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# Learning curve in relation to health-related quality of life in long-term, disease free survivors after McKeown minimally invasive esophagectomy

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## Abstract

**Background** The potential impact of learning curve on long-term health-related quality of life (QoL) after esophagectomy for cancer has not been investigated. The aim of this article is to investigate the relationship between learning curve for McKeown minimally invasive esophagectomy (MIE) and health-related quality of life (QoL) in long-term, disease free survivors up to 10 years after esophageal cancer resection.

**Methods** Esophageal cancer patients who underwent McKeown MIE between 2009 and 2019 were identified in which 280 who were free of disease at the time of survey and completed health-related QoL and symptom questionnaires, including EORTC QLQ-C30, EORTC QLQ-OES18, and Digestive Symptom Questionnaire. Patients were assessed in 3 cohorts according to the learning phases of expertise reported by our previous study: initial phase; plateau phase, and; experienced phase.

**Results** Median time from operation to survey was 5.8 years (interquartile range 4.6–8.2). The QLQ-C30 mean scores of functional scales, and symptom scales of respiratory and digestive systems including dyspnea ($P=0.006$), shortness of breath ($P=0.003$), and dysphagia ($P=0.031$) were significantly better in experienced phase group. Furthermore, in the subgroup analyses for patients without postoperative major complications, patients in the initial learning phase remained suffering from more symptoms of dyspnea ($P=0.040$) and shortness of breath ($P=0.001$).

**Conclusion** Esophageal cancer patients undergoing McKeown MIE in initial learning phase tend to suffer from a deterioration in long-term health-related QoL and higher symptomatic burden as compared to experienced learning phase, which did not improved over time and warranted more attention.

**Keywords** Esophageal cancer · Quality of life · Outcome · Learning curve · Minimally invasive surgery

For patients with potentially curable localized tumors, surgical resection via esophagectomy is still the primary form of treatment [1]. However, the implementation of this notoriously technically demanding procedure, unfortunately, is associated with a steep learning curve, considerable postoperative complications, and impaired health-related quality of life (QoL) with symptoms of dysphagia, regurgitation, coughing, and pain [2–6].

Over the last few decades, multiple studies have identified that several factors such as postoperative complications [6], anastomotic technique (circular stapled vs linear stapled) [7], site of surgical anastomosis (cervical vs intrathoracic) [8], and method of reconstruction (narrow gastric tube vs whole stomach) [9] did have a large effect on QoL after esophagectomy for cancer. However, the potential impact of learning curve on long-term health-related QoL after esophagectomy for cancer has not been investigated. As previous studies [2, 3, 6] demonstrated, the surgeon's experience did have a direct impact on the occurrence of postoperative adverse events such as anastomotic leak and pneumonia, which could negatively affect long-term health-related QoL after esophagectomy. Moreover, accumulated sufficient experience did have beneficial effects on protecting adjacent tissue and organs (e.g., thoracic duct and recurrent laryngeal nerve)

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against intraoperative injury, and would likely be conducive to improvement of QoL.

The purpose of this retrospective study was to compare the health-related QoL in long-term, disease free survivors after McKeown MIE for esophageal carcinoma among different groups: initial phase (1st–197th case); plateau phase (198th–314th case), and; experienced phase (315th–700th case), according to the learning curve of Dr Guo reported by our previous study on 700 consecutive patients [3].

## Materials and methods

### Patient eligibility

From September 2009 to June 2019, a total of 700 consecutive patients suffering from esophageal cancer underwent McKeown MIE by a single surgeon (Dr. Guo) in the Department of Thoracic Surgery at Daping Hospital. Data were collected retrospectively by chart review and analyzed in terms of demographic characteristics. Written consent was obtained from the patients associated with this study, and the study was approved by the Ethics Committee of Daping Hospital.

### Perioperative management

All patients underwent McKeown esophagectomy with systematic lymphadenectomy via video-assisted thoracoscopic-laparoscopic surgery. Neoadjuvant chemotherapy or chemoradiotherapy was performed for patients with clinical stage III or greater lesions. The tumor node metastasis stage was classified according to the staging protocol in the eighth edition of the American Joint Committee on Cancer Staging Manual [10].

