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Quality of Life and Its Associated Factors in Patients After Esophagectomy at a Single National Referral Center

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Abstract

Introduction. Esophagectomy is the standard surgical treatment for resectable esophageal cancer patients. However, the success rate for this procedure was about 25–35% and was associated with a severe risk of postoperative complications. In addition, patients after esophagectomy have decreased their quality of life (QOL), but no research has been done in Indonesia. Therefore, this study was conducted to determine the quality of life after esophagectomy in Indonesia based on the patient population at Dr. Cipto Mangunkusumo General Hospital (CMGH).

Method. A retrospective study was conducted using quality-of-life instruments issued by the European Organization for Research and Treatment of Cancer (EORTC). It consists of the module for esophageal cancer EORTC-QLQ-OES18 and the core questionnaire C30. Subjects were patients after esophagectomy in 2015–2021 at CMGH.

Results. About 35 subjects underwent esophagectomy and followed by reconstruction, which comprised 62.9% males and 37.1% females. The mean age was 43.8 ± 13.1 years. All subjects' median global health was 83.3 (IQR: 25.0). The overall functional scale question item with the lowest score was cognitive functioning (CF) 66.7 (IQR: 50.0). Meanwhile, based on the question items on the overall symptom scale, the worst scores were nausea and vomiting (NV) 16.7 (IQR: 50.0), pain (PA) 16.7 (IQR: 33.3), dysphagia (OESDYS) 33.3 (IQR: 33.3), eating (OESEAT) 34.5 (IQR: 23.9), choking (OESCH) 33.3 (IQR: 33.3), and coughing (OESCO) 33.3 (IQR: 33.3).

Conclusion. The overall QOL after esophagectomy at CMGH based on the EORTC-QLQ-C30 and OES18 questionnaires was good. However, prognostic factors associated with decreased quality of life should be better educated to patients and prepared well before the esophagectomy procedure, thus maximizing quality of life after esophagectomy.

Keywords: quality of life, esophagectomy, esophageal cancer

Introduction

Esophageal cancer is one of the malignancies in the gastrointestinal tract that has a poor prognosis with a five-year survival rate of only 15–50%. The incidence of esophageal cancer has continued to increase in recent decades.^{1–3} About 450,000 people worldwide have esophageal cancer. The high number of patients with esophageal cancer places it as the seventh most common malignancy and the sixth leading cause of death worldwide.⁴ Two geographic lines have the highest incidence. Firstly, the "Asian esophageal cancer belt" stretches from northeastern China to the Middle East, with an incidence of 100 cases per 100,000 people annually. Secondly, the path runs from east to south Africa.^{5,6} The squamous cell carcinoma type predominates in China, unlike most western countries.^{6,7} In the United States, the adenocarcinoma type is dominated by the incidence in Caucasian men of 0.4 per 100 thousand people in 1973 and increased to 2.8 per 100 thousand people in 2012.⁵ Based on data from Globocan 2020, the number of esophageal cancer in Indonesia reached 1,327 new cases and caused the death of up to 1,283 people.⁸ The number of cases of esophageal malignancy in Dr. Cipto Mangunkusumo General Hospital (CMGH) in 2020, 12 cases were reported. The surgical procedures performed are laparotomy to thoracotomy esophagectomy.

Esophagectomy is the standard surgical procedure for resectable esophageal cancer. However, the success rate for this procedure is only between 25–35% and is associated with a severe risk of postoperative complications.^{9–11} Patients after esophagectomy are known to have decreased quality of life (QOL) based on the assessment of physical function, role function, social function, vitality score, and health perception.^{12–14} These patients reported many complaints of weakness, difficulty breathing, reflux, diarrhea, loss of appetite, nausea, and vomiting.^{15–18} On the other hand, several QOL parameters increase after

esophagectomy. For example, pain relief, mental health, emotional, social, and cognitive function.^{12–14,17,19,20} Meanwhile, surgical techniques still provide various QOL outcomes.^{2,21} Subject characteristics such as age, gender, and body mass index were also not associated with quality of life. However, stage III to IV tumors, tumor location, and postoperative complications were predictors of decreased patient QOL scores.^{22,23}

No studies in Indonesia have published the quality of life in patients after esophagectomy. Most patients with esophageal cancer must be referred to a tertiary-level health facility because it requires more complex expertise and resource facilities. Therefore, this study was conducted to determine the quality of life after esophagectomy using instruments issued by the European Organization for Research and Treatment of Cancer (EORTC). It consists of the module for esophageal cancer EORTC-QLQ-OES18 and the core questionnaire C30. The questionnaire instrument will be used to assess the quality of life in the patient after esophagectomy, followed by esophageal reconstruction at Dr. Cipto Mangunkusumo General Hospital (CMGH), Jakarta.

Method

This retrospective cohort study included all adult patients after the esophagectomy procedure at Dr. Cipto Mangunkusumo National General Hospital (CMGH). Adult males and females underwent esophagectomy followed by reconstruction procedure (gastric pull-up, jejunal conduit, colon conduit, or distal gastroesophageal anastomosis) at CMGH between 2015–2021 were included in the study. Those with other malignancies (other than esophageal malignancies) and other surgical procedures (other than esophagectomy) were excluded from this study. Demographical data such as age, gender, body mass index, indication for surgery, tumor stage, tumor location, histopathological cell type, esophagectomy type, chemotherapy, and reconstruction type were recorded.

