

# Surgical cervicothoracic-flap repair of neoesophagus–airway fistula after esophagectomy for esophageal cancer: A retrospective cohort study



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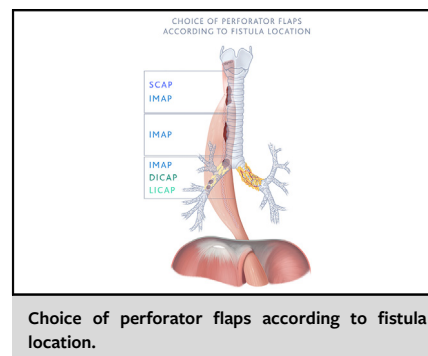
## ABSTRACT

**Objective:** To evaluate outcomes of surgical repair of postesophagectomy neoesophagus–airway fistulas (NEAFs).

**Methods:** We retrospectively included consecutive patients with NEAF managed by various techniques at our center between August 2009 and July 2021.

**Result:** Of the 11 patients (median age, 60 years; interquartile range, 58, 62), 4 had received induction chemoradiotherapy and 4 others induction chemotherapy. NEAF was mainly a complication of anastomotic leakage (n = 6) or attempted stenosis treatment (n = 3). The airway mainly involved was the trachea (n = 8). Airway defects were repaired by resection–anastomosis (n = 5), perforator flaps (n = 4), pedicled pericardium (n = 1), and/or direct suturing (n = 2). Gastric conduit defects were repaired by perforator flaps (n = 6), direct suturing (n = 2), or pedicled pericardium (n = 1). Of the 7 perforator flaps, 4 were internal mammary–artery, two dorsal intercostal–artery, and one supraclavicular–artery flaps. After a median follow-up of 100 months, 2 patients died on early postoperative course from NEAF repair failure and 3 from late NEAF recurrence at 4, 11, and 33 months. Among the remaining 6 patients, 1 died from local tumoral recurrence at 13 months, 1 was last on follow-up at 27 months, alive and eating normally. The other 4 were free from NEAF recurrence and dysphagia or swallowing disorder at 50 months' follow-up. These 4 results were obtained thanks to perforator flap interposition and airway resection anastomosis.

**Conclusions:** Surgical NEAF repair using perforator flap interposition may provide satisfactory long-term function after strong prehabilitation. (JTCVS Techniques 2024;23:123-31)



## CENTRAL MESSAGE

Neoesophagus–airway fistula is a life-threatening complication of esophagectomy for cancer: repair attempts have to follow rigorous prehabilitation.

## PERSPECTIVE

Neoesophagus–airway fistula is a life-threatening complication of esophagectomy for cancer. We achieved favorable results in repair attempts following rigorous prehabilitation: 4 of 11 patients showed no recurrence after a 50-month follow-up period. The use of perforator flap interposition appears to yield promising outcomes in such challenging situation.

The tracheobronchial tree is very close to the proximal esophagus and is therefore at high risk for injury during esophagectomy.<sup>1,2</sup> Reconstruction after esophagectomy usually involves creating a gastric conduit pulled up through the posterior mediastinum and anastomosed to

the esophageal stump in the neck or thorax. The proximity of this anastomosis to the membranous tracheobronchial wall carries a risk of fistula formation. Various perioperative and postoperative events may promote postesophagectomy neoesophagus–airway fistula (NEAF) formation.<sup>3</sup> For

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### Abbreviations and Acronyms

DFS	= disease free-survival
IQR	= interquartile range
MV	= mechanical ventilation
NEAF	= neoesophagus–airway fistula
OS	= overall survival
SEMS	= self-expanding metal stent

instance, radiotherapy and chemotherapy may decrease tissue viability and impair wound healing.<sup>4</sup> Tracheobronchial inflammation due to anastomotic leakage or endoscopic dilatation of a benign anastomotic stricture may also increase the risk of NEAF.<sup>5</sup> Other potential risk factors are airway ischemia after extensive dissection of the upper mediastinum, notably for extensive lymphadenectomy,<sup>6</sup> injury to the tracheobronchial tree during surgical dissection,<sup>7</sup> and cuff-induced tracheal necrosis during prolonged endotracheal intubation.<sup>8</sup>

NEAF formation in the neck or thorax has been reported in 0.3% to 1.9% of patients.<sup>9–11</sup> NEAFs vary widely in their clinical presentation, although the most common initial symptom is coughing after oral intake. Patients with NEAFs often experience life-threatening recurrent bronchopneumonia, mediastinitis, sepsis, and/or respiratory failure.

The optimal method for treating acquired nonmalignant NEAF is unclear. Studies have shown a distinctive profile regarding the surgical techniques and outcomes in those patients with previous esophagectomy.<sup>12–15</sup> The methods used include various surgical techniques and nonoperative stenting.<sup>16–18</sup> Among surgical methods, repair using interposition flaps<sup>19</sup> may be both effective and safe. The objective of this single-center retrospective observational study was to describe surgical techniques used to treat nonmalignant NEAF and to report the early and intermediate postrepair outcomes.

## METHODS

This retrospective single-center observational cohort study was approved by our institutional review board (DELIBERE\_CERC-SFCTCV-2022-01-17\_18377\_Olaf Mercier) and was conducted according to the ethical standards of the Committee on Human Experimentation of our institution. The need for informed patient consent was waived in compliance with French law on retrospective studies of de-identified healthcare data. The study is reported according to Strengthening the Reporting of Observational Studies in Epidemiology guidelines.<sup>20</sup>

### Patients and Study Design

Consecutive patients who underwent surgical repair of nonmalignant NEAF after esophagectomy for esophageal cancer between 2009 and 2021 at our tertiary thoracic surgery center (Marie Lannelongue Hospital, Le Plessis Robinson, France) were identified retrospectively by searching our department database. Surgical repair was attempted for all patients.