The details of our surgical techniques for McKeown MIE are available in our previously published article [3]. Briefly, During the thoracoscopic stage, standard trocars were placed at four sites and an artificial pneumothorax using carbon dioxide at a pressure of 8 mmHg was performed. After cavity inspection, the mediastinal pleura was cut and the azygos vein arch was cut off using a vascular stapler. Afterward, dissection of the lymph nodes around the right and left recurrent laryngeal nerve was performed as far as possible to the cervical region. Subsequently, the esophagus was mobilized caudally to the esophageal hiatus and cranially to the thoracic entrance, accompanied by lymphadenectomy of supraphrenic, paraesophageal, peripulmonary vein, subcarinal and paratracheal stations. During the laparoscopic stage, five trocars were placed and an artificial pneumoperitoneum at a pressure of 10 mmHg was performed. The stomach was mobilized with reserve of the right gastroepiploic artery, and pericardiac and celiac nodes were resected. Finally, a gastric tube was constructed via a stapler and a cervical end-to-side anastomosis was performed using a circular stapler.

All patients were subsequently transferred to the intensive care unit for ongoing management, and extubation was usually decided after a weaning readiness test involving spontaneous breathing on postoperative day 1. An iodine contrast examination was performed on postoperative day 7. If there was no leak, the chest tube was removed and liquid or semi-liquid diet started.

### Surgical outcome and postoperative adverse events

Postoperative adverse events included pulmonary complications and anastomotic leak. In detail, pulmonary complications included pneumonia, pleural effusion (requiring puncture and drainage), pneumothorax (requiring puncture and drainage), respiratory failure requiring reintubation, and acute respiratory distress syndrome. The definition of anastomotic leakage as well as other adverse events was same as described previously [11], according to the International Society for Diseases of the Esophagus and Esophagectomy Complications Consensus Group [12, 13].

According to the Clavien-Dindo grading system, major postoperative complications was defined as greater or equal to grade III [14].

### Measurement of QoL and postoperative follow-up

We used the validated simplified Chinese version of QLQ-C30 and QLQ-OES18 developed by the European Organization for Research and Treatment of Cancer (EORTC) to measure health-related QoL for patients with esophageal cancer, which has been demonstrated to be a reliable,valid, and acceptable in mainland China [15, 16]. In addition, each patients was also asked to complete digestive symptoms questionnaire [17]. All questionnaires were collected from patients via face-to-face, telephone, or sent electronically via a purpose designed on-line platform (www.wjx.cn). Each item was grouped into different QoL domains of global health status, symptom, and functional scales. All scale and item scores were linearly transformed to a 0–100 score according to the EORTC QLQ-C30 scoring manual [18]. High scores in the global QoL scale and functional scales indicate better levels of function and QoL, respectively (QLQ-C30), whereas high scores in the symptom scales and items represent worse symptoms (QLQ-C30, QLQ-OES18).

Patients were routinely invited for follow-up appointments in the outpatient department at intervals of 3 months for the first 2 years, and every 6 months until 5 years. Thereafter patients were invited to annual follow-up with surveillance imaging.

### Statistical analysis

Categorical data were compared using Fisher's exact test or Pearson chi-square tests, and continuous data were compared using one-way analysis of variance test or the Kruskal–Wallis test, as appropriate. Statistical analyses were performed by using IBM SPSS 25.0 software (IBM, Inc.). All significance tests were two tailed, with significance set at $P$ less than 0.05.

## Results

### Patient characteristics and perioperative parameters

A total of 287 patients were presumed to be alive and disease free after McKeown MIE at the time of analysis (June 2022). Of these, 280 agreed to participate in this study and completed all questionnaires, resulting in a response rate of 97% (Fig. 1). The demographics of the patients undergoing McKeown MIE during the study period are detailed in Table 1. Patients were divided into three groups: initial phase ($n=55$, 20%); plateau phase ($n=45$, 16%), and; experienced phase ($n=180$, 64%). Median time from operation to survey was 5.8 years (IQR 4.6–8.2); 10.4 years (IQR 9.9–11.7) in initial phase, 7.8 years (IQR 7.3–8.3) in plateau phase, and 5.0 years (IQR 4.1–5.7) in experienced phase.

