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Review Article

A Review of Complication Rates for Anterior Cervical Diskectomy and Fusion (ACDF)

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ABSTRACT

Background: There are multiple complications reported for anterior cervical diskectomy and fusion (ACDF), one of the most common cervical spine operations performed in the US (e.g. estimated at 137,000 ACDF/year).

Methods: Multiple studies analyzed the risks and complications rates attributed to ACDF.

Results: In multiple studies, overall morbidity rates for ACDF varied from 13.2% to 19.3%. These included in descending order; dysphagia (1.7%-9.5%), postoperative hematoma (0.4%-5.6% (surgery required in 2.4% of 5.6%), with epidural hematoma 0.9%), exacerbation of myelopathy (0.2%-3.3%), symptomatic recurrent laryngeal nerve palsy (0.9%-3.1%), cerebrospinal fluid (CSF) leak (0.5%-1.7%), wound infection (0.1-0.9%-1.6%), increased radiculopathy (1.3%), Horner's syndrome (0.06%-1.1%), respiratory insufficiency (1.1%), esophageal perforation (0.3%-0.9%, with a mortality rate of 0.1%), and instrument failure (0.1%-0.9%). There were just single case reports of an internal jugular veing occlusion and a phrenic nerve injury. Pseudarthrosis occurred in ACDF and was dependant on the number of levels fused; 0-4.3% (1-level), 24% (2-level), 42% (3 level) to 56% (4 levels). The reoperation rate for symptomatic pseudarthrosis was 11.1%. Readmission rates for ACDF ranged from 5.1% (30 days) to 7.7% (90 days postoperatively).

Conclusions: Complications attributed to ACDF included; dysphagia, hematoma, worsening myelopathy, recurrent laryngeal nerve palsy, CSF leaks, wound infection, radiculopathy, Horner's Syndrome, respiratory insufficiency, esophageal perforation, and instrument failure. There were just single case reports of an internal jugular vein thrombosis, and a phrenic nerve injury. As anticipated, pseudarthrosis rates increased with the number of ACDF levels, ranging from 0-4.3% for 1 level up to 56% for 4 level fusions.

Keywords: Anterior cervical, Diskectomy, Fusion, Risks, Complications, Adverse events

INTRODUCTION

Anterior cervical diskectomy and fusion (ACDF) is one of the most commonly performed spinal operations in the U.S. Between 2006-2013, one study cited an average of 137, 000 ACDF performed/year (total of 1,059,403 in 7 years) [Tables 1-3].[14] In a focused review of the ACDF literature, we evaluated the frequency of the various reported complications of ACDF procedures.

Table 1: Literature Review ACDF Complications 1989-2006.

Author Year	Number Patients	Design of Study	Findings	Findings	Conclusions
Bertalanffy[1] 1989	450 Pts ACD No Fusion 0% Mort 3.3% > Myel å	1.1% RLNP 1.1% HS 1.6% WI 1.3% >Rad 1.3% PH	1.1% RI 0.9% EDH 0.9% Instability 0.4% Nerve Root Lesion	0.4% SP 0.2% Pharyngeal Lesion 0.2% CSF Leak Meningitis	>Myelopathy Epidural Abscess (AE)
Ebraheim[4] 2000	28 Cadavers Anatomy Sympathetic Trunk (ST) > Damage C6 vs. C3	Between Medial Border LCM Diverge Progressively Cuadad C3 7.9 mm, to C6 13.8	ST > Converge Medially C3-C6 Average ST-LCM 10.6 mm +/- 2.6 mm	C6 Sympathetic Ganglion Closer to Medial Border LCM at C6	Damage ST HS; Ptosis, Meiosis Anhydrosis
Fujiba-yashi[8] 2001	Bilateral PNI Case Report OPLL	X-rays Both Diaphragm Paralysis	3 Weeks; Slight Return of Function	3 Months on ventilator	3 Years Still on Oxygen
Frempong-Boadu[7] 2002	23 Patients 22 M; 1 F Preoperative	MBS + Video-L Preop, 1 Week, 1 Month Postop	Dysphagia 11 Asymptomatic Abnormal Preop Studies	12 (51%) NL Preop Studies-No Dysphagia; Postop 8 Dysphagia-67%	0 Vocal Cord Paresis Preop: 2 Postop (1 Permanent)
Jankowski[9] 2003	Case Report Cervical EDH	32 yo F MR Cord Compression	C4-C5/C5-C6 ACDF	6 Hours Postop EDH on MR	Reoperation: Full Recovery
Jung[10] 2005	120 Patients RLNP Video-L	Preop 2 (1.6%) Asymptomatic Postop Symptomatic 8.3%	3 Months Postop 2.5% Symptomatic Postop Asymptomatic 15.9%	3 Months 10.8% 3 Months 2.5%	Symptomatic 10.8% Asymptomatic
Karim[11] 2006	1 Pt 35 yo F	Case Report ACDF C56	Increased Intraoperative Bleeding	Neck Swelling Dysphagia Postop Day 3-5	Postop day 5 Diagnosed IJ Thrombosis CT and US

