ORIGINAL ARTICLE





Comparison of Long-term Quality of Life in Patients with Esophageal Cancer after Ivor-Lewis, Mckeown, or Sweet Esophagectomy

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Abstract

Background The aim of this study was to compare the long-term quality of life (QoL) in patients after Sweet, Ivor-Lewis, or Mckeown esophagectomy.

Methods Esophageal cancer patients after Sweet, Ivor-Lewis, or Mckeown esophagectomy from 2010 to 2012 were included. QoL was assessed according to the European Organization for Research and Treatment of Cancer general questionnaire: QLQ-C30 and esophagus-specific questionnaire: QLQ-OES18.

Results A total of 126 qualified patients who have been alive for more than 3 years without tumor recurrence were divided into three groups: the Sweet group (n = 40), Ivor-Lewis group (n = 38), and Mckeown group (n = 48). Among these three groups, the QLQ-C30 mean scores of global health status, functional and symptom scales, and general QoL were similar. The symptom scales of QLQ-OSE18 showed that patients who had a Mckeown operation experienced more problem of eating (P = 0.029), choking when swallowing (P = 0.010) and coughing (P = 0.016), while patients undergoing Sweet operation complained more symptom of reflux (P = 0.003) and pain (P = 0.000).

Conclusions All three types of esophagectomy provided a generally good long-term QoL. However, patients in Sweet and Mckeown group tend to suffer from a higher symptomatic burden as compared to Ivor-Lewis approach.

Keywords Esophageal cancer · Quality of life (QoL) · QLQ-C30 · QLQ-OES18 · Esophagectomy

Introduction

Surgery remains the cornerstone of the multimodality treatment for advanced esophageal cancer. Various surgical approaches for esophageal cancer are currently being used, which can be divided into two groups: intrathoracic anastomosis group (Ivor-Lewis and Sweet) and cervical anastomosis group (transhiatal and Mckeown), according to the site of anastomosis. Still, there are no definitive guidelines for choosing a specific surgical approach for esophageal cancer.

Yu-Shang Yang and Qi-Xin Shang contributed equally to this work.

This work was presented at the 14th world conference of global perspectives in esophageal diseases (September 4, 2017, Geneva) and awarded best abstract.

Department of Thoracic Surgery, West China Hospital of Sichuan University, No. 37, Guoxue Alley, Chengdu 610041, Sichuan, China Ivor-Lewis and Mckeown have been gradually accepted as the standard and route procedure for esophageal cancer, while the approach of Sweet is debated, mainly for its limited extent of lymphadenectomy, especially for the dissection of the right upper mediastinal lymph nodes (RUM-LND). However, our previous study has investigated the efficiency of Sweet procedure with the RUM-LND resection. The result demonstrated a comparable overall survival between groups of Ivor-Lewis and Sweet. Hence, Sweet procedure maybe still worthwhile in modern esophagectomy.

Quality of life (QoL) plays an essential role postoperatively, which was seen as a prognostic value in patients with esophageal cancer. Different types of esophagectomy might have different impact on patients' QoL, which include the functional and symptomatic effects, and these impacts were correlated with patients' both short-term and long-term QoL. Although the effect of surgical approaches on QoL in esophageal cancer patients has been studied by several studies, most studies either have followed their cohorts for 2 years or less or, in case of longer follow-up, usually have not controlled for wide variations in elapsed time since



surgery within studied groups. 11–14 The aim of this study was to evaluate the long-term (> 3 years) QoL of patients after Ivor-Lewis, Sweet, and Mckeown esophagectomy without tumor recurrence using an available cancer-specific questionnaire with tumor-specific module.

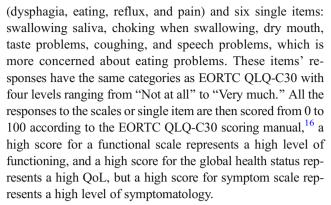
Materials and Methods

Patients

From May 2010 to May 2012, a total of 432 patients who had undergone esophagectomy were investigated. This study was approved by the ethics committee of West China Hospital, and informed consents were obtained from all included patients. The pathologic stage of esophageal cancer was diagnosed according to the American Joint Committee on Cancer/ Union for International Cancer Control, 7th edition. 15 Inclusion criteria for this study were as follows: (1) patients were diagnosed with esophageal squamous cell carcinoma; (2) esophagectomy with subtotal lymphadenectomy was performed via Ivor-Lewis, Mckeown or Sweet approach; (3) gastric conduit was used for esophageal replacement and posterior mediastinal route was used for reconstruction. The exclusion criteria used are as follows: (1) patients who lost to follow-up; (2) patients who have palliative surgery and R1 or R2 resection; (3) patients who died within 2 years; (4) patients who have tumor recurrence.

