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Original Article

Free Jejunal Graft Repair after Pharyngo-Laryngo-Esophagectomy-Risk Factor Analysis for Postoperative Dysphagia

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Purpose: Reconstruction with free jejunal graft (FJG) has been widely accepted for patients undergone pharyngo-cervical esophageal resection. Those patients often suffer variety of complications regarding postoperative peros function. We investigated risk factors especially focused on the development of dysphagia after FJG reconstruction.
Methods: A retrospective analysis was conducted using clinical chart review of 30 consecutive patients who underwent reconstruction with a FJG after pharyngo-laryngo-esophagectomy from 1995 to 2010. Mortality, morbidity, and postoperative dysphagia were investigated. Dysphagia was defined when the patients required enteral nutrition until later than 1 month postoperatively without any other complications, including anastomotic leakage, anastomotic stricture, FJG ischemic necrosis, and hospital death. Data on potential clinical factors were extracted and the relation of these variables to postoperative dysphagia was examined by univariate and multivariate analysis.
Results: There was one patient with hospital death over total 30 patients who deceased due to fatal postoperative bleeding from arterial anastomosis of FJG. Postoperative complications occurred in 14 patients (46.7%) those included respiratory complication in 5, anastomotic leakage 3, FJG ischemic necrosis 2, paralytic ileus 2, ischemic change of tracheostomy 2, anastomotic stricture 1 and dysphagia 9. Dysphagia was the most frequent in this series. Multivariate analysis demonstrated induction radiation (≥60 Gy) was independently significant factors for postoperative dysphagia.
Conclusion: FJG reconstruction may be safe and functionally satisfactory surgical option after pharyngo-laryngo-esophagectomy. Postoperative dysphagia may be induced prior radiation therapy.

Keywords: free jejunum graft, hypopharyngeal cancer, esophageal cancer, dysphagia, radiation therapy

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Introduction

Currently, reconstruction of digestive system using free jejunal graft (FJG) is widely accepted after laryngo-pharyngo-cervical esophagectomy. The procedure is complex, requiring both micro-vascular and intestinal anastomosis resulting in some unique postoperative problems. Those mainly include intestinal anastomotic complications such as stricture or leakage at pharyngo-jejuno or jejuno-esophageal anastomosis. Complication at vascular anastomosis such as stenosis or thromboembolic

occlusion is another serious problem which cause fatal FJG necrosis or edema. Of course those problems lead to decrease the patients quality of life or may cause life threatening situation. Incontinuity of digestive system after FJG reconstruction in addition of those FJG specific problems may therefore sometimes cause post-operative dysphagia. There have been only a few reports concerning the risks analysis associated with the development of a postoperative dysphagia after FJG reconstruction.[1)]

Materials and Methods

From 1995 to 2010, total 30 patients were performed laryngo-pharyngo-esophagectomy followed by reconstruction using FJG. Patients included 19 pharyngeal cancer, 7 laryngeal cancer, 2 cervical esophageal cancer, and 2 others. Clinical and surgical information were retrospectively corrected from the patients' medical chart. Written consents were obtained from all patients.

Table 1 The methods of reconstruction and intestinal anastomosis

Reconstruction (conduit)		N(%)
Free jejunal reconstruction (FJR)		28 (93.3)
FJR plus gastric tube		2 (6.7)
Intestinal anastomosis		
Proximal	Layer to layer	30
Distal	Layer to layer	15
	Instrumental (EEA)	15

Table 2 The methods of vascular anastomosis

Vascular anastomosis		n
Vein	Jugular. V (end-to-side)	30
Artery	Transverse cervical . A (end-to-end)	17
	Carotid. A (end-to-side)	14
	Superior thyroid. A (end-to-end)	2
	Lingual. A (end-to-end)	2
Artery	Single	25
	Double	5