F=Female, M=Male, MR=Magnetic Resonance Imaging, CT=Computed Tomography, US=Ultrasound, ACDF=Anterior Cervical Diskectomy/Fusion, IJ-Internal Jugular, CCA=Common Carotid Artery, VA=Vertebral Artery, PH=Postoperative Hematoma, HS=Horner's Syndrome, Pts=Patients, LC=Longus Colli Musculature, RLNP=Recurrent Laryngeal Nerve Palsy, Rad=Radiculopathy, Myel=Myelopathy, WI=Wound Infection, EDH=Epidural Hematoma, PH=Postop Hematoma, RI=Respiratory Insufficiency, Mort=Mortality, SP=Spondylodiscitis, CSF=Cerebrospinal Fluid Leaks, EA=Epidural Abscess, LCM=Longus Colli Muscles, ST=Sympathetic Trunk, PNI=Phrenic Nerve Injury, M=Male, MBS=Modified Barium Swallow, Video-L=Videolaryngoendoscopy, Postop=Postoperatively, ASC=Adjacent Segment Disease, PCF=Posterior Cervical Fusion, CHF=Congestive Heart Failure, CA=Cancer, DVT/PT=History of Deep Venous Thrombosis and Pulmonary Embolism, CAD=Coronary Artery Disease, LOS=Length of Stay, Pseud=Pseudarthrosis, NSQUIP=National Surgical Quality Improvement Program Database, JOA=Japanese Orthopedic Association, PEEK=Polyetheretherketone, AE=Adverse Events, NL=Normal, mos=Months, wk=Weeks, Avg.=Average, yo=Years Old

Rates of ACDF Performed From 2006-2013

Using the National Inpatient Sample (NIS) database, Saifi *et al.* (2017) reviewed the number of ACDF (1,059,403) vs. cervical disc arthroplasty (CDA; 13,099) performed in the U.S. between 2006 to 2013 [Table 2].[14] They noted a 5.7% increase in the frequency of ACDF from 2006 (average 120,617/year) to 2013 (127,500) (average 132,425/year), while CDA increased by 190% (540 in 2006, to 1,565 in 2013, averaging 1,637/year). Note the 81:1-fold difference in frequencies between the two procedures. Although ACDF patients had a longer average LOS vs. CDA (ACDF 2.3 vs. CDA 1.5 days), and were more expensive (average ACDF $16,178 vs. CDA $13,197), CDA required over double the revision rate (CDA 5.9% vs. ACDF 2.3%). The latter finding should in part explain the continued preference for ACDF, but other factors, such as reimbursement rates also likely apply.

Anatomical Considerations When Performing ACDF

Knowing the anatomy before performing an ACDF is critical to avoid unnecessary complications. In a study of 30 cadaveric specimens, Civelek *et al.* (2007) documented several common critical anatomical landmarks for performing ACDF surgery.[3] They found; the common carotid artery bifurcation mostly occurred at the C-4 level (78%); the inferior omohyoid belly crossed the field largely at the C5-6 level; the facial vein drained into the internal jugular vein predominantly at the C3-4 (54%) level; the superior sympathetic ganglion was located in most cases at C-4, while the location of the intermediate ganglion varied; the vertebral artery entered the transverse foramen at C-6 (90%), followed by C-7 (7%), and C4 (3%) respectively; finally, the inferior thyroid artery was usually found at the C6-7 level.[3]

Table 2: Literature Review ACDF Complications 2007-2017.

