主論文

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Postoperative Gastric Motility, Secretory Function, and Pre- and Postoperative Carbohydrate Metabolic States in Esophageal Cancer Patients

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Postoperative Gastric Motility, Secretory Function, and Pre- and Postoperative Carbohydrate Metabolic States in Esophageal Cancer Patients

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This study was undertaken to assess postoperative gastric motility and gastric acid secretion, and pre- and postoperative carbohydrate metabolism in patients with esophageal cancer. The gastric motility was compared among 3 different reconstruction routes in 26 patients who were divided into 2 groups according to the duration of postoperative follow-up; group A, 3 months or less; and group B, 18 months or more. The routes used for subtotal resection of the stomach were the posterior mediastinal, retrosternal, and subcutaneous routes. All patients showed positive resting pressure in the esophagus, but peristaltic waves did not reach the gastric tube at dry swallowing in any patients and peristaltic waves appeared after eating pudding only in 1 patient in group B. The resting pressure and gastric emptying time were similar among reconstruction routes, but the incidence and amplitude of metoclopramide (MCP)-induced peristaltic waves were significantly higher in group B than in group A. Furthermore, 24-h intragastric pH monitoring of gastic secretion in a group of 9 patients revealed individual variation in gastric secretion. Some patients showed high acidity soon after operation, suggesting the need for prophylactic treatment for preventing gastric ulcer. Postoperatively, postprandial serum gastrin levels were significantly higher than preoperative levels. In the other group of 11 patients tested, preoperative and postoperative carbohydrate metabolism were not significantly different. Postoperatively, carbohydrate metabolism recovered to preoperative levels after a transient decrease. These results demonstrated that postoperative motility improved over time although no difference was found among the 3 reconstruction routes used.

Key words: esophageal replacement, manometry, scintiscanning, 24-h pH monitoring, carbohydrate metabolism

In light of the improvement in survival of patients with esophageal cancer, the problem of long-term postoperative quality of life has come to the fore and esophageal replacement has drawn significant attention. Gastric reconstruction conduits and routes have been studied from various points of view based on the complaints of patients after surgery and on digestive and absorptive functions, motility, gastric secretion, and the state of food uptake (1-9).

In this study, we examined the postoperative function of the reconstructed gastric tube by comparing gastric motility and secretion among 3 different routes and also by comparing the motility between short- and long-term follow-up. We also compared glucose tolerance in pre- and postoperative states.

Patients and Methods

The standard operation for thoracic esophageal cancer used in our department is reconstruction surgery of subtotal stomach by the posterior mediastinal route with two- or three-field lymph node dissection. In this study, the cases of reconstruction using subtotal stomach by the retrosternal and subcutaneous routes were added to the cases of reconstruction by the posterior mediastinal route for comparison. All gastroesophagostomies were performed at the cervix with hands and pyloplasty was

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Table 1 Conditions of patients in groups A and B examined by manometry and gastroscintigraphy

Group	Patient no	Age	Sex	Reconstructive route used	Manometry	Scintigraphy	Postoprerative period (Months)
Group A							
	1	51	M	PM	+	+	2
	2	48	M	PM	+	+	2
	3	62	M	PM	+	+	2
	4	47	M	PM	+	+	2
	5	52	F	PM	+	+	2
	6	62	M	PM	+	+	2
	7	38	M	PM	+	−	1
	8	59	F	PM	−	+	2
	9	58	M	PM	+	+	2
	10	49	M	RS	+	+	1
	11	61	M	RS	+	+	2
	12	71	F	RS	+	+	1
	13	62	M	RS	+	+	1
	14	53	M	RS	+	−	2
	15	77	M	SC	+	+	1
	16	60	M	SC	+	+	2
Mean		56.9					1.7
Group B							
	1	64	M	PM	+	+	24
	2	49	M	PM	+	+	23
	3	53	M	PM	+	+	23
	4	49	M	PM	+	+	18
	5	71	M	PM	+	−	46
	6	74	M	RS	+	+	48
	7	57	M	RS	+	+	38
	8	76	F	SC	−	+	33
	9	79	M	SC	+	+	20
	10	81	M	SC	+	−	44
Mean		65.3					31.7

M: male; F: female; PM: Posterior mediastinum; RS: Retrosternum; SC: Subcutaneous; +: Patients who could be examined; −: Patients who could not be examined.

performed in all cases by pyloromyotomy of the anterior wall. All operations were performed by the same group of surgeons. Informed consent was obtained from all patients.

