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Review

Surgical complications and functional outcomes of 3191 jejunal free flaps used for reconstruction of circumferential defects following head and neck cancer resections: A systematic review

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ABSTRACT

Pedicled, fasciocutaneous and visceral flaps are all widely adopted for reconstruction after ablative surgery for advanced laryngeal, hypopharyngeal and cervical oesophageal cancers. With multiple options available, the choice depends on type and extent of the defect, patient's general conditions and institution expertise or preference.

Since its first description in 1959, the use of jejunal free flap (JFF) has been refined thanks to the introduction of microvascular anastomoses, progressively allowing to achieve low mortality and morbidity rates. Both swallowing and speech outcomes are also positively reported across studies.

A systematic review of English literature on JFF in H&N cancer reconstruction published after 2000 was carried out on Medline and Embase. Thirty-six studies were included in the analysis with a total of 3191 JFF reconstructions. Primary outcomes were surgical complications and functional outcomes (quality of speech and oral alimentation). A cumulative review was created pooling complication rates reported in single studies, and overall rates were obtained for fistulas (11.39%), strictures (14.17%), total and partial flap failure (4.79 and 6.15% respectively) and perioperative mortality (3.1%). Functional outcomes were variably reported, with different qualitative and quantitative assessment methods showing overall positive results. When reported, we've included impact of adjuvant radiotherapy and the ability of JFF to tolerate it has been widely confirmed. Above results have also been compared with same outcomes registered for different flaps.

Overall, studies over the past 20 years demonstrate good clinical and functional outcomes, proving JFF to be a reliable and safe method for reconstructing circumferential pharyngoesophageal defects.

Introduction

The management of advanced laryngeal, hypopharyngeal and cervical oesophageal cancers, often requires multimodal approach with surgery being either primary treatment or intervening as a salvage. Extensive resections are required to obtain negative margins, resulting in large circumferential defects. Reconstruction aims at maintaining a conduit for food passage as well as providing acceptable speech and swallow functions.

Over the years different reconstruction methods have been developed using various types of flaps. Two types of flaps are generally used, namely pedicled or free flaps. The choice depends on type and extent of the defect, patient's general conditions, previous treatments to the neck and institution expertise or preference.

Pectoralis major (PM) is the most commonly used pedicled flap for hypopharyngeal defect reconstructions; it is a versatile and reliable flap, easy to harvest and generally gives low donor site morbidity. It can however be too bulky and cause strictures.

Among free flaps, fasciocutaneous free flaps (FCFF) like radial forearm free flap (RFFF) and anterolateral thigh (ALT) are commonly used in reconstructing upper aerodigestive tract (UADT) defects. They are pliable, amenable to shaping and, particularly ALT, is suitable for reconstructing large defects. An issue commonly reported with free flaps is a higher fistula rate, likely related to the multiple suture lines.

Among visceral free flaps both jejunal free flap (JFF) and gastric pullup (GPU) can be used to reconstruct large circumferential pharyngo-

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esophageal defects. GPU has historically been associated with high mortality and morbidity [1].

The use of the JFF for reconstruction of the UADT was first described in 1959 by Seidenberg et al. who published their results of an experimental study where they used JFF following a pharyngolaryngectomy [2]. In 1961, Roberts et al. [3] published the first successful case report of this type of reconstruction, where the patient was reported to survive the procedure and regain swallowing function.

Since then, the technique has been progressively refined and higher success rates have been achieved thanks to the introduction and advancement of microvascular procedures [4–6]. Currently JFF are being used with reasonable outcomes and relatively low mortality and morbidity.

Good functional outcomes both in terms of swallowing and speech are reported for JFF. Advantages in swallowing outcomes are likely related to its intrinsic similarity to pharyngo-oesophageal structures, being jejunum a lubricated, mucosa-lined, tubular structure with peristaltic activity.

In terms of speech rehabilitation, it is generally believed that FCFF provide better voice quality compared to "wet voice" of JFF. However, highly functional tracheo-oesophageal voices following JFF reconstructions, non-inferior to that obtained with FCFF, have been described [7,8].

According to recent multidisciplinary guidelines on head and neck (H&N) cancers management, a jejunal flap would be indicated for a circumferential defect with less than 3.5 cm of residual pharyngeal mucosa and when the inferior anastomosis is above the clavicle [9].

The aim of this systematic review was to compile, evaluate and present surgical complications and provide an accurate representation of oncological and functional outcomes following pharyngoesophageal defects reconstruction with JFF.

Methodology

Search strategy

A systematic review of published literature on JFF in H&N cancer reconstruction was carried out in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Medline and Embase were searched with no search filters applied. Combinations of the following free terms and MeSH terms were used: "Jejunum"[Mesh], "Free Tissue Flaps"[Mesh], "Laryngeal Neoplasms"[Mesh], "Esophageal Neoplasms"[Mesh], jejun* free flap, pharyn* cancer*, laryn* cancer*, hypopharyn* cancer*, cervical esophag* cancer*, pharyngoesophageal defect*, laryn* defect*, circumferential defect*, laryngopharyngeal cancer*, laryngopharyngeal defect*. Truncation was used to ensure inclusion of most relevant studies. Duplicate articles were eliminated. Studies which reported at least one of the primary outcomes (defined below), and used JFF for circumferential defects, were included in our analysis. Animal studies, non-English articles, small case series (less than 10 subjects) and case reports, studies where the data of the target patient population could not be separated from other cohorts, review articles, articles with patients with partial or near circumferential pharyngoesophageal defects, patients with circumferential defects not related to H&N cancers (e.g. due to corrosive injuries), patients undergoing JFF where further reconstruction was done; and studies published before the year 2000, were all excluded from this review. In studies with overlapping patient populations, the most recent study was included. Relevant data was collected; data was excluded if not clear for our population of interest or not separated from other patient populations in the study.

