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Comparison of the short-term health-related quality of life in patients with esophageal cancer with different routes of gastric tube reconstruction after minimally invasive esophagectomy

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Abstract
Objective To compare the short-term health-related quality of life (HRQL) between the two different routes of gastric tube reconstruction after minimally invasive esophagectomy (MIE).
Methods From January 2007 to June 2009, 97 patients who underwent three-incision subtotal MIE were enrolled in this retrospective study. Among them, 49 patients followed prevertebral route and 48 patients followed retrosternal route. The questionnaires (EORTC QLQ C-30 and OES-18) were applied to assess the HRQL of the patients before and 2, 4, 12, 24 weeks after operation.
Results All the patients underwent operation with no mortality. No statistical difference was found in age, gender, serum albumin level, the level of growth in the esophagus, pathological diagnosis, tumor stage, operation time, blood loss or ICU stay between the two groups. The perioperative complication rate was 35.4% in retrosternal group and 32.7% in prevertebral group ($P = 0.774$). However, the rate of cervical anastomotic leak in the retrosternal group was much higher (20.8 vs. 6.1%, $P = 0.033$). But the rate of cardiac or pulmonary complication in the retrosternal group seemed to be lower (10.4 vs. 22.4%, $P = 0.110$). Besides, the rate of anastomotic stricture was similar (6.3 vs. 10.2%, $P = 0.735$). And all HRQL measures did not show major differences between the two groups before operation. However, at the time of 2 weeks after operation, the dysphagia and eating problem questionnaires scores were higher in retrosternal group than in prevertebral group, which meant that the patients in retrosternal group suffered more severe problems; meanwhile, the scores of global quality scale in retrosternal group was also lower, which indicated that the patients had a worse global quality of life. Whereas, at the time of 12 and 24 weeks after operation, the dyspnoea and reflux symptom questionnaire scores were lower in retrosternal group than in prevertebral group, which revealed that there were less problems in the patients of retrosternal group; meanwhile, the score of global quality scale in retrosternal group was higher conversely, which suggested that the patients gain a better status in global quality of life.
Conclusion Our results suggest that retrosternal route may be a good alternative choice for MIE in view of better HRQL after operation, although it has higher risk of anastomotic leak that might lead to worse HRQL in early period.

Keywords Minimally invasive esophagectomy (MIE) · Health-related quality of life (HRQL) · Route of reconstruction

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Introduction

In a disease such as esophageal cancer, which has a high morbidity and poor prognosis, survival alone may inadequately describe outcome. Researchers have paid more attention to patients' health-related quality of life (HRQL), which has been advocated as the second relevant outcome measure to assess the cancer therapy [1]. HRQL measures add another descriptive dimension that may be used to provide a better assessment of the effects of therapy and to compare one treatment to another.

Esophageal resection is the most established treatment that could offer a cure for patients with esophageal cancer in early stage. The factors that may be correlative with HRQL in patients after esophagectomy mainly include TNM stage, tumor location, pathological types (adenocarcinoma or squamous cell carcinoma), choice of conduit (stomach, colon or jejunum), location of anastomosis (thoracic or cervical), and route of reconstruction [2–4]. In the recent 20 years, minimally invasive esophagectomy (MIE) has been developed with various surgical types and may affect the post-operative HRQL compared with the conventional open surgery [5].

Three-incision subtotal esophagectomy with two or three fields lymph-node dissection is recommended for middle or some upper esophageal carcinoma [6, 7]. However, it is criticized with its high morbidities and poor post-operative HRQL, following the extensive trauma by the operation itself. We began the procedure of thoracoscopic esophagectomy or combined with laparoscopic gastric mobilization with the cervical anastomosis in 2004. More than 40 cases of MIE were done annually, which is now our first choice for clinical stage I and II esophageal carcinoma. And in our pilot study, the outcome showed that the short-term HRQL may be better in the MIE group compared with the open group [8].

On the other hand, in our former experience of open surgery, there were mainly two types (prevertebral and retrosternal) of the route for reconstruction. Preverteral route for the gastric tube was our routine choice. However, retrosternal route was also favored for its advantage of easy-making, less risk of gastric tube torsion, and possible benefit for adjuvant radiotherapy; therefore, it was kept especially for some cases of locally advanced caner.

And in our practice of MIE, prevertebral route for the gastric tube was also our routine choice. However, with the experience accumulated, we found that it was easier to make the retrosternal route through the minilaparotomy incision just below the xiphoid and no need for reestablishment of the pneumoperitoneum (the method will be described later). Thus, we were very interested to see the result of this route that was rarely reported under MIE, especially about the influence on HRQL, compared with that of the classical prevertebral route.

In this retrospective study, the EORTC (European organization for research and treatment of cancer, EORTC) quality of life core questionnaire (QLQ C-30) together with the esophageal-specific module (OES-18) was applied to compare the HRQL in patients with retrosternal or prevertebral reconstruction after MIE. Our unit had been given permission to use this tool prior to this study.

Patients and methods

Patients

From January 2007 to June 2009, 100 eligible patients with esophageal carcinoma were enrolled in this study. All patients had no history of previous thoracic or abdominal surgery. And they all performed esophagogastroduodenoscopy and acquired pathological diagnosis. Besides, CT scan or endoscopic ultrasonography was applied to exclude cases of local extension, massive lymph invasion, or organic metastasis. No chemotherapy or radiotherapy was performed before operation. All the patients in the two groups had goodish performance status with the Eastern Cooperative Oncology Group (ECOG) scores 0–1 before surgery.