Motor Function of Reconstructed Gastric Tube

From June 1989 to December 1992, 72 patients with esophageal cancer underwent operation in our department. Among these patients, 26 of the 47 patients whose subtotal stomach could be used for reconstruction surgery were randomly selected as subjects. Histologically, the tissues of all 26 patients appeared as squamous cell carcinoma and all patients underwent operation of over C_2. These 26 patients were divided into groups A and B based on the duration of follow-up: group A consisted of patients examined within 3 months after operation and group B consisted of patients examined more than 18 months after operation. All patients were followed up by intraluminal manometry and scintiscanning. Motility (peristalsis) of the reconstructed gastric tube was compared between groups A and B based on the intraluminal pressure of the esophagus and gastric emptying time. In groups A and B, both parameters were tested in most patients, but only one parameter was tested in some patients. The age distribution, sex, and the route of reconstruction in groups A and B are shown in Table 1. The peristaltic waves were classified according to Code *et al.* (10)

Table 2 Patients' conditions for 24-h pH monitoring

Patient no	Age	Sex	Reconstructive route used	Postoprerative period (Months)
1	38	M	PM	1
2	65	M	PM	2
3	49	M	RS	1
4	52	M	RS	3
5	57	M	SC	2
6	59	M	SC	2
7	72	M	SC	2
8	63	M	SC	3
9	57	M	SC	1
Mean	56.9			1.9

M: male; F: female; PM: Posterior mediastinum; RS: Retrosternum; SC: Subcutaneous.

Table 3 Conditions of patients for examining metabolism of carbohydrate

Patient no	Age	Sex	Reconstructive route used
1	62	F	PM
2	62	M	PM
3	47	M	PM
4	59	F	PM
5	68	M	PM
6	71	F	RS
7	49	M	RS
8	53	M	RS
9	89	M	SC
10	71	M	SC
11	60	M	SC
Mean	63.1		

M: male; F: female; PM: Posterior mediastinum; RS: Retrosternum; SC: Subcutaneous.

Manometric Study

An 8 Fr catheter tip pressure transducer (16 CT/8F-3, Gaeltec Co., Great Britain) was used for manometric study. RECTI-HORIZ8K23 (NEC Sanei, Japan) was used for recording. With the patient in the supine position, a catheter was inserted so that the tip of the sensor was 5 cm orad of the pylorus and the following parameters were measured: (a) resting pressure, (b) activity at resting, (c) activity at dry swallows, (d) response to eating pudding, and (e) response to injection of metoclopramide (MCP) 0.5 mg/kg.

Scintigram

After eating pudding labelled with Tc-Sn colloid, scintigrams were taken from the sternoclavicular joint to the epigastrium using a gamma camera (Diagnost C, Philips Co., Holland) in both the supine and sitting positions. The data obtained were analyzed using a gamma-Processor 673. (Philips Co., Holland) Radioactivity was counted every 30 sec and the percentage relative to the baseline was calculated at 5, 15, and 30 min. After the time-activity curve was obtained, the time to 50 % emptying of food ($T_{1/2}$) was calculated for comparison.