As shown in Table 1, patients in initial phase group were associated with older age at surgery ($P=0.008$), older age at survey ($P=0.02$), more female gender ($P=0.008$), less hypertension ($P=0.01$), more tumor located in the middle thoracic ($P<0.001$), and more advanced $T$ stage ($P=0.029$). The differences of postoperative outcomes among groups were significant in terms of major postoperative complications ($P<0.001$), pulmonary complications ($P<0.001$),

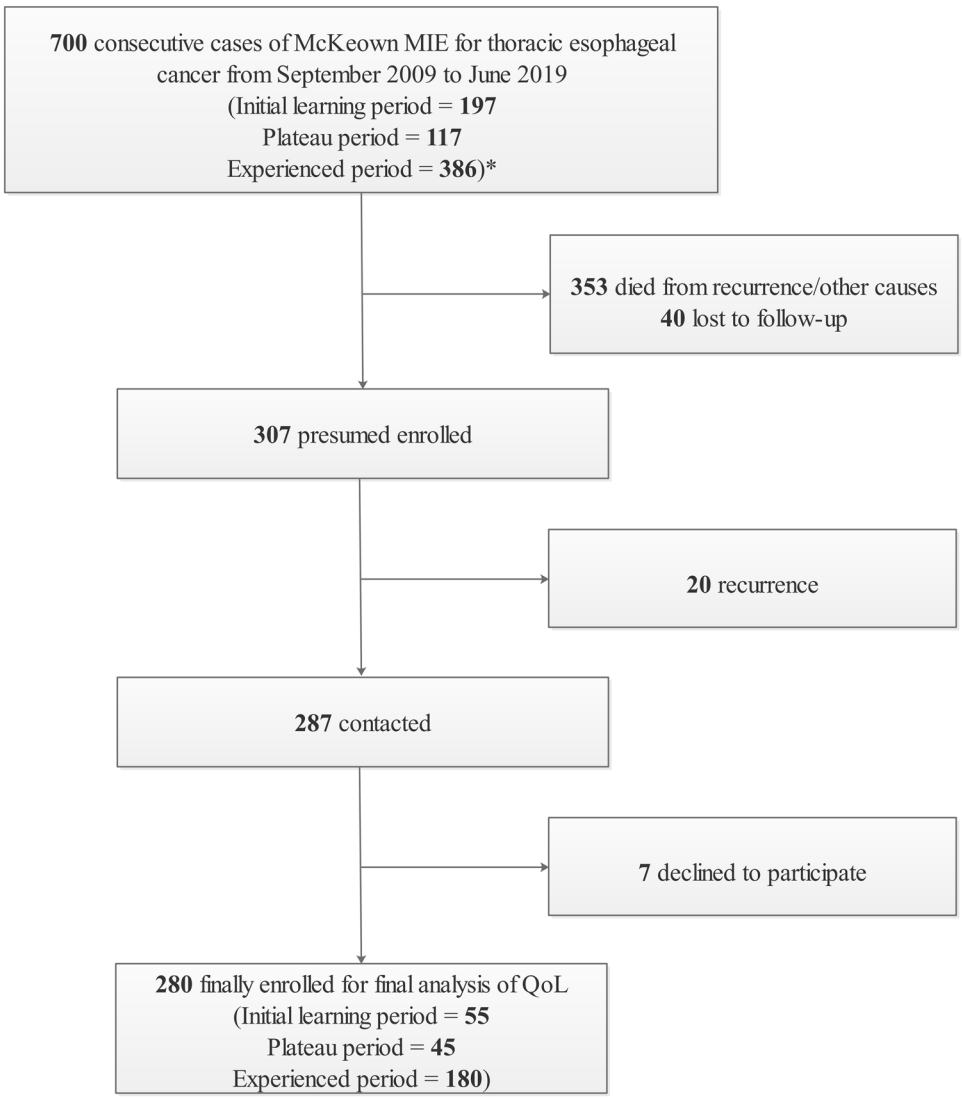


**Fig. 1** Study flowchart. *MIE* minimally invasive esophagectomy, *QoL* quality of life (*Bao et al. [7])

**Table 1** Characteristics and perioperative outcomes of patients

| Characteristics | Total ($n=280$) | Period 1 ($n=55$) | Period 2 ($n=45$) | Period 3 ($n=180$) | $P$* |
|---|---|---|---|---|---|
| Age at surgery, year (mean ± SD) | 62 ± 7 | 62 ± 7 | 60 ± 7 | 63 ± 7 | 0.008[a] |
| Age at survey, year (mean ± SD) | 68 ± 7 | 71 ± 7 | 67 ± 7 | 68 ± 7 | 0.027[a] |
| Female/male ratio | 55/225 | 19/36 | 7/38 | 29/151 | 0.008 |
| Smoking habit (smoker/ nonsmoker) | 185/95 | 31/24 | 34/11 | 120/60 | 0.130 |
| Co-morbidity | | | | | |
| COPD | 7 (2.5) | 0 | 1 (2.2) | 6 (3.3) | 0.403 |
| Hypertension | 29 (10.4) | 2 (3.6) | 1 (2.2) | 26 (14.4) | 0.010 |
| Diabetes mellitus | 5 (1.8) | 2 (3.6) | 0 | 3 (1.7) | 0.416 |
| Coronary artery disease | 5 (1.8) | 0 | 2 (4.4) | 3 (1.7) | 0.235 |
| Previous thoracic or abdominal surgery | 15 (5.4) | 4 (7.3) | 0 | 11 (6.1) | 0.188 |
| Tumor location | | | | | < 0.001 |
| Upper thoracic | 54 (19.3) | 10 (18.2) | 13 (28.9) | 31 (17.2) | |
| Middle thoracic | 153 (54.6) | 42 (76.4) | 20 (44.4) | 91 (50.6) | |
| Lower thoracic | 73 (26.1) | 3 (5.5) | 12 (26.7) | 58 (32.2) | |
| Pathological types | | | | | 0.413 |
| Squamous cell | 276 (98.6) | 53 (96.4) | 45 (100) | 178 (98.9) | |
| Others | 4 (1.4) | 2 (3.6) | 0 | 2 (1.1) | |
| Neoadjuvant therapy | 19 (6.8) | 1 (1.8) | 4 (8.9) | 14 (7.8) | 0.248 |