All patients underwent three-incision subtotal esophagectomy via MIE and reconstruction with gastric tube transposition by the same surgical group (Tan MD). In this series, prevertebral route reconstruction was performed in the first half of patients, and retrosternal route in the second half. And informed consents were obtained from all patients about the reconstruction route in the conversation before surgery. While conversion to thoracotomy or laparotomy was required in 3 patients (2 cases for thoracic extensive adhesion, 1 case for abdominal hemorrhage), they were excluded. Therefore, MIE was successfully completed in 97 patients (49 cases in prevertebral group and 48 cases in retrosternal group).

Operation procedure

Patients were general anesthetized with a double-lumen tube. The operation was composed of three stages. (1) Stage I: Thoracoscopic mobilization of intrathoracic esophagus with the tumor and dissection of lymph nodes (a detailed technique was described elsewhere [8]). Patients were placed in the left lateral decubitus position, and four thoracoscopic ports were placed on the patients. The operation began at dividing the inferior pulmonary ligament. Then, the mediastinal pleura overlying the esophagus were divided up to the level of the azygos vein. After double clipping of the azygos vein by Ham-o-lok at each side, the vessel was divided by harmonic scalpel (Ethicon Endosugery, Cicinatti, OH, USA). Circumferential mobilization of the entire esophagus was performed up to the thoracic inlet and down to the diaphragmatic reflection, including paraesophageal and subcarinal lymph nodes. Bilateral recurrent laryngeal nerve lymph nodes were cleaned by sharp dissection. After placing a single chest drain tube and closing the thoracic ports, the patient was turned to the supine position and re-draped. (2) Stage II:

Laparoscopic mobilization of the stomach with dissection of celiac lymph nodes. Five ports were set up similar to the descriptions of Luketich [9]. Complete mobilization of the stomach was performed by using harmonic scalpel, except for the clipping of the left gastric artery. Lymph nodes and fat tissue along the left gastric vessels, celiac axis, common hepatic artery, and splenic artery were dissected. After an oblique cervical incision along the left sternocleidomastoid was made, cervical esophagus was dissociated out. The esophagus was transected 2–3 cm distal to the upper esophageal sphincter. The specimen was pulled into the peritoneal cavity. Then the 5-mm port just below the xiphoid was extended to 4–5 cm. The specimen along with the stomach was pulled out of the mini-incision. And a 6-cm-wide gastric tube was made along the great curvature by linear cutter or hand sewing. Then, the specimen and proximal gastric cardia were moved. (3) Stage III: Gastroesophageal reconstruction with cervical anastomosis in different routes. In the group of prevertebral route, the gastric tube was pulled through posterior mediastinum under the laparoscopic guidance after closing the mini-incision and reestablishing of the pneumoperitoneum. A nasogastric tube and a feeding jejunum tube were placed through the nasal cavity. Finally, a wide gastroesophageal anastomosis was performed in side-to-side manner using linear cutter ETS45 (Ethicon Endosugery, Cicinatti, OH, USA). And in the group of retrosternal route, the nasogastric tube was inserted up to the neck through a gastrostomy in anterior gastric wall just 3–4 cm above the pylorus. The feeding jejunum tube was placed into the jejunum through the same gastrostomy or the other gastrostomy just below the first one. The gastrostomy was fixed on the peritoneum after completion of the anastomosis. Retrosternal route was easily made by blunt dissection through the mini-incision. The anastomosis method was the same as the prevertebral group. Pyloroplasty was never performed in both groups. The analgesia was used routinely in all patients by patient control epidural analgesia until thoracic drainage was removed (mostly within 3–5d).

HRQL Assessment

The assessment of HRQL was based on a previously validated cancer-specific core questionnaire, the QLQ-C30 (version 3.0, in Chinese) and the esophageal cancer-specific module QLQ-OES 18(in Chinese) both developed by EORTC. The QLQ-C30 includes one global QOL scale, five functional scales (physical, role, emotional, cognitive, and social), three general symptom scales (fatigue, nausea and vomiting and pain), and six single-item general symptom measures or problems (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). The QLQ OES-18 is composed of four symptom scales (dysphagia, eating, reflux, and esophageal pain), and six single items (swallowing saliva, choking when swallowing, dry mouth, taste problem, coughing and speech problem). After obtaining the informed consent of the patients, we requested everyone of them to fill out the questionnaires before operation and at the follow-up (2, 4, 12 and 24 weeks after operation) by letter visit or out patient consultant.

Statistical analysis

Scores, derived from the questionnaires were linearly transformed into a 0–100 scale according to the EORTC Scoring Manual [10]. A higher score in the functional and global HRQL scales represented a higher level of function and better global HRQL, whereas a higher score on symptom scales and items indicated more severe symptoms.

All data analyses were performed by using the statistical software SPSS 13.0 for Windows. Mean scores and standard deviations (SDs) were calculated. The unpaired *t*-test was used to examine statistical significance at the 5% level for the difference of scores between the two groups. Statistically speaking, P value of <0.05 was regarded as significance and <0.01 as prominent significance [11]. Besides, the data also were analyzed using nonparametric method, and the results were comparable to the parametric method.

Results

Clinical outcomes

All the patients underwent operation with no mortality within 30 days. The two groups were comparable with respect to their clinical characteristics (Table 1). No statistical significance was confirmed in the difference on age, gender, marital status, height, serum albumin level, the level of growth in the esophagus, pathological diagnosis, or tumor stage between the two groups by SPSS analysis.