Author Year	Number Patients	Design of Study	Findings	Findings
Civelek[3] 2007	30 Cadavers Anatomic Study Landmarks ACDF	CCA Bifurcation C-4 (78%); Inferior Omohyoid at C5-C6	Facial vein to IJ C3-4 (54%) Inferior Thyroid Artery C6-7	Superior Ganglion ST C-4, Intermediate Ganglion Varied
Fountas[6] 2007	1015 Primary 1-Level ACDF Followed 26.4 mos	Overall Morbidity Rate 19.3% 196/1015 Pts 9.5% dysphagia	5.6% postop hematoma; 2.4% PH required secondary surgery	3.1% RLNP 0.2% Worse Myelopathy 0.5% CSF Leak 0.3% esophageal perforation with
Epstein[5] 2011	60 ACDF 1 Level Iliac Autograft ABC Plate	100% Fused Avg. 3.8 mos 5 Smokers 6-8 Mos	2 Years Nurick Scores 3.3 to 0.3 (Mild Radiculopathy)	Odom's Criteria 52 Excellent 6 Good 2 Fail
Lord[13] 2017	21,5047 Medicare ACDF 89% No BMP 11% Used BMP	2005 11.84% 2007 16.73% 2011 12.01% Used BMP-Same Dysphagia,	Same Hoarseness, Neurologic, Medical, Other Complications	>Complications for ACDF 2.1% with BMP 1.9% without BMP
Traynelis[18] 2017	Multi-Center Retrospective Study	8887 ACDF Incidence of Horner's Syndrome (HS)	5 (0.06%) HS > Lateral Dissection of LCM	Recommend; Stay Medial When Dissecting LCM
Tasiou[16] 2017	114 Anterior Cervical Surgery 79% ACDF No plates 12.3% ACF	6.1% ACDF with Plates 1.7% Odontoid Screw 1 Anterior Osteophytectomy	Followed Avg 42.5 mos Complications 13.2% Overall ASD 2.7% Dysphagia 1.7%	Hematoma/ Swelling 1.7% CSF leak 1.7% Esophageal perforation 0.9% Worsening Myelopathy 0.9%
Saifi[14] 2017	US 2006-2013 ACDF 137,000/yr CDA 1637/yr	>LOS ACDF 2.3 vs. CDA 1.5 days	>Cost ACDF $16,178 vs. CDA $13,197	Reoperation >CDA5.9% vs. ACDF 2.3%

F=Female, M=Male, MR=Magnetic Resonance Imaging, CT=Computed Tomography, US=Ultrasound, ACDF=Anterior Cervical Diskectomy/Fusion, IJ-Internal Jugular, CCA=Common Carotid Artery, VA=Vertebral Artery, PH=Postoperative Hematoma, HS=Horner's Syndrome, Pts=Patients, LCM=Longus Colli, Musculature RLNP=Recurrent Laryngeal Nerve Palsy, Rad=Radiculopathy, Myel=Myelopathy, WI=Wound Infection, EDH=Epidural Hematoma, PH=Postop Hematoma, RI=Respiratory Insufficiency, Mort=Mortality, SP=Spondylodiscitis, CSF=Cerebrospinal Fluid Leak, EA=Epidural Abscess, LCM=Longus Colli Muscles, ST=Sympathetic Trunk, PNI=Phrenic Nerve Injury, M=Male, MBS=Modified Barium Swallow, Video-L=Videolaryngoendoscopy, Postop=Postoperatively, ASC=Adjacent Segment Disease, PCF=Posterior Cervical Fusion, CHF=Congestive Heart Failure, CA=Cancer, DVT/PT=History of Deep Venous Thrombosis and Pulmonary Embolism, CAD=Coronary Artery Disease, LOS=Length of Stay, Pseud=Pseudarthrosis, NSQUIP=National Surgical Quality Improvement Program Database, JOA=Japanese Orthopedic Association, PEEK=Polyetheretherketone, AE=Adverse Events, NL=Normal, mos=Months, wk=Weeks, Avg.=Average, yo=Years Old, CDA=Cervical Disc Arthroplasty

Esophageal Perforation Rate of 0.3%-0.9% with One Mortality

An esophageal perforation rate of 0.3%-0.9% was noted in several studies, accompanied by a single mortality.[1,7,17] In 1989, Bertalanffy and Eggert discussed a 0-mortality rate for 450 consecutive anterior cervical discectomy (ACD) without fusion.[1] Fountas *et al.* (2007), out of a 0.3% incidence of esophageal perforations occurring in 1015 ACDF, had 1 mortality (0.1%).[6] Although in Tasiou *et al.* study (2017) esophageal perforations occurred 0.9% of the 114 patients, there were no mortalities.[17]

