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Pharyngo-Esophageal Perforation Following Anterior Cervical Spine Surgery: A Single Center Experience and a Systematic Review of the Literature

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Abstract

Study Design: Case series and systematic review of the Literature.

Objectives: Pharyngo-esophageal perforation (PEP) is a rare, life-threatening complication of anterior cervical spine surgery (ACSS). Best management of these patients remains poorly defined. The aim of this study is to present our experience with this entity and to perform a systematic Literature review to better clarify the appropriate treatment of these patients.

Methods: Patients referred to our center for PEP following ACSS (January 2002-December 2018) were identified from our database. Moreover, an extensive review of the English Literature was conducted according to the 2009 PRISMA guidelines.

Results: Twelve patients were referred to our Institution for PEP following ACSS. Indications for ACSS were trauma (n = 10), vertebral metastases (n = 1) and disc herniation (n = 1). All patients underwent hardware placement at the time of ACSS. There were 6 early and 6 delayed PEP. Surgical treatment was performed in 11 patients with total or partial removal of spine fixation devices, autologous bone graft insertion or plate/cage replacement, anatomical suture of the fistula and suture line reinforcement with myoplasty. Complete resolution of PEP was observed in 6 patients. Five patients experienced PEP persistence, requiring further surgical management in 2 cases. At a median follow-up of 18.8 months, all patients exhibited permanent resolution of the perforation.

Conclusions: PEP following ACSS is a rare but dreadful complication. Partial or total removal of the fixation devices, direct suture of the esophageal defect and coverage with tissue flaps seems to be an effective surgical approach in these patients

Keywords

esophageal injury, esophageal perforation, anterior cervical spine, fusion, surgical flap, cervical spine

Introduction

The anterior approach for cervical spine surgery was first described in the 1950s and since then it has become a common procedure for many cervical spine conditions.[1,2] Although mortality remains low, this operation has considerable risk of morbidity (13.2% to 19.3% rates).[3] Pharyngo-esophageal perforation (PEP) is a rare complication of anterior cervical spine surgery (ACSS-incidence: 0,02%-1,62%).[3] It is associated with poor prognosis and a mortality rate that ranges from 12% to 20%.[4] Prompt recognition and treatment are mandatory

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to prevent adverse outcomes, such as mediastinitis, osteomyelitis and sepsis.[5] Evidence on this topic is based upon small reports and there are no guidelines for its management. Aim of this study is to better clarify the appropriate treatment of PEP after ACSS: our experience as a high-volume esophageal center is reported along with a systematic review of the English Literature.

Material and Methods

Demographic and Clinical Data

Patients referred to our center for PEP following ACSS (January 2002-December 2018) were identified from our database. Data regarding demographics, spine surgery, presenting symptoms, time between ACSS and PEP diagnosis, radiological and laboratory tests, surgery, hospital stay, outcome and follow-up was collected. All patients underwent a diagnostic work-up consisting of water-soluble contrast to assess the site, size and morphology of PEP. Endoscopy was performed only in selected cases, to detect penetration of spine hardware into the esophagus. All patients underwent CT scan and/or MRI to study neck, mediastinum, spine's stability and proper allocation of spine hardware. At our Center, all patients received a neurosurgical consultation prior to PEP repair to rule out the need for further spine stabilization after hardware removal or identifying a stable cervical spine that doesn't need further treatment.

Surgical Technique

PEP surgical strategy included a step-up approach with wound debridement and drainage when local infection was present, deferring definitive surgical treatment. Definitive PEP repair included defect suture and reinforcement with muscle flap. All patients underwent postoperative contrast swallow to assess PEP resolution which was defined as an absence of leak on clinical and radiological evaluation and initiation of oral intake. Persistence of fistula was defined according to radiological criteria or as reappearance of signs and symptoms suggestive of leak within 30 days after surgery. PEP recurrence was defined as a new onset of clinical and radiological signs 30 days after surgery, after radiological demonstration of first leak resolution. We subcategorized PEP in early when occurring within 30 days from spine surgery and as delayed when occurring 30 days after operation. The same time interval was adopted for definition of early and late complications after pharyngo-esophageal surgery.

Literature Review

A review of the English Literature was conducted according to the 2009 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[6]

Protocol and registration: Methods of the analysis and inclusion criteria were specified in advance and documented in a protocol.

Eligibility criteria: Only articles in English and human studies were included. Case reports and series with details regarding perforation and treatment were considered, while editorial, commentaries and duplicated articles were excluded. Papers were included when they contained: 1) history of cervical spine surgery, 2) documented PEP and 3) details on surgical approach and outcome. Studies reporting mixed causes of PEP were excluded.

Information sources: A systematic search was performed in MEDLINE, PubMED and Scopus on articles published from 1 January, 1980 to 31 December, 2019. Full-text papers were considered, and the related articles function was used for relevant papers not identified by the initial screening. References of the included papers were further checked to identify any additional study.

Search**:** Terms searched were: "anterior cervical spine surgery" AND "esophageal perforation", "pharyngo-esophageal perforation", "complication", "esophagus", "esophageal injury".

Study selection: Three different authors (LM, MV and ESP) screened all titles and abstract for eligible articles. Disagreements between reviewers were resolved by consensus.

Data collection process: A data extraction sheet was developed. We pilot-tested it on ten randomly-selected included studies, and refined it accordingly.

Data items: The included studies were analyzed in terms of first author, year of publication, numerosity, details of spine surgery, time and site of PEP, surgical intervention, morbidity, mortality and outcome. Data on outcome was recollected patient by patient from each case series.

Risk of bias in individual studies and across studies: To assess the risk of bias for each study, 2 reviewers independently investigated the individual studies (LM, ESP) and used The Cochrane Collaboration's tool for assessing risk of bias.[7] Bias risk assessment was performed at the study level. Inconsistencies in bias risk assessment were reconciled through discussion between 3 reviewers (LM, MV and ESP).

