NA, Magdycz WP, Zollinger PL, Carmouche JJ. Correlation of voice hoarseness and vocal cord palsy: A prospective assessment of recurrent laryngeal nerve injury following anterior cervical discectomy and fusion. *Int J Spine Surg* 2021;15:12-7.
- Fayed I, Conte AG, Keating G, Cobourn KD, Altshuler M, Makariou E, et al. Comparison of clinical and radiographic outcomes after standalone versus cage and plate constructs for anterior cervical discectomy and fusion. *Int J Spine Surg* 2021;15:403-12.
- Charalampidis A, Hejrati N, Ramakonar H, Kalsi PS, Massicotte EM, Fehlings MG. Clinical outcomes and revision rates following four-level anterior cervical discectomy and fusion. *Sci Rep* 2022;12:5339.
- Zhu D, Zhang D, Liu B, Li C, Zhu J. Can self-locking cages offer the same clinical outcomes as anterior cage-with-plate fixation for 3-level anterior cervical discectomy and fusion (ACDF) in mid-term follow-up? *Med Sci Monit* 2019;25:547-57.
- Lonjon N, Favreul E, Huppert J, Lioret E, Delhay M, Mraidi R. Clinical and radiological outcomes of a cervical cage with integrated fixation. *Medicine (Baltimore)* 2019;98:e14097.
- Shin JJ. Comparison of adjacent segment degeneration, cervical alignment, and clinical outcomes after one- and multilevel anterior cervical discectomy and fusion. *Neurospine* 2019;16:589-600.
- Zigler JE, Rogers RW, Ohnmeiss DD. Comparison of 1-level versus 2-level anterior cervical discectomy and fusion: Clinical and radiographic follow-up at 60 months. *Spine (Phila Pa 1976)* 2016;41:463-9.
- Yang S, Yu Y, Liu X, Zhang Z, Hou T, Xu J, et al. Clinical and radiological results comparison of allograft and polyetheretherketone cage for one to two-level anterior cervical discectomy and fusion: A CONSORT-compliant article. *Medicine (Baltimore)* 2019;98:e17935.
- Kapetanakis S, Thomaidis T, Charitoudis G, Pavlidis P, Theodosiadis P, Gkasdaris G. Single anterior cervical discectomy and fusion (ACDF) using self-locking stand-alone polyetheretherketone (PEEK) cage: Evaluation of pain and health-related quality of life. *J Spine Surg* 2017;3:312-22.
- El Baz EA, Sultan AM, Barakat AS, Koptan W, ElMiligui Y, Shaker H. The use of anterior cervical interbody spacer with integrated fixation screws for management of cervical disc disease. *SICOT J* 2019;5:8.
- Staatjes VE, de Wispelaere MP, Schröder ML. Recurrent laryngeal nerve palsy is more frequent after secondary than after primary anterior cervical discectomy and fusion: Insights from a registry of 525 patients. *World Neurosurg* 2018;116:e1047-53.
- Sejkorová A, Bolcha M, Beneš J, Kalhous J, Sameš M, Vachata P. Intraoperative measurement of endotracheal tube cuff pressure and its change during surgery in correlation with recurrent laryngeal nerve palsies, hoarseness, and dysphagia after anterior cervical discectomy and fusion: A prospective randomized controlled trial. *Global Spine J* 2023;13:1635-40.
- Luo CA, Lim AS, Lu ML, Chiu PY, Lai PL, Niu CC. The surgical outcome of multilevel anterior cervical discectomy and fusion in myelopathic elderly and younger patients. *Sci Rep* 2022;12:4495.
- Wang B, Lü G, Kuang L. Anterior cervical discectomy and fusion with stand-alone anchored cages versus posterior laminectomy and fusion for four-level cervical spondylotic myelopathy: A retrospective study with 2-year follow-up. *BMC Musculoskelet Disord* 2018;19:216.
- Chen X, Sial A, Stewart C, Vargas Castillo J, Diwan AD. Stand-alone anterior cervical decompression and fusion surgery: A cohort study evaluating a shaped cage without plates or screws. *Front Surg* 2022;9:934018.
- Al Eissa S, Konbaz F, Aldeghaither S, Annaim M, Aljehani R, Alhelal F, et al. Anterior cervical discectomy and fusion complications and thirty-day mortality and morbidity. *Cureus* 2020;12:e7643.
- Srikhande NN, Kumar VA, Sai Kiran NA, Ghosh A, Pal R, Moscote-Salazar LR, et al. Clinical presentation and outcome after anterior cervical discectomy and fusion for degenerative cervical disc disease. *J Craniovertebr Junction Spine* 2019;10:28-32.