Quality of life was assessed using a questionnaire from the European Organization for Research and Treatment of Cancer (EORTC). Patients were asked to fill out the Indonesian version of the EORTC-QLQ-C30 and OES18 questionnaires. In addition, subjects agreed to be interviewed by telephone or other communication methods (WhatsApp call/video, Zoom meeting). This questionnaire and its scoring manual are available on the EORTC website (<https://qol.eortc.org/questionnaires/>) used with permission. Unfortunately, no Indonesian version of the OES18 questionnaire is available. Thus, we provided the translation through a procedure following the EORTC manuals, adapted from the EORTC translation procedure published by Koller et al.²⁴ The process consists of drafting, forward translation, backward translation, and final discussion. Finally, the translation results are sent to an external proofreading agency. Furthermore, a pilot study was carried out on ten subjects.

All data were analyzed using IBM Statistical Package for the Social Sciences (SPSS) version 20. The normality test of data distribution used the Shapiro–Wilk test because the number of subjects was ≤ 50 . Numerical variables were expressed as mean (standard deviation, SD) or median (interquartile range, IQR). Categorical variables were presented as frequency (percentage). The normal distribution data were analyzed using the unpaired t-test (the independent variable with two groups) or one-way ANOVA (>2 groups). Alternatively, if the data distribution was not normal, then an alternative nonparametric Mann–Whitney test (two groups) or Kruskal–Wallis (>2 groups) was performed. Categorical variables in the 2x2 table were analyzed using the Chi-square test. The Committee of ethics, Faculty of Medicine, Universitas Indonesia, approved the study number KET-212/UN2.F1/ETIK/PPM.00.02/2022, protocol number 22–02–0228.

Results

Thirty-five subjects underwent esophagectomy and esophageal reconstruction at CMGH from 2015 to 2021: 22 males (62.9%) and 13 females (37.1%). The mean age was 43.8 ± 13.1 years. The majority of subjects were 18–40 years and 40–60 years; about 15 subjects (42.9%). The majority of body mass index (BMI) was classified as underweight, with 16 subjects (45.7%), followed by normal weight, and the least was the obese group, which only had one subject. Malignancy was the most indication of surgery, consisting of 24 subjects (68.6%), mainly in the stage III group (11 subjects, 31.4%), the most common histopathology was adenocarcinoma (21 subjects, 60.0%), and the number of patients with a history of chemotherapy reached 18 (51.4% of all subjects or 75.0% of all patients diagnosed with malignancy). The one-third lower distal part was the most common (23 subjects, 65.7%) pathological site, either due to tumor, trauma, caustic/corrosive injury, or other non-malignancy etiology. This also contributed to the high number of esophagectomies at the distal level. The type of esophageal reconstruction after esophagectomy performed at CMGH consisted of 11 (31.4%) gastric pull-ups and 24 (68.6%) other types. These other types included ileal conduit, colon conduit, and gastroesophageal anastomosis.

Quality of life after esophagectomy

The median quality of life (global health) of all subjects in this study was 83.3 (IQR: 25.0). Based on the functional scale group on the C30 questionnaire, which consists of elements of physical functioning (PF), role functioning (RF), emotional functioning (EF), and social functioning (SF), the median value was 93.3 (IQR: 33.3), 100.0 (IQR: 33.3), 83.3 (IQR: 26.7), and 100.0 (IQR: 0.0), respectively. These four groups of items had high value. Only the cognitive functioning (CF)

item had the lowest median value, 66.7 (IQR: 50.0). The interpretation of the score on the functional scale, if it is close to 100, indicates that the function is getting better. Meanwhile, based on the symptom scale group on the C30 questionnaire, which consists of items fatigue (FA), dyspnea (DYS), insomnia (SL), appetite loss (AP), constipation (CO), diarrhea (DI), financial difficulties (FI) had a median value range of 0.0 (IQR: 0.0) to 0.0 (IQR: 66.7). Only nausea and vomiting (NV) and pain (PA) items had the highest median scores, 16.7 (IQR: 50.0) and 16.7 (IQR: 33.3), respectively. The interpretation of the score on the symptom scale, if it is close to 0, indicates the symptoms the patient complains of are getting lower. Meanwhile, based on the OES18 questionnaire, item eating (OESEAT) had the highest median score, which was 34.5 (IQR: 23.9). Meanwhile, the items with a median score of zero number were trouble swallowing saliva (OSSV), dry mouth (OESDM), taste (OESTA), and speech (OESSP).

