Tonometer pH_i Monitoring of Free Jejunal Grafts following Pharyngolaryngoesophagectomy for Hypopharyngeal or Cervical Esophageal Cancer

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Key Words

Hypopharyngeal cancer · Cervical esophageal cancer · Free jejunal graft · Tonometer

Abstract

Background/Aims: Graft failure is a critical complication associated with vascular occlusion in esophageal reconstruction with a free jejunal graft following pharyngolaryngoesophagectomy. In this study, we evaluated the usefulness of intramucosal pH (pH_i) measurement using a tonometer to assess the graft viability. **Methods:** Two consecutive studies, the early phase study and the late phase study, were performed. Nineteen patients who underwent free jejunal transfer were enrolled in the early phase study before 1999 to determine the critical pH_i value. In the late phase study after 2000 (n = 16), anticoagulant treatment to prevent graft necrosis was performed in the patients having a pH_i value under the critical level. **Results:** In the early phase study, vascular obstruction was not seen in 16 patients with pH_i >7.10. Of 3 patients with pH_i <7.10, 2 underwent regrafting because of jejunal graft necrosis by vascular obstruction. In the late phase study, reoperation was not required in 3 of 4 patients with pH_i <7.10. Intraoperative vascular occlusion was found in 1 patient with a decline in pH_i value and anticoagulant treatment was effective in 2 others. **Conclusion:** The pH_i measurement using a tonometer is useful for finding vascular problems in free jejunal grafts.

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Introduction

Patients with hypopharyngeal or cervical esophageal cancer are commonly found at an advanced stage, resulting in poor prognosis. Recently, the effectiveness of chemoradiotherapy for these lesions has been reported [1] and this therapy may become curative treatment in cases of early stage disease [2]. However, the chemoradiotherapy does not always result in satisfactory outcome in the advanced cases and pharyngolaryngoesophagectomy as a salvage surgery is required for cases with residual or recurrent disease [3]. After pharyngolaryngoesophagectomy, reconstruction using a free jejunal graft (FJG) is regarded as the best optimum method. Several authors have reported the outcome of free jejunal transfer [4, 5]. Although the development in microsurgical techniques has been achieved, the most serious problem is failure of the vascular anastomosis, resulting in graft necrosis. This needs reoperation such as reanastomosis of the vessels or resection of the necrotic graft.

Accordingly, monitoring the viability of the graft is very important to detect vascular failure, but a convenient monitoring method has not yet been established. Various methods for monitoring have been reported: monitoring flap [6], the graft temperature, direct observation using endoscopy [7], and percutaneous Doppler ultrasound monitoring [7]. However, there are various problems with the latter methods, such as infection and a lack of objectivity. The intramucosal pH (pH_i) reflects

Table 1. Patients' characteristics

	Early group (n = 19)	Late group (n = 16)	p value
Age, range	64 (49–79)	61 (45–78)	NS
Sex			NS
Male	18	13	
Female	1	3	
Location			NS
Larynx	3	2	
Pharynx	11	13	
Cervical esophagus	5	1	
Histological type			NS
Squamous cell carcinoma	19	16	
Operative procedure			NS
Pharyngolaryngoesophagectomy	18	15	
Transhiatal esophagectomy and laryngectomy	1	1	
Reconstruction			NS
FJG	18	15	
Gastric pull-up and FJG	1	1	
TNM classification, stage			NS
I	1	2	
IIA	2	1	
IIB	1	1	
III	5	4	
IV	10	8	

the viability of the viscus, and tonometry is a less invasive method to assess pH_i in the gastrointestinal tract. Tonometric values of pH_i are correlated with pH values directly measured using a microprobe [8]. Also, pH_i is well correlated with intestinal oxygen consumption, therefore it is used as an indicator of intestinal ischemia [9, 10]. Based on these reports, we used a tonometer to monitor FJGs. The present study was performed to evaluate the usefulness of pH_i measurement to assess the viability of FJG.