Primary outcomes

- Surgical complications, recorded as number of events:
  - o Fistula and anastomotic leak rate
  - o Stricture rate
  - o Flap failure; reported cases of total flap loss and flap necrosis were counted under flap failure. Cases where patients were taken to theatre for exploration and review of the microvascular anastomosis, or where a partial flap loss was reported, were counted under partial flap failure
  - o Perioperative mortality; defined as 30 days *peri*-operatively or during hospital admission following reconstruction
  - o Peri-operative reoperation; defined as 30 days *peri*-operatively or during hospital admission following reconstruction
- Functional outcomes, described in quantitative or qualitative measures:
  - o Quality of speech
  - o Oral alimentation

Secondary outcomes

- Donor site morbidity
- Other complications

Complication rates recorded in each study were pooled to create a cumulative review.

Results

The initial search yielded 1233 articles. After elimination of duplicate results, 533 studies remained for further screening. A further 123 articles were excluded based on title alone, leaving 410 studies to undergo abstract screening to determine eligibility for inclusion. Of these, 163 articles were determined eligible for full text screening, of which 29 articles met the inclusion criteria (reasons for exclusion listed in Figure 1). Furthermore, 7 articles that met our inclusion criteria were identified through references of articles and were included in the analysis.

Patient demographics

A total of 3191 reconstructions were analysed, with a male predominance (992 males, 349 females) and a mean patient age of 62.5 years (range 25–93). Primary site of cancer was reported in 17 studies; the most common indication was hypopharyngeal cancer, reported as an indication in 597 patients, with oesophageal (263 patients) and laryngeal (66 patients) cancers ranking as second and third most common indications for reconstruction, respectively. Other indications for reconstruction included thyroid, advanced oropharyngeal and tracheal cancers. Mean hospital stay and follow-up were reported in 11 and 6 studies respectively; patients were hospitalized for a mean of 25.6 days (range 6–350), and followed for a mean of 30 months (range 0.1–162).

Clinical outcomes

All studies reported at least one of the primary clinical outcomes.

Fistula and anastomotic leak **(**Table 1**):**

Fistula and anastomotic leak were combined as a single outcome, and were collectively reported in 31 studies. A total of 301/2642 (11.39 %) patients developed fistulas, ranging between 0–35.29 %. Table 1 shows the relationship between developing fistula/anastomotic leak and previous RT (salvage cases); out of 175 salvage cases, 22 patients developed fistula (RR = 2.46, p = 0.004).

Stricture/stenosis **(**Table 2**):**

This complication was reported in 22 studies and was the most commonly reported primary outcome, occurring in 178/1256 patients (14.17 %; ranging from 0–33.3 % among studies). Five studies reported data on 67 patients who underwent adjuvant RT; 18 of these patients developed stricture, with a calculated relative risk (RR) of 4.83 (p = 0.0082)**.** One study [10] reported the rate of stricture in salvage cases

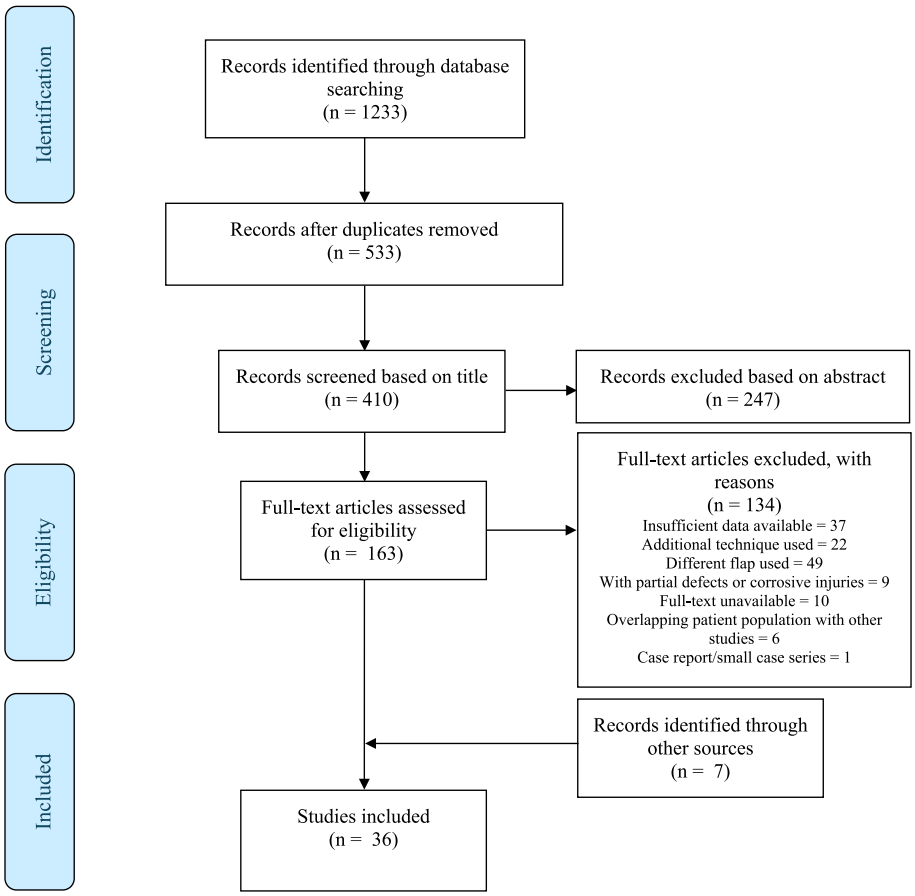

Figure 1. PRISMA flow chart.

(described in text as pre-operative RT), with stricture developing in 9/86 salvage cases (RR = 0.63, p = 0.24).

Flap failure **(**Table 3**):**

Flap failure was documented in 29 studies and affected 90/1880 patients (4.79 %), whereas partial flap failure was documented in 6 studies and affected 34/553 patients (6.15 %). In salvage cases, RR of flap failure = 1.28 (p = 0.68).