Table 1. Subjects' characteristic

Variables	Subjects (n = 35)	%
Age, mean (SD)	43.8 ± 13.1 years	
Age group		
18–40	15	42.9%
40–60	15	42.9%
>60	5	14.2%
Gender		
Male	22	62.9%
Female	13	37.1%
Body mass index		
Underweight	16	45.7%
Normal	14	40.0%
Overweight	4	11.4%
Obese	1	2.9%
Indication of surgery		
Malignancy	24	68.6%
Non-malignancy	11	31.4%
Tumor stage		
I	0	0.0%
II	7	20.0%
III	11	31.4%
IV	6	17.1%
Pathological site		
Upper third	8	22.9%
Middle third	4	11.4%
Lower third	23	65.7%
Esophagectomy level		
Distal	23	65.7%
Partial	0	0.0%
Total	12	34.3%
Reconstruction type		
Gastric pull up	11	31.4%
Others	24	68.6%
Histopathological type		
Adenocarcinoma	21	60.0%
Squamous cell carcinoma	3	8.6%
Non-cancer	11	31.4%
Chemotherapy		
Yes	18	51.4%
No	17	48.6%

In the C30 questionnaire, the question items that were statistically significant with prognostic factors include (1) physical functioning and gender; (2) role functioning and the tumor stage; (3) social functioning and histopathological types; (4) pain symptoms and gender; and (5) dyspnea symptoms and gender. Meanwhile, other prognostic factors were not statistically significant with the item questions on the C30 questionnaire.

In the OES18 questionnaire, the question items were statistically significant with prognostic factors, including (1) dysphagia symptoms (OESDYS) with tumor/non-tumor location; (2) feeding symptoms (OESEAT) with tumor/non-tumor location; (3) pain symptoms (OESPA) with gender; (4) choking symptoms (OESCH) with tumor/non-tumor location, esophagectomy level, esophageal reconstruction type, and chemotherapy; (5) tasting symptom (OESTA) with tumor/non-tumor location; (6) cough symptom (OESCO) with

Table 2. Factors associated with the EORTC-QLQ-C30 score

Variables	GH		PF		RF		EF		CF		SF		FA	
	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p
Overall subjects	83.3 (25.0)		93.3 (33.3)		100.0 (33.3)		83.3 (26.7)		66.7 (50.0)		100.0 (0.0)		0.0 (23.3)	
Age group		0.843		0.381		0.494		0.786		0.767		0.650		0.454
18–40	83.3 (25.0)		80.0 (40.0)		100.0 (33.3)		83.3 (33.3)		66.7 (50.0)		100.0 (0.0)		10.0 (43.3)	
40–60	83.3 (25.0)		93.3 (28.3)		100.0 (33.3)		90.0 (26.7)		75.0 (50.0)		100.0 (0.0)		0.0 (25.8)	
>60	83.3 (0.0)		76.7 (0.0)		100.0 (0.0)		83.4 (0.0)		75.0 (0.0)		100.0 (0.0)		0.0 (0.0)	
Gender		0.351		0.039*		0.119		0.231		0.075		0.860		0.076
Male	83.3 (25.0)		93.3 (26.7)		100.0 (16.7)		90.0 (26.7)		83.3 (50.0)		100.0 (0.0)		0.0 (13.3)	
Female	66.7 (25.0)		73.3 (46.7)		83.3 (58.4)		73.3 (38.3)		50.0 (41.7)		100.0 (0.0)		10.0 (61.7)	
Body mass index		0.463		0.517		0.335		0.299		0.756		0.757		0.822