Acid Secretory Function of Reconstructed Gastric Tube

Gastric acid secretion and reflux of bile acid were examined in 9 of 47 patients with esophageal cancer who were treated surgically in our department from July 1993 to May 1994. Acid secretory function was recorded continuously for 24 h of the reconstructed gastric tube using a monitor (Table 2). The electrode used for the experiment was a two-channel (situated 15 cm from each other) antimonic monopolar electrode and its tip was placed 5 cm orad of the pylorus. The data were recorded with a portable pH monitor (Digitraper MKII Gold; Synetics Medical Co., Sweden) and were analyzed using the Esophagram computer software package (Synetics Medical Co.). Postoperative gastrin levels 1 h after lunch were measured for comparison. The gastric acid response was examined after subcutaneous injection of tetragastrin (150 μg) on an empty stomach.

Pre-and Postoperative Carbohydrate Metabolism in Esophageal Cancer Patients

Serum levels of glucose, insulin, glucagon and somatostatin were measured in the other 11 of the 47 patients by intravenously injection of glucose 0.5 g/kg before and after the operation to compare the data (Table 3). After operation, these data were obtained when the patients were able to eat food. For comparison of data, the insulinogenic index (I.I) and values of K (11) were calculated.

Statistical Analysis

The values are expressed as mean ± SD, and Student's *t*-test was used to evaluate the statistical significance between the two groups.

Results

Intraluminal Pressure of Reconstructed Gas-

Table 4 Intraluminar pressure at rest, 50% emptying time (T 1/2), median pH values, and percentage of time of pH values less than 4

	PM	RS	SC
Motility test (Group A: n=16; Group B: n=10			
Intraluminal pressure (cmH_2O)			
Group A	6.5 ± 3.1 (8)	7.2 ± 2.6 (5)	6.0 ± 2.8 (2)
B	3.8 ± 0.4 (5)	2.5 ± 2.7 (2)	3.5 ± 2.1 (2)
Scintigram (min)			
Supine			
Group A	163.6 ± 129.6 (8)	127.6 ± 133.6 (4)	94.2 ± 6.0 (2)
B	191.8 ± 258.9 (4)	125.8 ± 94.3 (2)	68.7 ± 32.6 (2)
Sitting			
Group A	11.5 ± 7.3 (8)	31.7 ± 38.2 (4)	27.6 ± 2.4 (2)
B	17.8 ± 20.3 (4)	21.4 ± 5.5 (2)	262.8 ± 117.1 (2)
Secretion test (n=9)			
Median pH values			
Fundus	1.75 ± 2.05 (2)	6.80 ± 1.56 (2)	4.20 ± 2.56 (5)
Antrum	5.80 ± 0.71 (2)	6.95 ± 0.64 (2)	3.78 ± 2.10 (5)
Time % of pH value < 4			
Fundus	75.95 ± 14.07 (2)	4.25 ± 3.04 (2)	23.4 ± 35.21 (5)
Antrum	20.0 ± 7.21 (2)	4.80 ± 4.95 (2)	57.5 ± 38.2 (5)

PM: Posterior mediastinal route; RS: Retrosternal route; and SC: Subcutaneous route. Numbers in parentheses indicate numbers of the patients examined. There were no significant differences between groups A and B.

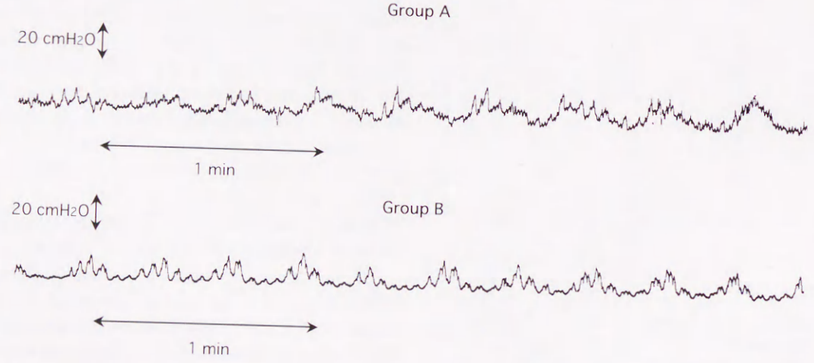


Fig. 1 Intraluminal resting mechanical activities of reconstructed gastric tube in groups A and B. The same type of waves (type I by Code's classification) appeared in groups A and B.