Morbidity Rates for ACDF Varied from 13.2%-19.3%

Several studies documented morbidity/complication rates of ACD and ACDF ranging from 13.2%-15.3%-19.3% [Tables 1-3].[1,6,17] In 1989, Bertalanffy and Eggert cited a morbidity rate of 15.3% for anterior discectomy without fusion (ACD) performed in 450 consecutive patients [Table 1].[1] Fountas *et al.* in 2007 observed a higher morbidity rate of 19.3% (196 patients) out of a series of 1015 patients undergoing ACDF utilizing Smith-Robinson autograft/allograft, with or without plates, followed an average of 26.4 mos. [Table 2].[6] Over a 6-year period, Tasiou *et al.* (2017) retrospectively reported a 13.2% morbidity rate for 114 patients undergoing ACDF (79% no plates, 6.1% ACDF with plates, 12.3% anterior corpectomy with fusion(ACF), two (1.7%) odontoid screws, and one anterior osteophytectomy) [Table 2].[17]

In descending order, the following complications rates were encountered in these three studies; dysphagia (1.7%-9.5%), worsening of the pre-existing myelopathy (3.3%), wound infection

Table 3: Literature Review ACDF Complications 2018-2019.

Author Year	Number patients	Design of Study	Findings	Findings	Conclusions
Zaki[22] 2018	ACDF 389 PCF 160 30 and 90 Day Readmissions	ACDF Readmit 5.1% 30 day 7.7% 90 day Infection 31.4% Pulmonary14.3%	PCF Readmit 11.2% 30 days 16.9% 90 days Wound Complication 19.4%	Risks Factors for ACDF: CHF, CA History DVT/PT, Surgery Complications	Risks Factors for PCF: CAD >Fused Levels > LOS
Saville[15] 2018	Postop Dysphagia ACDF 64 Patients	0 Profile 41 23 Plate/cage Dysphagia 83% Acute 35% Chronic	SWAL-QUOL Preop/ Postop: 6 wk,6 mos VAS/NDI 6 wk, 6 mos	Shorter Operative Time for 0 Profile 44 min vs. Plate/Cage 54 min	Comparable Postop Dysphagia
Bovonrat-wet[2] 2018	37,261 ACDF NSQUIP Database	148 (0.4%) Postop EDH + Reoperations 1/250 Patients	37% Post Discharge EDH-Risk Factors # or > levels Low BMI <24	Risk Factors EDH ASA 3 or > Male Preop Anemia	Risks Reop: Respiratory Infection Reintubation
Sharma[16] 2018	ACDF/no Plate 60 Iliac Autograft vs.60 PEEK	Both Improved JOA Scores Preop vs. 3 mos vs.6 mos, 1 yr	No Score Improvement Between 6 mos-1 year	Comparable fusion rates BOTH groups	Iliac Crest: 1 Level ACDF Fused 95.74% 2-Level 76%
Lee[12] 2019	1-4 Level PEEK ACDF with Plates 57 Pts/6 mos	Group I 17 Pts Group II 24 Pts Group III 12 Pts Group IV 4 Pts	Longer Time to Fuse with Longer Constructs (Avg.) 3 Levels 4.09 mos 4 Levels 5.25 mos	>>Subsidence Longer Fusions I 11.76% 2/17 II 20.83% 5/24 III 16.67% 2/12 IV 0.0% 0/04	>ASD Longer Fusions-Longer Time to Fuse
Wewel[19] 2019	Pseud rates 72 pts 232 Levels	3 Level ACDF 4 Level ACDF Pseud. 47 (14%) Levels	45.8% (33/72) Total Patients had Pseud	4 Level Pseud. 56% 9/16 Pts 3 Level Pseud. 42% 24/56 Pts	11.1% 8/72 Reoperations Symptomatic Pseud
Yerneni[21] 2019	Case-Delayed RLNP Postop C4-C7 ACDF	Postoperative Day 3: Onset Left RLNP	Treatment; Steroids	6 Months Later Resolved Deficit	1 Case Delayed 3 Day Postop RLNP
Yerneni[20] 2019	ACDF 21 Articles In v. Out Patient Surgery	Same Rates: Stroke, DVT/PE, Dysphagia, Clots	Avoid Out Patient ACDF with: >Age >Obesity Significant Myelopathy	Safe and effective Without Significant Comorbidities"	Out Patient ACDF: < Reoperation < Mortality < LOS