The operation time was 279 ± 64 min in retrosternal group and 266 ± 56 min in prevertebral group, with no statistical difference ($P = 0.275$) (Table 2). Blood loss (359 ± 156 vs. 336 ± 130 ml, $P = 0.436$) and ICU stay (2.5 ± 1.7 vs. 2.8 ± 1.9 d, $P = 0.572$) were also of no difference. 35.4% of the patients in retrosternal group had at least one perioperative complication, and contrastively, 32.7% in prevertebral group ($P = 0.774$) (Table 2). However, the rate of cervical anastomotic leak in the retrosternal group was much higher (20.8 vs. 6.1%, $P = 0.033$). But the rate of cardiac or pulmonary complication (arrhythmia, pulmonary infection or respiratory dysfunction) in the retrosternal group seemed to be lower (10.4 vs. 22.4%,

Table 1 Characteristics of 97 patients with esophageal cancer treated by surgery

	Retrosternal group ($n = 48$)	Prevertebral group ($n = 49$)
Age (mean)	60.3 ± 7.8	61.8 ± 8.7
Gender		
Male	32	30
Female	16	19
Marital status		
Single	2	2
Married	37	35
Separated, divorced, widowed	9	12
Height	167.6 ± 6.7	166.9 ± 6.5
Serum albumin level (g/L)	39.2 ± 5.2	38.6 ± 5.4
The level of growth in the esophagus		
Upper	7	5
Middle	32	34
Lower	9	10
Pathological diagnosis		
Squamous cell carcinoma	46	47
Adenocarcinoma	2	1
Undifferentiated	0	1
Tumor stage(p-TNM)		
0–I	11	12
IIa	26	29
IIb	5	4
III	6	4
IV	0	0

Table 2 Operative demographics

	Retrosternal group ($n = 48$)	Prevertebral group ($n = 49$)
Operation time (min)	279 ± 64	266 ± 56
Blood loss (ml)	359 ± 156	336 ± 130
ICU Stay (day)	2.5 ± 1.7	2.8 ± 1.9
Complication (perioperation)		
Cervical anastomotic leak	10	3
Chylothorax	1	1
Pulmonary infection	2	5
Respiratory dysfunction	0	1
Arrhythmia	3	5
Pulmonary embolism	1	1
Complication (long-term)		
Anastomotic stricture	3	5

$P = 0.110$). Besides, the rate of anastomotic stricture between the two groups was similar (6.3 vs. 10.2%, $P = 0.735$).

Comparison of HRQL of the two groups

The response of the QOL measures was almost 95.1% in total during the entire follow-up period (229/240 [95.4%] questionnaires were fed back in the retrosternal group and 232/245 [94.7%] in the prevertebral group). The detail scores were shown in Table 3. All patients were alive during the 6-month follow-up; however, recurrence of mediastinal lymph node occured in one patient of retrosternal group 5.5 months after operation.

In the assessment of the HRQL before operation, the scores of every scale and item between the two groups were adjacent, with no statistical difference. However, the scores of global quality of life scale, dysphagia, and eating symptom scales between the two groups presented statistical difference at the time of 2 weeks after operation. Meanwhile, the scores of global quality, dyspnoea, and reflux between the two groups also presented statistical difference at the time of 12 and 24 weeks after operation. And the scores of the other scales or single symptoms did not show statistical differences.

The mean scores of dysphagia scale and eating scale of the two groups improved rapidly after operation, and then descended gradually after 2 weeks later. The scores in retrosternal group were much higher than in prevertebral group, especially during the early period(0–2 week), which revealed that the problem of dysphagia, and eating was more severe in the patients of retrosternal group. However, the scores between two groups became closer gradually with the follow-up time going on. And at the 12th week, the score in retrosternal group had almost drawn up to prevertebral group (Table 3, Figs. 1, 2).

The mean scores of dyspnoea items of the two groups improved rapidly after operation, and then descended gradually. The scores in two groups were adjacent in the early period. However, after the 12th week, the scores in prevertebral group were much higher than in retrosternal group (Table 3, Fig. 3), which meant that the problem of dyspnoea was more severe in the patients of prevertebral group.

The mean scores of reflux scale of both groups increased continuously after operation. The scores in two groups were adjacent in the early period. However, after the 12th weeks, the scores in prevertebral group were much higher than in retrosternal group (Table 3, Fig. 4), which indicated that the patients in prevertebral group had more severe suffering from reflux.

Besides, the mean scores of the global HRQL were lower in retrosternal group than in prevertebral group in the early period (2nd week: 53.5 ± 16.7 vs. 60.9 ± 15.6, $P = 0.026$), whereas higher in the later period conversely (12th week: 71.0 ± 13.1 vs. 64.8 ± 14.2, $P = 0.028$; 24th week: 71.9 ± 9.7 vs. 66.7 ± 11.3, $P = 0.017$) (Table 3,