Re-operation **(**Table 4**):**

In 10 studies, a total of 89/834 patients (10.67 %) underwent re-operation. The most common indications were revision of the micro-vascular anastomosis (documented here as partial flap failure) and flap failure (3 % and 2.64 %, respectively). Other indications included bleeding (0.96 %), management of anastomotic leak, and donor-site complications. Perez-Smith et al. [11] mentioned that 25 patients were re-operated on for either partial flap failure or evacuation of haematoma; these cases were counted as "other/not specified" as no distinction was made.

Peri-operative mortality **(**Table 4**):**

Twenty-one articles recorded *peri*-operative mortality rate as defined previously, with a total of 49/1580 (3.1 %, range 0–17.39 %) deaths within 30 days from the operation or within hospital admission for surgery.

Donor site morbidity:

A total of 91/1249 patients experienced complications related to donor site (7.29 %) as reported by 12 studies. The majority were related to surgical wound including infection, dehiscence and bleeding (4.56 %), followed by functional complications including ileus, pyloric spasm, intussusception and intestinal torsion causing obstruction (1.6 %), and other unspecified complications (14 %).

Other complications:

Other complications were reported in 694/1902 patients (36.49 %), most of which were infective (15.09 %), followed by medical (5.57 %), operative-site (5.52 %), functional (3.52 %), haemorrhagic (2.21 %), and tracheostomy-related complications (1.47 %). Others included iatrogenic injuries and otherwise non-specified complications (3.1 %).

Long-term survival:

This outcome was reported in 11 studies**.** Survival rates at 1 year were reported in 4 articles, ranging from 70.5 % – 83.8 %. Five studies reported 2 years survival rates, ranging between 49.4 % and 84 %. Four studies reported survival at 3 years, ranging from 47 % to 67.6 %. Survival rates at 5 years were reported in 8 articles (26 % – 54 %.) Two studies reported survival at 10 years, rates recorded were 15 % and 19 %.

Functional outcomes

Feeding/swallowing **(**Table 5**):**

A total of 13 studies provided a qualitative assessment of swallowing. Only 58 % of patients were able to return to a solid diet (ranging between 20.45–100 % as reported in single studies); however, 86.26 % of patients maintained a fully oral diet without the need for any additional feeding adjuncts. Use of feeding adjuncts was reported in 7 studies; 3 studies reported on the use of tube feeding post-operatively, with a total of 22/67 patients reliant partially or fully on tube feeds for their diet (32.84 %). Four studies reported on the use of gastrostomy feeding; out of 436 patients, 31 were partially or fully reliant on gastrostomy feeds (6.80 %).

Additionally, 4 articles performed quantitative assessment using scales or other defined outcomes. Radionuclide oesophageal scintigraphy was used to assess clearance rates and compare them to physiologic rate (> 90 % clearance), with 12 jejunal flaps averaging 69 % ± 17 % (10). The University of Washington Quality of Life (UW-QOL)

Table 1
Fistula/anastomotic leak rates, and rates in salvage cases.

Reference	Patient No.	No. included	Leak/fistula	Percentage
Daiko et al. [33]	50	50	2	4.00 %
Elfeky et al. [44]	37	37	3	8.11 %
Ikeguchi et al. [26]	22	22	2	9.09 %
Lee et al. [22]	32	32	1	3.13 %
Miyata et al. [34]	58	58	10	17.24 %
Ferahkose et al. [27]	14	14	0	0.00 %
Ott et al. [35]	109	109	29	26.61 %
Numajiri et al. [25]	10	10	0	0.00 %
Ida et al. [36]	14	14	1	7.14 %
Laing et al. [18]	31	31	3	9.68 %
Yu et al. [32]	31	31	1	3.23 %
Chang et al. [20]	168	168	23	13.69 %
Triboulet et al. [45]	77	77	25	32.47 %
Chan et al. [46]	89	86[1]	4	4.65 %
Chen et al. [47]	12	12	0	0.00 %
Hanson et al. [15]	23	23	0	0.00 %
Hong et al. [48]	18	18	1	5.56 %
Hsieh et al. [49]	16	16	5	31.25 %
Lewin et al. [31]	31	31	1	3.23 %
Nyquist et al. [23]	24	19[2]	4	21.05 %
Perez- Smith et al. [11]	368	368	30	8.15 %
Sharp et al. [39]	19	19	2	10.53 %
Walker et al. [19]	104	104	11	10.58 %
Omura et al. [50]	10	10	0	0.00 %
Park et al. [29]	61	61	18	29.51 %
Tan et al. [24]	10	10	3	30.00 %
Mehrara etl al. [38]	105	105	8	7.62 %
Miyamoto et al. [37]	274	274	7	2.55 %
Denewer et al. [30]	28	25[1]	2	8.00 %
Sugiyama et al. [21]	773	757[3]	87	11.49 %
Keereweer et al. [51]	51	51	18	35.29 %
Total	**2669**	**2642**	**301**	**11.39 %**

Reference	No.	Salvage cases	Fistula/leak total	Fistula/leak in salvage cases	RR	P-Value
Hsieh et al. [49]	16	5	5	2		
Laing et al. [18]	31	11	3	3		
Miyamoto et al. [37]	274	79	7	4		
Chang et al. [20]	168	80	23	13		
Total	**489**	**175**	**38**	**22**	**2.46**	**0.004**

No.: patient number; RR: relative risk.
[1] Some patients excluded from further analysis due to flap failure.
[2] Some patients excluded from further analysis due to mortality or flap failure.
[3] Some patients excluded from further analysis as no information recorded about fistula.

Questionnaire [12] was used in one study with 8 patients scoring an average of 68.8 and 71 for chewing and swallowing, respectively (11).