tric Tube

There was no significant difference in intraluminal pressure between groups A and B for a given reconstruction route, but the intraluminal pressure at rest tended to be higher in group A than in group B (Table 4). Mechanical activity at rest was seen in 3 of 14 (21.4%) patients tested in group A and in 3 of 9 (33.3%) patients tested in group B. The peristaltic waves which appeared were those of type 1 classified by Code *et al.* (10) in groups A and B (Fig. 1). The peristaltic waves on dry swallows reached the residual esophagus but did not reach the reconstructed gastric tube in any patient in either group. Peristaltic waves were evoked by eating pudding in only one patient in group B and in no patients in group A. The shape of the waves was that of type 3. Peristaltic waves were evoked by MCP 0.5 mg/kg i. v. and increased in amplitude in 8 of the 14 patients in group A (57.1%) and in 7 of the 9 in group B (77.8%). The peristaltic waves appeared 105.0 ± 48.6 sec after the injection of MCP in group A and 121.4 ± 160.0 sec in group B. The duration of the waves was 9.8 ± 3.9 min in group A and 12.0 ± 3.9 min in group B. The average amplitude in group A (14.1 ± 7.0 cmH_2O) was significantly lower than that in group B (64.0 ± 9.9 cmH_2O), and the waves seen in group A were type 1 and those in group B were type 3 (Fig. 2).

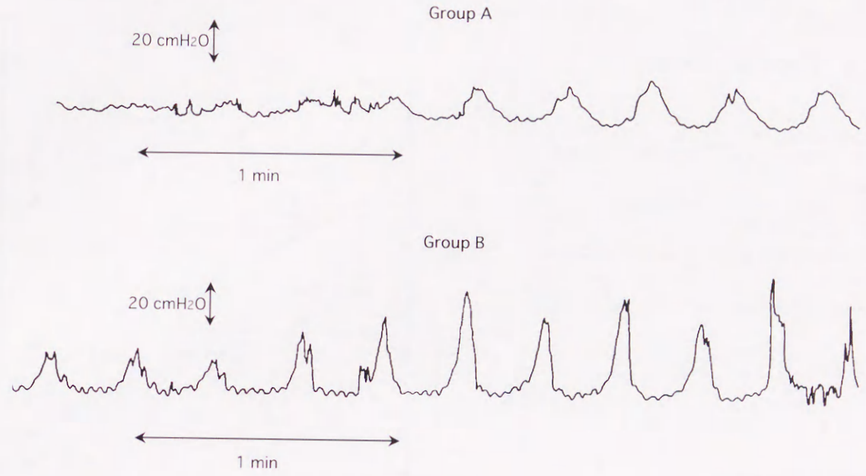


Fig. 2 Response to injection of metoclopramide (MCP) after 240 sec in group A and after 40 sec in group B. Group A showed type I and group B showed type 3 waves in response to MCP.

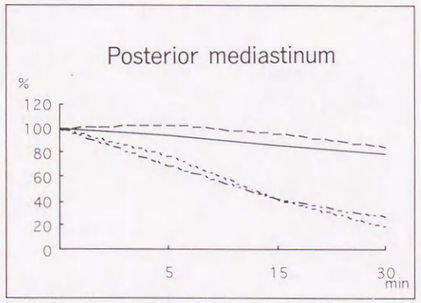
Scintigraphy

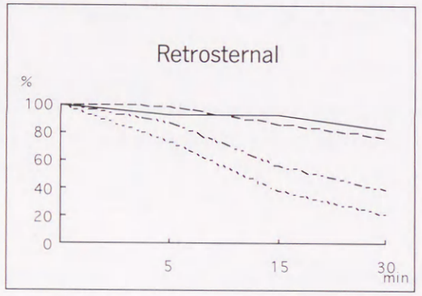
In the sitting position, the tendency to stasis of food was observed in the subtotal stomach in patients treated by the subcutaneous route in group B. There were no differences between the posterior mediastinal and retrosternal gastric routes in groups A and B (Table 4, Fig. 3). The tendency of gastroduodenal reflux was seen in the restored posterior mediastinal routes in the supine position.