- Alhashash M, Allouch H, Boehm H, Shousha M. Results of four-level anterior cervical discectomy and fusion using stand-alone interbody titanium cages. *Asian Spine J* 2022;16:82-91.
- Lau D, Chou D, Mummaneni PV. Two-level corpectomy versus three-level discectomy for cervical spondylotic myelopathy: A comparison of perioperative, radiographic, and clinical outcomes. *J Neurosurg Spine* 2015;23:280-9.

31. Tasiou A, Giannis T, Brotis AG, Siasios I, Georgiadis I, Gatos H, et al. Anterior cervical spine surgery-associated complications in a retrospective case-control study. *J Spine Surg* 2017;3:444-59.
32. Yagi K, Nakagawa H, Okazaki T, Irie S, Inagaki T, Saito O, et al. Noninfectious prevertebral soft-tissue inflammation and hematoma eliciting swelling after anterior cervical discectomy and fusion. *J Neurosurg Spine* 2017;26:459-65.
33. Rasouli J, Fiani B, Belding J, Moore TA. Anterior cervical discectomy and fusion with “kissing” allograft interbodies. *Cureus* 2021;13:e19499.
34. Soliman MA, Alkhamees AF, Khan A, Shamisa A. Instrumented four-level anterior cervical discectomy and fusion: Long-term clinical and radiographic outcomes. *Neurol India* 2021;69:937-43.
35. Jack MM, Lundy P, Reeves AR, Arnold PM. Four-level anterior cervical discectomy and fusions: Results following multilevel cervical fusion with a minimum 1-year follow-up. *Clin Spine Surg* 2021;34:E243-7.
36. Chong E, Mobbs RJ, Pelletier MH, Walsh WR. Titanium/polyetheretherketone cages for cervical arthrodesis with degenerative and traumatic pathologies: Early clinical outcomes and fusion rates. *Orthop Surg* 2016;8:19-26.
37. Hisey MS, Zigler JE, Jackson R, Nunley PD, Bae HW, Kim KD, et al. Prospective, randomized comparison of one-level mobi-C cervical total disc replacement versus anterior cervical discectomy and fusion: Results at 5-year Follow-up. *Int J Spine Surg* 2016;10:10.
38. Buttermann GR. Anterior cervical discectomy and fusion outcomes over 10 years: A prospective study. *Spine (Phila Pa 1976)* 2018;43:207-14.
39. Shibani E, Gapon K, Wostrack M, Meyer B, Lehmborg J. Clinical and radiological outcome after anterior cervical discectomy and fusion with stand-alone empty polyetheretherketone (PEEK) cages. *Acta Neurochir (Wien)* 2016;158:349-55.
40. Mullins J, Pojskić M, Boop FA, Arnautović KI. Retrospective single-surgeon study of 1123 consecutive cases of anterior cervical discectomy and fusion: A comparison of clinical outcome parameters, complication rates, and costs between outpatient and inpatient surgery groups, with a literature review. *J Neurosurg Spine* 2018;28:630-41.
41. Kreitz TM, Hollern DA, Padegimas EM, Schroeder GD, Kepler CK, Vaccaro AR, et al. Clinical outcomes after four-level anterior cervical discectomy and fusion. *Global Spine J* 2018;8:776-83.
42. Wang SJ, Ma B, Huang YF, Pan FM, Zhao WD, Wu DS. Four-level anterior cervical discectomy and fusion for cervical spondylotic myelopathy. *J Orthop Surg (Hong Kong)* 2016;24:338-43.
43. Alonso F, Rustagi T, Schmidt C, Norvell DC, Tubbs RS, Oskouian RJ, et al. Failure patterns in standalone anterior cervical discectomy and fusion implants. *World Neurosurg* 2017;108:676-82.
44. Gornet MF, Lanman TH, Burkus JK, Hodges SD, McConnell JR, Dryer RF, et al. One-level versus 2-level treatment with cervical disc arthroplasty or fusion: Outcomes up to 7 years. *Int J Spine Surg* 2019;13:551-60.
45. Mathews WE. C5 Palsy Following Anterior Cervical Discectomy and Fusion. *American Academy of Neurological and Orthopaedic Surgeons*; 2014. Available from: <https://aanos.org>. [Last accessed on 2022 Oct 21].
46. Zavras AG, Nolte MT, Sayari AJ, Singh K, Colman MW. Stand-alone cage versus anterior plating for 1-level and 2-level anterior cervical discectomy and fusion: A randomized controlled trial. *Clin Spine Surg* 2022;35:155-65.
47. Bydon M, Xu R, De la Garza-Ramos R, Macki M, Sciubba DM, Wolinsky JP, et al. Adjacent segment disease after anterior cervical discectomy and fusion: Incidence and clinical outcomes of patients requiring anterior versus posterior repeat cervical fusion. *Surg Neurol Int* 2014;5:S74-8.