The Performance Status Scale for Head and Neck Cancer Patients (PSS-HN) [13], was used in one study with 83.3 % of patients scoring 50 or above, and none of the patients having a completely normal diet (12). Another study (13) used the Royal Brisbane Hospital Outcome Measure for Swallowing (RBHOMS) [14]: results showed 10 patients reaching optimal swallowing function, and 8 patients regaining pre-morbid swallowing function.

Speech **(**Table 6**):**

This outcome was assessed in 11 studies; 9 articles included a qualitative assessment of speech, 6 of which focused on speech quality following tracheoesophageal puncture (TEP). In total, 63.13 % of patients were described to have acceptable speech, while 75.76 % of patients who underwent TEP had acceptable speech. The other 3 studies showed a cumulative acceptable speech rate of 84.24 %.

Three studies performed quantitative assessment of speech. Hanson et al. [15] used UW-QOL Questionnaire [12], with 8 patients averaging a score of 50. Fukushima et al. [8] used the Understandability of Speech Subscale of the PSS-HN [13]; 78.46 % of patients scored 75 or 100 and were considered to have adequate speech restoration. Deschler et al. [7] assessed speech by having subjects undertake 4 standardized tasks to assess the quality of the voice; trained as well as naïve listeners evaluated voice recording of 10 subjects and marked their fluency on a ruler from 1 to 100. The mean score for fluency was 51.1 according to naïve listeners, and 63.5 as marked by trained listeners.

Discussion

Surgical management of advanced UADT cancers depends on multiple factors: tumour location and extension, patient's comorbidities, previous treatments, and surgeon's preference and expertise. Advanced UADT cancers are known to have poor prognosis, with 5-year survival rates ranging from 35–68 % [16].

Surgical treatment needs to be carefully planned to offer these patients a safe single-stage procedure which is oncologically sound, with low morbidity and mortality, allowing for short hospital stay and quick recovery. Simultaneously, it is imperative to pursue good functional outcomes in terms of speech and swallowing to allow for a good quality of life.

Due to extensive resections, surgical treatment requires reconstruction to recreate a well-matched and patent pharyngo-oesophageal conduit with adequate blood supply and a safe airway. Pedicled, fasciocutaneous and visceral flaps are all widely used and clinical and functional outcomes are variably reported in the literature.

Since its first description in 1959 [2], the JFF has been widely adopted for reconstruction of pharyngo-oesophageal defects. Particularly after introduction of microvascular anastomoses, its use has been extensively adopted and cited in the literature with detailed description of the technique [5].

Table 2
Stricture/stenosis, and association between stricture/stenosis and adjuvant radiotherapy.

Reference	Patient No.	No. included	Stricture	Percentage
Chan et al. [46]	89	86[1]	2	2.33 %
Chen et al. [47]	12	12	0	0.00 %
Hanson et al. [15]	23	23	7	30.43 %
Hong et al. [48]	18	18	6	33.33 %
Hsieh et al. [49][a]	16	16	1	6.25 %
Ikeguchi et al. [26]	22	22	3	13.64 %
Laing et al. [18]	31	31	3	9.68 %
Lee et al. [22][b]	32	32	3	9.38 %
Lewin et al. [31]	31	31	6	19.35 %
Ni et al. [52]	18	18	3	16.67 %
Nyquist et al. [23][c]	24	19[2]	5	26.32 %
Perez- Smith et al. [11]	368	368	40	10.87 %
Sharp et al. [39]	19	19	6	31.58 %
Yu et al. [32]	31	31	6	19.35 %
Ferahkose et al. [27]	14	14	1	7.14 %
Ott et al. [35]	109	109	27	24.77 %
Park et al. [29]	61	61	19	31.15 %
Sarukawa et al. [10]	183	183	25	13.66 %
Tan et al. [24][b]	10	10	0	0.00 %
Denewer et al. [30]	28	25[1]	1	4.00 %
Triboulet et al. [45]	77	77	9	11.69 %
Keereweer et al. [51]	51	51	5	9.80 %
Total	**1267**	**1256**	**178**	**14.17 %**

Reference	Patient No.	Adjuvant RT	Stricture total	Stricture with RT	RR	P Value
Chen et al. [47]	12	12	0	0		
Hanson et al. [15]	23	11	7	6		
Laing et al. [18]	31	17	3	3		
Nyquist et al. [23]	24	14	5	5		
Yu et al. [32]	31	13	6	4		
Total	**121**	**67**	**21**	**18**	**4.83**	**0.0082**

No.: number; RT: radiotherapy; RR: relative risk.
[1] Some patients excluded from further analysis due to flap failure.
[2] Some patients excluded from further analysis due to mortality or flap failure.
[a] Proximal anastomosis.
[b] Distal anastomosis.
[c] Distal anastomosis, with tracheoesophageal puncture (TEP).

Generally, the advantages of JFF are: one surgical session; fast recovery of physiological alimentation; ability to reconstruct large defects from nasopharynx to retrosternal space [11]; compatibility with RT with suitability of irradiated tissues to sustain procedure and healing, as well as capacity to resist adjuvant radiation treatment. The disadvantages of this flap include: requirement for laparotomy, and requirement for a microvascular anastomosis. JFF is contraindicated in patients with abdominal comorbidities such as ascites, history of extensive abdominal surgery, chronic intestinal disease or invasion of the thoracic oesophagus by the tumour [15].

Fistula

Fistula is an early event that can complicate recovery after UADT reconstructions. It delays resumption of oral feeding and, if not responsive to conservative management, it requires a return to theatre likely with the need to harvest another flap. Fistulas also increase the risk of dreaded complications such as wound disruption and carotid blow out. Correlation is also shown between fistula formation and development of stricture [17,18].

In our systematic review the proportion of fistula formation is 11.39 %, ranging from 0 to 35.29 % in single studies. Walker et al. [19] report fistulas occurring in 11 % of their patients with management equally distributed between conservative and closure with a flap, most commonly a pectoralis major (PM) flap.