Underweight	83.3 (25.0)		86.7 (31.7)		100.0 (33.3)		78.3 (33.3)		66.7 (33.3)		100.0 (0.0)		0.0 (27.5)	
Normal	75.0 (27.1)		90.0 (43.3)		91.7 (50.0)		83.3 (30.8)		91.7 (50.0)		100.0 (0.0)		5.0 (56.7)	
Overweight	87.5 (20.8)		93.3 (5.0)		100.0 (0.0)		100.0 (12.5)		75.0 (62.5)		100.0 (0.0)		5.0 (20.0)	
Obese	–		–		–		–		–		–		–	
Indication of surgery		0.322		0.560		0.664		0.343		0.912		0.971		0.285
Malignancy	83.3 (25.0)		93.3 (26.7)		100.0 (16.7)		100.0 (26.7)		66.7 (50.0)		100.0 (0.0)		0.0 (10.0)	
Non-malignancy	83.3 (25.0)		90.0 (38.3)		100.0 (45.8)		83.3 (31.7)		75.0 (50.0)		100.0 (0.0)		5.0 (50.9)	
Tumor stage		0.261		0.605		0.047*		0.243		0.605		0.402		0.057
I	–		–		–		–		–		–		–	
II	83.3 (16.6)		93.3 (33.3)		100.0 (33.3)		90.0 (26.7)		83.3 (50.0)		100.0 (0.0)		0.0 (33.3)	
III	83.8 (26.6)		93.3 (33.3)		100.0 (16.7)		83.3 (33.3)		66.7 (50.0)		100.0 (0.0)		0.0 (10.0)	
IV	66.7 (8.3)		63.3 (55.0)		50.0 (54.2)		70.0 (32.4)		66.7 (75.0)		100.0 (16.7)		40.0 (49.2)	
Pathological location		0.898		0.717		0.197		0.539		0.872		0.436		0.183
Upper third	83.3 (25.0)		73.3 (35.0)		83.3 (33.3)		81.7 (33.3)		75.0 (62.5)		100.0 (0.0)		5.0 (35.0)	
Middle third	83.3 (25.0)		86.7 (28.3)		100.0 (0.0)		73.3 (25.0)		50.0 (37.5)		100.0 (0.0)		0.0 (0.0)	
Lower third	83.3 (25.0)		93.3 (33.3)		100.0 (33.3)		90.0 (26.7)		83.3 (50.0)		100.0 (0.0)		10.0 (33.3)	
Esophagectomy level		0.957		0.433		0.757		0.490		0.900		0.198		0.304
Distal	83.3 (25.0)		93.3 (33.3)		100.0 (33.3)		90.0 (26.7)		83.3 (50.0)		100.0 (0.0)		10.0 (33.3)	
Partial	–		–		–		–		–		–		–	
Total	83.3 (25.0)		76.7 (30.0)		100.0 (29.2)		73.3 (31.7)		58.4 (50.0)		100.0 (0.0)		0.0 (10.0)	
Reconstruction type		0.798		0.956		0.782		0.710		0.714		0.200		0.351
Gastric pull up	83.3 (25.0)		90.0 (26.7)		100.0 (29.2)		83.3 (26.7)		83.3 (50.0)		100.0 (0.0)		10.0 (23.3)	
Others	83.3 (25.0)		93.3 (33.3)		100.0 (33.3)		90.0 (33.3)		50.0 (50.0)		100.0 (0.0)		0.0 (33.3)	
Histopathological type		0.595		0.642		0.908		0.537		0.620		0.001*		0.516
Adenocarcinoma	83.3 (25.0)		93.3 (26.7)		100.0 (16.7)		100.0 (26.7)		66.7 (50.0)		100.0 (0.0)		0.0 (10.0)	
Squamous cell carcinoma	83.3 (25.0)		93.3 (36.7)		100.0 (41.7)		83.3 (30.0)		66.7 (50.0)		100.0 (0.0)		10.0 (45.0)	
Non-cancer	83.3 (0.0)		86.7 (0.0)		100.0 (0.0)		73.3 (0.0)		100.0 (0.0)		83.3 (0.0)		0.0 (0.0)	
Chemotherapy		0.919		0.565		0.633		0.447		0.878		0.563		0.287
Yes	83.3 (50.0)		90.0 (35.0)		100.0 (37.5)		83.3 (33.3)		75.0 (50.0)		100.0 (0.0)		10.0 (39.2)	
No	83.3 (25.0)		93.3 (26.7)		100.0 (25.0)		90.0 (26.7)		66.7 (50.0)		100.0 (0.0)		0.0 (16.7)	