For each patient, the data were extracted from the medical records. NEAF was defined as an endoscopically or radiographically evident fistulous communication between the central airway (trachea or proximal bronchus) and the anastomosis or gastric conduit after esophagectomy. Tracheal membranous defects were localized by bronchoscopy, and distances from the vocal cords and carina were measured to guide future surgery. We did not include patients with fistulas to the lung parenchyma or pleural cavity, malignant NEAF, or NEAF after surgical procedures other than esophagectomy with esogastric anastomosis. All patients had undergone esophagectomy elsewhere and were referred to our hospital for NEAF management.

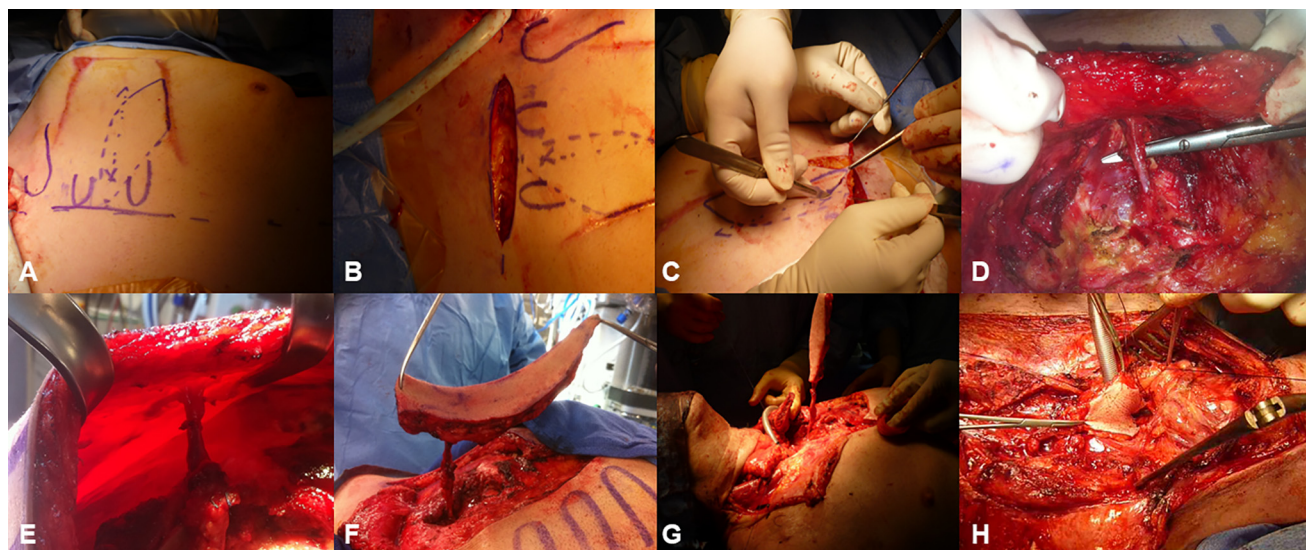
### Management of NEAF

**Preoperative conditioning.** According to the presentation in each patient, components of the preoperative management included weaning off mechanical ventilation (MV), improvement of the nutritional status, treatment of bronchial inflammation and/or lower respiratory tract infection, and treatment of sepsis. When achieving these goals was not feasible, the digestive tract was excluded and continuity restored later. In patients who required MV, we performed a tracheotomy and placed the balloon distal to the fistula to protect the airway and accelerate weaning off the ventilator. The tracheotomy was positioned as near as possible to the fistula. Nutritional preparations were administered either enterally through a jejunostomy or gastrostomy or parenterally. Nasogastric tube insertion was avoided to minimize stress on the fistula. Bronchial secretion samples were collected routinely for microbiological studies, and antibiotic therapy was given routinely when the results indicated lower respiratory tract infection or colonization. Life-threatening condition was defined as any organ failure found in Sepsis-related Organ Failure Assessment (ie, SOFA) score in addition to respiratory failure.<sup>21</sup>

### Surgical Technique

The approach was decided according to fistula size and location. For tracheal NEAF in patients who had not received radiotherapy, we used the collar incision.<sup>22</sup> This anterior approach allows direct visualization for gastric-conduit repair, resection of the damaged tracheal segment, and sparing of the airway blood supply and recurrent nerves. In our practice, previous radiotherapy precludes distal tracheal mobilization. In this situation, we used cervicothoracic approaches, with clavicular swing or clavicular head resection, allowing tracheal suturing at the manubrium level or even more distally at the carina. In addition, laryngeal release maneuvers were preferentially used with supra or subhyoid muscles section (Montgomery<sup>23</sup> or Dedo-Fishman maneuvers<sup>24</sup>) to maintain appropriate tension of the tracheal anastomosis. In patients with gastric-conduit defects that were not amenable to suturing, we restored digestive-tract integrity using perforator flaps (internal mammary artery perforator flap; supraclavicular artery perforator flap; dorsal intercostal artery perforator flap; or lateral intercostal artery perforator flap) (Figures 1, 2, and 3), depending on flap availability and fistula location. Perforator flaps were used when the size of the NEAF does not allow tracheal resection–anastomosis.

For bronchial NEAF, we performed posterolateral thoracotomy, resection of the fistula, bronchial anastomosis, and gastric-conduit defect repair using a perforator flap. We excluded the gastric conduit (neoesophagus) only when needed to control a life-threatening condition. In this situation, the gastric conduit was completely excluded by proximal esophagostomy and distal stapling, and feeding was via a jejunostomy. A tracheostomy is performed during the same surgery below the NEAF if possible. After improvement of the clinical condition, the esophagus was reconstructed using colon tissue or a jejunal-free flap and the membranous posterior wall of the airway with perforator flaps.