QoL Assessment

The qualified patients' health-related QoL was assessed according to the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 (version 3.0)¹⁶ and (esophagus-specific) QLQ-OES18 developed by Blazeby. 17,18 Structured questionnaires were used to collect data from patients via face-to-face, telephone, or mail interview. EORTC QLQ-30 is a worldwide and cancer-specific questionnaire used for evaluating the QoL of patients with malignant diseases, which incorporates five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), a global health status/QoL scale, and a number of single items assessing additional symptoms commonly reported by cancer patients (dyspnea, loss of appetite, insomnia, constipation, and diarrhea) and perceived financial impact of the disease. Each scale refers to several questions while each single item corresponds to single question, and all items' responses have been classified into four levels which represent "Not at all," "A little," "Quite a bit," and "Very much" in order corresponding to 1-4, consequently except for the global health status which includes 7-point items ranging from "very poor" to "excellent". The QLQ-OES18 consists of four scales



The calculated results of QoL were compared among different surgical approaches. EORTC QLQ-C30 and QLQ-OSE18 values of each surgical approach group were also compared with the available reference healthy population (RHP) published by Scott¹⁹ and Derogar²⁰, respectively.

Statistical Analysis

The clinicopathologic features among different surgical approach groups were analyzed by the Fisher exact test and chi-square test. The mean values with standard deviation (SD) were used to present the data of QoL and the outcomes of QoL comparison among different groups were achieved by the analysis of variance (ANOVA). At the same time, when comparing the mean score of each item to RHP, Student's *t* test was applied. The statistical significance was regarded as the probability value < 0.05. Statistical analyses were conducted by IBM® SPSS® Statistics Version 21.0.

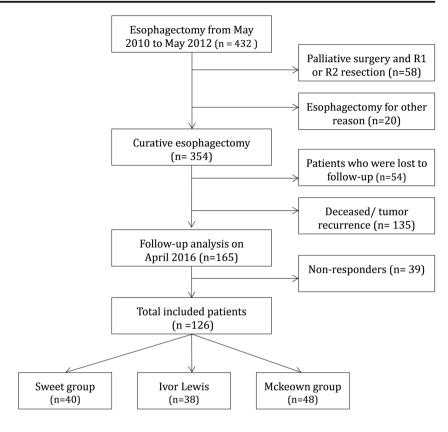
Results

A total of 354 esophageal cancer patients were included in the analyses. Of these, 135 patients (38.1%) were already deceased or suffered recurrences, and 54 patients (15.2%) were lost to follow-up at the time of analysis (April 2016). Of the remaining 165 patients, 39 patients refused to respond, and 126 patients were eligible for completing questionnaires and finally included in our study. The specific study population selection is exhibited in Fig. 1.

After that, the patients were divided into three groups: the Sweet group (open left-thoracic esophagectomy with thoracic anastomosis), 40 patients (31.7%); the Ivor-Lewis group (abdominal and right-thoracic esophagectomy with thoracic anastomosis), 38 patients (30.2%); the Mckeown group (abdominal, right-thoracic and cervical esophagectomy with cervical anastomosis.), 48 patients (38.1%). The clinicopathologic features among the three groups are shown in Table 1.



Fig. 1 Flow diagram of the study population selection



QLQ-C30

In about 3 to 5 years after curative-intent esophagectomy for esophageal cancer, the three patient groups stratified by surgical approaches shared virtually comparable mean scores of global health/QOL, general symptom scales, and function scales. The comparisons of QLQ-C30 questionnaire among three groups are shown in Table 2. We also compared the mean scores of each group with that of the reference healthy population (RHP) available from EORTC.^{20,21} The result showed that social function deficits irrespective of type of surgical approaches were observed when contrasted to the RHP (P = 0.040 in the Sweet group, P = 0.001 in the Ivor-Lewis group, P = 0.049 in the Mckeown group) (Fig. 2). Role and emotional and cognitive function, however, were similar with that of the RHP. For general symptom scales, a higher burden of appetite loss, diarrhea, nausea, and vomiting was found in each group when compared to RHP, indicating that the digestive symptoms were the most striking complaint among these patients.