Chang et al. [20] compared salvage and primary surgeries with the former having higher fistula rates. Equally, they report how single layer anastomoses are associated more commonly with fistula formation compared to double-layer. In their study, fistulas are mostly reported at the proximal anastomosis. As commonly mentioned [17],this is related to size discrepancy between pharyngeal and jejunal ends. In addition to that, irregular border of tongue base can be a factor together with swallowing movements adding shear and tension to the suture line. Interestingly, fistulas in salvage surgeries were mostly reported at the distal anastomosis where soft tissue is scarcer and therefore the area is more affected by RT effects. Possibly for the same reason, proximal fistulas in their series closed spontaneously more frequently.

Sugiyama et al. [21] demonstrated how cardiovascular disease, specifically atherosclerosis, is a risk factor for fistula formation, attenuating circulation of healing mucosa.

Comparing fistula rates of JFF to that of FCFF or pedicled flaps, better outcomes are commonly reported for JFF. The explanation for this could be related to fewer suture lines and therefore less tension as opposed to the need of T junctions and an additional vertical suture required to insert tubed pedicled and FCFF [17]. A further element is related to the difficult integration of muco-cutaneous sutures [15].

Stricture

Stricture manifests as a late complication that can cause major detriment on quality of life as it can result in malnutrition, hospital admission, need for repeated endoscopic dilatations, and eventually definitive feeding tube dependance.

Our systematic review reveals an overall 14.17 % rate of stricture and stenosis, ranging between 0 and 33.3 % among studies. Both Chan et al. [17] and Fukushima at al. [8] report strictures occurring mostly or exclusively at the proximal anastomosis; likely due to discrepancy between pharyngeal and jejunal lumens. Conversely, Lee at al. [22] and

Table 3
Flap failure rates, and rates in salvage cases.

Reference	Patient No.	Failure	Percentage	Partial failure	Percentage
Chan et al. [46]	89	3	3.37 %		
Chen et al. [47]	12	0	0.00 %	0	0.00 %
Daiko et al. [33]	50	3	6.00 %		
Elfeky et al. [44]	37	2	5.41 %		
Hanson et al. [15]	23	2	8.70 %	4	17.39 %
Hong et al. [48]	18	3	16.67 %		
Hsieh et al. [49]	16	2	12.50 %		
Ikeguchi et al. [26]	22	1	4.55 %		
Laing et al. [18]	31	0	0.00 %		
Lee et al. [22][a]	32	3	9.38 %		
Lewin et al. [31]	31	2	6.45 %	1	3.23 %
Miyata et al. [34]	58	3	5.17 %		
Nouarei et al. [9]	123	3	2.44 %		
Nyquist et al. [23]	24	2	8.33 %		
Perez- Smith et al. [11]	368	11	2.99 %		
Walker et al. [19]	104	3	2.88 %	11	10.58 %
Yu et al. [32]	31	2	6.45 %		
Ferahkose et al.[27]	14	1	7.14 %		
Mura et al.[40]	58	4	6.90 %		
Ott et al. [35]	109	12	11.01 %	10	9.17 %
Park et al. [29]	61	5	8.20 %		
Tan et al. [24]	10	0	0.00 %		
Numajiri et al. [25]	10	0	0.00 %		
Mehrara et al. [38]	105	3	2.86 %		
Miyamoto et al. [37]	274	6	2.19 %	8	2.92 %
Ida et al. [36]	14	1	7.14 %		
Denewer et al. [30]	28	3	10.71 %		
Triboulet et al. [45]	77	5	6.49 %		
Keereweer et al. [51]	51	5	9.80 %		
Total	**1880**	**90**	**4.79 %**	**34**	**6.15 %**

Reference	No.	Salvage cases	Failure total	Failure in salvage cases	RR	P-value
Hsieh et al. [49]	16	5	2	0		
Nyquist et al. [23]	24	23	2	1		
Miyamoto et al. [37]	274	79	6	3		
Total	**314**	**107**	**10**	**4**	**1.28**	**0.68**

No.: patient number; RT: radiotherapy; RR: relative risk.
[a] Intra-operative flap failure with immediate re-harvesting of another flap.

Nyquist et al. [23] registered more strictures at distal anastomoses. Nyquist et al. [23] found an increased incidence between stricture formation and primary TEP. They've explained their finding with proximity of TEP to distal anastomosis contributing to compromised blood flow, inflammation, fibrosis and stricture formation. No other study reported analogous conclusions.

A retrospective study comparing visceral, pedicled and FCFF, reports an overall stenosis rate of 23.6 % with more than half of the cases occurring with visceral flap reconstruction (31). They mention that visceral flaps were more commonly JFF, however, that is not further clarified. Moreover, visceral flaps were mostly used for circumferential defects as opposed to pedicled and fasciocutaneous, and this renders this comparison, as many others in the literature, less clear.

Comparing JFF to PM and ALT, Chan et al. [17] reported a significantly higher stricture rate in non-visceral flaps (2.3 % in JFF vs. 27.2 % in PM and 12.5 % in ALT). The explanation would be related to the presence of stratified epithelium at anastomosis site combined with higher fistula rates that they also reported. This would lead to prolonged inflammation, scarring, scar contraction and stricture.

Correlation between early fistula and late stricture formation in also demonstrated by Laing et al. [18] in their series, with 2 out of 3 strictures occurring after earlier fistula.

Flap failure

Several case series were published in the 1980 s on the use of JFF for pharyngoesophageal reconstruction, with a relatively high failure rate. Higher success rates recorded thereafter are likely due to the introduction and advancement of microvascular techniques [4–6]; in this review, this is further supported by the 0 % failure rate recorded by 2 studies incorporating the vascular supercharge [24,25], a technique to reinforce blood flow to the flap with an additional microvascular anastomosis.