**FIGURE 1.** Technical features of the internal mammary artery perforator flap (IMAP) for acquired nonmalignant postesophagectomy neoesophagus–airway fistula (NEAF) as performed at our center. A, Preoperative skin markings for harvesting a right IMAP flap based on the second intercostal space internal mammary artery perforator. B, The initial step involves making a midline skin incision along the sternum, precisely at the level of the second and third intercostal spaces, extending through the skin down to the fascia. C, Subfascial dissection is carried out until the identification of the IMAPs. D, Individualization of IMAPs. It is crucial to choose the IMAP with the greatest diameter if multiple IMAPs are identified. E, The chosen perforator is dissected in a retrograde manner, passing through both the pectoralis major and intercostal muscle fibers until it reaches its point of origin on the internal mammary artery (IMA). F, The perforator flap is rotated upward to cover the NEAF. G, The IMAP is sutured to the gastric conduit defect with the skin toward the digestive lumen. H, Suture of the skin pad at the level of the digestive defect.

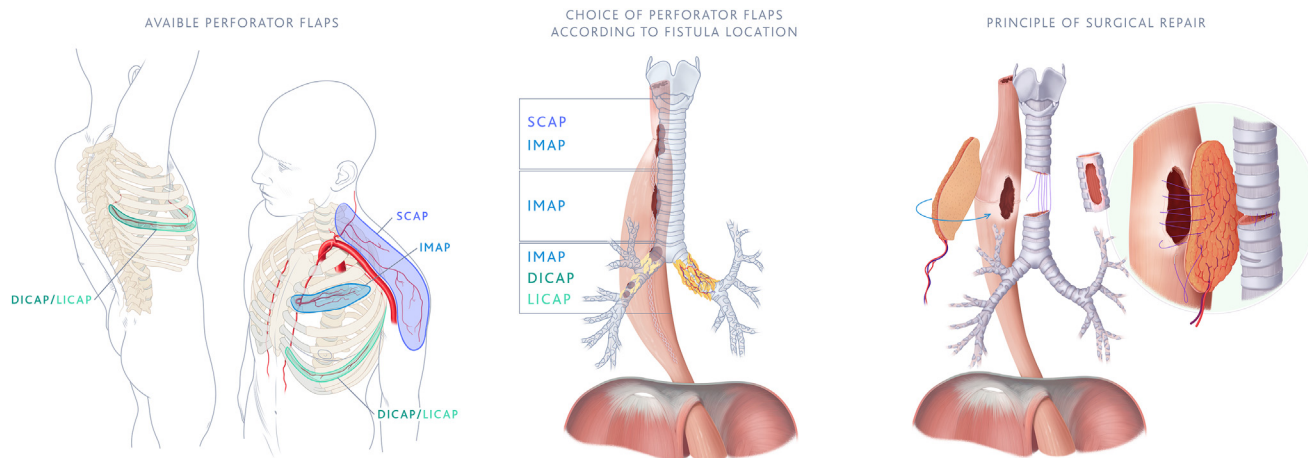
**Postoperative Management**

Patients were extubated as early as possible. Initial empirical systemic broad-spectrum antibiotic therapy was secondarily adjusted based on the microbiological studies of preoperative and intraoperative samples. Tracheobronchial endoscopy was performed routinely during the postoperative period and repeated if needed. Nutritional support was given enterally (jejunostomy or gastrostomy) or parenterally. Oral intake was permitted

after fistula healing was documented by bronchoscopy or upper gastrointestinal follow-through.

**Follow-up**

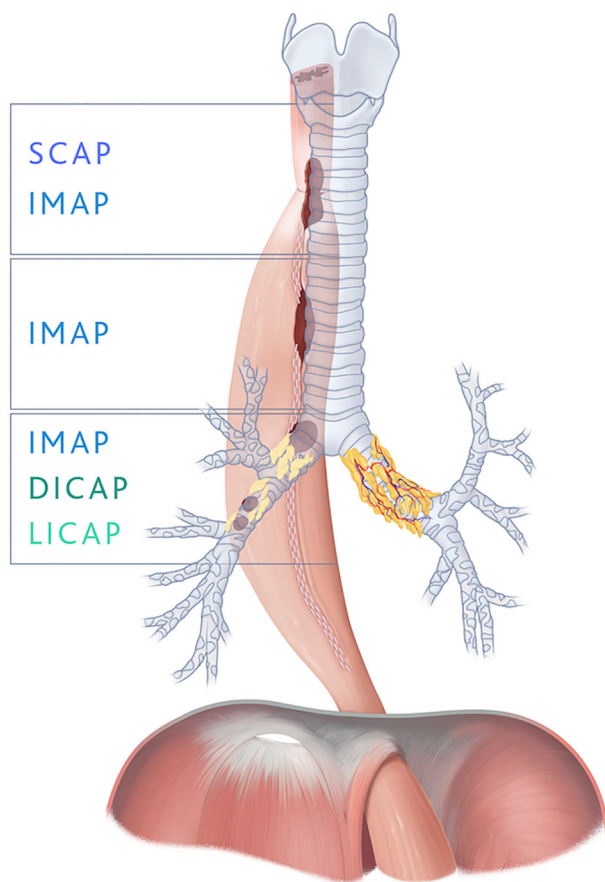
The first follow-up visit occurred 1 month postoperatively at our institution, after discharge. Subsequently, follow-up was provided by the referring center.



**FIGURE 2.** Perforator-flap surgical strategy for acquired nonmalignant postesophagectomy neoesophagus–airway fistula (NEAF) repair used at our center. *Left panel*, 3 types of chest perforator flaps used at our institution to repair NEAF: SCAP, ie, supraclavicular artery perforator flap; IMAP, ie, internal mammary artery perforator flap; and DICAP, ie, dorsal intercostal artery perforator flap, or LICAP, ie, lateral intercostal artery perforator flap. *Middle panel* demonstrates the choice of perforator flap according to the fistula level. Each perforator flaps could manage 3 different level of fistula without compromising their perfusion. *Right panel* illustrates surgical technique of gastric conduit repair using skin pad suture and tracheal repair with resection and direct anastomosis. One should consider the additional role of the flap as vascularized tissue interposition between gastric and tracheal sutures.