Summary measures and planned methods of analysis: Continuous variables are represented as means $\pm$ SD or medians with ranges, and categorical variables as percentages or frequencies. Correlations were evaluated using Chi square test. Statistical analyses were performed in JMP statistical software version 14.3.0 (SAS Institute Inc., New York, NY, USA).

The study was approved by the Institutional Review Board of our Department. All patients signed informed consent for data collection.

Results

Twelve patients (4F/8 M, mean age 49 years; range 19-74) were referred to our Institution for PEP following ACSS. Indications for spine surgery were traumatic cervical spine fracture (n = 10), vertebral metastases (n = 1) and disc herniation (n = 1). Among the ten patients who experienced prior cervical trauma, 8 presented with tetraplegia. Spine injuries occurred at a single vertebra in 2, double in 7 and multiple levels in 1 case. Patient 8#

Table 1. Patients' Demographics, Indications and Characteristics of Anterior Cervical Spine Surgery.

Case	Sex/Age	Reason for SS	Neurological status	Hardware	Time between SS and PEP
1	F/46	C6-C7 Trauma	Quadriplegic	Anterior plate + posterior fixation	22 days
2	M/19	C6-C7 Trauma	Quadriplegic	Anterior plate + posterior fixation	30 days
3	M/66	C6-C7 Trauma	Quadriplegic	Plate	156 months
4	M/74	C6-C7 Trauma	Quadriplegic	Plate + bone graft	12 days
5	M/19	C6-C7 Trauma	Quadriplegic	Anterior plate + posterior fixation	7 days
6	M/52	C7 Vertebral metastasis	Quadriplegic	Plate	30 days
7	M/49	C5-C7 Trauma	Quadriplegic	Anterior plate and cage + posterior fixation	9 months
8	F/69	C4-C5-C6 Disc herniation	Cervical myelopathy	Mesh + plate	33 months
9	M/39	C5 Trauma	Quadriplegic	Plate + cage	40 months
10	F/46	C6-C7 Trauma	Quadriplegic	Plate + cage	12 months
11	M/62	C6-C7 Trauma	Cervical myelopathy	Plate + bone graft	9 days
12	F/47	C4 Trauma	Left-sided hemiparesis	Plate + cage	154 months

F=female; M=male; SS=spine surgery, PEP=pharyngo-esophageal perforation

had multiple vertebral degenerative disease and presented with cervical myelopathy. With regard to previous spine surgery, anterior cervical corpectomy and fusion had been performed in 4 cases, anterior cervical discectomy and fusion in 8. All patients underwent hardware placement at the time of ACSS as well as additional posterior fixation in patients 1#, 2#,5# and 7#. Table 1 reports the type of hardware used for each patient. In 6 patients PEP was discovered in the early postoperative period (median: 17 days, range 7-30), while a delayed perforation was detected in 6 patients (median 35.5 months, range 9-156 months). Presenting symptoms included dysphagia (n = 5), incision swelling (n = 4), fever (n = 3), odynophagia and dysphonia (n = 2), cough and regurgitation (n = 1), and alimentary fluid leakage from cervical drainage (n = 1). No patient was septic at the time of observation, however 6 patients presented with a neck abscess and esophago-cutaneous fistula.

Preoperative Evaluation

Esophagogram correctly detected a pharyngo-esophageal leak in 11/12 cases (91,7%) (Figure 1), in one patient a false negative occurred. CT scan revealed a fluid collection in 8 patients and in one patient it showed air bubbles near the spine hardware. In 3 patients, CT scan resulted negative: completed with oral contrast, it confirmed the leakage without abscess. Esophagogastroduodenoscopy detected PEP in 6/7 cases (85,7%). In 6 patients, the fistula was located in the esophagus, while in the remaining cases it involved the hypofaryngeal walls or both the hypopharynx and the esophagus, with a mean size of 2 cm. (Table 2). Five patients had initial management of PEP performed elsewhere: in 3 cases neck exploration and drain was performed, in 2 an esophageal suture plus sternocleidomastoid (SCM) flap was done while in 1 case a primary closure a was attempted. All 5 patients experienced PEP persistence. At our Institution, all patients received an evaluation by a spine surgeon. In order to correctly evaluate the spine fusion and stability, as well as the location of the prosthetic materials, all patients underwent a neck X ray and CT scan and/or MRI. Six patients had a stable spine; 4 patients required posterior fixation due to incomplete spine fusion (in 3 patients it was performed prior to esophageal operation, in 1 during esophageal

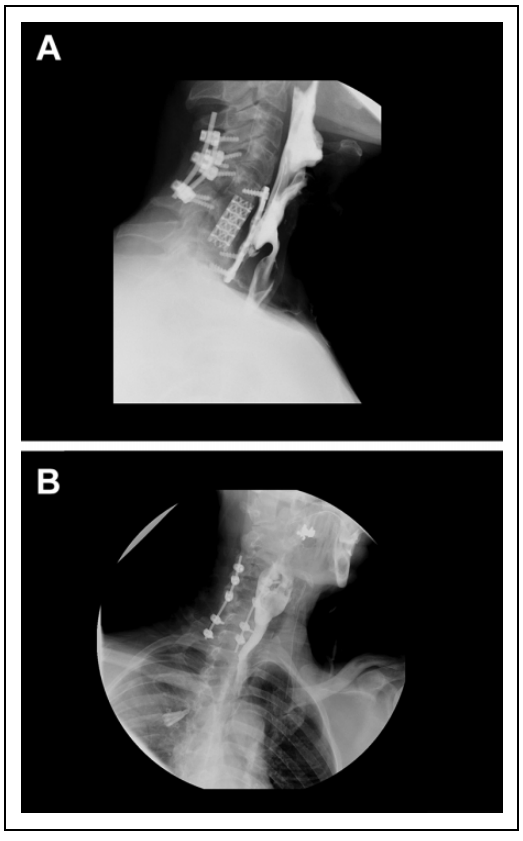

Figure 1. Fig1A: contrast oesophagram showing posterior esophageal leakage (case 7#). Fig 1B. contrast oesophagram performed after surgical procedure showing resolution of esophageal perforation (case 7#).