Notes: GH = global health; PF = physical functioning; RF = role functioning; EF = emotional functioning; CF = cognitive functioning; SF = social functioning; FA = fatigue; NV = nausea and vomiting; PA = pain; DY = dyspnea; SL = insomnia; AP = appetite loss; CO = constipation; DI = diarrhea; FI = financial difficulties; IQR = interquartile range; * = significant (p < 0.05)

Table 2. Factors associated with the EORTC-QLQ-C30 score (cont.)

Variables	NV		PA		DY		SL		AP		CO		DI		FI	
	Median (IQR)	P	Median (IQR)	P	Median (IQR)	P	Median (IQR)	P	Median (IQR)	P	Median (IQR)	P	Median (IQR)	P	Median (IQR)	P
Overall subjects	16.7 (50.0)		16.7 (33.3)		0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
Age group					0.0 (0.0)		0.0 (66.7)		0.0 (0.0)		0.0 (0.0)		0.0 (0.0)		33.3 (66.7)	
18-40	16.7 (50.0)	0.772	16.7 (0.0)	0.478	33.3 (33.3)	0.414	16.7 (66.7)	0.393	0.0 (0.0)	0.144	0.0 (0.0)	0.834	0.0 (0.0)	0.868	0.0 (66.7)	0.425
40-60	0.0 (50.0)		16.7 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
>60	25.0 (0.0)		8.4 (0.0)		0.0 (0.0)		0.0 (0.0)		33.3 (0.0)		0.0 (0.0)		0.0 (0.0)		0.0 (0.0)	
Gender					0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
Male	8.4 (37.5)	0.085	16.7 (16.7)	0.024*	0.0 (0.0)	0.009*	0.0 (66.7)	0.757	0.0 (33.3)	0.640	0.0 (0.0)	0.833	0.0 (0.0)	0.665	0.0 (66.7)	0.807
Female	33.3 (66.7)		16.7 (33.3)		50.0 (50.0)		0.0 (50.0)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (0.0)	
Body mass index					0.0 (0.0)		0.0 (58.4)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		33.3 (91.7)	
Underweight	16.7 (33.3)		16.7 (29.2)		0.0 (0.0)		0.0 (58.4)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		33.3 (91.7)	
Normal	8.4 (50.0)	0.963	16.7 (20.8)	0.503	33.3 (33.3)	0.481	0.0 (66.7)	0.853	0.0 (33.3)	0.676	0.0 (0.0)	0.377	0.0 (66.7)	0.720	0.0 (66.7)	0.443
Overweight	25.0 (50.0)		8.4 (16.7)		0.0 (0.0)		0.0 (75.0)		0.0 (25.0)		0.0 (50.0)		0.0 (25.0)		0.0 (50.0)	
Obese	-		-		-		-		-		-		-		-	
Indication of surgery					0.0 (0.0)		0.0 (33.3)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
Malignancy	16.7 (50.0)	0.985	16.7 (16.7)	0.393	0.0 (0.0)	0.957	0.0 (33.3)	0.364	0.0 (33.3)	0.597	0.0 (0.0)	0.913	0.0 (0.0)	0.847	0.0 (66.7)	0.379
Non-malignancy	16.7 (50.0)		16.7 (33.3)		0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		16.7 (66.7)	
Tumor stage					0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		66.7 (100.0)	
I	-		-		0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
II	16.7 (50.0)	0.561	16.7 (33.3)	0.111	0.0 (0.0)	0.505	0.0 (66.7)	0.136	0.0 (33.3)	0.873	0.0 (0.0)	0.587	0.0 (0.0)	0.895	66.7 (100.0)	0.299
III	16.7 (33.3)		16.7 (16.7)		0.0 (0.0)		0.0 (33.3)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
IV	33.4 (66.7)		33.3 (29.1)		41.7 (41.7)		50.0 (50.1)		0.0 (66.7)		0.0 (8.3)		0.0 (8.3)		16.7 (75.0)	
Pathological location					0.0 (33.3)		0.0 (58.4)		0.0 (25.0)		0.0 (0.0)		0.0 (0.0)		66.7 (91.7)	
Upper third	0.0 (29.2)	0.476	16.7 (25.0)	0.399	33.3 (33.3)	0.220	0.0 (58.4)	0.215	0.0 (25.0)	0.736	0.0 (0.0)	0.761	0.0 (0.0)	0.752	66.7 (91.7)	0.131
Middle third	25.0 (41.7)		8.4 (16.7)		0.0 (0.0)		0.0 (0.0)		0.0 (25.0)		0.0 (0.0)		0.0 (0.0)		0.0 (75.0)	
Lower third	16.7 (50.0)		16.7 (33.3)		0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
Esophagectomy level					0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
Distal	16.7 (50.0)	0.381	16.7 (33.3)	0.458	-	0.427	0.0 (66.7)	0.541	0.0 (33.3)	0.868	0.0 (0.0)	1.000	0.0 (0.0)	0.753	0.0 (66.7)	0.157
Partial	-		-		0.0 (25.0)		0.0 (58.4)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		50.0 (100.0)	
Total	8.4 (33.3)		16.7 (16.7)		0.0 (0.0)		0.0 (58.4)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		50.0 (100.0)	
Reconstruction type					0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
Gastric pull up	16.7 (50.0)	0.641	16.7 (12.5)	0.955	0.0 (0.0)	0.255	0.0 (66.7)	0.572	0.0 (33.3)	0.597	0.0 (0.0)	0.227	0.0 (0.0)	0.847	0.0 (66.7)	0.118
Others	0.0 (50.0)		16.7 (33.3)		33.3 (33.3)		0.0 (33.3)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		33.3 (100.0)	
Histopathological type					0.0 (0.0)		0.0 (33.3)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
Adenocarcinoma	16.7 (50.0)	0.892	16.7 (16.7)	0.679	0.0 (0.0)	0.818	0.0 (33.3)	0.661	0.0 (33.3)	0.325	0.0 (0.0)	0.861	0.0 (0.0)	0.501	0.0 (66.7)	0.342
Squamous cell carcinoma	16.7 (50.0)		16.7 (33.3)		0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
Non-cancer	16.7 (0.0)		16.7 (0.0)		0.0 (0.0)		0.0 (0.0)		0.0 (0.0)		0.0 (0.0)		0.0 (0.0)		33.3 (0.0)	
Chemotherapy					0.0 (0.0)		0.0 (66.7)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (66.7)	
Yes	16.7 (50.0)	0.544	16.7 (33.3)	0.492	0.0 (0.0)	0.339	16.7 (66.7)	0.303	0.0 (33.3)	0.680	0.0 (0.0)	0.610	0.0 (0.0)	0.905	0.0 (66.7)	0.772
No	0.0 (50.0)		16.7 (16.7)		16.7 (16.7)		0.0 (50.0)		0.0 (33.3)		0.0 (0.0)		0.0 (0.0)		0.0 (83.4)	

Notes: GH = global health; PF = physical functioning; RF = role functioning; EF = emotional functioning; CF = cognitive functioning; SF = social functioning; FA = fatigue; NV = nausea and vomiting; PA = pain; DY = dyspnea; SL = insomnia; AP = appetite loss; CO = constipation; DI = diarrhea; FI = financial difficulties; IQR = interquartile range; * = significant (p < 0.05)