Surgical technique

A FJG about 20 cm long of jejunal segment was harvested at 20 cm–30 cm distal from the treitz ligament through small size 10 cm median laparotomy. One or two jejunal arteries were prepared and served as donor artery. One jejunal vein with adequate size was chosen as donor vein. The donor artery was gently flushed-out using normal saline solution containing 1% heparin sodium and kept in ice cold saline solution until intransplantation. After pharyngo- laryngo-esophagectomy, intestinal anastomoses were applied followed by the vascular anastomoses. In all FJG reconstruction, intestinal anastomosis at proximal side (pharyngo-jejuno) was carried out using hand sawn anastomosis in all cases, however, distal anastomosis (jejuno-esophago) was carried out by hand sawn (n = 15) or instrumental anastomosis (EEA) (n = 15) (**Table 1**). Vascular anastomosis were done under microscopic surgical technique using 5 × magnified surgical scope. All vascular anastomosis were performed using interrupted suturing technique with 8-0 monofilament suture. Venous drainage was established by end-to-side anastomosis between jejunal vein and the jugular vein in all cases. Recipient transverse cervical artery was chosen for recipient artery in majority of cases after careful inspection of its adequate blood supply. When TCA pulsation seemed to be insufficient, carotid artery was chosen. When artery blood supply seemed to be necessary, thyroid artery or lingual artery was chosen for recipient artery by end-to-side anastomosis (**Table 2**). A tube jejunostomy for postoperative enteral diet is made before closing the abdominal wound. Pulsation was monitored by Doppler blood flow monitoring system (ES-100V3, Hadeco inc., Kawasaki, Japan) every 6 hours after surgery until postoperative day (POD) 3. No anticoagulative agents were given, however, PGE1(3γ) was continuously injected to maintain blood flow to the FJG. Normal oral feeding was started around day 7 after surgery. Nutritional support was decreased based on oral nutritional uptake.

Assessment

Postoperative dysphagia was defined if patients required additional or full enteral nutrition support beyond 1 month postoperatively without any other complications including anastomotic leakage, anastomotic stricture, FJG ischemic necrosis, and hospital death.

All data are expressed as mean ± standard deviation.

Statistical methods

Univariate analysis was performed using the unpaired Student's *t*-tests or χ^2 test, and multivariate analysis was performed using logistic regression. All statistical analyses were done using the Stat View-J 5.0 software package (Abacus Concepts Inc., Berkeley, California, USA),

Table 3 Characteristics of 30 patients performed FJG reconstruction

Sex	M:F	26:4
Age		64.7±10.0
Disease	Pharyngeal ca	19 (63.3)
	Laryngeal ca	7 (23.3)
	Cervical esophageal ca	2 (6.7)
	Others	2 (6.7)
Induction	Radiation alone	4 (13.3)
	Radiation + Chemotherapy	20 (66.0)
Radiation dose	≥60 Gy	6 (20.0)
	<60 Gy	18 (60.0)

and all *p* values that were two-sided at a value of <0.05 were considered to be statistically significant.

Result

The clinical characteristics of the 30 patients are summarized in **Table 3**.

A total of 24 male and 6 female with a mean age of 64.7 ± 10.0 years (range: 37 to 76 years) were included in this study. Out of those 30 cases, 24 patients had undergone radiation therapy before surgery (80%), including, 6 patients who received radical radiation dose over 60 Gy.

Pharyngo-laryngo-cervical esophagectomy was performed on 28 cases, and combined pharyngo-total esophagectomy was done for 2 cases with extended esophageal cancer. Those two cases were reconstructed surgically with FJG plus gastric tube (**Table 1**). The mean operation time and blood loss was 738.7 ± 166.1 min and 707.4 ± 530.2 ml, respectively. There was one early death as a result of massive bleeding from the arterial anastomosis between carotid artery and jugular artery on POD10 (mortality = 3.3%). Complications occurred in 14 cases (morbidity 46.7%). Those included respiratory complication in 5 (16.7%), anastomotic leakage in 3 (10%), FJG necrosis in 2 (6.7%), paralytic ileus in 2 (6.7%), and ischemic change of tracheostomy in 2 (6.7%) anastomotic stricture in 1 (3.3%), postoperative dysphagia in 9 cases (**Table 4**). One anastomotic stricture was observed at distal anastomosis with mechanical (EEA). This case was treated with repeated endoscopic balloon dilation. When entire FJG necrosis was confirmed, the FJG was immediately extracted and re-reconstruction using skin flap or redo FJG reconstruction was done later.

Nine cases (30%) suffered postoperative dysphagia and required enteral nutrition support more than 1 month after surgery. It was impossible for the patients with dysphagia to intake rice-gruel, although the passage was no problem. Radiation or clinical inspection revealed that those dysphagia may be caused by compression of FJG caused by skin stiffness, or poor peristalsis of jejunal segment. Nine patients underwent rehabilitation, mainly for swallowing and feeding. Three patients needed enteral nutrition more than 1 month but less than 2 months. Six patients needed more than 2 months but less than 3 months.