Table 2. Characteristics of Pharyngo-Esophageal Perforation.

Case	Site of PEP	Size of PEP (cm)	Cause of PEP	Culture isolates
1	hypopharyngeal	2	plate decubitus	*Staphylococcus epidermidis*
2	left pyriform sinus	2,5	plate decubitus	*Candida glabrata*
3	cervical esophagus	nr	plate decubitus	*Citrobacter koseri*
4	pharyngo-esophageal	nr	intraoperative injury	*Stenotrophomonas maltophilia, Staphylococcus aureus, Candida glabrata*
5	cervical esophagus	3,5	intraoperative injury	*Staphylococcus aureus, Candida glabrata*
6	pharyngo-esophageal	nr	plate decubitus	*Morganella morganii, Peptostreptococcus sp.*
7	cervical esophagus	0,5	plate decubitus	*Pseudomonas aeruginosa*
8	cervical esophagus	1	nr	*Staphylococcus epidermidis*
9	hypopharyngeal	2,5	plate migration	*Candida albicans*
10	cervical esophagus	1	plate decubitus	*Stenotrophomonas maltophilia, Candida albicans*
11	cervical esophagus	2	intraoperative injury	*Staphylococcus epidermidis*
12	hypopharyngeal	3	plate migration	Negative

PEP= pharyngo-esophageal perforation; nr=not reported

surgery). In 1 patient, bone graft placement from iliac crest was performed, while in another case Halo-vest fixation was positioned during PEP repair. Indications for the removal of fixation devices were plate/screw decubitus and/or migration. Removal of the anterior hardware was performed in 10 patients, either prior to esophageal surgery (n = 2) or during surgery (n = 8). In case 6#, hardware removal was not performed because of poor general condition for metastatic cancer. In case 8#, anterior plate was not removed because there were no signs of dislocation.

All patients underwent culture-directed IV antibiotics (Table 2). Special attention was paid to restore nutritional status by parenteral (n = 2) or preferably enteral (n = 10) nutrition.

Surgery for PEP

All patients received surgical treatment for PEP. Initial approach with wound debridement and drainage was performed in 4 patients due to significant local infection. In case 11# a conservative treatment with fasting and IV antibiotics was undertaken due to absence of inflammation: a PEP persistence was observed and the patient underwent PEP repair. Eleven patients underwent definitive surgical treatment of PEP: in all cases a suture of the fistula and reinforcement with muscle flaps was performed in 11 patients (SCM flap in 10, pectoralis major -PM- flap in 1) (Figure 2). Drains were always placed and removed after fistula resolution. In case 10# esophageal repair was achieved in 2 steps: first posterior esophageal defect was sutured and a protective esophagostomy was performed; 4 months later, esophagostomy was closed with complete resolution of PEP. In case 6# a conservative approach with toilette and drainage was undertaken, because of metastatic disease from prostatic cancer; he eventually died of progression of oncologic disease after 4 months.

Outcome and Follow-Up

After index surgery, resolution of PEP was observed in 6 patients. Five patients experienced a persistent fistula. Case 7# underwent a revision of cervical wound with debridement and drainage. Due to leak persistence, a third operation was performed with re-suture of esophageal dehiscence and PM flap, obtaining resolution. In case 2#, a salivary output from drains occurred 4 days after surgery, requiring a revision with drains re-positioning. A lower salivary output was then observed and was treated with a conservative approach: the patient was discharged with a neck drain and with an oral soft diet until resolution 365 days after surgery. In case 8#, an endoscopic stent was placed, with resolution of the leak. Finally, case 4# and 5# were successfully treated conservatively by maintaining cervical drainage (Table 3). Median hospital stay was 26.5 days (range 12-127 days). Median time from index surgery to oral feeding was 21.5 days (9-120). Early complications included 1 hematoma and 1 neck fluid collection which required surgical revision. One patient died of pulmonary complications 16 days after successful pharyngeal repair. Late complications included 4 esophageal pseudodiverticula: in 2 asymptomatic cases no treatment was necessary, 2 patients complained of dysphagia and the pseudodiverticulum was treated with endoscopic septotomy. One patient (who did not undergo removal of anterior hardware) developed PEP recurrence 24 months after esophageal surgery; esophagogastroscopy documented an esophageal diverticulum with anterior spine hardware dislocation. She underwent posterior stabilization and cervical revision, removal of anterior hardware, esophageal suture and cover with SMC flap.

Median follow-up was 18.8 months (range 17.7-154). At the time of last follow-up, no PEP recurrences were reported.