Table 3. Factors associated with the EORTC–QLQ–OES18 score

Variables	OESDYS		OESEAT		OESRFX		OESPA		OESSV	
	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p
Overall subjects	33.3 (33.3)		34.5 (23.9)		16.7 (33.3)		23.3 (33.3)		0.0 (66.7)	
Age group										
18–40	23.3 (46.7)	0.426	40.9 (26.8)	0.310	33.3 (33.3)	0.826	33.3 (23.3)	0.114	0.0 (66.7)	0.455
40–60	33.3 (23.3)		30.9 (21.4)		0.0 (50.0)		10.0 (33.3)		0.0 (66.7)	
>60	16.7 (0.0)		18.4 (11.8)		16.7 (0.0)		5.0 (0.0)		0.0 (0.0)	
Gender										
Male	28.3 (39.2)	0.809	29.3 (22.7)	0.092	0.0 (37.5)	0.148	10.0 (25.8)	0.007*	0.0 (41.7)	0.477
Female	33.3 (33.3)		43.3 (23.9)		33.3 (33.3)		33.3 (16.7)		0.0 (66.7)	
Body mass index										
Underweight	28.3 (20.0)	0.237	38.6 (24.4)	0.116	8.4 (33.3)	0.846	16.7 (33.3)	0.503	0.0 (58.4)	0.252
Normal	23.3 (35.8)		31.7 (21.6)		16.7 (37.5)		23.3 (33.3)		0.0 (66.7)	
Overweight	55.0 (78.4)		17.5 (18.5)		25.0 (62.5)		21.7 (38.3)		0.0 (0.0)	
Obese	–		–		–		–		–	
Indication of surgery										
Malignancy	33.3 (43.4)	0.166	41.2 (24.9)	0.264	16.7 (33.3)	1.000	23.3 (23.3)	0.812	33.3 (66.7)	0.202
Non-malignancy	23.3 (33.3)		31.4 (23.3)		16.7 (45.8)		23.3 (33.3)		0.0 (33.3)	
Tumor stage										
I	–	0.307	–	0.126	–	0.481	–	0.732	–	0.575
II	33.3 (20.0)		42.9 (22.1)		33.3 (50.0)		10.0 (33.3)		0.0 (33.3)	
III	10.0 (23.3)		21.2 (24.6)		16.7 (50.0)		10.0 (43.3)		0.0 (0.0)	
IV	38.3 (39.2)		36.7 (15.8)		0.0 (25.0)		28.3 (15.8)		16.7 (66.7)	
Pathological location										
Upper third	50.0 (58.4)	0.048*	60.4 (25.1)	0.001*	8.4 (45.8)	0.725	16.7 (40.8)	0.495	33.3 (66.7)	0.181
Middle third	28.3 (60.0)		20.0 (8.2)		8.4 (29.2)		5.0 (27.5)		0.0 (0.0)	
Lower third	23.3 (33.3)		27.9 (18.5)		16.7 (50.0)		23.3 (33.3)		0.0 (66.7)	
Esophagectomy level										
Distal	23.3 (33.3)	0.085	30.1 (21.8)	0.138	16.7 (50.0)	0.484	23.3 (33.3)	0.497	0.0 (33.3)	0.421
Partial	–		–		–		–		–	
Total	38.3 (60.9)		42.8 (26.3)		8.4 (33.3)		10.0 (33.3)		16.7 (66.7)	
Reconstruction type										
Gastric pull up	23.3 (33.3)	0.350	31.1 (22.9)	0.233	16.7 (33.3)	0.970	23.3 (33.3)	0.622	0.0 (58.4)	1.000
Others	33.3 (20.0)		41.8 (25.2)		16.7 (50.0)		10.0 (33.3)		0.0 (66.7)	
Histopathological type										
Adenocarcinoma	33.3 (43.4)	0.248	41.2 (24.9)	0.434	16.7 (33.3)	0.790	23.3 (23.3)	0.947	33.3 (66.7)	0.436
Squamous cell carcinoma	23.3 (33.3)		30.2 (23.2)		16.7 (50.0)		23.3 (33.3)		0.0 (50.0)	
Non-cancer	33.3 (0.0)		40.0 (26.5)		0.0 (0.0)		23.3 (0.0)		0.0 (0.0)	
Chemotherapy										
Yes	23.3 (33.3)	0.176	22.6 (17.1)	0.001	8.4 (37.5)	0.529	23.3 (33.3)	0.825	0.0 (41.7)	0.379
No	33.3 (38.4)		47.1 (23.9)		33.3 (41.7)		23.3 (28.3)		0.0 (66.7)	

Notes: OESDYS = *dysphagia*, OESEAT = *eating*, OESRFX = *reflux*, OESPA = *pain*, OESSV = *trouble swallowing saliva*, OESCH = *choking*, OESDM = *dry mouth*, OESTA = *taste*, OESCO = *cough*, OESSP = *speech*, IQR = *interquartile range*, * = significant (p < 0.05).

Table 3. Factors associated with the EORTC-QLQ-OES18 score (cont.)