### CHOICE OF PERFORATOR FLAPS ACCORDING TO FISTULA LOCATION



**FIGURE 3.** Choice of perforator flaps according to fistula location. *SCAP*, Supraclavicular artery perforator flap; *IMAP*, internal mammary artery perforator flap; *DICAP*, dorsal intercostal artery perforator flap; *LICAP*, lateral intercostal artery perforator flap.

Each follow-up visit included a physical examination and radiologic screening for local and distant recurrences. All adjuvant treatments and new surgeries were recorded.

Day-90 mortality was the primary end point. Overall survival (OS) was calculated from the date of NEAF first repair to the date of death, and censored at the date of last follow-up for patients found to be alive at the most recent follow-up. Disease-free survival (DFS) was calculated from the date of NEAF first repair to the date of first NEAF recurrence evidence, or death, or censored at the date of last follow-up. Postoperative morbidity and functional outcomes were secondary end points. Postoperative morbidity was defined as any postoperative complication within 90 days after the surgery and was classified as described by Dindo and colleagues.<sup>25</sup> Satisfactory long-term function was defined as the absence of dysphagia, or swallowing disorder.

#### Statistical Analysis

Continuous variables were described as median (interquartile range [IQR]) and categorical variables as number (%). OS and DFS were calculated according to Kaplan–Meier. Median follow-up was estimated by reversed Kaplan–Meier. Statistical analysis was performed using SPSS

20.0 for Windows software (IBM Corp). Missing data were managed by contacting the addressing center, general surgeon, and general practitioner of the patient.

## RESULTS

### Patient Characteristics and Details on the Primary Tumor and Fistula

Between August 2009 and July 2021, 11 patients were treated for NEAF at our center. Table 1 provides details on their features, neoadjuvant treatments, and surgical techniques. Details on the fistulas are given in Table 2. Ten patients had had 2-field lymphadenectomy and one (#3) 3-field lymphadenectomy. Gastric reconstruction was through the posterior mediastinum in all patients. Median time between esophagectomy and NEAF diagnosis was 5 months (0.4–21 months). Primary esophagectomies were complicated in 6 cases with an anastomotic leak, 3 cases an anastomotic stenosis and in 2 cases where NEAF occurred from the onset.

### Preoperative Management

Median time from NEAF diagnosis to surgical repair was 42 days [IQR, 35, 110]. The main presenting symptoms were pneumonia and coughing triggered by eating. Three patients (#2, #8, and #10) with early NEAF had septic shock from pneumonia or mediastinitis requiring intensive care unit admission and reintubation; the condition was immediately life-threatening in 2 of these patients (#8 and #10) due to superimposed acute renal failure and central nervous system (Glasgow Coma Scale score 9) alteration. The airway end of the NEAF was in the trachea in 8 patients, left main bronchus in 2 patients, and right main bronchus in 1 patient. NEAF diameter ranged from 0.5 to 4 cm.

Five patients had a tracheostomy at presentation (#1, #2, #3, #9, and #11). Nine patients were weaned off ventilatory assistance before NEAF repair; the other 2 patients (#8 and #10) were those with life-threatening illness. Eight patients had severe undernutrition, with a median body mass index of 20.7 kg/m<sup>2</sup> [IQR, 18, 23] and a median albuminemia of 24.6 g/L [IQR, 23, 34]. Nutritional support was provided via a jejunostomy in 9 patients and via a gastrostomy in 1 patient (#9); the remaining patient (#10) required emergent NEAF repair. The mean calorie intake was 2300 kcal [IQR, 1646, 2475] during prehabilitation. Six patients met criteria for pneumonia,<sup>26,27</sup> and 2 others had also positive bronchial-aspirate cultures; these 8 patients were given antibiotic therapy active on the recovered microorganisms. Before surgical repair, 4 patients (#3, #4, #5, and #8) had implantation of an esophageal self-expanding metal stent (SEMS) positioning to cover the fistula. The preoperative management let us resume MV weaning, infectious control, and weight loss stop in all patients except #8 and #10.

TABLE 1. Esophageal cancer history of 11 patients with nonmalignant acquired postesophagectomy neoesophagus–airway fistula (NEAF) treated in our center

Patient	Sex	Age, y	Comorbidity	Tumor histology	Tumor staging	Tumor location by esophageal third	Primary tumor neoadjuvant/ adjuvant treatment	Esophagectomy surgical approaches	Esophagectomy anastomotic complication	Endoscopic previous treatment
1	M	69	Tobacco	SCC	T3N0R1	Superior		Ivor Lewis followed by pharyngolaryngectomy for positive margins, cervical mechanical anastomosis, full open	Anastomotic fistula followed by anastomotic stenosis	Endoscopic dilatation, esophageal stent
2	F	48	Tobacco, alcohol	SCC	T3N0R0	Middle	5FU plus cisplatin, 45 Gy/70 Gy	McKeown, cervical manual anastomosis, full open	Anastomotic fistula	
3	M	62	Coronaryopathy, diabetes mellitus	ADC	T1N0R0	Inferior	Epirubicin, oxaliplatin plus capecitabine	Transhiatal, cervical mechanical anastomosis, full open	Anastomotic stenosis	Endoscopic dilatation, esophageal stent
4	M	58	Coronaryopathy, LEAD, COPD, tobacco	SCC	T2N0R0	Inferior		Transhiatal, cervical manual anastomosis, full open	Anastomotic stenosis	Endoscopic dilatation, esophageal stent
5	M	61	Hypertension, COPD, diabetes mellitus, tobacco	SCC	T2N0R0	Inferior	Paclitaxel, cisplatin, epirubicin	Ivor Lewis, thoracic mechanical anastomosis, full open	Anastomotic fistula	
6	M	58	LEAD, tobacco	SCC	T3N0R0	Superior	5FU plus cisplatin, 45 Gy	McKeown, cervical mechanical anastomosis, full open	Anastomotic fistula	Esophageal stent
7	M	58	LEAD, tobacco	ADC	T2N0R0	Inferior	5FU plus cisplatin, 45 Gy	McKeown, cervical manual anastomosis, full open	Anastomotic fistula on gastroplasty necrosis	Endoscopic dilatation, esophageal stent
8	M	60	COPD, tobacco	ADC	NA	Inferior	5FU plus oxaliplatin/ 5FU plus cisplatin	Ivor Lewis, thoracic mechanical anastomosis, full open	Anastomotic fistula followed by anastomotic stenosis	
9	M	75	LEAD, hypertension, tobacco	ADC	T1N0R0	Inferior		Transhiatal, cervical manual anastomosis, full open	NEAF	
10	M	53	COPD, tobacco	SCC	T0N1R0	Middle	Carboplatin plus paclitaxel, 41.4 Gy	McKeown, cervical manual anastomosis, coeli thoracoscopy	Anastomotic fistula on gastroplasty necrosis	
11	M	61	Tobacco, cirrhosis, alcohol	ADC	T2N0R0	Superior	LV5FU2 plus cisplatin	McKeown, cervical manual anastomosis, full open	NEAF	