Table 3 HRQL Scores of patients with esophageal cancer treated by surgery

	Retrosternal group					Prevertebral group				
	Pre-operation	2 weeks post-operation	4 weeks post-operation	12 weeks post-operation	24 weeks post-operation	Pre-operation	2 weeks post-operation	4 weeks post-operation	12 weeks post-operation	24 weeks post-operation
QLQ-C30										
Global quality of life scale[a]	71.4 ± 8.7	53.5 ± 16.7*	59.7 ± 17.4	71.0 ± 13.1*	71.9 ± 9.7*	72.3 ± 10.3	60.9 ± 15.6	63.6 ± 15.8	64.8 ± 14.2	66.7 ± 11.3
Functioning scale[a]										
Physical functioning	81.4 ± 9.1	64.7 ± 9.0	73.6 ± 10.9	78.7 ± 9.8	79.7 ± 9.7	82.0 ± 9.6	68.0 ± 8.9	76.0 ± 10.4	79.6 ± 9.6	80.1 ± 9.3
Role functioning	70.8 ± 7.3	51.4 ± 13.7	56.6 ± 16.0	69.1 ± 11.4	70.5 ± 9.8	69.4 ± 6.2	54.1 ± 15.8	58.2 ± 17.1	68.0 ± 8.9	68.7 + 8.1
Emotional functioning	69.8 ± 8.2	64.4 ± 8.6	67.5 ± 8.5	70.8 ± 8.4	73.1 ± 6.9	70.7 ± 9.6	66.0 ± 8.8	68.9 ± 8.3	71.1 ± 8.5	72.3 ± 7.9
Cognitive functioning	73.4 ± 6.1	69.3 ± 7.9	70.1 ± 10.8	75.2 ± 7.0	75.0 ± 6.4	73.0 ± 6.2	70.9 ± 9.0	70.9 ± 10.8	73.3 ± 7.6	74.1 ± 6.8
Social functioning	62.5 ± 12.2	48.3 ± 12.1	61.5 ± 14.6	65.0 ± 9.2	66.0 ± 7.7	62.9 ± 12.4	50.0 ± 13.6	62.9 ± 15.3	66.0 ± 9.6	66.7 ± 9.0
General symptom scales[b]										
Fatigue	22.7 ± 9.1	47.4 ± 14.1	33.8 ± 16.5	27.5 ± 11.2	26.6 ± 10.4	21.7 ± 8.2	44.9 ± 11.8	31.9 ± 15.8	27.4 ± 11.8	27.0 ± 10.9
Nausea and vomiting scale	11.5 ± 7.8	17.0 ± 10.0	14.3 ± 9.1	12.5 ± 8.1	12.2 ± 7.5	11.6 ± 7.8	15.3 ± 10.1	12.9 ± 9.8	12.3 ± 8.9	12.3 ± 8.9
Pain	16.7 ± 8.4	37.8 ± 17.1	26.0 ± 11.3	20.5 ± 13.0	20.1 ± 12.4	17.4 ± 9.6	35.4 ± 15.8	24.1 ± 11.8	19.7 ± 12.6	19.7 ± 11.6
General symptom items[b]										
Dyspnoea	27.1 ± 20.2	56.3 ± 21.9	43.7 ± 19.7	31.2 ± 25.2*	29.9 ± 25.0*	26.5 ± 20.4	58.5 ± 17.4	46.9 ± 21.5	41.5 ± 24.1	40.8 ± 24.8
Insomnia	25.0 ± 14.6	35.4 ± 18.7	29.8 ± 18.5	26.4 ± 18.1	25.7 ± 17.2	23.8 ± 15.2	32.6 ± 14.4	27.9 ± 15.7	25.1 ± 17.4	23.8 ± 16.7
Appetite loss	28.5 ± 16.8	43.7 ± 18.4	34.0 ± 16.1	26.4 ± 16.8	25.7 ± 17.2	27.2 ± 17.6	38.1 ± 18.0	30.6 ± 17.8	25.1 ± 17.4	24.5 ± 17.7
Constipation	22.2 ± 15.9	29.8 ± 17.2	25.7 ± 17.2	21.5 ± 16.1	22.2 ± 15.9	22.4 ± 15.8	28.6 ± 18.0	23.8 ± 18.0	22.4 ± 15.8	21.7 ± 16.0
Diarrhea	20.8 ± 16.3	26.4 ± 16.8	22.9 ± 17.0	20.8 ± 16.3	20.1 ± 16.5	20.4 ± 16.4	26.5 ± 16.6	21.7 ± 17.4	21.1 ± 16.2	20.4 ± 16.4
Financial difficulties	25.7 ± 17.2	31.9 ± 15.3	34.7 ± 16.8	27.8 ± 15.9	25.7 ± 15.7	25.8 ± 15.6	29.2 ± 14.6	29.9 ± 15.6	26.5 ± 15.2	25.1 ± 14.5
QLQ-OES18										
General symptom scales[b]										
Dysphagia	36.8 ± 15.4	46.0 ± 25.2**	34.9 ± 27.8	25.7 ± 15.0	24.5 ± 12.3	37.8 ± 17.5	31.7 ± 22.1	26.7 ± 19.7	22.7 ± 13.8	22.9 ± 12.5
Eating	36.9 ± 16.1	48.8 ± 30.8**	34.2 ± 25.9	24.6 ± 11.3	24.2 ± 12.9	36.1 ± 18.2	32.9 ± 26.5	27.1 ± 20.8	22.7 ± 14.3	22.4 ± 14.4
Reflux	18.1 ± 9.0	26.4 ± 15.3	28.8 ± 16.4	31.2 ± 16.3*	31.2 ± 15.2*	18.3 ± 8.3	30.6 ± 15.3	34.0 ± 15.9	38.4 ± 17.4	38.8 ± 16.5
Pain	20.6 ± 8.3	22.7 ± 10.5	20.8 ± 8.1	13.9 ± 6.7	13.4 ± 6.5	19.7 ± 9.4	24.2 ± 10.5	21.1 ± 8.8	13.4 ± 6.0	13.1 ± 6.3
General symptom items[b]										
Swallowing saliva	18.4 ± 7.9	24.3 ± 11.9	18.8 ± 8.8	14.3 ± 7.7	13.9 ± 7.2	19.1 ± 9.6	25.2 ± 13.6	18.7 ± 10.5	14.0 ± 7.9	13.3 ± 7.6