Variables	OESCH		OESDM		OESTA		OESCO		OESSP	
	Median (IQR)	p	Median (IQR)	p	Median (IQR)	P	Median (IQR)	p	Median (IQR)	p
Overall subjects	33.3 (33.3)		0.0 (33.3)		0.0 (0.0)		33.3 (33.3)		0.0 (0.0)	
Age group										
18–40	33.3 (33.3)	0.829	33.3 (33.3)	0.109	0.0 (66.7)	0.421	33.3 (66.7)	0.770	0.0 (33.3)	0.081
40–60	33.3 (33.3)		0.0 (8.3)		33.3 (41.7)		0.0 (0.0)			
>60	16.7 (0.0)		0.0 (0.0)		16.7 (0.0)		0.0 (0.0)			
Gender										
Male	16.7 (33.3)	0.352	0.0 (33.3)	0.291	0.0 (0.0)	0.471	33.3 (41.7)	0.942	0.0 (0.0)	0.435
Female	33.3 (33.3)		0.0 (33.3)		33.3 (50.0)		0.0 (16.7)			
Body mass index										
Underweight	33.3 (33.3)	0.900	0.0 (33.3)	0.333	0.0 (83.3)	0.187	33.3 (58.4)	0.623	0.0 (0.0)	0.257
Normal	33.3 (33.3)		0.0 (41.7)		33.3 (33.3)		0.0 (0.0)			
Overweight	16.7 (33.3)		0.0 (0.0)		33.3 (50.0)		0.0 (25.0)			
Obese	–		–		–		–			
Indication of surgery										
Malignancy	33.3 (66.7)	0.121	0.0 (33.3)	0.569	0.0 (66.7)	0.645	33.3 (33.3)	0.649	0.0 (33.3)	0.045
Non-malignancy	16.7 (33.3)		0.0 (33.3)		33.3 (58.4)		0.0 (0.0)			
Tumor stage										
I	–	0.101	–	0.115	–	0.494	–	0.259	–	0.587
II	33.3 (0.0)		0.0 (0.0)		33.3 (66.7)		0.0 (0.0)			
III	0.0 (33.3)		0.0 (0.0)		33.3 (33.3)		0.0 (0.0)			
IV	0.0 (33.3)		33.3 (75.0)		33.3 (50.0)		0.0 (8.3)			
Pathological location										
Upper third	50.0 (58.4)	0.029*	33.3 (58.4)	0.103	83.4 (100.0)	0.005*	16.7 (66.7)	0.205	16.7 (100.0)	0.009*
Middle third	33.3 (0.0)		0.0 (0.0)		50.0 (58.4)		0.0 (25.0)			
Lower third	0.0 (33.3)		0.0 (33.3)		33.3 (33.3)		0.0 (0.0)			
Esophagectomy level										
Distal	0.0 (33.3)	0.023*	0.0 (33.3)	0.757	0.0 (0.0)	0.246	33.3 (33.3)	0.504	0.0 (0.0)	0.072
Partial	–		–		–		–			
Total	33.3 (25.1)		0.0 (33.3)		33.3 (66.7)		0.0 (33.3)			
Reconstruction type										
Gastric pull up	0.0 (33.3)	0.007*	0.0 (33.3)	0.598	0.0 (0.0)	0.121	33.3 (33.3)	0.012*	0.0 (0.0)	0.914
Others	33.3 (33.4)		0.0 (66.7)		33.3 (33.4)		0.0 (0.0)			
Histopathological type										
Adenocarcinoma	33.3 (66.7)	0.285	0.0 (33.3)	0.119	0.0 (66.7)	0.718	33.3 (33.3)	0.168	0.0 (33.3)	0.076
Squamous cell carcinoma	0.0 (33.3)		0.0 (16.7)		33.3 (33.3)		0.0 (0.0)			
Non-cancer	33.3 (0.0)		100.0 (0.0)		66.7 (0.0)		0.0 (0.0)			
Chemotherapy										
Yes	0.0 (33.3)	0.007*	0.0 (33.3)	0.399	0.0 (0.0)	0.056	33.3 (33.3)	0.470	0.0 (0.0)	0.056
No	33.3 (50.1)		0.0 (33.3)		33.3 (66.7)		0.0 (33.3)			

Notes: OESDYS = dysphagia, OESEAT = eating, OESRFX = reflux, OESPA = pain, OESSV = trouble swallowing saliva, OESCH = choking, OESDM = dry mouth, OESTA = taste, OESCO = cough, OESSP = speech, IQR = interquartile range, * = significant (p < 0.05).

esophageal reconstruction type; and (7) speech symptoms (OESSP) with tumor/nontumor location. Other prognostic factors were not statistically significant with the item questions on the OES18 questionnaire.

Discussion

In this study, most subjects were male, as in several similar studies in Sweden,²⁵ Texas,²⁶ Germany,^{27,28} and Seattle.²⁹ However, the mean age of the subjects in this study was younger than the mean age in those five studies. After being grouped by age, the patient population at CMGH, esophageal cancer that requires an esophagectomy procedure is more likely to occur at a young age. Most subjects had underweight and normal body mass index (BMI), thus slightly different from Poh et al., who showed that the subject population consisted of patients with normal BMI.²⁶ The low BMI of patients at the CMGH should be suspected because most patients have trouble with food intake due to obstruction in the esophagus.

Esophagectomy remains the primary choice in resectable esophageal cancer.⁹ Most esophagectomy was performed at the distal level, corresponding to the most common pathological location in the lower third. This finding is similar to the results of a study by Gockel et al., which was also dominated by 62% of patients with distal tumor locations.²⁸ The most common histopathological type found in this study was adenocarcinoma. It is different from the study in Germany by Gockel et al., which was dominated by squamous cell carcinoma.²⁸ However, another study conducted in Germany by Gutschow et al. showed that 68.7% of patients had adenocarcinoma cell type cancer.²⁷ More than 50% of patients in CMGH were known to have received chemotherapy before the surgical procedure compared to those who did not. The high number of subjects who received chemotherapy could be attributed to many patients with advanced malignancy. A study in Germany by Gutschow et al. showed that the percentage of patients who received neoadjuvant therapy such as radiotherapy or chemotherapy was less than 50% because the early tumor stages dominated the population.²⁷