Literature Review

The initial PubMed search returned 1964 studies and 8 additional records were identified in references. After eligibility assessment a total of 68 studies were included (Figure 3).[5,8-74] There were 62 case reports and case series ($\leq$5 patients)[5,7-31,33,34,36-57,59,61-68,72,73] and 6 retrospective studies (>5 patients).[39,42,63,65,73,74] All included studies were level 4 evidence. Data on 159 patients was available: M/F 107/

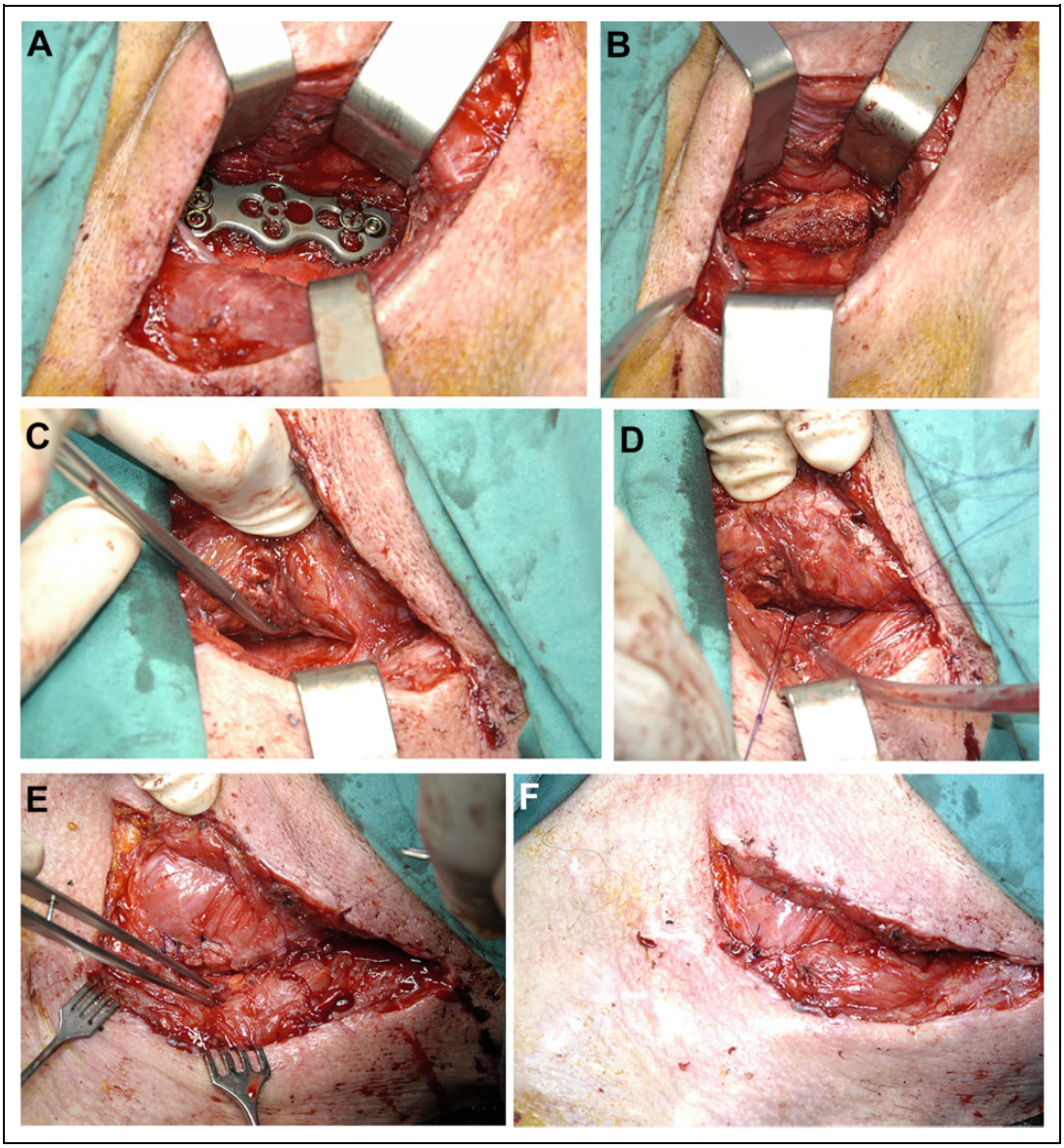

Figure 2. PEP surgical management (case 7#): anterior hardware removal, bone graft placement from iliac crest, anatomical suture of the fistula and suture line reinforcement with pectoralis major flap. Fig2A: fixation device (plate) prior to removal. Fig2B: bone graft placement. Fig2C: esophageal perforation. Fig2D: esophageal perforation suture. Fig2E: pectoralis major flap. Fig2F: final result.

38 (sex not reported for 14), with a mean age of 45.2 years (range 14-85 years). Indications for ACSS and presentation of PEP are summarized in Table 4. Perforation was an incidental finding in 5 patients (3.1%). PEP occurred early in the postoperative period in 65 patients (40.9%): in 8 cases PEP was discovered intraoperatively, while in the remaining it was documented later with a median interval of 5.5 days (range 1-30). There were 94 delayed perforations (59.1%), diagnosed at a median time of 24.0 months from ACSS (range 1.1-300). Early and delayed perforations differed in presentation: acute inflammatory symptoms were more frequent in early perforation (p.008 and .003) while dysphagia was more common in delayed PEP (p.005) (Table 4). A total of 147 patients underwent surgery for PEP. Twelve patients received non-surgical management for poor general condition (n = 3) or for leakage characteristics (absent or minor fistula, absent or mild infection, no sepsis) (n = 9). These cases were treated with drainage, nasogastric tube, antibiotics, enteral and/or parenteral nutrition and in 10 cases healing was achieved (83.3%). One patient died because of cardiac arrest (8.3%) while 1 patient was lost to follow-up (8.3%). Among the 147 surgical patients, 58 (36.4%) were initially managed with a conservative approach with medications, iv antibiotics and enteral or parenteral nutrition, or with debridement, drainage ± hardware removal without pharyngo-esophageal repair. Reasons for initial conservative approach were local inflammation and infection (n = 50, 86.2%) or no evidence of fistula during revisional surgery (n = 8, 13.8%). In 14 of these patients (24.1%),

Table 3. Surgical Management of Pharyngo-Esophageal Perforation and Outcome.