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(0.1-0.9%-1.6%), new radicular symptoms (1.3%), postoperative wound hematoma (1.3%-5.6% (2.4% requiring surgery), and 0.9% epidural hematoma), symptomatic recurrent laryngeal nerve palsy (0.9%-1.1%-3.1%) adjacent disc degeneration (2.7%), postoperative soft tissue swelling/hematoma (1.7%), respiratory insufficiency (1.1%), cerebrospinal fluid (CSF) leak (0.5%-1.7%), Horner's syndrome (0.06%-0.1%-1.1%), aggravation of preexisting myelopathy (0.9%), instrument/ mechanical failure/instability (0.1%-0.9%), esophageal perforation (0.3%-0.9%; one mortality 0.1%), new nerve root lesions (0.4%), aseptic spondylodiscitis (0.4%), exacerbation of myelopathy (0.2%), meningitis due to a dural perforation (0.2%), transient additional myelopathy (0.2%), and an epidural abscess(0.2%) [Tables 1-3].[1,6,17]

Rates of Immediate Postoperative Dysphagia After ACDF Ranged from 1.7% to 67%

Several series documented that for patients undergoing ACDF, the most common and immediate postoperative complaint was dysphagia, ranging in frequency from 1.7%-67%

[Tables 1-3].[6,7,15,17] Frempong-Boadu *et al.* in 2002 evaluated ACDF-related postoperative dysphagia, vocal cord paralysis, and speech dysfunction in 23 patients averaging 59 years of age [Table 1].[7] Patients underwent modified barium swallows and videolaryngoendoscopy preoperatively, plus 1 week, and 1 month postoperatively. Preoperative swallowing studies were abnormal in 11 (48%) asymptomatic patients, but normal in 12 patients (52%). Postoperatively, 8 patients exhibited new swallowing abnormalities (67%). Preoperative vocal cord function was normal in all patients, but postoperatively 2 showed vocal cord paresis (one transient; one permanent). Interestingly, swallowing dysfunction correlated with; advanced age, a prior history of such dysfunction, longer surgical procedures, and a trend toward increased dysphagia with multilevel surgery attributed to greater soft tissue swelling/retraction injury. In 2007, Fountas *et al.* observed postoperative dysphagia in 9.5% of 1015 patients undergoing ACDF [Table 2].[6] The postoperative dysphagia rate in Tasiou's *et al.* study (2017) was 1.7% out of 114 patients undergoing anterior cervical procedures [Table 2].[17] Other reports had cited immediate postoperative dysphagia rates of 93% and chronic rates of 35%.

Saville *et al.* (2018) evaluated postoperative dysphagia rates after 64 ACDF utilizing 41 zero-profile devices, and 23 plate/cage constructs. [Table 3].[15] They utilized dysphagia and SWAL-QOL scores (i.e. preoperatively, postoperatively at 6 weeks 12 weeks), along with outcomes analyzed with the Visual Analog Scale (VAS), and the Neck Disabilityu Index (NDI) (i.e. preoperatively, 6 weeks and at 6 months postoperatively). For the zero-profile group, surgical time was reduced vs. plate/cages (e.g.44.88±6.54 min vs 54.43±14.71min), but postoperative, dysphagia rates were the same.

Acute (0.9%-8.3%) and Chronic (2.5%) Symptomatic Postoperative Recurrent Laryngeal Nerve Palsy (RLNP) After ACDF

In multiple series, the rates of symptomatic postoperative recurrent laryngeal nerve palsies (RLNP) ranged from 0.9%-8.3% [Tables 1-2].[1, 6,10,17] Bertalanffy and Eggert (1989) found a 1.1% incidence of RLNP out of 450 ACD [Table 1].[1] Jung *et al.* (2005) prospectively evaluated the frequency of RLNP before and after 120 ACDF utilizing preoperative and postoperative laryngoscopy [Table 1].[10] Preoperatively, 2 (1.6%) patients had asymptomatic RLNP (e.g. hoarseness). Postoperatively, symptomatic RLNP was found in 8.3% of patients (e.g. hoarseness), but asymptomatic RLNP was also documented in 15.9% of patients (i.e. total: 24.2%). At 3 postoperative months, the incidence of symptomatic RNLP was a lesser 2.5%, while asymptomatic RNLP was still documented in 10.8% of cases. The incidence of RLNP in Fountas *et al.* (2007) was 3.1% out of 1015 primary single-level ACDF [Table 2].[6] Further, in Tasiou *et al.* (2017), RLNP occurred in 0.9% of 114 anterior cervical cases [Table 2].[17]

Delayed RLNP

In Yemeni *et al.* a 75-year-old female, 3 days after a C4-7 ACDF, developed a delayed recurrent laryngeal nerve palsy (RLNP) [Table 3].[21] The left vocal cord paralysis was treated with a course of steroids, and 6 months later, her deficit resolved. The most likely etiology of the delayed RLNP was "neurapraxia caused by intraoperative compression or traction on the nerve", but other potential factors included; direct nerve injury, ischemia, vasospasm, or viral factors