48. Ghobrial GM, Harrop JS, Sasso RC, Tannoury CA, Tannoury T, Smith ZA, et al. Anterior cervical infection: Presentation and incidence of an uncommon postoperative complication. *Global Spine J* 2017;7:12S-16S.
49. Chen YC, Zhang L, Li EN, Ding LX, Zhang GA, Hou Y, et al. Late deep cervical infection after anterior cervical discectomy and fusion: A case report and literature review. *BMC Musculoskelet Disord* 2019;20:437.
50. Klingler JH, Krüger MT, Sircar R, Kogias E, Scholz C, Volz F, et al. PEEK cages versus PMMA spacers in anterior cervical discectomy: Comparison of fusion, subsidence, sagittal alignment, and clinical outcome with a minimum 1-year follow-up. *ScientificWorldJournal* 2014;2014:398396.
51. Han SY, Kim HW, Lee CY, Kim HR, Park DH. Stand-alone cages for anterior cervical fusion: Are there no problems? *Korean J Spine* 2016;13:13-9.
52. Yahanda AT, Pennicooke B, Ray WZ, Hacker CD, Kelly MP, Dorward IG, et al. Pharyngoesophageal damage from hardware extrusion at an average of 7.5 years after anterior cervical discectomy and fusion: A case series, discussion of risk factors, and guide for management. *World Neurosurg* 2022;160:e189-98.
53. Amhaz HH, Kuo R, Vaidya R, Orlewicz MS. Esophageal perforation following cervical spine surgery: A review with considerations in airway management. *Int J Crit Illn Inj Sci* 2013;3:276-8.
54. Krishnan P, Kartikueyan R, Patel SM, Bose PP, Mukherjee KK. Two cases of esophageal injury following anterior cervical discectomy and fusion: One overt and one covert. *Ann Neurosci* 2017;24:126-30.
55. Lee SH, Mesfin A, Riew KD. Delayed esophageal perforation after anterior cervical fusion and retropharyngeal steroid use: A report of two cases. *Spine J* 2015;15:e75-80.
56. Park MK, Cho DC, Bang WS, Kim KT, Sung JK. Recurrent esophageal perforation after anterior cervical spine surgery: Case report. *Eur Spine J* 2018;27:515-9.
57. Zakkó P, Rontal M, Park D. Delayed Esophageal Perforation Diagnosed 12 Years After Anterior Cervical Discectomy and Fusion: A Case Report and Review of Current Literature. *J Am Acad Orthop Surg Glob Res Rev* 2022;6: e22.00080.
58. Gibson AW, Gobillot TA, Bass DI, Zakarevicius Z, Rizvi ZH, Ravanpay AC. Case of esophageal perforation and repair with a supraclavicular artery island fascial flap 15 years after anterior spine surgery. *World Neurosurg* 2020;143:102-7.
59. Yerneni K, Burke JF, Nichols N, Tan LA. Delayed recurrent laryngeal nerve palsy following anterior cervical discectomy and fusion. *World Neurosurg* 2019;122:380-3.
60. Huang WC, Tan EC, Chang CC, Kuo YH, Hsu XT, Chang WK, et al. Effect of tracheal intubation mode on cuff pressure during retractor splay and dysphonia recovery after anterior cervical spine surgery: A randomized clinical trial. *Spine (Phila Pa 1976)* 2020;45:565-72.
61. Huschbeck A, Knoop M, Gahleitner A, Koch S, Schrom T, Stoffel M, et al. Recurrent laryngeal nerve palsy after anterior cervical discectomy and fusion – Prevalence and risk factors. *J Neurol Surg A Cent Eur Neurosurg* 2020;81:508-12.
62. Perrone O, Tassi V, Mattioli B, Daddi N, Uneddu M, Borghesi I, et al. Pharyngo-oesophageal perforation following anterior cervical discectomy and fusion: Management and results. *Eur J Cardiothorac Surg* 2017;51:160-8.
63. Wu CH, Yang EW, Lor KK. Contralateral recurrent laryngeal nerve palsy in revision anterior cervical discectomy and fusion (ACDF): A cautionary tale. *Biomedicine (Taipei)* 2021;11:51-5.
64. Syre P, Bohman LE, Baltuch G, Le Roux P, Welch WC. Cerebrospinal fluid leaks and their management after anterior cervical discectomy and fusion: A report of 13 cases and a review of the literature. *Spine (Phila Pa 1976)* 2014;39:E936-43.
65. McGirt MJ, Rossi V, Peters D, Dyer H, Coric D, Asher AL, et al. Anterior cervical discectomy and fusion in the outpatient ambulatory surgery setting: Analysis of 2000 consecutive cases. *Neurosurgery* 2020;86:E310-5.