Case	Initial conservative management[#]	Cervical incision	PEP repair	Outcome	Further treatment	Oral feeding* (days)	Hospital stay (days)
1	no	Right cervicotomy	Double-layer suture + SCM flap	Resolution	-	14	18
2	no	Left cervicotomy	Double-layer suture + SCM flap	Persistence	Surgical drainage	99	109
3	no	Left cervicotomy	Double-layer suture + SCM flap	Resolution	-	11	16
4	Surgical drainage	Left cervicotomy	Double-layer suture + SCM flap	Persistence (low output)	Conservative	10	70
5	no	Collar cervicotomy	Double-layer suture + SCM flap	Persistence (low output)	Conservative	28	63
6	Percutaneous drainage	-	-	Persistence	-	-	22
7	no	Collar cervicotomy	Double-layer suture + PM flap	Persistence	Surgical drainage. Esophageal suture + PM flap	99	127
8	no	Left cervicotomy	Double-layer suture + SCM flap	Persistence	Endoscopic stent	22	31
9	Surgical drainage	Left cervicotomy	Double-layer suture + SCM flap	Resolution	-	-[§]	16
10	Surgical drainage	Left cervicotomy	Double-layer suture + SCM flap + cervical esophagostomy	Resolution	-	120	37
11	NPO, antibiotics	Left cervicotomy	Double-layer suture + SCM flap	Resolution	-	9	12
12	no	Left cervicotomy	Double-layer suture + SCM flap	Resolution	-	21	22

PEP=pharyngo-esophageal perforation; SCM= sternocleidomastoid flap; PM= pectoralis major flap
[#]Initial conservative management includes NPO, antibiotics, naso-gastric tube insertion, surgical drainage when indicated.
*after index surgery
[§]postoperative death

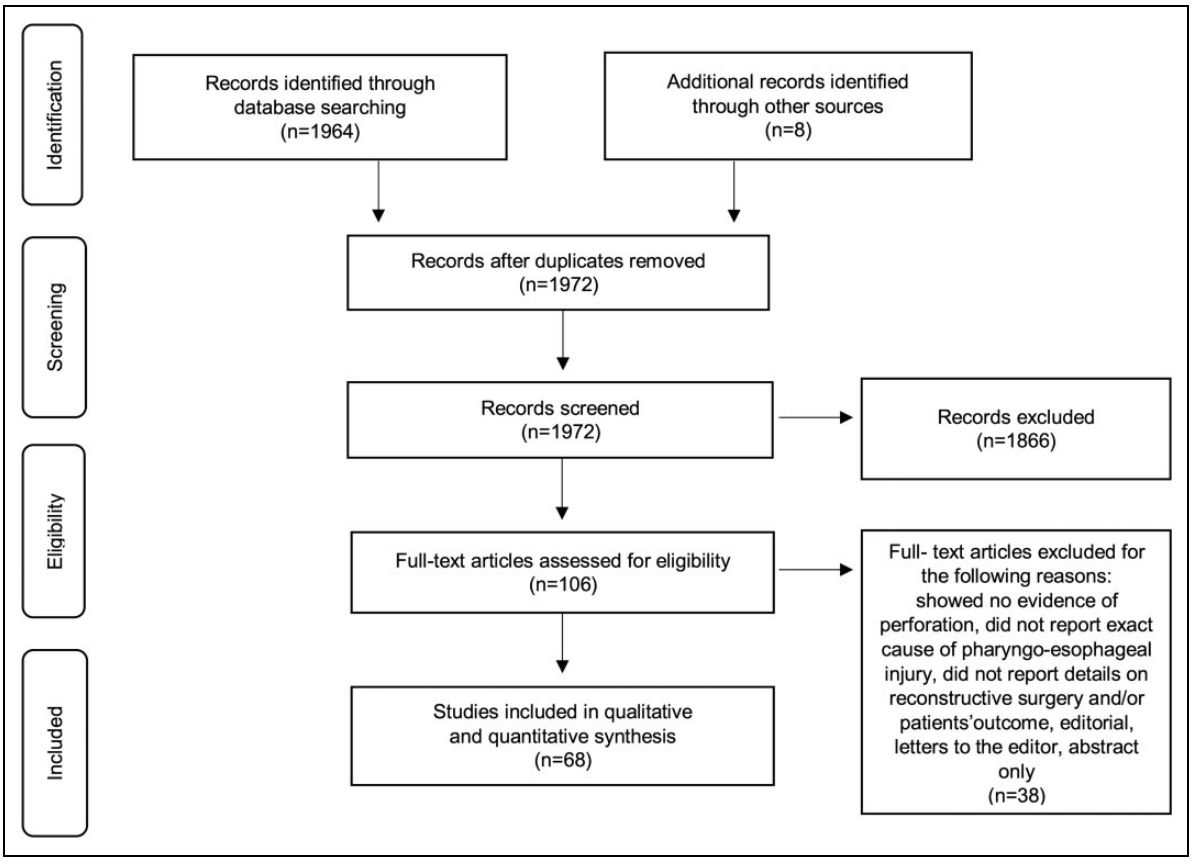

Figure 3. Literature review according to the 2009 preferred reporting items for systematic reviews and meta-analyses PRISMA guidelines.

Table 4. Clinical Characteristics, Treatment Methods and Outcome of PEP in the Sturdies Included in the Literature Review.