In the sitting position, there were three different types of time-activity curves according to the classification of Shiraha *et al.* (3): (a) slow type, which drew slow curves while the contents was gradually emptied into the subtotal stomach; (b) delayed type, which drew slow curves after most of the contents was rapidly emptied; and (c) rapid type, in which most of the contents was rapidly emptied. According to this classification, 6 patients were classified as slow type, 7 as delayed type and 1 as rapid type in group A and 6 patients were classified as slow type and 2 as delayed type in group B. In group A, many patients showed delayed type in the reconstructed subtotal stomach when the posterior mediastinal route was used.

Secretory Function of Gastric Tube

The secretory function of the reconstructed gastric tube showed individual differences irrespective of the route of reconstruction (Table 4). According to the classification of Takahashi *et al.* (12), one patient was type 1 (high acidity), two were type 2 (intermediate), five were type 3 (low acidity), and one was type 4 (antral high acidity). In all but two patients, pH values decreased in response to tetragastrin (Fig. 4). This effect was





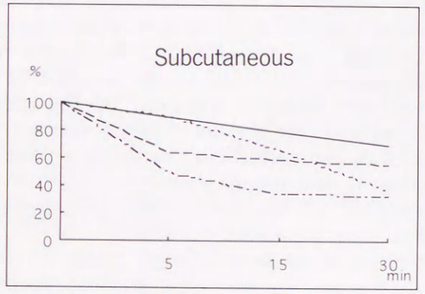


Fig. 3 Mean percentage curves of retention activities of Tc-Sn colloid in groups A and B. In supine position, there were no differences according to the route of reconstruction in either group. In sitting position, the tendency to stasis of food was observed only in patients treated by the subcutaneous route in group B. Numbers of patients examined were 14 in group A and 8 in group B.
(----) sitting A; (——) supine A; (– – –) supine B; (–·–·–) sitting B.

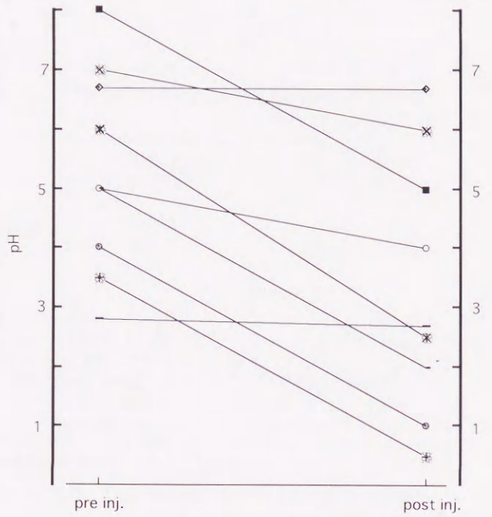


Fig. 4 Effects of tetragastrin injection on the reconstructed gastric tube. After injection of tetragastrin, pH values in the gastric tube decreased in all but two patients. This decrease lasted for about 27.8 ± 20.0 min.
(-■-) case 1; (-◆-) case 2; (-●-) case 3; (-✳-) case 4; (-✱-) case 5; (-✕-) case 6; (—) case 7; (-○-) case 8; (—) case 9.

maintained for 10–70 min (27.8 ± 20.0 min). The serum gastrin levels 1 h after a meal before the operation (92.9 ± 40.2 pg/ml) were significantly lower than after the operation (207.8 ± 114.6 pg/ml).