66. Lubelski D, Pennington Z, Sciubba DM, Theodore N, Bydon A. Horner syndrome after anterior cervical discectomy and fusion: Case series and systematic review. *World Neurosurg* 2020;133:e68-75.

67. Traynelis VC, Malone HR, Smith ZA, Hsu WK, Kanter AS, Qureshi SA, *et al.* Rare complications of cervical spine surgery: Horner's syndrome. *Global Spine J* 2017;7:103S-8S.
68. Ren H, Wang J, Yu L. Retropharyngeal hematoma following anterior cervical spine surgery: Lessons from a case report (CARE-compliant). *Medicine (Baltimore)* 2019;98:e17247.
69. Elder BD, Theodros D, Sankey EW, Bydon M, Goodwin CR, Wolinsky JP, *et al.* Management of cerebrospinal fluid leakage during anterior cervical discectomy and fusion and its effect on spinal fusion. *World Neurosurg* 2016;89:636-40.
70. Yeh KT, Chen IH, Yu TC, Peng CH, Liu KL, Wu WT. Management and outcome of cerebrospinal fluid leakage during anterior cervical fusion for an ossified posterior longitudinal ligament. *Tzu Chi Med J* 2013;25:249-52.
71. Weinheimer WJ, Rowley JG, Otto R, Floyd J, Chen PG. Oropharyngeal CSF leak secondary to anterior cervical discectomy and fusion. *Case Rep Otolaryngol* 2018;2018:7629184.
72. Choi DH, Lee JW, Kim CH, Choi YS. Indirect repair with surgicel® and fibrin glue for postoperative cerebrospinal fluid leakage after cervical anterior foraminotomy: A case report. *J Korean Soc Spine Surg* 2016;23:171-6.
73. Rozen TD, Kline MT. Chronic persistent Horner's syndrome in trigeminal autonomic cephalalgia subtypes and alleviation with treatment: Two case reports. *J Med Case Rep* 2019;13:60.
74. Song KJ, Choi BW, Lee DH, Lim DJ, Oh SY, Kim SS. Acute airway obstruction due to postoperative retropharyngeal hematoma after anterior cervical fusion: A retrospective analysis. *J Orthop Surg Res* 2017;12:19.
75. Hao Q, Ding Q, Yang H, Tan K, Wang ZH, Wang S, *et al.* Symptomatic postoperative spinal epidural hematoma preferentially occurs after anterior cervical discectomy and fusion versus anterior cervical corpectomy and fusion: A retrospective study. *Ann Palliat Med* 2022;11:2025-32.
76. Protzman NM, Kapun J, Wagener C. Thoracic spinal subdural hematoma complicating anterior cervical discectomy and fusion: Case report. *J Neurosurg Spine* 2016;24:295-9.
77. Chin KR, Seale J, Butron V, Cumming V. Postoperative cervical haematoma complicated by ipsilateral carotid thrombosis and aphasia after anterior cervical fusion: A case report. *Case Rep Med* 2013;2013:590639.
78. McDowell MM, Parry PV, Agarwal N, Miele VJ, Maroon JC. Long term delay in onset of prevertebral hematoma following anterior cervical discectomy and fusion: A case report. *J Clin Neurosci* 2019;62:234-7.
79. Thompson SE, Smith ZA, Hsu WK, Nassr A, Mroz TE, Fish DE, *et al.* C5 palsy after cervical spine surgery: A multicenter retrospective review of 59 cases. *Global Spine J* 2017;7:64S-70S.
80. Takase H, Murata H, Sato M, Tanaka T, Miyazaki R, Yoshizumi T, *et al.* Delayed C5 palsy after anterior cervical decompression surgery: Preoperative foraminal stenosis and postoperative spinal cord shift increase the risk of palsy. *World Neurosurg* 2018;120:e1107-19.
81. Oh JK, Hong JT, Kang DH, Kim SW, Kim SW, Kim YJ, *et al.* Epidemiology of C5 palsy after cervical spine surgery: A 21-center study. *Neurospine* 2019;16:558-62.
82. Krätzig T, Mohme M, Mende KC, Eicker SO, Floeth FW. Impact of the surgical strategy on the incidence of C5 nerve root palsy in decompressive cervical surgery. *PLoS One* 2017;12:e0188338.
83. Sinensky AM, Kaye ID, Li WT, Wagner SC, Butler JS, Sebastian AS, *et al.* Radiographic measures of spinal alignment are not predictive of the development of C5 palsy following anterior cervical discectomy and fusion surgery. *Int J Spine Surg* 2021;15:213-8.