Table 3 continued

	Retrosternal group				Prevertebral group			
	Pre-operation	2 weeks post-operation	4 weeks post-operation	12 weeks post-operation	24 weeks post-operation	Pre-operation	2 weeks post-operation	4 weeks post-operation	12 weeks post-operation	24 weeks post-operation
Choking when swallowing	32.6 ± 16.1	33.3 ± 15.4	23.6 ± 17.8	20.8 ± 16.3	20.1 ± 16.5	31.9 ± 15.2	32.6 ± 18.6	22.4 ± 17.2	19.7 ± 16.5	19.7 ± 16.5
Dry mouth	22.6 ± 11.6	29.9 ± 17.5	20.8 ± 11.1	20.1 ± 11.4	19.8 ± 11.2	21.8 ± 11.9	26.9 ± 17.3	20.4 ± 11.4	19.7 ± 11.1	19.7 ± 10.6
Taste problems	27.8 ± 15.9	39.6 ± 16.4	31.2 ± 12.7	25.0 ± 14.6	24.3 ± 15.0	26.5 ± 13.6	36.7 ± 17.0	29.9 ± 15.6	23.8 ± 18.0	23.8 ± 16.7
Coughing	18.4 ± 9.9	32.3 ± 15.5	25.0 ± 13.7	20.8 ± 9.4	20.2 ± 9.7	19.1 ± 10.7	36.0 ± 17.1	27.5 ± 14.2	23.1 ± 10.1	22.8 ± 10.0
Speech problem	16.0 ± 7.7	34.7 ± 17.1	25.0 ± 17.5	18.1 ± 11.3	17.7 ± 11.6	16.3 ± 8.7	32.0 ± 12.7	23.5 ± 13.6	17.7 ± 11.0	17.4 ± 10.7

[a] Score range 0–100. Higher score represents a better quality of life or a higher level of functioning

[b] Score range 0–100. Higher score represents more severe symptoms

* P value < 0.05

** P value < 0.01

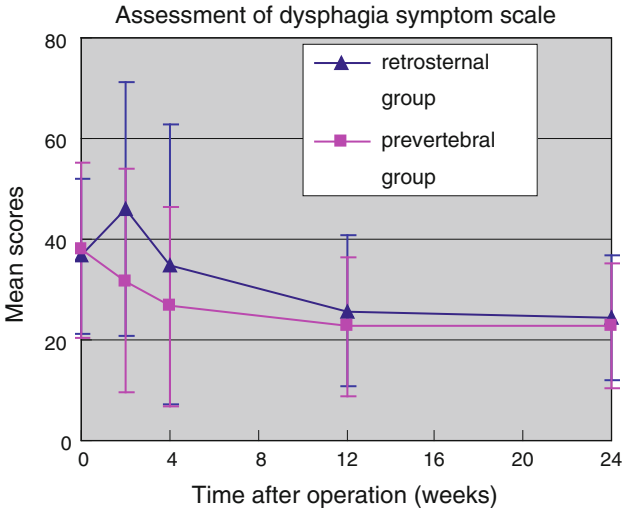

Fig. 1 Assessment of dysphagia symptom scale between the retrosternal group and prevertebral group before operation and during follow-up. Higher scores represent more severe dysphagia problem

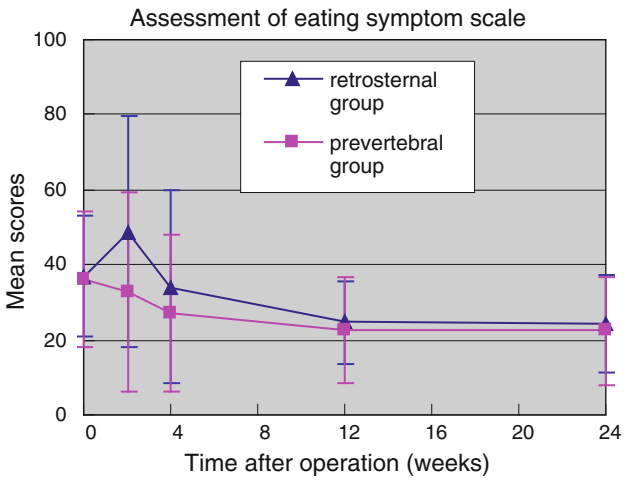

Fig. 2 Assessment of eating symptom scale between the retrosternal group and prevertebral group before operation and during follow-up. Higher scores represent more severe eating problem

Fig. 5). These suggested that the patients in retrosternal group had a worse HRQL in the early period; however, they recovered to a better status in the later period, compared with the prevertebral group.