Materials and Methods

Patients

Thirty-five patients underwent free jejunal transfer after resection of laryngeal, hypopharyngeal, and cervical esophageal cancer and the pH_i of these grafts was measured by tonometry between January 1994 and December 2002. The patients consisted of 31 men and 4 women, ranging in age from 45 to 79 years with an average age of 62.6 years. The locations of the tumors were the hypopharynx in 24 patients, the cervical esophagus in 6, and the larynx in 5. All 35 patients had squamous cell carcinoma. The clinical stage (TNM classification) was I in 3 patients, II in 5, III in 9, and IV in 18. Of the 35 patients, 23 underwent preoperative treatment, which consisted of chemotherapy in 13, radiotherapy in 5, and chemoradiotherapy in 5 patients. 33 pa-

tients underwent pharyngolaryngoesophagectomy and esophageal reconstruction using a FJG, while 2 patients underwent transhiatal total esophagectomy with laryngectomy and reconstruction using gastric pull-up with a FJG. Bilateral neck dissection was performed in all 35 patients. In this report, we designed two studies: the early phase study before 1999 ($n = 19$), in which pH_i of FJGs was measured to determine the critical value of pH_i , and the late phase study after 2000 ($n = 16$), in which anticoagulant treatment was performed in the patients having a pH_i value under the critical value established in the early phase study. There was no significant difference in the clinicopathological characteristics between the early phase group and the late phase group (table 1).

Surgical Technique and Postoperative Medication

Pharyngolaryngoesophagectomy was performed by a team of otolaryngologists for hypopharyngeal and laryngeal cancers, and by a team of surgeons for cervical esophageal cancers. Reconstruction with a FJG was performed by the surgeons' team, and microvascular anastomosis was done by a plastic surgeon. The superior thyroidal artery or transverse cervical artery was used as the feeding artery, while the external jugular vein or superior thyroidal vein was used as the drainage vein. Urokinase (Mitsubishi Pharma, Osaka, Japan) (24×10^4 units/day) and prostaglandin E_1 (Ono Pharmaceutical, Osaka, Japan) (80 $\mu\text{g/day}$) were intravenously administered continuously until the 5th postoperative day in all 35 cases. In the late phase study, heparin sodium (Aventis Pharma, Tokyo, Japan) (200 units/kg/day) was administered to patients whose pH_i value fell to <7.10 in addition to urokinase and prostaglandin E_1 .

Table 2. Postoperative complications

Complications	Early group (n = 19)		Late group (n = 16)	
	n	%	n	%
Obstruction of vessel anastomosis	3	16	1	6
Necrosis of FJG	2	11	1	6
Anastomosis leakage (minor)	4	21	2	13
Anastomosis stenosis	4	21	1	6
Bleeding	1	5	2	13

Assessment of pH_i

Blood circulation of the FJG was assessed by measuring the pH_i using a tonometer (TRIP Sigmoid Catheter, Tonometrics Division, Instrumentarium Corp., Helsinki, Finland) during and after the operation. The pH_i was assessed indirectly using a trans-nasal sampling tube with a silicone balloon which was impermeable to gas. The tonometer was positioned in the middle of the FJG intraoperatively and the tube was fixed on the nose to prevent moving away from the correct position. The pH_i was measured immediately after completion of anastomosis and at 6- to 12-hour intervals until 5 days after the operation. The regional PCO_2 ($PrCO_2$) was calculated from the measured PCO_2 multiplied by an equilibration factor, with the factors for periods of 60 min and >90 min being 1.19 and 1.17, respectively. The pH_i was calculated using the following version of the Henderson-Hasselbalch equation:

$$pH_i = 6.1 + \{\log_{10} [HCO_3^-]/PrCO_2 \times 0.03\}$$

$$(PrCO_2 = \text{measured } PCO_2 \times k)$$

where $[HCO_3^-]$ is the actual bicarbonate concentration (mmol/l) of the arterial blood sample and k is the equilibration factor (1.19 or 1.17).

Statistical Analysis

The pH_i data are expressed as the mean $\pm$ SD. The significance of differences was determined using the two-sided Student's *t* test. The Fisher's exact test was used to compare postoperative complications. A *p* value <0.05 was considered significant for all analyses.

Results

Postoperative Complications

In the early phase study, postoperative complications occurred in 10 (53%) of the 19 patients: obstruction of the graft vessels in 3 (16%) (2 of them suffered from graft necrosis), minor digestive anastomotic leakage in 4 (21%), and digestive anastomotic stenosis in 4 (21%) (table 2). The 3 patients with obstruction of the graft, vessels did not have any diseases predisposing to vascular occlusion, but all of them had received preoperative treatment, with radiotherapy (32–66 Gy) being performed in all 3 patients and chemotherapy (5-FU and/or CDDP) being

done in 2 patients. The causes of vascular obstruction were compression by hematoma, thrombus at the arterial anastomosis and thrombus at the venous anastomosis, respectively. Blood flow of the graft successfully restored with removal of the hematoma in 1 patient, but the other 2 patients required regrafting because of necrosis of the original graft. The course after reoperation was uneventful in all 3 patients. Digestive anastomotic leakage and stenosis were treated conservatively in all cases.