| Depth of tumor invasion[†] | | | | | 0.029 |
| T0 or Tis | 30 (10.7) | 3 (5.5) | 7 (15.6) | 20 (11.1) | |
| T1 | 76 (27.1) | 8 (14.5) | 12 (26.7) | 56 (31.1) | |
| T2 | 59 (21.1) | 19 (34.5) | 10 (22.2) | 30 (16.7) | |
| T3 | 103 (36.8) | 20 (36.4) | 15 (33.3) | 68 (37.8) | |
| T4 | 12 (4.3) | 5 (9.1) | 1 (2.2) | 6 (3.3) | |
| Lymph node metastasis[†] | | | | | 0.830 |
| N0 | 210 (75.0) | 39 (70.9) | 35 (77.8) | 136 (75.6) | |
| N1 | 50 (17.9) | 13 (23.6) | 8 (17.8) | 29 (16.1) | |
| N2 | 19 (6.8) | 3 (5.5) | 2 (4.4) | 14 (7.8) | |
| N3 | 1 (0.4) | 0 | 0 | 1 (0.6) | |
| Postoperative complications | | | | | |
| Clavien-Dindo grade ≥ III | 55 (19.6) | 24 (43.6) | 11 (24.4) | 20 (11.1) | < 0.001 |
| Pulmonary complications | 41 (14.6) | 19 (34.5) | 5 (11.1) | 17 (9.4) | < 0.001 |
| Anastomotic leak | 52 (18.6) | 19 (34.5) | 9 (20.0) | 24 (13.3) | 0.002 |

*COPD* chronic obstructive pulmonary disease, *IQR* interquartile range, *SD* standard deviation

*Chi-squared test or Fisher's exact test unless otherwise indicated

[a]One-way analysis of variance test among groups

[b]Kruskal–Wallis test among groups

[†]8th edition of the American Joint Committee on Cancer Staging Manual

and anastomotic leak ($P=0.002$), which were similar to the results of our previous study [3].

## QoL assessments and symptoms reported

EORTC QLQ-C30: as shown in Table 2, mean functional QoL scores such as physical functioning ($P<0.001$), role functioning ($P<0.001$), emotional functioning ($P=0.007$), cognitive functioning ($P<0.001$), and social functioning ($P<0.001$) were lower (indicating worse function), and symptom scores such as fatigue ($P=0.004$), pain ($P=0.021$), dyspnea ($P=0.004$), appetite loss ($P=0.007$), and constipation ($P=0.007$) generally higher (more symptoms) in initial phase group. There was no association between learning curve and other symptoms such as nausea and vomiting ($P=0.863$), insomnia ($P=0.158$), and diarrhea ($P=0.351$).