Postoperative Hematomas with ACDF

Incidence of Postoperative Hematomas Following ACDF (1.3-5.6%)

Multiple ACDF series demonstrated that postoperative wound hematomas occurred in from 1.3%-5.6% of cases, with epidural clots specifically found in 0.9% of patients [Tables 1, 2].[1,6,17] Out of 450 ACD without fusion performed in 1989, Bertalanffy and Eggert found a 1.3% incidence of postoperative wound hematomas, and a 0.9% frequency of epidural hematomas [Table 1].[1] Tasiou *et al.* (2017) observed postoperative hematomas/significant wound swelling in 1.7% of 114 patients undergoing ACDF [Table 2].[17] Out of 1015 patients, Fountas *et al.* (2007) found postoperative hematomas in 5.6% of patients [Table 2].[6]

Secondary Surgery Required for Postoperative Hematomas after ACDF (0.4%-2.4%)

One case study and several large series documented that following ACDF, there was a 0.4%-2.4% incidence of postoperative cervical hematomas warranting secondary surgery [Table 1-3].[2,6,9] In 2003, Jankowski *et al.* evaluated a 32-year-old female who 6 hours following a C4-C5/C5-C6 ACDF became quadriplegic; following resection of a large epidural hematoma, the patient fully recovered neurological function [Table 1].[9] Fountas *et al.* (2007) found postoperative hematomas in 5.6% of patients undergoing 1015 ACDF; 2.4% (slightly less than half of the 5.6%) warranted secondary surgery [Table 2].[6] Using the National Surgical Quality Improvement Program database (NSQUIP) to assess 37,261 ACDF performed between 2012-2016, Bovonratwet *et al.* (2018) determined that 1 of 250 (0.4%) patients undergoing ACDF developed a postoperative hematoma warranting secondary surgery within 30 postoperative days [Table 3].[2] There were 148 (0.4%) patients with hematomas who required reoperations; notably, 37 occured after discharge. Risk factors for hematomas requiring secondary surgery included; 3 or more level surgery, lower body mass index (BMI ≤24), American Society of Anesthesiologists classification ≥3, anemia, and male sex. Those having reoperations prior to discharge had longer LOS, and were at greater risk for respiratory complications (e.g. pneumonia, reintubation), and infections.

30 (5.1%) and 90 Day (7.7%) Readmissions Rates Following ACDF

Zaki *et al.* (2018 Spine) retrospectively evaluated unplanned readmissions 30 and 90 days after 389 ACDF vs. 160 posterior cervical fusions (PCF) (2013-2014) [Table 3].[22] The 30- and 90-day unplanned readmissions respectively occurred at lower rates for ACDF (5.1% and 7.7%) vs. PCF (11.2% and 16.9%). Typically, readmissions addressed; infection/sepsis for 31.4% having ACDF, and 25.8% for PCF, pulmonary adverse events for ACDF (14.3%), and wound complications with PCF (19.4% readmitted). Risks factors for ACDF readmissions included; "heart failure, history of malignancy, history of deep vein thrombosis/ pulmonary embolism, and intraoperative untoward events". Risks for complications after PCF included; a history of cardiac disease, more fusion levels, and more prolonged LOS.

Anatomy of Sympathetic Trunk and Risk of Horner's Syndrome (0.06%-0.1%-1.1%) with ACDF

Anatomy of the Sympathetic Trunk

Damage to the sympathetic trunk (i.e. Horner's syndrome characterized by ptosis, miosis, and anhidrosis) is more likely to occur during more caudad anterior cervical surgery. In their anatomic study of 28 adult cadavers, Ebraheim *et al.* (2000) found the longus colli muscles (LCM) progressively diverged laterally from C3 (distance between LCM 7.9 mm) to C6 (distance between LCM 13.8 mm), while the sympathetic trunk locations (average 10.6 mm) progressively converged medially [Table 1].[4] Therefore, at lower cervical levels, the sympathetic trunk was more susceptible to injury during ACDF.

Frequency of Horner's Syndrome with ACDF

In three clinical studies, the frequency of Horner's Syndromes ranged from 0.06-0.1%-1.1% [Tables 1-2].[1,6,18] In 1989, Bertalanffy and Eggert noted a 1.1% risk of a Horner's Syndrome out of 450 ACD [Table 1].[1] When Fountas *et al.* (2007) evaluated 1015 patients undergoing initial ACDF, over an average of 26.4 postoperative months, 0.1% of patients developed Horner's syndromes [Table 2].[6] A multicenter retrospective study of 8887 ACDF performed by Traynelis *et al.* (2017), revealed a 0.06% (5 patients) rate of Horner's Syndromes occuring most frequently with C5-C6 level surgery; the majority of these deficits partially recovered [Table 2].[18] To reduce these injures in the future, Traynelis *et al.* recommended more restricted medial dissection of the LCM with very limited lateral retraction, particularly at the more distal cervical levels.