Pre- and Postoperative Metabolism of Carbohydrates

There were no significant differences in the serum levels of glucose, insulin, glucagon, and somatostatin in the empty stomach between pre- and postoperative data. Time-activity curves following intravenous glucose tolerance testing are shown in Fig. 5; the only significant difference between pre- and postoperative values was serum glucagon at 30 min. Preoperative K values were 2.2 ± 0.8 and postoperative K values were 1.5 ± 0.7, showing no significant difference. However, glucose tolerance tended to decrease after the operation. Preoperative I.I was 0.24 ± 0.36 and postoperative I.I was 0.21 ± 0.16, and the difference was not significant.

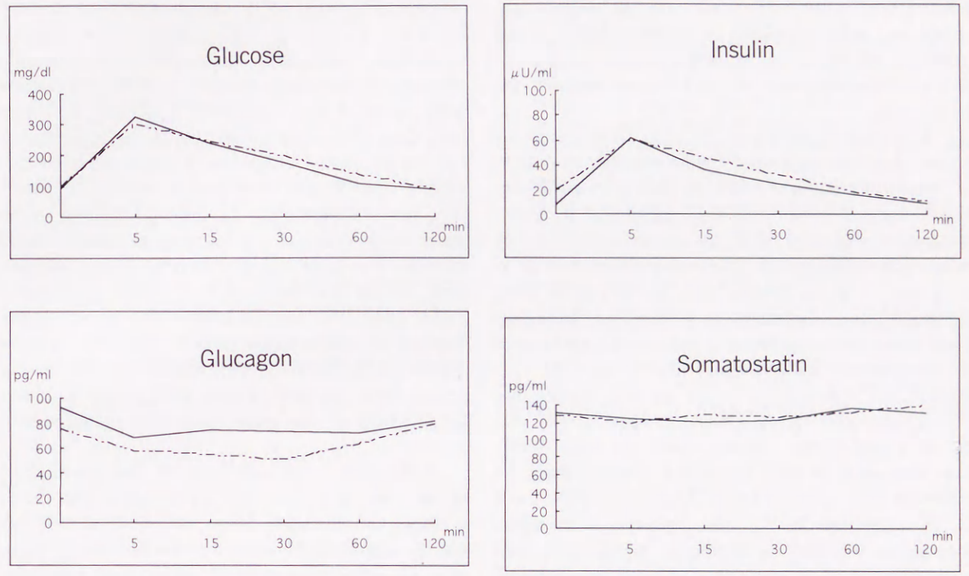


Fig. 5 Time-activity curve of carbohydrate metabolism before and after operation. Serum levels of glucose, insulin, glucagon and somatostatin in the empty stomach were measured. Pre and postoperative data showed a significant difference only in glucagon levels at 30 min after operation. (——) Preoperative, (- - - - -) Postoperative.

Discussion

Surgical resection of esophageal cancer often involves the use of pedicled jejunal grafts, pedicled colon grafts and gastric tubes for esophageal reconstruction. Among these, the gastric tube is most frequently used. In this study, we examined the functions of esophageal motility (peristalsis) and secretion in the reconstructed gastric tube by focusing on the subtotal stomach by the posterior mediastinal route, which is the standard operative procedure for esophageal cancer. We also examined pre- and postoperative glucose tolerance to compare the data.

In our study, the resting pressure in the reconstructed gastric tubes showed little difference among the three surgical routes we used, and the pressure was positive in both groups. Yoshino *et al.* (13) reported that intragastric pressure at rest varied according to the route of reconstruction, but Miller *et al.* (14) reported positive resting pressure in all gastric tubes irrespective of the route, showing an average of 3.7 cmH_2O. Lam *et al.* (15) conjectured that the positive intragastric resting pressure of 1–7 mmHg seen in their cases was due to truncal vagotomy. We consider, however, that the positive pressure may have been due to the gastric tube, because the tube is apt to be affected by abdominal pressure owing to the loss of the esophageal sphincter.