To reduce the impact of flap compromise, early detection of microvasculature thrombosis is mainstay. Prolonged microvascular compromise causes extended subepithelial oedema with reduced blood flow and ischemic time leading the flap to necrosis and failure [26]. Anastomoses on large vessels such as internal jugular vein and external carotid artery have been proven to be safe even in salvage cases [27].

Total and partial JFF failure rates in this review were 4.79 % and 6.15 % respectively, as opposed to 1.7 % and 1.9 % failure rates quoted in a review on FCFF [28]. Although these results may show unfavourable outcome for JFF, it should be noted that there is large discrepancy in the number of patients in each review (3191 in this review vs. 413 in the FCFF review).

A study comparing pedicled, visceral and free flaps, found flap compromise to be comparable (10.2 %) between each reconstructive method regardless of treatment type, defect type or history of RT [29]. Analysing patients' comorbidities; renal failure and hypoalbuminaemia were found to be risk factors for flap failure.

Walker et al. [19] weighed flaps survival vs. failure against presence of ischaemic heart disease, vessels used for the anastomosis, ischaemic time and whether the operator used a microscope or loupes. There were no significant differences, however, loupes were noted to bring on a more favourable outcome; that may have been a biased conclusion as use of microscope was earlier in the series, when they were less experienced. Overall, with earlier detection and re-exploration of anastomoses, they report a flap survival of 97 %. A low threshold for re-exploration of any suspected vascular compromise is generally

Table 4
Peri-operative re-operation and mortality.

Reference	Patient No.	Partial failure	Total failure	Bleeding	Other/not specified	Re-operation	Percentage
Chen et al. [47]	12	0	0			0	0.00 %
Chan et al. [46]	89				2	2	2.25 %
Daiko et al. [33]	50		3			3	6.00 %
Hanson et al. [15]	23	4	2			6	26.09 %
Hsieh et al. [49]	16		2	2		4	25.00 %
Laing et al. [18]	31			1		1	3.23 %
Lee et al. [22]	32			1	1	2	6.25 %
Perez- Smith et al. [11]	368				25*	25	6.79 %
Walker et al. [19]	104	11	3			14	13.46 %
Ott et al. [35]	109	10	12	4	6	32	29.36 %
Total	**834**	**25 (3 %)**	**22 (2.64 %)**	**8 (0.96 %)**	**34 (4.08 %)**	**89**	**10.67 %**

Reference	Patient No.	Peri-op mortality	Percentage
Chen et al. [47]	12	0	0.00%
Daiko et al. [33]	50	0	0.00%
Elfeky et al. [44]	37	1	2.70%
Hanson et al. [15]	23	4	17.39%
Hsieh et al. [49]	16	1	6.25%
Ikeguchi et al. [26]	22	1	4.55%
Laing et al. [18]	31	2	6.45%
Lee et al. [22]	32	0	0.00%
Lewin et al. [31]	31	0	0.00%
Miyata et al. [34]	58	3	5.17%
Nouarei et al. [9]	123	8	6.50%
Nyquist et al. [23]	24	3	12.50%
Perez- Smith et al. [11]	368	14	3.80%
Yu et al. [32]	31	0	0.00%
Ferahkose et al. [27]	14	1	7.14%
Ott et al. [35]	109	3	2.75%
Sarukawa et al. [10]	183	0	0.00%
Miyamoto et al. [37]	274	0	0.00%
Ida et al. [36]	14	1	7.14%
Triboulet et al. [45]	77	5	6.49%
Keereweer et al. [51]	51	2	3.92%
Total	**1580**	**49**	**3.10%**

Other causes of reoperation: fistula/leak (n = 5), donor-site related (n = 4).
*Returned to theatre for partial flap failure or evacuation of haematoma.

Table 5
Qualitative assessment of diet.

Reference	No.	No. included	Normal diet*	%	Fully oral diet**	%	Tube feeding	%	Gastrostomy feeding	%
Chan et al. [46]	89	84[1]	52	61.90 %	–	–	–	–	–	–
Chen et al. [47]	12	12	10	83.33 %	–	–	–	–	–	–
Laing et al. [18]	31	25[2]	11	44.00 %	19	76.00 %	–	–	3	12.00 %
Lewin et al. [31]	31	26[3]	14	53.85 %	19	73.08 %	7	26.92 %	–	–
Nyquist et al. [23]	24	15[2]	–	–	9	60.00 %	6	40.00 %	–	–
Perez- Smith et al. [11]	368	368	–	–	337	91.58 %	–	–	18	4.80 %
Sharp et al. [39]	19	19	–	–	18	94.74 %	–	–	1	5.26 %
Walker et al. [19]	104	44[2]	9	20.45 %	32	72.73 %	–	–	9	20.45 %
Yu et al. [32]	31	26[4]	15	57.69 %	17	65.38 %	9	34.62 %	–	–
Omura et al. [50]	10	10	9	90.00 %	–	–	–	–	–	–
Deschler et al. [7]	10	10	10	100.00 %	–	–	–	–	–	–
Denewer et al. [30]	28	25[1]	20	80.00 %	–	–	–	–	–	–
Chang et al. [20]	168	23[5]	17	73.91 %	20	86.96 %	–	–	–	–
Total	**925**	**687**	**167**	**58.60 %**	**471**	**86.26 %**	**22**	**32.84 %**	**31**	**6.80 %**

*Patients described to resume normal/regular/solid/unlimited diet.
**Patients who relied on soft or pureed food but did not require feeding adjuncts.
[1] Some patients excluded from further analysis due to flap failure or stricture.
[2] Swallowing outcome available for patients assessed at long-term follow-up only (6–24 months).
[3] Swallowing outcomes available for this number of patients only.
[4] Some patients excluded from further analysis due to fistula, flap failure, recurrence of disease or inadequate follow-up.
[5] Only patients with fistula were included in the analysis.

adopted to reduce the risk of flap failure [15].

Morbidity and perioperative mortality

Postoperative complications have significant impact on hospital stay, permanent sequelae, initiation of adjuvant treatment, patient and

Table 6
Qualitative assessment of speech.