QLQ-OSE18

From the analysis of variance, the symptom scales of QLQ-OSE18 showed that patients who had a Mckeown operation experienced more problem of eating (P = 0.029), choking when swallowing (P = 0.010), and coughing (P = 0.016), while patients undergoing the Sweet operation complained

more symptom of reflux (P = 0.003) and pain (P = 0.000)(Table 3). Then, the comparisons of the mean scores of each group with that of the RHP were carried out (Fig. 3). Similarly, eating problem was observed in every group when contrasted to RHP (P = 0.001 in the Ivor-Lewis group, P = 0.000 in both the Sweet group and Mckeown group). More complaints of reflux (P = 0.000), pain (P = 0.009), and trouble talking (P =0.036) in the Sweet group, more choking when swallowing (P = 0.000), swallowing saliva (P = 0.038) and trouble with taste (P = 0.006) in the Mckeown group, and more choking when swallowing (P = 0.015) in the Ivor-Lewis were reported as compared with that of RHP. Of these symptoms, choking when swallowing was the most striking complaint with the maximal difference between the mean scores of each group and that of the RHP, followed by the reflux and eating with trouble.

Discussion

To date, there is still a significant debate regarding the best surgical approaches for esophagectomy. In addition to the survival after operation, long-term QoL represents the other important issues for patients. R,10 Our study provided further insight into the long-term quality of life in patients with esophageal cancer according to surgical approaches. Outcomes from the questionnaire of QLQ-C30 showed that neither was there a significant difference of mean sores in global health status nor



Table 1 Patient and tumor characteristics of patients undergoing three types of esophagectomy

		Sweet $n = 40$	Ivor-Lewis $n = 38$	Mckeown $n = 48$	P			
					S vs I	S vs M	I vs M	S vs I vs M ^a
Sex	Male	31 (77.5)	26 (68.4)	36 (75.0)	0.366	0.781	0.499	0.642
	Female	9 (22.5)	12 (31.6)	12 (25.0)				
Age	≤60	21 (52.5)	22 (57.9)	30 (62.5)	0.632	0.344	0.664	0.639
	>60	19 (47.5)	16 (42.1)	18 (37.5)				
Technique	Open	40 (100.0)	22 (57.9)	32 (66.7)	0.000	0.000	0.183	0.000
	MIE	0 (0)	6 (15.8)	2 (4.2)				
	Hybrid	0 (0)	10 (26.3)	14 (29.2)				
Differentiated	Well	4 (10.0)	6 (15.8)	12 (25.0)	0.549	0.135	0.171	0.207
	Moderate	29 (72.5)	28 (73.7)	26 (54.2)				
	Poor	7 (17.5)	4 (10.5)	10 (20.8)				
Location	Upper	4 (10.5)	3 (7.5)	3 (6.25)	0.202	0.721	0.243	0.402
	Middle	18 (47.4)	25 (62.5)	25 (52.1)				
	Lower	16 (42.1)	10 (25.0)	16 (33.3)				
	GEJ	2 (5.0)	0 (0)	4 (8.3)				
TNM stage	0	1 (2.5)	2 (5.3)	6 (12.5)	0.160	0.921	0.450	0.425
	I	10 (25)	10 (26.3)	14 (29.2)				
	II	23 (57.5)	20 (52.6)	18 (37.5)				
	III	6 (15)	6 (15.8)	10 (20.8)				
Adjuvant therapy	No	22 (55)	22 (57.9)	20 (41.7)	0.212	0.797	0.135	0.266
	Yes	18 (45)	16 (42.1)	28 (58.3)				
Dilation*	No	38 (95.0)	35 (92.1)	38 (79.2)	0.671	0.031	0.096	0.049
	Yes	2 (5.0)	3 (7.9)	10 (20.8)				

^a S Sweet, I Ivor Lewis, M Mckeown; *treatment for benign anastomotic strictures after esophagectomy)

in general QoL among three groups. Meanwhile, none of the groups showed any significant difference in global quality of life, role, and emotional or cognitive function as compared to RHP. Several reasons may explain the above outcomes. On the one hand, QoL would drop immediately following operation because of surgical trauma, which recovers during the

postoperative rehabilitation period. Even the long-term QoL would get close to that of RHP but never reach to the preoperative level, which was confirmed by Egberts et al.²² On the other hand, during the recovery period, patients adapt to the situation of coexisting with esophageal cancer and do not act out of fear, anger, and unacceptability, which allowed achieving