M, Male; SCC, squamous cell carcinoma; F, female; 5FU, fluorouracil; ADC, adenocarcinoma; LEAD, lower extremity artery disease; COPD, chronic obstructive pulmonary disease; NA, not available; NEAF, neoesophagus–airway fistula.

TABLE 2. Fistula characteristics and surgical repair in the 11 patients with nonmalignant acquired postesophagectomy neoesophagus–airway fistula (NEAF)

Patient no.	Time from esophagectomy to fistula diagnosis, mo	Fistula location, length (cm), and carina-vocal cords distance, cm	Time from fistula diagnosis to repair, d	Surgical techniques for fistula repair	Time to fistula closure in months in days since surgery	Follow-up since surgery	Outcome at last follow-up
1	32	Gastrotracheal 0.6 (3.5/7.5)	109	Dartevelle transclavicular approach for DICAP flap patched on the trachea and gastric conduit		4	Died with late* fistula recurrence
2	0.5	Gastrotracheal 3 (6/4)	96	Cervicomantubriotomy for IMAP flap patched on the gastroplasty, and tracheal resection-anastomosis with the Montgomery maneuver	15	70	Died without fistula recurrence
3	8	Gastrotracheal 1.5 (3/6)	5	Cervicomantubriotomy for IMAP flap patched on the gastric conduit, and tracheal resection-anastomosis	8	21	Lost to follow-up
4	19	Gastrotracheal 3 (7/3)	74	Cervicomantubriotomy for pedicled pericardial flap patched on the gastric conduit, and tracheal resection-anastomosis with Dedo-Fishman maneuver	9	118	Died without fistula recurrence
5	0.5	Gastro–left main bronchus 1	206	Right thoracotomy for direct suture of the gastric conduit and pedicled pericardial flap patched on the bronchus		0.7	Died with early* fistula recurrence
6	2	Gastrotracheal 1 (5/5)	42	Dartevelle transclavicular approach for IMAP flap patched on the gastric conduit and tracheal resection-anastomosis with Dedo-Fishman maneuver	168	13	Died with local tumor recurrence
7	23	Gastro–right main bronchus 2	36	Right thoracotomy for esophagostomy, gastric conduit resection, IMAP flap patched on the bronchus	11	100	Alive without upper airway or digestive tract dysfunction
8	0.5	Gastrotracheal 1.5 (2/10)	35	Right thoracotomy for esophagostomy, direct tracheal suture covered by serratus anterior flap		0.5	Died with early* fistula recurrence
9	195	Gastrotracheal 0.5 (8/3)	38	Cervicotomy for direct suture of the gastric conduit with sealant, tracheotomy and direct suture of the fistula	10	27	Alive without upper airway or digestive tract dysfunction

(Continued)

TABLE 2. Continued

Patient no.	Time from esophagectomy to fistula diagnosis, mo	Fistula location, length (cm), and carina-vocal cords distance, cm	Time from fistula diagnosis to repair, d	Surgical techniques for fistula repair	Time to fistula closure in days since surgery	Follow-up since surgery	Outcome at last follow-up
10	0.3	Gastro–left main bronchus 1	8	Right thoracotomy for DICAP flap patched on the bronchus, covering the gastroplasty		34	Died with late* fistula recurrence
11	5	Gastrotracheal 4 (4/5.3)	176	Cervicomansubriotomy for SCAP flap patched on the gastric conduit, and tracheal resection–anastomosis covered by the tracheotomy		11	Died with late* fistula recurrence

DICAP, Dorsal intercostal artery perforator flap; IMAP, internal mammary artery perforator flap; SCAP, supraclavicular artery perforator flap. \*The cutoff for distinguishing early from late NEAF recurrence was postoperative day 90.

### Surgical Techniques

Table 2 provides details on the surgical procedures. A flap was used in 10 of the 11 patients; 7 were perforator flaps, 2 pericardial flaps, and 1 a serratus anterior flap. Of the 8 patients with tracheal fistulas, 5 underwent tracheal resection–anastomosis.

Direct suturing was performed to close the tracheal defect in 2 patients and the gastric defect in 2 other patients. Of the 2 patients diverted, one had an esophagostomy and the other an esophagostomy and gastric–conduit resection.

### Postoperative Management and Complications

Median length of stay was 32 days. Nutritional support was restarted as soon as possible with a median daily intake of 2147 kcal [IQR, 1646, 2475]. Weaning off MV was achieved after a median of 1 day [IQR, 1, 2]. In 1 patient (#8), severe refractory pneumonia required extracorporeal membrane oxygenation.