Reference	No.	No. included	Acceptable speech	%	TEP*	Acceptable speech	%
Lewin et al. [31]	31	8[1]	5	62.50 %	8[a]	5	62.50 %
Ni et al. [52]	18	18	4	22.22 %	2	2	100.00 %
Perez- Smith et al [11]	368	136[1]	78	57.35 %	96	78	81.25 %
Sharp et al. [39]	19	19	11	57.89 %	18[b]	11	61.11 %
Yu et al. [32]	31	9[1]	2	22.22 %	10[c]	2	20.00 %
Fukushima et al. [8]	130	130	102	78.46 %	130[d]	102	78.46 %
Total	**597**	**320**	**202**	**63.13 %**	**264**	**200**	**75.76 %**

Reference	No.	No. included	Acceptable speech	%
Laing et al. [18]	31	31	24	77.42%
Walker et al. [19]	104	44	31	70.45%
Ott et al. [35]	109	109	100	91.74%
Total	**244**	**184**	**155**	**84.24%**

*Tracheoesophageal puncture.
[1] Speech outcomes available for this number of patients only.
[a] Four primary TEP (3 with acceptable speech), 4 secondary (2 acceptable).
[b] Seventeen primary TEP, 1 secondary.
[c] Five primary TEP (1 lost to follow-up, 0 acceptable), 5 secondary (2 acceptable).
[d] All secondary TEP.

carers' quality of life and health care expenses.

Harvesting of JFF involves a laparotomy, prolonged operative time and possible abdominal complications. Compared to a myocutaneous flaps, JFF is more time consuming, technically demanding and has a higher donor site morbidity risk. Often surgeons are inclined to choose "easier" flaps, mostly in frail patients that are not considered good candidates for major operations [30]. Furthermore, many patients with H&N cancers, owing to history of smoking, have chronic obstructive pulmonary disease and minimal pulmonary reserve, thus avoiding abdominal surgery in this population would be desirable. One study [31] compared duration of ventilator support and ICU/hospital stay and found them to be longer after JFF compared to ALT flaps. However, the overall incidence of postoperative complications did not differ significantly.

Literature divides donor site morbidity of JFF into laparotomy and motility related, with multiple complications recorded such as wound infection or cellulitis, dehiscence, hematoma, ileus, torsion and intussusception leading to bowel obstruction. Yu et al. [32] found faster postoperative recovery and shorter hospital stay in patient undergoing reconstruction with ALT flaps compared with JFF. They reported various donor site complications such as small bowel obstruction, nausea and vomiting leading to malnutrition and readmission to hospital. Conversely among ALT patients, donor site morbidity was minor and limited to seromas and hematomas.

Comparing JFF donor site morbidity to that of GPU, the former appears to have fewer/less severe complications. In GPU the oesophagus requires dissection and mobilisation from adjacent thoracic structures, carrying a high rate of cardiopulmonary complications [27,33]. Moreover, longer operative time and excessive blood loss have been reported in GPU procedures (27). Also, Denewer et al. [30] highlighted how morbidity and mortality increase when mediastinum is addressed due to increased operative trauma. Sugiyama et al. [21] presume an association between longer operative time in JFF and an increased risk of infective complications due to higher likelihood of intraoperative wound contamination.

Across studies, perioperative mortality is variably defined as occurring in the first 30 postoperative days or during the same admission of the procedure. Perioperative mortality after JFF reconstructions in this review was 3.1 %, ranging from 0 to 17.39 % in single studies.

A UK national analysis [9] on pharyngolaryngectomy reconstructions identified age, surgery during an emergency admission, major acute cardiovascular events, respiratory complications, sepsis, acute renal failure, surgical site complications including carotid or jugular hemorrhage, and reconstructive failure as independent risk factors for perioperative mortality. In their analysis, GPU had significantly worse outcomes both compared to FCFF and JFF.

Miyata et al. [34] analysed cervical oesophagectomies with JFF in larynx-preserving surgeries and found a hospital mortality rate of 5.1 %, with no significant difference when the larynx was preserved.

Ott et al. [35], despite reporting a high complication and reoperation rate, had low mortality and good long-term survival in their series; accurate patient selection, early recognition and management of complications and surgical expertise are all regarded as factors improving morbidity and mortality.

The importance of surgical expertise has been proven in 2 consecutive series from the same institution; the more recent series recorded improvements of mortality rates, fistula rates, major medical complications and mean length of hospital stay [32].

Impact of radiotherapy

The impact of preoperative RT on reconstruction outcomes is variably reported in the literature. Irradiation renders surgery more demanding due to alteration of tissue planes, fibrosis, and disruption of microcirculation leading to poor blood flow and poor healing. Moreover, preoperative RT induces suppression of immune function, rendering postoperative complications more common [36]. However, many studies in this review [10,22,26] did not report worse clinical outcomes in irradiated patients.

Park et al. [29] found a 2.99-fold higher risk of fistula in salvage surgeries but no difference in flap compromise rates after RT. Fukushima et al. [8] found significantly longer hospitalisation in patients undergoing salvage compared to primary surgeries.

Only one study in this review measured impact of RT on JFF reconstructions based on severity of complications rather than only their frequency [37]; postoperative complications had significantly higher Clavien-Dindo (CD) grades in the RT group compared to the non-RT group. Conversely, frequency of complications did not differ significantly, hence the risk of underestimating RT impact when not grading severity of complications.

As for the ability of JFF to tolerate adjuvant RT, this is widely reported in the literature [15,17,19].

Survival rates

Prognostic factors for long term survival in patients with hypopharyngeal and cervical oesophageal cancers are: T stage, particularly T3 and above if with vocal fold palsy and tumour size > 5 cm; N stage,

particularly palpable cervical nodes, extracapsular spread and involvement of mediastinal nodes; positive surgical margins; and postoperative complications [33]. All these factors should be considered when selecting candidates for surgery.