Table 2 EORTC QLQ-C30 outcomes for the Sweet, Ivor-Lewis, and Mckeown groups

	$M \pm SD$			P	
	Sweet	Ivor-Lewis	Mckeown		
Global quality of life	70.54 ± 20.62	72.33 ± 22.86	70.67 ± 21.23	0.174	
General symptom scales					
Fatigue	27.68 ± 23.23	26.73 ± 26.31	27.72 ± 24.53	0.158	
Nausea/vomiting	26.81 ± 16.08	22.32 ± 17.75	21.5 ± 12.39	0.756	
Pain	20.26 ± 24.32	12.35 ± 22.28	20.93 ± 21.83	0.072	
General symptom items					
Dyspnea	23.67 ± 30.29	22.11 ± 28.67	25.68 ± 19.22	0.086	
Insomnia	19.37 ± 23.26	16.22 ± 26.66	22.14 ± 18.54	0.135	
Appetite loss	21.26 ± 20.35	23.33 ± 19.47	21.39 ± 26.75	0.096	
Constipation	13.03 ± 18.36	15.75 ± 15.72	15.23 ± 23.26	0.314	
Diarrhea	18.51 ± 13.7	17.35 ± 18.42	23.77 ± 17.72	0.258	



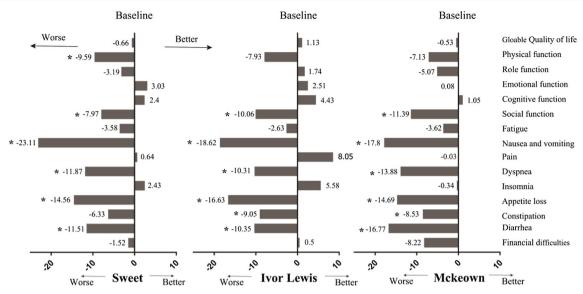


Fig. 2 The difference of EORTC QLQ-C30 mean scores between each surgical approach and reference group

a new set of knowledge based on the self-knowledge of each patient which contributed for an improved overall QoL. ^{7,21,22}

For the symptom scales in the QLQ-C30, the result showed that most patients suffered from almost the same symptoms as most of researches had ever reported: diarrhea, appetite loss, nausea and vomiting, and function decrease. ^{7,13,14} While advances in surgical technique for esophagectomy, the surgical trauma continues to be appreciably higher than other similarly complex operations such as pancreatectomy, gastrectomy, and hepatectomy. ^{23–25} Not surprisingly, the considerably anatomical and physiological changes by this surgery will lead to long-lasting symptoms.

The EORTC QLQ-OSE18 questionnaire was confirmed as the only suitable measure in accompany with the QLQ-C30 to assess QoL of patients with esophageal cancer. ^{13,14,22,26} In our study, reflux is the most striking complaint in the Sweet group, while choking when swallowing in the Mckeown group. The reasons for reflux are the removal of esophagogastric junction,

which destroys its anti-reflux barrier, and the difference in pressure change also contributes to the reflux. In addition, lower anastomotic location has been demonstrated with higher risk of reflux.²⁷ The Sweet operation was preferentially performed in patients with tumor in lower thoracic esophagus in our study, and its esophagogastric anastomosis usually completed at a relatively lower level. Hence, the site of anastomosis may play a non-neglectable role in the striking burden of reflux in the Sweet group. And longer gastric conduit blood supply, tension of anastomosis, and the extrinsic compression are also some of the possible explanations.^{28,29}

Choking when swallowing caused the greatest impact on patients in the Mckeown group from our studies; however, there is no difference found in dysphagia among the three groups. As compared with intrathoracic esophagogastric anastomoses, the cervical esophagogastric anastomoses has been reported with a relative higher risk of hematoma in the neck and recurrent laryngeal nerve palsy duo to cervical esophageal

Table 3 EORTC QLQ-OSE18 outcomes for the Sweet, Ivor-Lewis, and Mckeown groups and pairwise contrast

	$M \pm SD$				
	Sweet	Ivor-Lewis	Mckeown		
Dysphagia	10.56 ± 17.6	2.92 ± 10.23	7.87 ± 16.68	0.089	
Eating problems	8.54 ± 9.53	6.14 ± 7.17	11.81 ± 11.64	0.029	
Reflux	21.67 ± 21.08	10.53 ± 12.51	11.11 ± 14.31	0.003	
Pain	9.99 ± 11.47	4.68 ± 8.42	1.39 ± 3.71	0.000	
Trouble swallowing saliva	0.83 ± 5.27	3.51 ± 10.37	9.72 ± 28.32	0.074	
Choked when swallowing	8.33 ± 14.62	10.53 ± 15.7	19.44 ± 21.56	0.010	
Dry mouth	8.33 ± 16.45	14.03 ± 16.68	9.72 ± 18.14	0.314	
Trouble with taste	5 ± 12.05	1.75 ± 7.54	12.5 ± 25.38	0.016	
Trouble with coughing	12.5 ± 22.24	7.02 ± 17.6	8.33 ± 17.53	0.414	
Trouble talking	7.5 ± 15.99	7.02 ± 13.77	8.33 ± 22.28	0.943	