In the late phase study, postoperative complications occurred in 8 (50%) of the 16 patients: graft necrosis in 1 (6%), minor anastomotic leakage in 2 (13%), anastomotic stenosis in 1 (6%) and postoperative bleeding in 2 (13%) (table 2). One of 2 patients with postoperative bleeding received intravenous heparin sodium administration in addition to urokinase and prostaglandin E_1 because of a falling pH_i value.

Postoperative Change of pH_i in the Early Phase Group

The postoperative changes of pH_i in all patients of the early phase group are shown in figure 1. In the 16 patients without obstruction of the graft vessels, pH_i values were stable and the lowest pH_i was >7.10 throughout the postoperative course. The mean value of pH_i immediately after surgery in these patients was 7.32 ± 0.11 . The mean value gradually increased and was stable between 7.32 and 7.41. On the other hand, in the 3 patients with vascular obstruction, the pH_i fell to <7.10. Decline in the pH_i value <7.10 occurred within 30 h after operation in 2 patients with vascular obstruction by thrombus and at 54 h after operation in 1 patient with obstruction by hematoma. The pH_i value of these 3 patients continued to fall to 6.72 ± 0.16 within 24 h after the value decreased to <7.10. Based on the results of pH_i in the early phase study, we determined that the critical value of pH_i was 7.10.

Outcomes of Patients Whose pH_i Values Were <7.10

In the early phase study, all 3 patients whose pH_i value was <7.10 had vascular obstruction of the graft ves-

Fig. 1. Postoperative changes of the pH_i of the FJG in the early phase study ($n = 19$). The pH_i value was <7.10 in 3 patients with obstruction of the graft vessels ($\circ$). In the 16 patients ($\bullet$), whose pH_i values were always >7.10 , vascular obstruction was not found.

Table 3. Patients with obstruction of pedicle vessels in the early phase group

Patient No.	Past history	Preoperative treatment	Periods until reoperation, h	pH_i		Cause of vessel obstruction	Reoperation
				before	after		
1	–	Radiotherapy (32 Gy)	54	6.94	7.37	Oppression by hematoma	Removal of the hematoma
2	Esophageal cancer	Radiotherapy (40 Gy) chemotherapy	6	6.82	7.36	Arterial thrombus	Regraft
3	–	Radiotherapy (66 Gy) chemotherapy	30	6.67	NM	Venous thrombus	Regraft

NM = Not measured; before = before reoperation; after = after reoperation.

sels and underwent reoperation (table 3). Postoperative courses were uneventful and the mean hospital stay was 58.7 ± 31.5 days.

Outcomes of Patients in the Late Phase Group

In the late phase group, pH_i values fell to <7.10 in 4 patients (table 4). Thrombus in the anastomotic artery was found in 1 patient with a pH_i value of 7.08 just before wound closure. Reanastomosis of the artery was immediately performed and pH_i values never fell to 7.10, resulting in uneventful postoperative course. In the remaining 3 patients, the pH_i values immediately after surgery were 7.08, 7.30 and 7.12, and decreased gradually to 6.65, 7.07 and 7.00 by 6 h after the operation, respectively. Intrave-

nous administration of heparin sodium was added in these patients. Among them, 2 patients recovered gradually without reoperation. In 1 case, the pH_i value decreased to 6.59 by 12 h after the operation without improving regardless of heparin sodium administration, and regrafting was performed (fig. 2).

Discussion

Several advantages of FJGs have been reported when compared with other reconstructive methods. Schusterman et al. [11] reported that reconstruction with a FJG was associated with fewer complications and a higher

Fig. 2. Postoperative changes of the pH_i in 4 patients whose pH_i was <7.10 in the late phase study. In 1 patient (●), reanastomosis of the artery was immediately performed just before wound closure. In the 3 patients (○), administration of additional heparin sodium was performed.

Table 4. Patients whose pH_i value fell to <7.10 in the late phase group

Patient No.	Detection time (h after operation)	pH _i		Cause of vessel obstruction	Treatment	Outcome
		before	after			
1	0	7.08	7.40	Arterial thrombus	Reanastomosis	Recovered
2	6	7.07	7.24	Unknown	Heparin sodium	Recovered
3	6	7.00	7.32	Unknown	Heparin sodium	Recovered
4	6	6.65	6.59	Venous thrombus	Heparin sodium	Graft necrosis (regraft)

Detection time = The time decreased pH_i fell to <7.10 after operation; before = before treatment; after = after treatment.

success rate in comparison with gastric pull-up reconstruction. Low mortality, early intake of food, fewer cardiac or pulmonary complications, and a shorter hospital stay are also advantages of this method [12]. Despite these advantages, however, postoperative complications are not rare. There were 13 operative failures (13.5%) including arterial obstruction, venous anastomotic problems, and carotid blowout and 5 perioperative deaths (6%) among 96 patients in the series of Coleman et al. [12]. In the series of Julieron et al. [13], there were 2 postoperative deaths (2.4%), 4 graft failures (4.8%) and 11 salivary fistulas (13.3%) among 83 patients undergoing pharyngo-esophageal reconstruction with a FJG.