Discussion

This study has shown that the total perioperative complication rate was equivalent in the two reconstruction groups. However, the rate of cervical anastomotic leak was higher in the retrosternal group, while the rate of cardiac or pulmonary complication was higher in the prevertebral group. HRQL showed deterioration after operation. And in

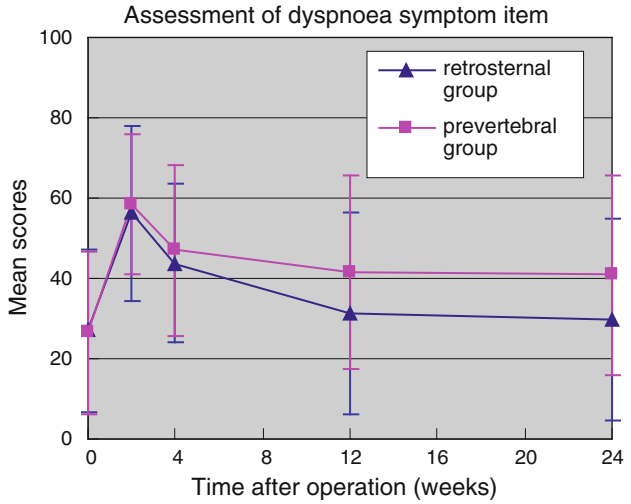

Fig. 3 Assessment of dyspnoea symptom item between the retrosternal group and prevertebral group before operation and during follow-up. Higher scores represent more severe dyspnoea problem

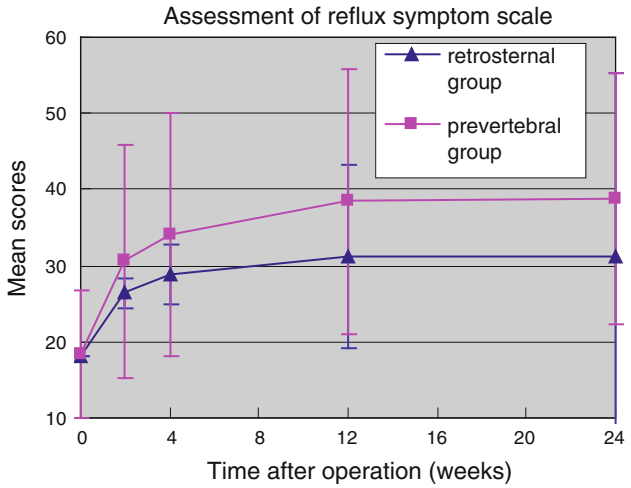

Fig. 4 Assessment of reflux symptom scale between the retrosternal group and prevertebral group before operation and during follow-up. Higher scores represent more severe reflux problem

the early period (2 weeks after operation), the patients in retrosternal group had more severe dysphagia and eating problem and had worse global quality of life. Whereas, in the later period (12 and 24 weeks after operation), the patients in retrosternal group had less problems of dyspnoea and reflux symptom and gained a better status in global quality of life.

The conventional open three-incision subtotal esophagectomy was censured for its demerits of extensive trauma, intense pain, and slow recovery. However, MIE (especially thoracoscopic or thoracolaparoscopic esophagectomy) was applied originally in 1992 [12] and has been developing rapidly in various types. As a minimally invasive approach, it may be beneficial for patients with esophageal cancer.

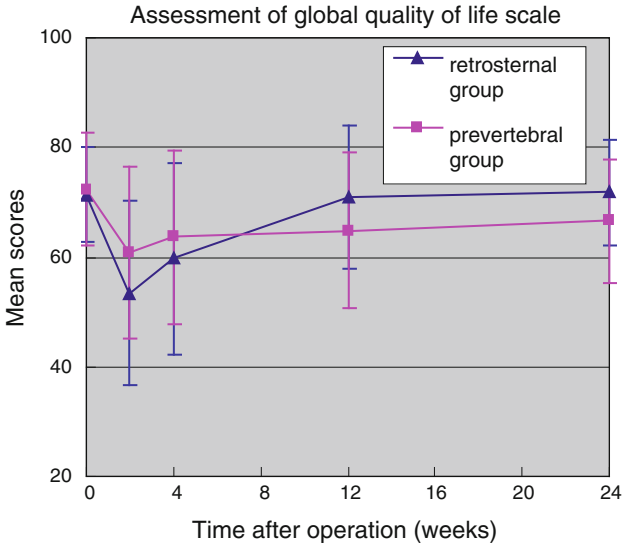

Fig. 5 Assessment of global quality of life scale between the retrosternal group and prevertebral group before operation and during follow-up. Higher scores represent better global quality of life

Compared with other booming minimally invasive surgical procedures, MIE is technically demanding, and it is still done at few medical centers. We started our practice of MIE in 2004 [13] and were interested to do some amelioration of the operation, such as patient's position, anastomosis technique, and gastric tube reconstruction route. However, the report of retrosternal route via MIE was rare, let alone the comparison with the prevertebral route.

Recent advances of self-administered structured and validated tools for the assessment of HRQL established by EORTC, designed for patients with cancer (QLQ-C30), as well as the esophageal-specific module (QLQ-OES 18), have developed HRQL research. Several Clinical trials accomplished had proved the feasibility, reliability and validity to assess HRQL of patients with esophageal cancer pre- or post-operation [14].

In this study, no statistical significance was confirmed in the prevalence of the major peri-operative complication between the two routes, although retrosternal group seemed to have a little higher rate than prevertebral group (35.4 vs. 32.7%). And in a prospective randomized study [15], which contained 26 patients who were randomly allocated to either retrosternal ($n = 14$) or posterior mediastinal ($n = 12$) reconstruction after gastric tube formation, retrosternal reconstruction also showed an increased morbidity (15 vs. 13 major complications) and mortality (14.2 vs. 8.3%). However, this difference was also of no statistically significant.