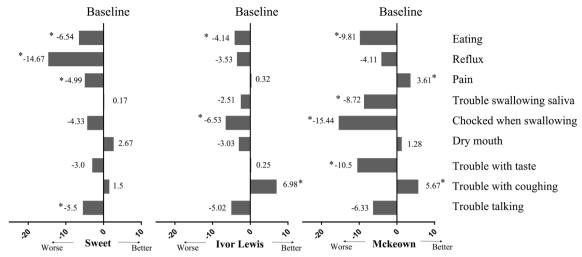


Fig. 3 The difference of EORTC QLQ-OES18 mean scores between each surgical approach and reference group

mobilization³⁰ and a predisposition of benign stricture formation duo to a high incidence of anastomotic leakage.³¹ Thus, the abovementioned potential factors may increase the complaint of choking when swallowing and ultimately worsens global quality of life. The explaination of the comparable dysphagia is that the removal of the cancer-related stenosis in esophagus contributed to the improvement in dysphagia after operation and patients complained less about dysphagia and gradually adapted to the new eating conditions though the swallowing function was not the same as that before the operation. Egberts et al.²² once prospectively assessed the QoL of 105 patients who underwent esophagectomy for esophageal cancer by means of EORTC QLQ-C30 and QLQ-OSE18 and reported an improvement in dysphagia even 3 months after discharge from hospital.

Pain after operation is another main complaint. From our study, the Sweet group showed the highest mean score of pain. The first probable explanation is the difference of surgical procedures. Although the Sweet procedure requires only one incision through left chest, mobilization of the stomach is done with manual manipulation through the cut-opened hiatus and diaphragm and a larger incision for thoracotomy is inevitable, and the bigger surgical wound contributes to more pain in patients even 2 years after operation. However, more than half of patients who accepted the Ivor-Lewis or Mckeown procedure underwent through thoracoscopy and laparoscopy, and these minimally invasive surgeries are correlated to less postoperative pain for patients. Different location of anastomosis was also associated with pain among esophageal cancer patients. Both Wormald et al.²¹ and Blazeby et al.¹⁰ had reported that scores for pain were significantly higher among the group of patients with intrathoracic anastomosis compared to those with cervical anastomosis. The results were also confirmed by the observations in a longitudinal study by Egberts et al.²² who compared the QoL of patients in cervical and intrathoracic anastomosis groups separately.

Several limitations to this study should be mentioned, such as its retrospective work with the potential for selection bias. Another limitation of this study was that we did not evaluate the postoperative QoL at multiple time points and therefore cannot comment the dynamic effect of different surgical approaches. Several studies have demonstrated the benefit in QoL among esophageal cancer patients who experience minimally invasive surgery. Thus, the variable surgical technique among the three groups would potentially introduce bias in the comparison of QoL across surgical approaches. However, the subgroup analysis by stratifying these patients based on surgical technique was confined, since the high risk of type II error caused by the relatively small number of patients receiving MIE and the different types of minimally invasive procedures (total or hybrid).

Conclusion

Our study highlighted that, although the three surgical approaches (the Ivor-Lewis, Mckeown, or Sweet) shared a comparable general health-related QoL for esophageal cancer patients in about 3 to 5 years after curative-intent esophagectomy, a higher burden of digestive disorder were associated with the Sweet and Mckeown operation. Meanwhile, further studies on researching the impact of the surgical approaches on patients' postoperative QoL are needed.

Authors' Contributions (I) Conception and design: Long-Qi Chen, Yu-Shang Yang, and Yong Yuan;

- (II) Administrative support: Wei-Peng Hu and Yu-Shang Yang;
- (III) Provision of study materials or patients: Qi-Xin Shang and Yu-Shang Yang;
- (IV) Collection and assembly of data: Yu-Shang Yang, Xiao-Ying Wu, and Qi-Xin Shang;
- $\left(V\right)$ Data analysis and interpretation: Qi-Xin Shang, Wei-Peng Hu, and Yong Yuan;



(VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Compliance with Ethical Standards

Competing Interests The authors declare that they have no competing interests.

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