	Overall	Early Perforations	Delayed Perforations	*p*
Patients *n (M/F*	159 (107/38)	65 (47/13)	94 (60/25)	-
Age *mean (range)*	45.2 yr (14-85)	45.1 yr (14-83)	44.8 yr (18-85)	-
Indication for SS *n (%)*				*0.123*
Trauma	88 (55.3)	34 (52.3)	54 (57.4)	
Disc herniation	22 (13.8)	13 (20.0)	9 (9.5)	
Spondylosis	24 (15.1)	8 (12.3)	16 (17.0)	
Ossification of the posterior Longitudinal ligament	2 (2.5)	0 (0)	2 (2.1)	
Tumor	4 (2.5)	0 (0)	4 (4.2)	
Ankylosing spondylitis	7 (4.4)	3 (4.6)	4 (4.2)	
Tuberculosis	2 (1.3)	1 (1.5)	1 (1.7)	
Other	3 (1.9)	2 (3.0)	1 (1.7)	
Unreported	4 (2.5)	4 (6.1)	3 (3.2)	
Symptoms *n (%)*				
Dysphagia	**59 (37.1)**	**14 (21.5)**	**45 (47.9)**	***0.005***
Fever	27 (17.0)	11 (16.9)	16 (17.0)	*0.929*
Cervical swelling	**25 (15.7)**	**18 (27.7)**	**7 (7.4)**	***0.0008***
Neck abscess	23 (14.5)	11 (16.9)	13 (13.8)	*0.491*
Odynophagia	22 (13.9)	10 (16.7)	12 (12.8)	*0.814*
Salivary leakage	18 (11.3)	10 (15.3)	9 (9.6)	*0.426*
Neck pain	17 (10.7)	5 (7.7)	12 (12.8)	*0.285*
Purulent drainage	**14 (8.8)**	**12 (18.5)**	**2 (2.1)**	***0.0003***
Repetitive respiratory events	11 (6.9)	1 (1.5)	10 (10.6)	*0.013*
Alimentary fluid leakage	8 (5)	6 (9.2)	2 (2.1)	*0.046*
Dyspnea/cough	5 (3.1)	3 (4.6)	2 (2.1)	*0.391*
Incidental finding	**5 (3.1)**	**0 (0)**	**5 (5.3)**	***0.019***
Neurological symptoms	4 (2.5)	2 (3.1)	2 (2.1)	*0.72*
Dysphonia	4 (2.5)	3 (4.6)	1 (1.1)	*0.165*
Regurgitation	3 (1.9)	1 (1.5)	2 (2.1)	*0.776*
Bleeding	3 (1.9)	1 (1.5)	2 (2.1)	*0.776*
Foreign material extruded during coughing	2 (1.2)	0 (0)	2 (2.1)	*0.143*
Subcutaneous emphysema	2 (1.2)	2 (3.0)	0 (0)	*0.058*
Sepsis	2 (1.2)	2 (3.0)	0 (0)	*0.058*
Mediastinitis	1 (0.6)	0 (0)	0 (0)	*0.182*
Interval from SS to PEP *mean (range)*	-	8.9 d (0-30)	52.34 mo (1.1-300)	-
Surgery for PEP *n (%)*				
Initial conservative therapy	58 (36.4)	27 (41.5)	31 (33.0)	*0.251*
Resolution with conservative therapy	14 (24.1)	6 (22.2)	8 (25.8)	*0.396*
Surgical approach for PEP	127 (79.9)	52 (80)	75 (80.0)	*0.936*
Repair without flap	52 (40.6)	20 (38.4)	32 (42.7)	*0.575*
Resolution	37 (71.1)	12 (60)	25 (78.1)	*0.583*
Repair with flap	75 (59.1)	32 (61.5)	43 (57.3)	*0.392*
Resolution	58 (77.3)	26 (81.2)	32 (74.4)	*0.572*
Outcome				
n (%)				
Postoperative mortality	3 (2.3)	2 (3.8)	4 (5.3)	*0.824*
mean (range)				
Postoperative length of stay	39.2 d (8-191)	45.4 d (8-191)	28.8 d (5-70)	*0.244*
Time to refeeding	40.9 d (4-480)	37.9 d (6-186)	43.2 d (4-480)	*0.701*
Follow-up	15.9 mo (1-72)	11.6 mo (1-48)	18.0 mo (1-72)	-

SS=spine surgery; PEP=pharyngo-esophageal perforation; yr= year; mo=months; d=days.

resolution of perforation was achieved, with a median time to refeeding of 31 days (range 4-119). Three patients required further neck irrigation and 3 died of pulmonary complications. Thirty-eight patients subsequently underwent pharyngo-esophageal repair: in 14 cases a direct suture was performed while a muscular flap was adopted in 24 patients. Immediate resolution of leakage was achieved in 11/14 patients with primary PEP repair (78.6%) and in 19/24 patients with muscle flap repair (79.2%), while in 8 patients repeated surgery was necessary for leak persistence. Eighty-nine patients underwent repair as primary treatment: 38 cases were treated with primary pharyngo-esophageal suture (42.7%), 48 with muscular flap

Table 5. Literature Review: Summary of Therapeutic Approach for PEP. Table 5 Compares Surgical vs Non Surgical Approach for PEP and Among Surgical Patients, PEP Direct Repair vs Repair with Flap.

	PEP treatment: overall (n = 159)		p	PEP treatment: surgically treated only (n = 127)		p
	Non surgical	Surgical		PEP direct repair	Repair with flap*	
Patients n (%)	32 (20.1%)	127 (79.9%)	-	52 (32.5%)	76 (47.5)	-
Outcome	Persistence n = 8 Resolution n = 24	Persistence n = 32 Resolution n = 95	.927	Persistence n = 15 Resolution n = 37	Persistence n = 18 Resolution n = 58	.513
Time to refeeding (mean; range)**	43.4; 0-120	40.7; 4-480	.862	52.0; 7-480	31.9; 4-270	.155
Hospital stay (mean; range)**	NA	41.5; 8-191	-	51.5; 10-191	35.1; 8-150	.295
Number of treatments (mean)	NA	1.5	-	1.7	1.3	.114
Mortality (n; %)	4; 12.5%	3; 2.3%	.05	0; 0%	3; 3.9%	**.039**
Follow-up§ (mean; range)	7.1; 1-24	17.5; 1-72	-	18.2; 1-72	17.0; 1-60	-