Worsening Myelopathy (0.2%-3.3%) and Radiculopathy (1.3%) Attributed to ACDF

Worsening of preoperative myelopathy and/or radiculopathy were variously reported in different ACDF studies [Table 1-2].[1,6,17] One study (1989) documented worsening of the pre-existing myelopathy in 3.3% of cases, 1.3% exhibited worsening of preoperative radiculopathy, while new nerve root lesions (iatrogenic) occurred in 0.4% of cases [Table 1].[1] Two other ACDF studies reported worsening of preexisting myelopathy; one study cited a 0.2% incidence (2 out of 1015; 2017), while the other reported this in 0.9% of cases (out of 114; 2017) [Table 2].[7,17]

Other Complications of ACDF (Up to 2.7%)

Multiple other complications were reported following ACDF [Tables 1, 2].[1,17] A 1989 study of 450 ACD reported; respiratory insufficiency (1.1%), instability (0.9%), aseptic spondylodiscitis (0.4%), and a pharyngeal lesion (0.2%) [Table 1].[1] Nearly three decades later, Tasiou *et al.* (2017) observed several additional complications following 114 anterior cervical procedures; a 2.7% incidence of adjacent segment degeneration (ASD), and a 0.9% frequency of mechanical failures of instrumentation [Table 2].[17]

Higher Complications Rates (2.1%) for ACDF Performed with Bone Morphogenetic Protein (BMP/Infuse)

Lord *et al.* (2017) retrospectively evaluated the trends, costs, and complication occurring within 90 days of 215,047 ACDF performed in Medicare patients using BMP/Infuse "off-label" (2005-2011) [Table 2].[13] In 2005, BMP was used in 11.84% of cases; this increased to 16.73% in 2007, and decreased to 12.01% by 2011. Notably, the FDA had required that Medtronic issue a warning against using BMP/Infuse for anterior cervical surgery in 2008. The overall complication rate was a higher 2.1% with BMP vs. 1.9% without; there was also a higher wound complication rate with BMP. In the 90-day perioperative period, BMP charges were 17.6% greater than those for non-BMP users. Notably, similar rates of "dysphagia/hoarseness, neurologic, medical, or other complications" were observed for both groups.

Intraoperative Cerebrospinal Fluid Fistulas During ACDF (0.2%- 1.7%)

Three studies documented dural fistulas/cerebrospinal fluid leaks as occurring in from 0.2%-1.7% of ACDF [Tables 1, 2].[1,6,17] In Bertalanffy and Eggert (1989), one patient with a dural fistula developed meningitis (0.2% out of 450 non-plated ACD) [Table 1].[1] A 0.5% incidence of CSF fistulas occurred out of 1015 primary ACDF in Fountas *et al.* (2007) study [Table 2].[6]. Dural tears occurred in 1.7% of 114 anterior cervical procedure performed by Tasiou *et al.* (2017) [Table 2].[17]

Wound Infections after ACDF (0.1%- 1.6%)

Three studies documented different infection rates following ACDF ranging from 0.1%-0.2% up to 1.6% [Tables 1-2].[1,7,17] In one study involving 450 ACD, the wound infection rate was 1.6%, there was one instance of meningitis (0.2%) attributed to

a dural perforation, and another patient developed an epidural abscess (0.2%) [Table 1].[1] Two other series (2007), documented superficial postoperative wound infections in 0.1% (out of 1015 ACDF; 2007), and 0.9% of patients resepctively (out of 114 anterior cervical procedures) [Table 2].[7,17]

Fusion and Pseudarthrosis Rates Following ACDF

Fusion Rates and Pseudarthrosis Rates for 1-2 Level ACDF

Higher fusion rates were typically noted following 1-level vs. 2-level ACDF.[5,16] When Epstein (2011) evaluated fusion rates for 60 ACDF utilizing dynamic plates and iliac crest autograft, both CT and dynamic X-rays confirmed a 100% fusion rate over an average 3.8-months duration (range 2.5-8 months); the 5 smokers exhibited delayed fusions (i.e. over 6-8 months) [Table 2].[5] In another study, Sharma *et al.* (2018) documented comparable fusion rates for 1-2 level ACDF using stand-alone tricortical iliac crest autograft (60 patients) vs. stand-alone polyetheretherketone (PEEK) cages (60 patients); however, statistically significant higher fusion rates occurred for 1-level ACDF (95.74%) vs. 2-level ACDF (76.00%) [Table 3].[16].