Pneumonia developed postoperatively in 5 patients and consistently responded to antibiotic therapy. One patient (#3) experienced manubrium necrosis and another (#11) mediastinitis; surgical treatment was successful in both. Tracheal stenosis developed in 1 patient (#6) and was treated initially by endoscopic dilatation followed on postoperative day 140 by resection anastomosis; the stenosis had not recurred when this patient died at 13 months from tumor recurrence at the carina. Patient #7 underwent digestive-tract continuity restoration using a jejunal-free flap at 5 months.

### Other Outcomes

Median follow-up was 100 months (Table 2). Median OS was 34 months and median DFS 11 months. One patient was lost to follow-up. Of the remaining 9 patients, 2 were alive with good upper airway and digestive-tract function, 27 and 100 months after surgery, respectively.

NEAF healing was documented by endoscopy (not systematic) in 6 patients at a median of 11 days [IQR, 9, 53] after surgery. At last follow-up, all 6 reported being able to eat normally. Two of these patients had dysphonia related to unilateral recurrent nerve palsy. Four of the 5 patients managed by tracheal resection–anastomosis experienced fistula healing, after a median follow-up of 50 months. Fistula healing was also documented in 1 of the 4 patients managed using an airway patch and in 1 of the 2 patients managed with direct fistula suturing (#8 and #9).

### NEAF Recurrence

All 5 patients with NEAF recurrence died during follow-up. Two of these patients had early fistula recurrence and died within 90 days after the first repair procedure despite emergency salvage surgery. Three patients (#1, #10, and #11) had late recurrence, after day 90. One of these patients (#1) died from aspiration pneumonia on day 128 after surgery in circumstances that precluded a second repair attempt. Another (#10) had repeat surgery 10 months after the initial procedure for flap repositioning with interrupted sutures through a sternotomy; a further recurrence 1 year later led to the implantation of a tracheal SEMS to prevent pneumonia followed by direct gastric–conduit suturing and latissimus dorsi interposition through a right lateroposterior thoracotomy. This patient died from a further NEAF recurrence 30 months after the initial procedure. Finally, patient #11 was treated 3 months after the initial repair by direct NEAF suture and a new supraclavicular artery perforator flap but experienced another recurrence and died 10 months after the initial repair.

In this group of patients, primary esophagectomy always included mediastinal lymph node dissection and no one underwent transhiatal approach. Time from primary esophagectomy to diagnosis was shorter with a median of

0.5 months [IQR, 0.5, 5] versus 13.5 months [IQR, 3.5, 22]. Finally, time from diagnosis to NEAF repair was longer with a median of 109 days [IQR, 35, 176] versus 40 days [IQR, 36.5, 66].

## DISCUSSION

Of the 11 patients who underwent NEAF surgical repair at our center over a 10-year period, 6 experienced NEAF healing and resumed oral intake. The NEAF recurred in 5 patients, all of whom died. A flap was used in all the patients but one, and tracheal resection–anastomosis was performed in 5 of the 8 patients with tracheal fistulas.

Airway resection–anastomosis for NEAF repair has been described as inadvisable.<sup>28,29</sup> However, of the 6 patients whose fistula healed in our study, 4 had had airway resection–anastomosis. Once the fistula is established, tracheal resection–anastomosis may be preferable over direct suturing or patching of an ischemic and inflammatory site. According to one view, the airway abnormality responsible for fistula formation is confined to the membranous wall and should be managed with primary repair or patch reconstruction.<sup>28,29</sup> However, for tracheal fistulas, an anterior approach allows perforator-flap repair of the gastric conduit. A short tracheal resection–anastomosis is then reasonable, as the perforator flap supplies blood vessels and the remaining vessels are spared by using the anterior approach. Moreover, a perforator flap allows tension-free closure of the digestive fistula orifice with no further risk of stenosis.<sup>30</sup> As demonstrated for pharyngoesophageal reconstruction, the musculocutaneous part of the perforator flap provides good swallowing function.<sup>31</sup> For tracheal mobilization, the Dartevelle approach and Dedo–Fishman or Montgomery maneuver can be used to remain consistent with recommendations by Grillo regarding the transtracheal approach for gastric repair.<sup>22–24,32</sup> Similarly, for bronchial NEAF, using a perforator flap provides tension-free posterior-wall closure and material-free airway repair, thereby minimizing the risk of subsequent bronchomalacia and stenosis.<sup>33</sup> In our 3 patients with bronchial fistulas, perforator flap reconstruction produced airtight wall closure with a skin-based rigid structure capable of resisting damage from digestive-tract secretions. In addition, perforator flaps offer the versatility and plasticity needed to reach any fistula site, and they also fill the mediastinal space with no risk of airway or gastric conduit compression.

In critically ill patients, tracheal or bronchial resection after esophagectomy would carry an unacceptably high risk of anastomotic complications. NEAF often results in life-threatening conditions such as severe sepsis and undernutrition. Measures must therefore be taken to improve health before surgery. They include weaning off MV, providing nutritional support, treating airway and pulmonary inflammation or infection, and controlling sepsis. These measures were applied in our patients; however, 2 patients (#8 and

#10) could not be weaned off MV due to life-threatening illness and, among them, one (#10) required emergent surgery before the initiation of nutritional support. Preoperative implantation of an esophageal SEMS, as performed in 2 of our 6 patients with NEAF healing (#3 and #4), may be helpful. In a retrospective study of 58 patients with gastric-airway fistulas, single stent implantation achieved sealing in three-quarters and healing in a third of cases; 7 patients were alive and eating normally at the end of follow-up, which ranged from four to 61 months.<sup>34</sup> Placement of 2 stents, each covering one of the fistula orifices, obviated the need for emergency surgery in 11 of 13 patients with NEAF after esophagectomy for cancer, allowing improvements in health status.<sup>35</sup> Nonetheless, caution may be in order, as stenting worsen local ischemia between the gastric conduit and trachea; of our 11 patients, 5 had been treated with esophageal stenting before the diagnosis of NEAF. Moreover, stenting has been reported to increase NEAF size, notably with double tracheal and digestive stenting.<sup>16</sup> Prompt surgical repair of stented but unhealed NEAF may therefore be required to prevent stent-induced tracheal and gastric-conduit injury. We suggest leaving previously deployed stents in place until surgical repair can be performed and removing the stents during surgery.