In the univariate analysis, female sex ($p = 0.0441$) and induction radiation (≥60 Gy) ($p = 0.0383$) revealed to be significant covariate associated with postoperative dysphagia (**Table 5**). Multivariate analysis demonstrated induction radiation (≥60 Gy) was only one independently significant factors for postoperative dysphagia ($p = 0.0457$) (**Table 6**).

Discussion

FJG is mainly used as a reconstruction of digestive tract after pharyngo-laryngo-esophagectomy or cervical esophagectomy, however, is rarely used for esophageal reconstruction after short segment cervical esophagectomy alone without pharyngeal resection. In another rare setting, FJG was used as an offset additional reconstruction segment when the intestinal defect is too long to cover by gastric tube alone after laryngo-pharyngo-total esophagectomy.

FJG is thought to be physiologically superior than muscle or skin flap.[2] The use of skin or muscle graft as digestive conduit which has no peristaltic function or mucous lining may leads difficulty of swallowing or food pass. Chan, et al.[3] have suggested that FJG reconstruction of circumferential pharyngectomy defects achieves a better functional outcome than non-intestinal substitute such as a pectoralis major flap or a free anterolateral thigh reconstruction. In addition, FJG is considered to be less invasive reconstruction option than the use of gastric tube for the selected cases such as extended cervical esophageal cancer.[4] However, patients who undergo FJG reconstruction sometimes suffer from dysphagia, and this is the most frequent complication.[5]

FJG repair includes some specific surgical or physiological aspects which leads distinct complications. FJG require microvascular anastomosis on which the graft viability completely depends. Problems on vascular anastomosis leads rapid fatal condition or some other ischemic problems. The FJG is placed in subcutaneous lesion after laryngopharyngectomy which require wide range surgical insults around neck lesion. The subcutaneous

Table 4 The results of FJG reconstruction (Overlapping distribution)

Operation time (min)		738.7 ± 166.1
Blood loss (ml)		707.4 ± 530.2
Hospital stay (day)		67.4 ± 40.6
Complications	Respiratory complication	5 (16.7%)
	Anastomotic leakage	3 (16.7%)
	FJG ischemic necrosis	2 (6.7%)
	Ischemic change of tracheostomy	2 (6.7%)
	Anastomotic stricture	1 (3.3%)
	Dysphagia*	9 (30%)
Surgical mortality		1 (3.3%)**

* Patients who required enteral nutrition on 1 month without other complications including anastomotic leakage, FJG ischemic necrosis, anastomotic stricture, and hospital death

** Massive bleeding from vascular anastomosis

Table 5 Univariate analysis in postoperative dysphagia

		Dysphagia (+) (n = 9)	Dysphagia (–) (n = 16)	*p* value
Age		68.4 ± 6.8	60.9 ± 11.2	0.0797
Sex	M	5	15	0.0403
	F	4	1	
Radiation	≥60 Gy	4	1	0.0403
	<60 Gy	5	15	
Chemotherapy	Yes	8	10	0.3548
	No	1	6	
Intestinal anastomosis (anal side)	Layer to layer	3	8	0.6766
	EEA	6	8	
Blood loss (ml)		556.8 ± 359.0	758.3 ± 656.1	0.4056
Operation time (min)		719.1 ± 174.5	750.9 ± 185.3	0.6781

Table 6 Multivariate analysis in postoperative dysphagia

	Odds ratio	95% CI	*p* value
Age	1.054	0.914–1.215	0.4722
Sex; M	0.075	0.004–1.309	0.0759
Radiation ≥60 Gy	16.572	1.103–249.053	0.0423

space at neck lesion is sometimes very limited. The patient lose swallowing function after laryngo-pharyngo-surgery, and thus combined effect with compression in neck subcutaneous space. In addition, the redundancy of the proximal jejunal part led to the formation of a reservoir pouch with subsequent dysphagia.[5)]

Radiation therapy has generally been recommended for the patient with advanced pharyngeal cancer before surgery.[6)] It has been well known that radiation therapy causes radiation dermatitis or tissue fibrosis.[7)] Those radiation induced tissue damage result in skin or connective tissue stiffness. Lecleire, et al.[8)] described that high dose radiation therapy leads to impeded blood flow which cause tissue inflammation, or fibrosis of adjacent soft tissues. Nguyen, et.al.[9)] mentioned that radiation therapy has been shown to induce hyperactivation of transforming growth factors beta 1 (TGFβ1), which is a peptide to increase synthesis or inhibits degradation of collagen. Its autocrine hypertension following radiation increases the fibrosis of normal organs in the radiation fields producing a decrease in their blood supply, hypoxemia, and ultimately functional damage. The impeded blood flow and skin stiffness may finally result in decreasing FJG mortility and circumferential compression.