In our study, the finding that peristaltic activity did not reach the intragastric tube at dry swallows was considered to have been caused by the discontinuity of the function to connect the residual esophagus with the reconstructed gastric tube. Instead, the food is considered to have passed through the gastric tube by gravity.

As peristaltic activity appeared in response to eating pudding only in one patient, although the amount consumed was small, it remains to be seen whether or not peristaltic waves will appear when patients eat enough food to fill the intragastric tube and to give pressure to the gastric wall.

The dopamine antagonist MCP is widely used for enterokinesis and antiemesis, but its use in the evaluation of reconstructive gastric tubes has been reported in only a few papers. As expected, the amplitude of the peristaltic waves evoked by MCP was greater in group B than in group A. Although the precise mechanism of MCP in the periphery has not been clarified, the effect of MCP on the gastric tube is considered to be based on the antagonistic action on the peripheral dopamine receptor because truncal vagotomy was performed. Miller *et al.* (14), who injected MCP intravenously to six patients, reported that type 2 peristaltic waves appeared within 2.5 min and persisted until 10 min. In our study, the same results were obtained in group B, but we were not sure about the difference in the response to MCP between groups A and B. We conjecture that the following problems are inherent during the early postoperative period when unphysiologically constructed routes are used for esophageal reconstruction: (a) reduced blood flow in the reconstructed stomach, (b) persistent edema in the wall of the gastric tube, and (c) different sensitivities of dopamine receptors in the wall of the gastric tube.

The scintigrams revealed no difference between the posterior mediastinal route and the retrosternal route in either the sitting or supine positions. When reconstruction was performed by the posterior mediastinal route, excretion of food tended to be faster in the sitting position, similar to the physiological route, but the food tended to reflux in the supine position (Fig. 3). The difference between the sitting and supine positions was caused by the force of gravity in both groups. Furthermore, the motility of the gatric tube reconstructed by any route was not seen even after a long period postoperatively.

There was one case with high acidity, type 1 as classified by Hashimoto *et al.* (12). There were four patients with median pH values of less than 4, three with pH 4–7, and two with pH over 7. As a whole, there were many patients with decreased acid secretion. This result, however, is considered to have been the result of individual differences, not due to differences among the gastric routes. By scintigraphy, the tendency of gastroduodenal reflux was seen in the restored posterior mediastinal routes in the supine position. By 24-h pH monitoring as well, reflux of bile was observed more frequently in patients treated by restored posterior mediastinal routes than by other routes showing the same tendency. In our study, the postoperative serum gastrin levels increased more significantly than those of preoperation. Lam *et al.* reported that the fasting and postprandial serum gastrin levels significantly increased after surgery when truncal vagotomy was added to the operation; they described that the loss of feedback in the gastric tubes by truncal vagotomy was responsible for this increase. We agree with this opinion. There have been some reports describing cases of hemorrhagic ulcer in gastric tubes (16). Individual differences in the secretory function of reconstructed gastric tubes was great, as pointed out in this study, and some patients showed high acidity during the early postoperative period. Therefore, the possibility of ulcer in the gastric tube should be borne in mind.

In this study, postoperative serum glucagon tended to be decreased and there was no indication that glucose tolerance was disturbed due to surgery. Although there was no significant difference between pre- and postoperative I.I values, postoperative carbohydrate metabolism tended to decrease in K values. Pre- and postoperative carbohydrate metabolism in the patients with esophageal cancer was complexly affected by various factors such as the state of blood flow in the reconstructed gastric tubes, truncal vagotomy, and the secretion of various hormones. Therefore, no significant differences were seen in pre- and postoperative carbohydrate metabolism, and glucose metabolism appeared to recover to the preoperative state 2–3 months postoperatively.

In the present study, most patients in group B responded to the injection of MCP, suggesting that the motility of the reconstructed gastric tube has improved with time.

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