Eleven studies in this review reported data on long-term survival outcomes. Nouraei et al's UK national analysis [9] reports survival rates in patients undergoing JFF at years 1, 2, 3, 5 and 10. Overall survival decreases from 79 % at 1 year to 54 % at 5 and 19 % at 10 years. Compared with JFF survival outcomes appear to be better in patient undergoing FCFF reconstruction and worse, however not significantly, for GPUs.

Commenting on survival data relative to JFF reconstruction needs to take into account the advanced stage of the disease for which such procedure is offered, the multiple comorbidities affecting H&N cancer patients, and frequent high degree of social deprivation. Undergoing surgery during an emergency admission also appears to be a factor impacting both postoperative and long-term mortality [9].

Another aspect to consider is relative to different subsites of primary tumours needing JFF reconstruction. Ideally, outcomes for cervical oesophageal and hypopharyngeal primaries should be analysed separately given differences in the affected anatomical location and tumour biology; they are however often pooled together, adding bias to survival calculations [35].

Swallowing

Dysphagia may be an early or late complication in UADT reconstructive surgery. Many different factors contribute to swallowing impairment and are frequently cited in the literature: fistulas and delayed wound healing, cranial nerve palsies, flap redundancy, tongue base retraction, strictures and dysmotility impairing bolus transit through the neopharynx. Less commonly, factors such as dentition, age, appetite, taste and food preference are considered in the evaluation of final diet levels [31], therefore, comparisons between studies are not always accurate.

Many studies in this review reported positive swallowing outcomes with restoration of oral feeding with JFF. Laing et al. [18] describe meticulous care in placing the flap in an isoperistaltic manner and under some degree of tensions to avoid flap redundancy, achieving functional swallowing in 84 % of patients. Perez Smith et al. [11] and Mehrara et al. [38] report even higher success rates with 91.6 % and 87 % of patients, respectively, being able to maintain adequate oral nutrition.

Apart from the functional success of normal oral feeding, Sharp et al. [39] highlight its social and psychological importance with reduced levels of handicap, distress, frustration and withdrawal.

Comparing different reconstruction techniques, Chan et al. [17] recorded a 61.9 % of resumption of normal oral diet with JFFs as opposed to 35.8 % in PMs and 38.2 % in ALTs. They account the presence of mucus and peristalsis as contributing factors for better outcomes in JFFs, particularly in salvage cases. Mura et al. [40] report higher chances of restoration of normal feeding with free flaps, including JFF, compared to PM flaps. Another study showed a significantly higher resumption of oral diet with ALT compared to JFF (91 % vs 73 %), however patients with JFF were more likely to resume a full oral diet, whereas ALT patients tended to consume pureed or soft diets [31].

Speech

Restoration of a socially acceptable and functional voice is another challenge of UADT reconstructions. Different types of alaryngeal speech include use of electrolarynx, oesophageal and tracheoesophageal speech [41]. Electrolaryngeal voice, although understandable, is not favoured by patients due to its mechanical quality [42]. Oesophageal voice requires prolonged rehabilitation with unpredictable outcomes, and is often unsuccessful both for pedicled and free flaps. Pedicled flaps and FCFF are usually too thick and stiff to vibrate, whereas a JFF does not allow passage of air due to its intrinsic peristalsis [40].

Articles included in this review, mainly evaluate tracheoesophageal speech following primary or secondary TEP. Despite the scarce data and variable methods of assessing speech restoration, the cumulative results of this review were reassuring, with 75.76 % of patients who underwent TEP having at least understandable speech. Sharp et al. [39] reported no evidence of dysphonia in patients using tracheoesophageal voice, as well as reduced levels of disability. Walker et al. [19] report that at 2-years follow up, 70 % of patients who underwent jejunal reconstruction were able to use their voice in daily circumstances, with half of them being able to communicate on the phone. Deschler et al. [7] report equal outcomes in conversational intensity in pharyngolaryngectomies with no flap, JFF and RFFF. They also report a detailed subjective analysis done with evaluation of speaking rate, communication effectiveness, use of pitch, fluency, pleasantness, wetness and extraneous speech noise; their study concluded no differences between JFF and RFFF. Fukushima et al. [8] rated speech intelligibility according to PSS-HN [13], and registered a successful prosthesis voice restoration in 78.4 % of patients. They also report no difference between insertion sites (oesophageal or jejunal), or between salvage and primary cases.

The most commonly reported drawback of jejunal voice is its wet, gurgly, low pitch and cavernous quality [5,23,43] that would often lead patients to deem it socially unacceptable, occasionally to the point of not routinely using their new voice to communicate [31].

One study compared voice outcome after JFF and ALT, and fluency and use of tracheoesophageal voice for routine conversation was in favour of ALT [31]. Fluency was defined as the ability to produce 10 to 15 words per breath, and sustain vowel production for 10 s.

Conclusions

Reconstruction of large pharyngoesophageal defects resulting from extensive H&N cancer ablation is a surgical challenge with several options available. Usually when multiple options are available, each has advantages and disadvantages and the choice of reconstructive method needs to be tailored to each case.

This systematic review offers a comprehensive analysis on current literature on JFF to provide a better understanding of its strengths and weaknesses, by comparing clinical and functional outcomes. Comparisons were seldom simple and straightforward, mainly due to the retrospective nature of most studies and inconsistent record of variables.

Overall, JFF proves to be a reliable, safe and effective method for reconstructing circumferential pharyngoesophageal defects, with studies over the past 20 years demonstrating good clinical and functional outcomes.

CRediT authorship contribution statement

Sarah Mortaja: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Francesca Angela Chiumenti:** Writing – original draft, Validation, Investigation. **Deepak M. Kalaskar:** Visualization, Supervision, Project administration. **Raghav C. Dwivedi:** Writing – review & editing, Visualization, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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