Cervical anastomotic leak was distinctly much more in retrosternal group than in prevertebral group (20.8 vs. 6.1%, $P = 0.033$) in this study. Consequently, more patients in

retrosternal group suffered dysphagia and eating problems in the early period after operation. The high prevalence of leak may correlate to the poor oxygen supply. Anegg et al. [16] reported 29 patients who underwent gastric transposition via an orthotopic ($n = 14$) or retrosternal ($n = 15$) route. Interstitial partial pressure of oxygen (PO_2) of the stomach in the anastomotic region was measured during esophagectomy and after operation. Levels were higher in orthotopic group than in retrosternal group (68.2 vs. 24.6 mmHg, $P = 0.001$), which revealed that oxygen supply at the anastomosis of the gastric tube was better after orthotopic than retrosternal gastric transposition. The pressure of manubrium was suggested to be the main reason for hypoxia. Accordantly, Kunisaki et al. [17] reported that partial resection of the manubrium could significantly reduced the incidence of leak in the retrosternal procedure (4/29 vs. 31/68, $P = 0.0305$). In our experience, the anastomotic leak was mostly evident through the neck. And it usually closed up in 4–8 weeks with the treatment of thorough drainage, enough nutrition supply and anti-inflammation if necessary.

The prevertebral route theoretically has the disadvantage of the compression on the lung by the dilatation of the stomach with air and or digestive solution to increase the possibility of pulmonary implications [18]. In this study, the patients in prevertebral group complained more dyspnoea problem after operation, especially in the later period(12 weeks after operation). Thus, it is suggested that retrosternal route may be a better choice for the patients with poor respiratory function.

Duodenogastric reflux (DGR) is a common sequel of subtotal esophagectomy with gastric pull-up. In this study, patients in prevertebral group complained more DGR than retrosternal group after operation. Moreover, this difference became more and more evidently during the follow-up, especially after the 12th week. Katsoulis [19] investigated the effect of the reconstruction route on the DGR by 24-hour ambulatory bilirubin monitoring on patients who underwent transhiatal subtotal esophagectomy and a gastric tube interposition either in the posterior mediastinum (PM group, $n = 11$) or in retrosternal space (RS group, $n = 8$) and the control group of 8 healthy volunteers. The median percentage of reflux time, the median number of reflux episodes, and the median number of reflux episodes longer than 5 min in PM versus RS groups, were 29.1 versus 0.15% ($P < 0.001$), 185 versus 8 ($P = 0.002$) and 10 versus 0 ($P = 0.001$), respectively. The values of the above variables in PM versus control groups were 29.1 versus 3.95% ($P = 0.007$), 185 versus 21 ($P = 0.02$), and 10 versus 2 ($P = 0.009$), respectively, whereas in RS versus control groups they were 0.15 versus 3.95% ($P = 0.01$), 8 versus 21 ($P = 0.04$), and 0 versus 2 ($P = 0.05$), respectively. Thus, the author concluded that posterior mediastinal route seemed to be associated with high reflux of duodenal contents, whereas retrosternal route could minimize the reflux at levels even lower than those of the healthy individuals. Therefore, the reconstruction of retrosternal route may be suitable for the patients with long life expectancy.

Whether the anastomosis with linear staple would worsen the reflux symptom is an interesting topic. Besides, there is no report directly discussing linear staple and reflux. However, as to our experience, it is hard to draw the conclusion. On the one hand, it was reported that there was a statistically significant difference between the hand-sewn (end-to-end) group of patients and the linear staple(side-to-side) group with respect to mean anastomotic diameters (1.688 ± 0.26 vs. 3.012 ± 0.17 cm, $P = 2.10*10^{-8}$) [20]. Thus, the broader anastomosis may worsen the reflux. And on the other hand, it is our perception that gastroesophageal reflux was minimized if the end of the cervical esophagus was anastomosed to the anterior gastric wall in the neck a short distance below the top of the stomach in several patients. In this way, a short retroesophageal gastric pouch was formed, which could partly minimize gastroesophageal reflux. Therefore, further studies are needed to definitude this issue.

Above all, in view of the global HRQL, the scores were poor in retrosternal group than prevertebral group in the early period after operation. The reason might be that the risk of cervical anastomotic leak was higher, as we hypothesized. However, in the later period, the scores in retrosternal group were better, owing to its less impact on respiratory function and duodenogastric reflux.

Meanwhile, HRQL after MIE was also reported in rare literatures [21, 22]. Parameswaran et al. [22] studied the clinical outcomes of 58 patients who underwent MIO for cancer or high-grade dysplasia. The validated questionnaires of EORTC QLQ-C30 and QLQ-OES18 were used to assess the HRQL before surgery and at 6 weeks, 3, 6, and 12 months after surgery. In result, 2 patients had partial conversion to open surgery, and 52 patients were alive at 1 year. Patients reported deterioration in functional aspects of HRQL and more symptoms than baseline levels at 6 weeks after MIO. However, most cases improved by 3 months and had returned to baseline levels by 6 months. These levels were maintained 1 year after surgery, with 85% of patients recovering in more than 50% of the HRQL domains. Therefore, they drew the conclusion that MIO could lead to a rapid restoration of HRQL.

However, at present, there is still no consensus for the optimal route of reconstruction for three-incision subtotal esophagectomy. Although both approaches have been widely used, there are still controversies in many aspects with regard to the issue of which one is more advantageous.