In our series, there was no patient death during the perioperative period but complications associated with surgical procedure were not uncommon. Leakage of the

pharyngojejunal anastomosis occurred in 21% and esophagojejunal stenosis was seen in 21% in the early phase group. However, all of these operative complications were cured with conservative treatment. Obstruction of the vascular anastomosis was the most undesirable complication because reoperation to replace a FJG increases the hospital stay and medical expenses. Monitoring of jejunal graft viability is essential to avoid such reoperation. Several monitoring methods for FJGs have been evaluated and reported in reconstruction of the pharynx and cervical esophagus [6, 7]. Among them, the clinical assessment of using the monitoring flap has some disadvantages including the difficulty of evaluating ischemia. Changes of the serosal surface of the monitoring flap induced by infection can make it difficult to correctly evaluate the status of the jejunal graft. Laryngoscopy has also

been used for monitoring of the jejunal flaps, but this method is obviously invasive and is not accurate enough because the change of mucosal color caused by ischemia needs a long time after vascular obstruction. On the other hand, tonometry is the quantitative and objective evaluation method.

The current results demonstrated that real-time monitoring of pH_i was helpful in detecting vascular damage immediately and in preventing reoperation by administration of heparin sodium in 2 of the 3 patients. In 1983, Fiddian-Green et al. [8] used a tonometer to predict the prognosis of patients with hemorrhagic shock caused by a bleeding gastric ulcer. Since then the tonometer has been applied to patients with acute circulatory failure [14], adult respiratory distress syndrome [15], and multiple organ failure [16]. pH_i has also been used to evaluate ischemia of the sigmoid colon after surgery for abdominal aortic aneurysm [17, 18]. A few investigators have advocated the use of gastrointestinal tonometry to calculate pH_i values for prediction of the postoperative outcome in patients at risk of inadequate splanchnic perfusion [19, 20]. Grum et al. [9] reported that there was a strong correlation between the changes of pH_i and intestinal O_2 consumption under conditions where O_2 delivery was decreased. Based on these observations, it was determined whether the pH_i measured by tonometry is useful as a monitoring method of tissue perfusion in FJGs after pharyngolaryngoesophagectomy in our series.

From our data in the early phase study, we considered the critical pH_i value induced by vascular complication in a FJG to be 7.10. When the pH_i value was ≥ 7.10 , obstruction of the pedicle vessels was not observed. We performed additional therapy by administering heparin sodium to patients whose pH_i value fell to < 7.10 expecting to avoid graft necrosis. The addition of heparin to uroki-

nase and prostaglandin E_1 improves the efficacy of thrombolysis and vasodilation by preventing both the formation and the incorporation of new fibrin into the thrombus. Hirigoyen et al. [21] noted thrombus formation in venules after ischemia-reperfusion injury and described the washout by urokinase and general administration of heparin to be effective against thrombus formation in the microcirculation. However, it is possible that heparin increases the risk of bleeding tendency. This suggests that the selection of the cases for the administration of heparin sodium is important. In our late series, early detection of vascular occlusion followed by additional treatment prevented regrafting in 3 of 4 patients with low pH_i values. On the other hand, we failed to prevent reoperation in 1 patient whose pH_i was falling in spite of the administration of heparin sodium. We opted for reoperation when the pH_i value reached 6.59 after 12 h. When pH_i does not recover within several hours by additional treatment, reoperation should be performed. Moreover, obstruction by the thrombus in the early and late phase study occurred in all patients within 30 h after the operation and vessel damage by hematoma occurred 54 h after the operation. These findings suggest that it is important to monitor the values of pH_i by tonometry for 2 days after surgery to detect vascular obstruction by thrombus, and to continue the monitoring by tonometry until 3 days after the operation at least.

In conclusion, pH_i measurement with a tonometer is useful for detecting vessel damage before necrosis appears after reconstruction with a FJG. When the pH_i value falls to < 7.10 , the jejunal graft is undergoing a severe disturbance induced by vascular obstruction. Additional treatment such as administration of heparin sodium should be given to such patients immediately to avoid reoperation.

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