In this study, 24 out of 30 cases were performed induction radiation therapy. Six out of these were performed with definitive therapeutic dosage of above more than 60 Gy. Postoperative complication was seen on 14 patients (46.7%). Most frequent postoperative problem was dysphagia which was noted on 9 patients in this series. Univariate and multivariate analysis for possible factors excluding cases of anastomotic stenosis or leakage association with this complication revealed induction radiation (≥60 Gy) was only one significant covariate

which affect this complication. Out data indicated that postoperative dysphagia may be led by prior radiation damage in the neck lesion.

A great variety of prevention technique against these complications has been evolved. Decreased blood flow on recipient artery such as TCA after radiation may lead graft ischemia which resulting in impaired peristalsis. Numajiri, et al.[10] advocated the use of two or more recipient artery to donor artery of FJG to increase graft blood flow. A double arterialized free jejunal graft might reduce the risk of venous thrombosis and increase the peristaltic motion which might be a possible countermeasure. Hospers, et al.[11] suggested that medications with radioprotector effect such as amifostine may be used to decrease radiation damage to the normal muscles. Lazarus, et al.[12] mentioned that early therapeutic regimens of swallowing exercises increase the precision of movements, and maintain range of motion provide the best prevention of long-term swallowing dysfunction in patients who have undergone radiation therapy.

Conclusion

FJG reconstruction may be safe and functionally acceptable surgical option with limited surgical insult after pharyngo-laryngo-esophagectomy. The preoperative radiation cases, however, tend to cause postoperative dysphagia. Particular consideration and close monitoring is required.

Disclosure Statement

We have no financial or other interest in the manufacture or distribution of the device.

References

1) Sharp DA, Theile DR, Cook R, et al. Long-term functional speech and swallowing outcomes following pharyngolaryngectomy with free jejunal flap reconstruction. Ann Plast Surg 2010; **64**: 743-6.
2) Moradi P, Glass GE, Atherton DD, et al. Reconstruction of pharyngolaryngectomy defects using the jejunal free flap: a 10-year experience from a single reconstructive center. Plast Reconstr Surg 2010; **126**: 1960-6.
3) Chan YW, Ng RW, Liu LH, et al. Reconstruction of circumferential pharyngeal defects after tumor resection: reference or preference. J Plast Reconstr Aesthet Surg 2010; **64**: 1022-8.
4) Ferahkose Z, Bedirli A, Kerem M, et al. Comparison of free jejunal graft with gastric pull-up reconstruction after resection of hypopharyngeal and cervical esophageal carcinoma. Dis Esophagus 2008; **21**: 340-5.
5) Keereweer S, Sewnaik A, Kerrebijn JD, et al. Dysphagia after an L-shaped reconstruction technique of the free jejunum graft. J Plast Reconstr Aesthet Surg 2010; **63**: 1820-4.
6) Nguyen NP, Frank C, Moltz CC, et al. Risk of aspiration following radiation for non-nasopharyngeal head and neck cancer. J Otolaryngol Head Neck Surg 2008; **37**: 225-9.
7) Krieg T, Meurer M. Systemic scleroderma. Clinical and pathophysiologic aspects. J Am Acad Dermatol 1988; **18**: 457-81.
8) Lecleire S, Di Fiore F, Ben-Soussan E, et al. Prior chemoradiotherapy is associated with a higher life-threatening complication rate after palliative insertion of metal stents in patients with oesophageal cancer. Aliment Pharmacol Ther 2006; **23**: 1693-702.
9) Nguyen NP, Antoine JE, Dutta S, et al. Current concepts in radiation enteritis and implications for future clinical trials. Cancer 2002; **95**: 1151-63.
10) Numajiri T, Sowa Y, Nishino K, et al. Double arterialized free jejunal flap. J Reconstr Microsurg 2010; **26**: 165-70.
11) Hospers GA, Eisenhauer EA, de Vries EG. The sulfhydryl containing compounds WR-2721 and glutathione as radio- and chemoprotective agents. A review, indications for use and prospects. Br J Cancer 1999; **80**: 629-38.
12) Lazarus CL, Logemann JA, Pauloski BR, et al. Swallowing disorders in head and neck cancer patients treated with radiotherapy and adjuvant chemotherapy. Laryngoscope 1996; **106**: 1157-66.