EORTC QLQ-OES18: symptom scores such as dry mouth ($P=0.001$) and speech difficulty ($P=0.001$) generally higher (more symptoms) in initial phase group. In

**Table 2** EORTC QLQ-C30

| | Total ($n=280$) | Initial phase ($n=55$) | Plateau phase ($n=45$) | Experienced phase ($n=180$) | $P$* |
|---|---|---|---|---|---|
| Global health status | 79.3 ± 19.0 | 76.5 ± 23.6 | 73.4 ± 15.7 | 81.6 ± 17.8 | 0.018 |
| Physical functioning | 90.4 ± 14.0 | 83.3 ± 19.5 | 93.6 ± 9.3 | 91.7 ± 12.2 | < 0.001 |
| Role functioning | 93.4 ± 15.9 | 85.7 ± 26.1 | 97.7 ± 9.2 | 94.7 ± 12.1 | < 0.001 |
| Emotional functioning | 93.1 ± 13.1 | 88.3 ± 17.0 | 92.9 ± 11.3 | 94.6 ± 11.8 | 0.007 |
| Cognitive functioning | 90.4 ± 17.4 | 82.4 ± 20.6 | 96.2 ± 8.7 | 91.4 ± 17.2 | < 0.001 |
| Social functioning | 92.1 ± 17.0 | 84.2 ± 25.5 | 92.4 ± 13.1 | 94.4 ± 13.7 | < 0.001 |
| Fatigue | 12.5 ± 19.6 | 19.7 ± 23.7 | 14.1 ± 19.2 | 10.0 ± 17.8 | 0.004 |
| Nausea and vomiting | 6.4 ± 15.7 | 6.9 ± 14.2 | 5.3 ± 13.3 | 6.5 ± 16.8 | 0.863 |
| Pain | 7.8 ± 15.2 | 11.2 ± 16.0 | 11.3 ± 15.5 | 5.9 ± 14.6 | 0.021 |
| Dyspnea | 10.8 ± 20.0 | 18.7 ± 27.0 | 9.0 ± 16.6 | 8.8 ± 17.7 | 0.004 |
| Insomnia | 19.7 ± 29.1 | 20.0 ± 26.9 | 27.2 ± 32.3 | 17.8 ± 28.8 | 0.158 |
| Appetite loss | 11.3 ± 21.9 | 15.0 ± 24.0 | 18.9 ± 25.3 | 8.4 ± 19.9 | 0.007 |
| Constipation | 7.3 ± 18.9 | 12.7 ± 24.4 | 11.3 ± 20.2 | 4.7 ± 16.1 | 0.007 |
| Diarrhea | 16.3 ± 25.5 | 20.6 ± 28.3 | 16.6 ± 24.3 | 14.9 ± 24.9 | 0.351 |
| Financial difficulties | 16.3 ± 28.0 | 23.6 ± 34.3 | 19.6 ± 28.1 | 13.2 ± 25.5 | 0.038 |

*One-way analysis of variance test among groups

addition, participants in initial phase group tend to be more likely to be associated with eating difficulty ($P=0.072$), dysphagia ($P=0.097$), and pain ($P=0.068$) (Table 3).

Digestive Symptom Questionnaire: participants in initial phase group reported statistically significantly more problems with swallowing solid food ($P=0.031$), appetite loss ($P<0.001$), and shortness of breath ($P=0.003$). In addition, more than 50% participants experienced regurgitation, which did not differ significantly among the three groups ($P=0.659$, Table 4).

Furthermore, as shown in supplemental Tables 1, 2, and 3, in the subgroup analyses for patients without major complications, patients in the initial learning phase suffering from more symptoms of dyspnea ($P=0.040$) or shortness of breath ($P=0.001$).