Quality of life after esophagectomy and its associated factors

The quality of life of post-esophagectomy patients at CMGH is quite good. Global health item scores are higher than the study by Gockel et al., which only had a median of 83.3,²⁸ also higher than Gutschow et al. and the reference value from EORTC.²⁷ In this study, the lowest score in the C30 functional scale item questionnaire was cognitive functioning (CF). At the same time, the highest scores were role functioning (RF) and social functioning (SF). This result differs from Gockel et al., which showed that the highest score was on CF items, and the lowest was on RF and SF items.²⁸ The CF score of this study is even lower than the reference value from EORTC.²⁷ In this study, the C30 questionnaire for symptoms, nausea, vomitus (NV), and pain (PA) had the highest score. In the study by Gockel et al., PA items were also reported by some patients, although their values were lower than in this study.²⁸ The NV symptom score in this study is higher than the reference value from EORTC.²⁷

The results of symptom scores on the OES18 questionnaire are also similar to the results of a study by Gockel et al. Trouble swallowing saliva (OSSV), dry mouth (OESDM), taste (OESTA), and speech (OESSP) items all scored 0. Reflux (OESRFX) and pain (OESPA) were also common symptoms. The different results were dysphagia (OESDYS), eating (OESEAT), choking (OESCH), and coughing (OESCO) items which were zero in the study by Gockel et al. but were widely reported in this study. Although many items have zero scores,

these items have varying IQR scores. Therefore, there is still the possibility of differences in the degree of symptoms reported by patients.²⁸ All the results in C30 and OES18 scores should be affected or related by some factors, including gender, tumor stage, histopathological types, tumor location, and reconstruction type.

Gender was significantly related to the C30 questionnaire score on physical functioning, pain, and dyspnea symptoms. The male gender had a higher median physical functioning than the female. While the median value on symptom items did not differ, both scores were zero and statistically significant. A study in Sweden by Djarv et al. showed that the median score in male patients was higher than that of female patients. Although based on statistical analysis, both gender is worse off than their population's reference score.¹⁵

The tumor stage was significantly related to role functioning. Subjects with tumor stage IV had the lowest median score = 50 (IQR: 54.2). The low score of the role functioning items can be suspected as a result of patients following routine chemotherapy and periodic controls, thus limiting them from being more active in the community, which decreases their quality of life. Although the study by Gutschow et al. failed to demonstrate the effect of tumor stage on quality of life.²⁷

Histopathological types were significantly related to social functioning. Squamous cell carcinoma had a lower score than adenocarcinoma. A study that found the relationship between histopathological types and quality of life was conducted by Gockel et al. However, the related item was pain based on the OES18 questionnaire. Squamous cell carcinoma is significantly associated with a higher score of pain symptom complaints than adenocarcinoma.²⁸ The high score of pain may indirectly affect the social functioning item. Even though in this study, the histopathological type was significantly associated with pain symptoms. However, the female factor had a higher median pain score than the male one.

Tumor location was significantly related to many items in the OES18 questionnaire, starting from dysphagia (OESDYS), eating (OESEAT), choking (OESCH), tasting (OESTA), and speech (OESSP). The tumor location that triggers more of these symptoms is the upper third. It is suspected that this is related to the function of the epiglottis, larynx, and tongue, which are located more proximal.

In this study, gastric pull-up reconstruction had a higher median score than other techniques (jejunal conduit, distal gastroesophageal anastomosis, colon conduit). It was statistically significant ($p = 0.007$) on the OESCH and OESCO items in the OES18 questionnaire. OESCH is a parameter to assess complaints of choking when eating, and OESCO is a parameter to assess cough problems. The two are interconnected because the choking state will trigger a cough response. The inability to cough can worsen the choking condition. Based on the study by Stephens et al., complaints of reflux, dumping, or dysphagia after gastric pull-up procedures should not be different from other reconstruction techniques.³⁰ Although the gastric pull-up technique is relatively easy to perform, the outcome of this procedure is associated with frequent complaints of reflux, uncontrolled gastric emptying, and various other postprandial symptoms.³¹ This reflux state continues to cause dysphagia. However, the 10-year QOL following esophagectomy with esophageal reconstruction using the gastric pull-up technique showed better results. Patient satisfaction in consuming their food increases, and their postprandial symptoms improve.³²

The limitation of this study is the lack of literature that discusses the relationship between each prognostic factor and quality of life items. Furthermore, most published studies only convey the overall median

QoL without stratification. Therefore, measuring the quality of life was proceeded only once and without precise boundaries/intervals—for example, three months and six months after esophagectomy. In addition, this study had not collected baseline QoL values from the normal population in CMGH and Indonesia. Thus, they still had to rely on references from EORTC and other research that could give inaccurate results.

Conclusions

The overall quality of life in patients after esophagectomy at CMGH based on the EORTC-QLQ-C30 and OES18 questionnaires were good. Prognostic factors associated with decreased quality of life should be better educated to patients and prepared well before the esophagectomy procedure, thus maximizing quality of life after esophagectomy. Quality of life assessment should be carried out in patients after esophagectomy procedure at certain time intervals and more than one measurement.

Disclosure

The authors declare no conflict of interest.

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Conceptualization ASP, Data curation DHS, Formal analysis DHS, Funding acquisition DHS, Investigation DHS, Methodology DHS, Project administration ASP, Resources DHS, Software DHS, Supervision ASP, Validation DHS ASP, Visualization ASP, Writing original draft preparation DHS ASP, Writing review and editing DHS ASP.

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