PEP= pharyngo-esophageal perforation; NA= not applicable
*Repair with flap comprehends repair with AlloDerm® Matrix, Surgisis® Mesh, jejunal loop interposition
**days
§months

(53.9%), 2 biological mesh repair (2.2%), 1 with esophageal resection and jejunal auto-transplant (1.1%). Resolution after surgery was reported for 26/38 patients treated with direct suture (68.4%) and for 39/48 with muscular flap reconstruction (81.2%) (Table 5). Anterior hardware was removed in 105/147 patients (71.4%). There were 3 postoperative deaths with a mortality rate of 2.3%. Among surgical patients, mean time to oral feeding was 40.7 days (range 4-480), while mean hospital stay was 41.5 days (range 8-191). There were no significant differences in postoperative outcomes between early and delayed perforation.

Discussion

Anterior approach to the cervical spine is well-established procedure for several conditions. It is considered effective and safe, although it can carry a significant burden in terms of complications.[43] PEP incidence is low and ranges from 0% to 1.49%.[13,20] The most frequent site of injury is the Killian triangle[39]: here the esophageal mucosa is unprotected by the muscular layer and is separated from the retroesophageal space only by the buccopharyngeal fascia.[73] Another area of weakness is the lateral wall of the pyriform sinus.[38] Traumatic spinal injuries represent the most frequent indication for ACSS in our review (57.5% of cases) as well as in our case series, followed by degenerative disease and disc herniation. Cervical trauma may be a predisposing factor for hardware dislodgment after surgery and may itself facilitate esophageal lesions through bone fragments or hyperextension trauma.[75]

PEP can be diagnosed intraoperatively, early postoperatively or can be delayed years after spine surgery.[73] Among early PEP (40.5%), intraoperative injury with immediate identification represented 12.3% of cases in our review, whereas early postoperative diagnosis was far more common. Early presentation is linked to iatrogenic injury such as retraction or improper placement of plates, screws or bone grafts.[35] Delayed PEP (59.1% in the Literature) is usually related to chronic compression, dislodgement of hardware, screw migration or instrumentation failure.[64] The long-time interval between spine surgery and delayed PEP (mean 52.34 months, range 1.1-300) exceeds the usual 1-year follow-up after spine operation. This prompts the need for a longer follow-up and for a careful patient education about possible late complications and presenting symptoms.

Presentation of PEP is variable and goes from neck abscess to hardware dislodgement in the esophageal lumen. Symptoms can be overlooked or misdiagnosed as PEP is uncommon. Therefore a high index of suspicion is necessary for prompt recognition ad correct management.[12] Neck pain, dysphagia, odynophagia, fever, surgical site swelling and drainage were the most typical presenting signs and symptoms reported both in the Literature and in our case series. Sometimes patients can be asymptomatic and PEP is detected during regular follow-up.[19,41,61,64,74] When a PEP is suspected, appropriate investigations must follow. Radiographs can show indirect signs of cervical perforation, such as widening of retropharyngeal space, subcutaneous emphysema or prevertebral air, and loose or missing hardware.[73] Esophagogram can identify the leak, showing contrast in the prevertebral space or in the operative site.[76] Moreover, contrast swallow can determine leak extent and its relationship with adjacent structures and anatomical spaces. Endoscopy, executed by an experienced endoscopist