Higher Pseudarthrosis Rates for 3-4 Level ACDF

For 3 and 4-level ACDF, higher pseudarthrosis rates were observed [Table 3].[12,19] Lee *et al.* (2019) looked at fusion rates for 1-level vs. multilevel ACDF using polyetheretherketone (PEEK) cage-plate fusions in 57 patients followed at least 6 months [Table 3].[12] It took significantly longer for 3-4 multilevel constructs to fuse vs. single level ACDF (e.g. 3-level (4.09 mos.) and 4-level (5.25 mos.)), and there was greater caudal adjacent segmental disc disease following multilevel procedures. Wewel *et al.* (2019) also retrospectively evaluated fusion and pseudarthrosis rates for 72 patients undergoing 3 and 4-level ACDF (232 levels fused) [Table 3].[19] Pseudarthrosis was observed at 47 (14%) total levels, with 45.8% of patients (33/72) exhibiting at least one level that failed to fuse (e.g. typically, the most caudal level). Furthermore, 4-level ACDF incurred a higher pseudarthrosis rate of 56% (9/16 patients) vs. a rate of 42% for 3-level ACDF (24/56 patients). Additionally, 11.1% (8/72 patients) of patients with symptomatic postoperative pseudarthrosis required secondary surgery.

Internal Jugular Venous Thrombosis After ACDF: Single Case Study

Karim *et al.* (2006) presented what they considered to be the first case of internal jugular venous thrombosis attributed to an ACDF.[11] This involved a 35-year-old female, without significant comorbidities, who underwent a C5-C6 ACDF. During the surgery, there was "significant venous bleeding" that was routinely controlled. The patient was discharged 1 day postoperatively without complaints. On postoperative day 3 and progressing by postoperative day 5, she developed mild dysphagia and increased neck swelling on the right side, the site of surgical access, without symptoms/signs of respiratory distress. Although they anticipated finding a postoperative hematoma, the cervical CT "suggested" and the ultrasound "confirmed" right internal jugular venous thrombosis. She was seen by vascular surgery, and sent home after a 3-day hospital stay, during which time she was placed on Warfarin.

Bilateral Phrenic Nerve Injuries with ACDF: Case Report

In 2001, Fujibayashi *et al.* observed bilateral phrenic nerve palsies resulting from an ACDF performed in one patient for ossification of the posterior longitudinal ligament (OPLL).[8] In this case, bilateral phrenic nerve paralysis was documented on a chest X-ray showing bilateral "laxity of the diaphragm". Diaphragmatic motion began to reappear 3 weeks later, and the patient was off the ventilator by the third postoperative month; yet she still required oxygen 3 years later." Various etiologies for unilateral/bilateral phrenic nerve injuries occurring during ACDF included; stretch injuries to the C4 roots, iatrogenic injury to the ventral horn, ischemia/spinal edema, or cord compression. Interestingly, the author (Epstein) could not find any other ACDF studies in the literature that cited such a deficit. However, most such injuries are reported following cardiovascular procedures.

Risks of Out-Patient Cervical Surgery

Yerneni *et al.* (2019) performed a met-analysis involving 21 articles (up to April 2018), most of which were retrospective studies, looking at the safety of performing outpatient ACDF [Table 3].[20] They noted no "statistically significant difference between inpatient and outpatient ACDF in overall complications; incidence of stroke, thrombolytic events, dysphagia, and hematoma development." Nevertheless, those having outpatient ACDF were "well-selected", a factor which they readily admitted significantly contributed to their lower reoperation rates, reduced mortality, and lesser length of stay. Furthermore, they acknowledged that; " advanced age and comorbidities such as obesity and significant myelopathy are likely not suitable for outpatient ACDF." Their recommendation was for future larger prospective randomized control trials to determine the safety of outpatient ACDF.

CONCLUSION

Although the mortality rates for ACDF remain low, these operations carry significant morbidity rates varying from 13.2%-19.3% [Tables 1-3].[1,7,17] Therefore, patients should be carefully selected to undergo these procedures, and operative intervention should be limited only to those who warrant it based on the correlation of neurological deficits with significant MR/CT/X-ray abnormalities.

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