First, from the view of anatomy, the reconstruction route, which is relatively shorter in distance of conduit

required to reach the neck, could translate to reduced tension for the anastomosis. The previously series based on the cadavers reported that retrosternal route was approximately 2–3 cm longer than prevertebral route [23–25]. However, a recent prospective study by Chen et al. [26] is opposed to this standpoint. They performed measurements with gastric conduit from the cricoid cartilage to the pyloric ring after esophagectomy but before reconstruction in sixty consecutive patients, and the result showed that the length of the retrosternal route was significantly shorter than the prevertebral route (32.68 ± 2.67 vs. 35.48 ± 2.93 cm, $P < 0.001$). However, the reference points used in these studies were not uniform. And at the same time, the differentia of races may make this issue complicated.

Second, regarding the surgical maneuver, both approaches were not very difficult in technique under MIE. However, in our experience, retrosternal route has a little advantage. It is easy and quick to insert the nasogastric tube and the feeding jejunum tube through the gastrostomy by an open fashion via the mini-incision below the xiphoid. The avoidance of placement through the nasal cavity could decrease relative morbidities [27].

Third, as to the peri-operation morbidity, many surgeons preferred the prevertebral route because of the perception that it might be associated with fewer complications. However, this finding has not been supported by enough studies. Urschel et al. [28] demonstrated that no significant differences could be found in the post-operative morbidity and mortality comparing the two approaches in their meta-analysis.

Fourth, in spite of this study, rare reports also discuss the HRQL of different reconstruction route [29, 30]. In a recent research, Nakajima et al. [30] investigated 37 patients with esophagectomy. The anastomosis was made at the cervical location by the retrosternal route in 12 patients (RS group), at the high thoracic location by the posterior mediastinal route in 18 patients (HT group), and at the cervical location by the posterior mediastinal route in 7 patients (PM group). The score revealed that reflux were few in the HT group. Patients suffered from dumping syndrome were significantly few in the HT group ($P = 0.0399$). The percentage time of pH $<$ or $=$ 4.0 was shortest in the HT group at the position of the esophagogastric anastomosis ($P < 0.0281$). Body weight recovery was best in HT group ($P < 0.0001$). Therefore, the authors suggested that QOL was best in patients with the anastomosis at the high thoracic location by the posterior mediastinal route.

Finally, in view of the post-operative treatment, retrosternal route could avoid the tumor recurrence within the gastric conduit, in which way malignant dysphagia could be prevented. At the same time, it is convenient to differentiate metastatic mediastinal lymph node from gastric conduit by CT scan [31], with no necessity of expensive PET-CT scan, and this is especially significative in developing countries. And the further advantage of retrosternal reconstruction is avoiding gastric conduit from irradiation during the post-operative radiation therapy for tumor residua or recurrence cases [32]. On the other hand, the retrosternal gastric conduit makes cardiac surgery unnecessarily complicated [33]. Thus, for patients with expectation of long-term survival who might eventually develop cardiac disease and require cardiac surgery, retrosternal route is not appropriate.

Basing on this study, we suggest that retrosternal route may be an alternative choice for MIE, in view of better HRQL in the later period after operation, together with other advantages.

However, this study had limitations. The selection of patients for the prevertebral or retrosternal group was not strictly randomized, which may lead to bias. Besides, some of the difficulties and problems, which were correlative with learning curve of surgical technique, had been avoided or reduced in the later patients, and this would also lead to bias. And a single hospital-based design may be another cause of selection bias.

Meanwhile, the impact on HRQL by adjuvant chemoradiotherapy was not referred in this study. However, many studies showed that definitive chemoradiotherapy might have a similar survival rates but much lesser impact on HRQL, in comparison with surgery. In a randomized trial [34] that compared HRQL after chemoradiation alone and chemoradiation with surgery for esophageal cancer using the Spitzer Quality of Life Index, the overall index was significantly worse after surgery than after definitive chemoradiation, but the longitudinal HRQL outcomes were similar over time in both groups. And in another research, Avery et al. [35] compared HRQL between patients with locally advanced esophageal cancer selected for chemoradiotherapy ($n = 51$) and those who had combination treatment including oesophagectomy ($n = 81$). At the worst expected time point after treatment, surgery was associated with a greater reduction in HRQL from baseline than chemoradiotherapy. Recovery of HRQL was achieved within 6 months after chemoradiotherapy, but complete recovery had not occurred 6 months after surgery and there was persistent significant deterioration in some aspects. Thus, the negative impact of chemoradiotherapy on short-term HRQL is less than that experienced with combination treatment including surgery, and HRQL assessment is valuable to inform clinical decision-making.

Besides, the outcomes of longer term HRQL is still to be defined, as Lagergren et al. [36] revealed that patients who underwent esophagectomy suffered persistent problems with physical function, breathlessness, diarrhea, and reflux even after 3 years. These findings might be used to inform patients of the long-term consequences of surgery. On the

other hand, the assessment of HRQL in our study was based on the questionnaires, which were self-administered structured tools. And it would be more comprehensive if the additional objective parameters could be contained in the further study, such as post-operative weight loss, nutritional condition, pulmonary function, SpO2, and pH monitoring.

Therefore, further prospective randomized controlled trials are needed to validate the discrepancies of HRQL in patients with esophageal cancer with different routes of gastric tube reconstruction after MIE.

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