Neoadjuvant therapy was given to 8 of our 11 patients before esophagectomy. This proportion is substantially greater than in other cohorts,<sup>16,35,36</sup> suggesting that our patients had more advanced esophageal cancer and may therefore have been at high risk for NEAF repair failure. Use of a perforator flap can bridge large defects with well-vascularized tissue that constitutes a strong barrier between the repaired airway and the digestive tract.

The limitations of our study include the retrospective design, which may have resulted in information bias. Although this case series is relatively small, it provides valuable insights, given the condition's high mortality rate. With 11 repairs performed and 6 long-term survivors, this dataset offers robust guidance for managing this challenging condition. Changes in management may have occurred during the 10-year recruitment period. All patients were managed at the same high-volume university center, limiting the general applicability of our data. We advocate the presence of specialized plastic surgeon for this complex surgery. The high proportion of patients given neoadjuvant therapy before esophagectomy suggests selection bias. Other studies of NEAF repair also used a single-center retrospective design. A meta-analysis of these studies and ours might produce a greater level of evidence.

In conclusion, NEAF healing can be achieved by surgery after preoperative treatment to improve the health status. Perforator-flap repair of the gastric conduit, and tracheal resection–anastomosis in patients with tracheal involvement, could provide satisfactory outcomes for swallowing disorder and dysphagia.



### Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

### References

- Koshenkov VP, Yakoub D, Livingstone AS, Franceschi D. Tracheobronchial injury in the setting of an esophagectomy for cancer: postoperative discovery a bad omen. *J Surg Oncol*. 2014;109:804-7. <https://doi.org/10.1002/jso.23577>
- Maruyama K, Motoyama S, Sato Y, Hayashi K, Usami S, Minamiya Y, et al. Tracheobronchial lesions following esophagectomy: erosions, ulcers, and fistulae, and the predictive value of lymph node-related factors. *World J Surg*. 2009;33:778-84. <https://doi.org/10.1007/s00268-008-9871-7>
- Gudovsky LM, Koroleva NS, Biryukov YB, Chernousov AF, Perelman MI. Tracheoesophageal fistulas. *Ann Thorac Surg*. 1993;55:868-75. [https://doi.org/10.1016/0003-4975\(93\)90108-t](https://doi.org/10.1016/0003-4975(93)90108-t)
- Mendelsohn FA, Divino CM, Reis ED, Kerstein MD. Wound care after radiation therapy. *Adv Skin Wound Care*. 2002;15:216-24. <https://doi.org/10.1097/00129334-200209000-00007>
- Kron IL, Johnson AM, Morgan RF. Gastrotracheal fistula: a late complication after transhiatal esophagectomy. *Ann Thorac Surg*. 1989;47:767-8. [https://doi.org/10.1016/0003-4975\(89\)90139-2](https://doi.org/10.1016/0003-4975(89)90139-2)
- Fujita H, Kawahara H, Hidaka M, Nagano T, Yoshimatsu H. An experimental study on viability of the devascularized trachea. *Jpn J Surg*. 1988;18:77-83. <https://doi.org/10.1007/BF02470850>
- Hulscher JBF, ter Hofstede E, Kloek J, Obertop H, de Haan P, van Lanschot JJB. Injury to the major airways during subtotal esophagectomy: incidence, management, and sequelae. *J Thorac Cardiovasc Surg*. 2000;120:1093-6. <https://doi.org/10.1067/mtc.2000.110182>
- Nordin U. The trachea and cuff-induced tracheal injury. An experimental study on causative factors and prevention. *Acta Oto-Laryngol Suppl*. 1977;345:1-71.
- Buskens CJ, Hulscher JBF, Fockens P, Obertop H, van Lanschot JJB. Benign tracheo-neo-esophageal fistulas after subtotal esophagectomy. *Ann Thorac Surg*. 2001;72:221-4. [https://doi.org/10.1016/S0003-4975\(01\)02701-1](https://doi.org/10.1016/S0003-4975(01)02701-1)
- Song S-W, Lee H-S, Kim MS, Lee JM, Kim JH, Zo JI. Repair of gastrotracheal fistula with a pedicled pericardial flap after Ivor Lewis esophagogastrctomy for esophageal cancer. *J Thorac Cardiovasc Surg*. 2006;132:716-7. <https://doi.org/10.1016/j.jtcvs.2006.05.030>
- Yasuda T, Sugimura K, Yamasaki M, Miyata H, Motoori M, Yano M, et al. Ten cases of gastro-tracheobronchial fistula: a serious complication after esophagectomy and reconstruction using posterior mediastinal gastric tube. *Dis Esophagus*. 2012;25:687-93. <https://doi.org/10.1111/j.1442-2050.2011.01309.x>
- Muniappan A, Wain JC, Wright CD, Donahue DM, Gaissert H, Lanuti M, et al. Surgical treatment of nonmalignant tracheoesophageal fistula: a thirty-five year experience. *Ann Thorac Surg*. 2013;95:1141-6. <https://doi.org/10.1016/j.athoracsur.2012.07.041>
- Mathisen DJ, Grillo HC, Wain JC, Hilgenberg AD. Management of acquired nonmalignant tracheoesophageal fistula. *Ann Thorac Surg*. 1991;52:759-65. [https://doi.org/10.1016/0003-4975\(91\)91207-C](https://doi.org/10.1016/0003-4975(91)91207-C)
- Dartevelle P, Macchiarini P. Management of acquired tracheoesophageal fistula. *Chest Surg Clin N Am*. 1996;6:819-36.
- Macchiarini P, Verhoye JP, Chapelier A, Fadel E, Dartevelle P. Evaluation and outcome of different surgical techniques for postintubation tracheoesophageal fistulas. *J Thorac Cardiovasc Surg*. 2000;119:268-76. [https://doi.org/10.1016/S0022-5223\(00\)70182-6](https://doi.org/10.1016/S0022-5223(00)70182-6)
- Lambertz R, Hölscher AH, Bludau M, Leers JM, Gutschow C, Schröder W. Management of tracheo- or bronchoesophageal fistula after Ivor-Lewis esophagectomy. *World J Surg*. 2016;40:1680-7. <https://doi.org/10.1007/s00268-016-3470-9>
- Schweigert M, Dubez A, Beron M, Muschweck H, Stein HJ. Management of anastomotic leakage-induced tracheobronchial fistula following oesophagectomy: the role of endoscopic stent insertion. *Eur J Cardiothorac Surg*. 2012;41:e74-80. <https://doi.org/10.1093/ejcts/ezr328>
- Bartels HE, Stein HJ, Siewert JR. Respiratory management and outcome of non-malignant tracheo-bronchial fistula following esophagectomy. *Dis Esophagus*. 1998;11:125-9. <https://doi.org/10.1093/dote/11.2.125>
- Hammoudeh ZS, Gursel E, Baciewicz FA. Split latissimus dorsi muscle flap repair of acquired, nonmalignant, intrathoracic tracheoesophageal and bronchoesophageal fistulas. *Heart Lung Circ*. 2015;24:e75-8. <https://doi.org/10.1016/j.hlc.2014.12.166>
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Bull World Health Organ*. 2007;85:867-72. <https://doi.org/10.2471/BLT.07.045120>
- Gyawali B, Ramakrishna K, Dhamoon A. Sepsis: the evolution in definition, pathophysiology, and management. *SAGE Open Med*. 2019;7:205031211983504. <https://doi.org/10.1177/2050312119835043>
- Grillo HC, Moncure AC, McEnany MT. Repair of inflammatory tracheoesophageal fistula. *Ann Thorac Surg*. 1976;22:112-9. [https://doi.org/10.1016/s0003-4975\(10\)63971-9](https://doi.org/10.1016/s0003-4975(10)63971-9)
- Montgomery WW. The surgical management of supraglottic and subglottic stenosis. *Ann Otol Rhinol Laryngol*. 1968;77:534-46. <https://doi.org/10.1177/000348946807700314>
- Dedo HH, Fishman NH. Laryngeal release and sleeve resection for tracheal stenosis. *Ann Otol Rhinol Laryngol*. 1969;78:285-96. <https://doi.org/10.1177/000348946907800208>
- Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205-13. <https://doi.org/10.1097/01.sla.0000133083.54934.ae>
- Low DE, Alderson D, Ceccanello I, Chang AC, Darling GE, D'Journo XB, et al. International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG). *Ann Surg*. 2015;262:286-94. <https://doi.org/10.1097/SLA.0000000000001098>
- Jensen GL, Cederholm T, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition: a consensus report from the global clinical nutrition community. *J Parenter Enter Nutr*. 2019;43:32-40. <https://doi.org/10.1002/jpen.1440>
- Balakrishnan A, Tapias L, Wright CD, Lanuti MX, Gaissert HA, Mathisen DJ, et al. Surgical management of post-esophagectomy tracheo-bronchial-esophageal fistula. *Ann Thorac Surg*. 2018;106:1640-6. <https://doi.org/10.1016/j.athoracsur.2018.06.076>
- Shen KR, Allen MS, Cassivi SD, Nichols FC, Wigle DA, Harmsen WS, et al. Surgical management of acquired nonmalignant tracheoesophageal and bronchoesophageal fistulas. *Ann Thorac Surg*. 2010;90:914-9. <https://doi.org/10.1016/j.athoracsur.2010.05.061>
- Bertheuil N, Duisit J, Isola N, Lengelé B, Bergeat D, Meunier B. Perforator-based intercostal artery muscle flap: a novel approach for the treatment of tracheoesophageal or bronchoesophageal fistulas. *Plast Reconstr Surg*. 2021;147:795e-800e. <https://doi.org/10.1097/PRS.00000000000007892>
- Huang TC, Hsu YC, Chen HC, Chang SC, Chen HH. Functional outcome analysis after anterolateral thigh flap reconstruction of pharyngo-esophageal defect. *Ann Plast Surg*. 2015;75:174-9. <https://doi.org/10.1097/SAP.0000000000000073>
- Dartevelle P, Chapelier A, Macchiarini P, Cerrina J. Transcervical excision of bronchopulmonary cancers with apical invasiveness. *Rev Pneumol Clin*. 1992;48:211-6.
- Favere K, Vanderbiest K, Bresseleers J, Depuydt P. Benign gastrobronchial fistula following oesophagectomy in a patient presenting with respiratory failure. *BMJ Case Rep*. 2019;12:e228537. <https://doi.org/10.1136/bcr-2018-228537>
- Wang H, Tao M, Zhang N, Zou H, Li D, Ma H, et al. Single application of airway stents in thoracogastric-airway fistula: results and prognostic factors for its healing. *Ther Adv Respir Dis*. 2019;13:1753466619871523. <https://doi.org/10.1177/1753466619871523>
- Elbe P, Lindblad M, Tsai J, Juto J-E, Henriksson G, Agustsson T, et al. Non-malignant respiratory tract fistula from the oesophagus. A lethal condition for which novel therapeutic options are emerging. *Interact Cardiovasc Thorac Surg*. 2013;16:257-62. <https://doi.org/10.1093/icvts/ivs478>
- Lindner K, Lübke L, Müller A-K, Palmes D, Senninger N, Hummel R. Potential risk factors and outcomes of fistulas between the upper intestinal tract and the airway following Ivor Lewis esophagectomy. *Dis Esophagus*. 2017;30:1-8. <https://doi.org/10.1111/dote.12459>

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