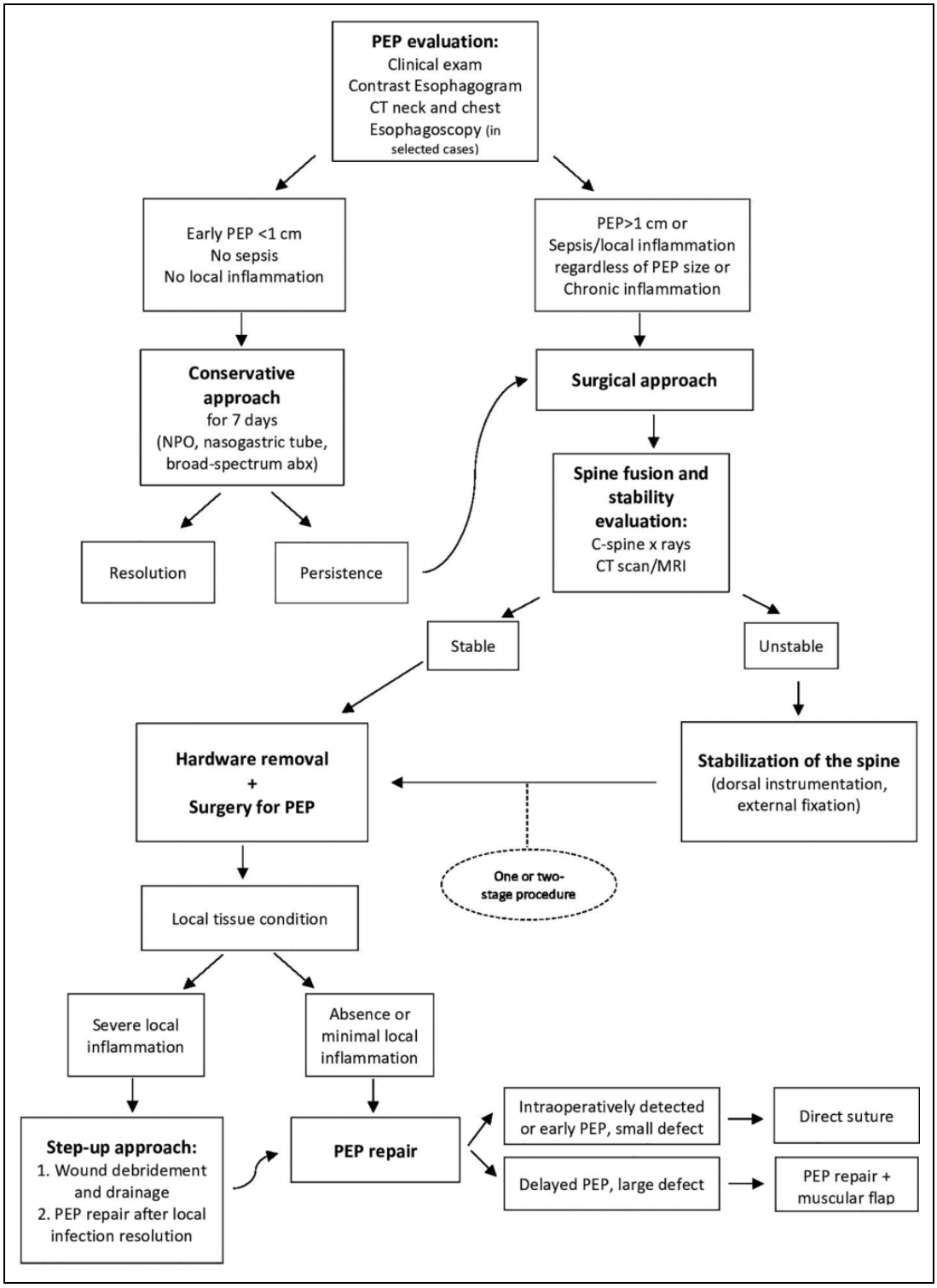

Figure 4. Proposed algorithm in the management of pharyngo-esophageal perforations following anterior cervical spine surgery.

to avoid risk of further tearing during air insufflation, can show perforation and can detect penetration of spine hardware into the esophagus.[5] Computed tomography (CT) can detect an abscess or fluid collections and can verify the placement of spine hardware. Cervical spine fusion can be evaluated with cervical CT or X-ray to establish the need for supplementary fixation once removed the anterior hardware.[56] In our case series, contrast swallow study and CT scan were performed in all patients: esophagogram was able to detect PEP in 11/12 cases (91,7%) and CT scan guided treatment through the demonstration of air and fluid collections and evaluation of spine stability.

Patients with PEP usually undergo a long period of fasting. Restoring an adequate nutritional status is of paramount importance to improve healing, prevent weight loss and reduce the hospital stay.,[77,78] In the Literature, type of feeding is reported for 94/159 patients, with enteral nutrition being the most used (82% of cases). In our case series, all patients received nutritional support, with 10/12 patients receiving enteral feeding.

Currently, there are no definite guidelines on correct management of PEP and treatment options range from conservative approach to surgery. An interdisciplinary strategy is necessary: as a matter of fact, apart from PEP repair, an evaluation by a spine surgeon is mandatory in order to decide the potential implant removal and the need for further spine stabilization. The only late recurrence we experienced was linked to dislocation of the hardware (not removed at the time of PEP repair) in the esophagus. This underlines the importance of hardware removal, above all in delayed perforations in which the injury mechanism is mainly linked to hardware presence. Regarding PEP repair, a conservative approach could be suggested for small, early-recognized PEP, without signs of abscess, whereas surgery should be preferred in case of defects >1 cm and/or more prominent clinical presentation. In case of important local inflammation, a step-up approach should be preferred, with a first intervention aimed at improving local tissue conditions, postponing perforation repair once infection has resolved. Pharyngo-esophageal suture must be performed in a tension-free manner to avoid strictures. Particular attention should be given to the removal of poorly viable tissue prior to suture. A muscle flap can be associated to pharyngo-esophageal primary repair: the interposition of muscle protects the suture from compression or friction by the surrounding tissues, and it can be used to close larger defects. As already reported by Hershman et al, various flap options have been explored to repair PEP.[67] The SCM flap is the most frequently adopted in the Literature (62.7%). In our experience it has proved to be effective, easy to harvest and with a reliable blood supply. Regarding the choice of performing a direct suture or a reinforcement with a flap, there are no standard protocols available. In our Literature review we did not find statistically relevant differences in the use of the 2 approaches. Postoperative outcomes were similar even if both postoperative hospital stay and time to refeeding tended to be longer for direct sutures. This suggests that a tailored approach is necessary: for PEP detected intraoperatively or very early a direct suture could be adequate, while in larger and delayed defects a flap should be preferred (see Figure 4). Moreover, it must be noted that many cases will require repeated operations regardless of the chosen approach. In the Literature, multiple operations were performed in 36/147 patients (24.5%), with a mean of 2.7; similarly, in our series only 6/11 patients achieved PEP resolution after 1 single procedure. The fact that for some patients a single operation is ineffective underlines the important morbidity linked with PEP and the technical difficulty of the surgical approach required for its resolution. This is also demonstrated by the mortality rate associated with the surgical treatment of PEP. In the Literature review, surgery for PEP presented a mortality rate of 3.8% in early and 5.3% in delayed perforations. In our case series, we also experienced a postoperative death due to pulmonary complications in a weakened patient. Once more, despite the rarity of PEP, when this complication does occur, the consequences for the patient can be grave.

Even though the numerosity of our series is superior to the majority of the published reports, our study has some limitations: data was collected retrospectively therefore some bias may be present in the data analysis.

Conclusions

We report the experience of a tertiary referral center for esophageal surgery with PEP following ACSS. Successful management of this complication depends on prompt recognition and treatment. We recommend a tailored and multidisciplinary approach: partial or total removal of the fixation devices, wound debridement, removal of poorly viable tissues, attempt tension-free suture repair and coverage with muscle flaps in cases where soft tissues are amendable.

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