## Discussion

The main finding of our present study was that the initial learning phase of McKeown MIE could adversely affect postoperative complications such as pulmonary complications and anastomotic leak, and further lead to a deterioration in long-term health-related QoL and higher symptomatic burden as compared to experienced learning phase. To the best of our knowledge, this study was the first survey to investigate the potential impact of learning curve for MIE on long-term health-related QoL to date. In addition, we found that approximately 20–50% patients undergoing McKeown MIE would always suffer from adverse digestive and respiratory symptoms such as regurgitation, dysphagia, shortness of breath, and chronic cough, which persisted as long as

**Table 3** EORTC QLQ-OES18

| | Total ($n=280$) | Initial phase ($n=55$) | Plateau phase ($n=45$) | Experienced phase ($n=180$) | $P$* |
|---|---|---|---|---|---|
| Eating difficulty | 6.9 ± 9.4 | 9.2 ± 10.9 | 7.7 ± 10.3 | 6.0 ± 8.6 | 0.072 |
| Dysphagia | 8.8 ± 12.7 | 9.2 ± 11.0 | 12.4 ± 15.1 | 7.7 ± 12.4 | 0.097 |
| Reflux | 14.9 ± 16.7 | 13.9 ± 14.9 | 17.8 ± 18.3 | 14.6 ± 16.9 | 0.467 |
| Pain | 4.5 ± 11.8 | 5.6 ± 15.4 | 7.7 ± 15.9 | 3.3 ± 9.0 | 0.068 |
| Trouble swallowing saliva | 5.0 ± 14.6 | 6.6 ± 17.4 | 6.2 ± 18.1 | 4.2 ± 12.6 | 0.475 |
| Choking with swallow | 2.9 ± 9.9 | 3.0 ± 9.6 | 4.6 ± 13.7 | 2.5 ± 8.9 | 0.472 |
| Dry mouth | 13.7 ± 21.4 | 21.2 ± 26.7 | 18.6 ± 24.4 | 10.3 ± 18.0 | 0.001 |
| Trouble with taste | 1.7 ± 8.9 | 1.2 ± 6.2 | 2.3 ± 8.5 | 1.8 ± 9.7 | 0.825 |
| Cough | 5.0 ± 14.6 | 7.8 ± 19.2 | 4.6 ± 11.6 | 4.2 ± 13.6 | 0.268 |
| Speech difficulty | 3.2 ± 12.7 | 8.4 ± 22.4 | 4.6 ± 13.7 | 1.2 ± 6.4 | 0.001 |

*One-way analysis of variance test among groups

**Table 4** Digestive symptom questionnaire

| | Total ($n=280$) | Initial phase ($n=55$) | Plateau phase ($n=45$) | Experienced phase ($n=180$) | $P$* |
|---|---|---|---|---|---|
| Do you have difficulty swallowing? | 45 (16.1) | 13 (23.6) | 7 (15.9) | 25 (13.8) | 0.240 |
| Do you have difficulty swallowing solid food? | 78 (27.9) | 20 (36.4) | 17 (38.6) | 41 (22.7) | 0.031 |
| Do you have difficulty swallowing liquid? | 15 (5.4) | 3 (5.5) | 2 (4.5) | 10 (5.5) | 1.000 |
| Do you feel any pain when swallowing? | 13 (4.6) | 5 (9.1) | 3 (6.8) | 5 (2.8) | 0.075 |
| Do you feel a sticking sensation in your throat when you eat? | 70 (25.0) | 10 (18.2) | 8 (18.2) | 52 (28.7) | 0.153 |
| Score your appetite from 0 to 10 (mean score) | 9 (7–10) | 7 (6–9) | 9 (6–10) | 9 (8–10) | <0.001[a] |
| Do you feel nausea when you see the food? | 2 (0.7) | 0 | 0 | 2 (1.1) | 1.000 |
| How many meals do you eat per day? (mean) | 3 (3–3) | 3 (3–3) | 3 (3–4) | 3 (3–3) | 0.533[a] |
| Can you eat more than 50% of your meal? | 227 (81.1) | 46 (83.6) | 36 (81.8) | 145 (80.1) | 0.857 |
| Are you always the last to finish eating? | 80 (28.6) | 22 (40.0) | 11 (25.0) | 47 (26.0) | 0.113 |
| Do you have heart palpitation when you eat? | 4 (1.4) | 0 | 2 (4.5) | 2 (1.1) | 0.190 |
| Do you have sweating when you eat? | 12 (4.3) | 1 (1.8) | 5 (11.4) | 6 (3.3) | 0.058 |
| Do you have sweating after you eat? | 12 (4.3) | 2 (3.6) | 3 (6.8) | 7 (3.9) | 0.619 |
| Do you get full easily when you eat? | 100 (35.7) | 29 (52.7) | 12 (27.3) | 59 (32.6) | 0.011 |
| Do you have more than 3 episodes of diarrhea a day? | 26 (9.3) | 6 (10.9) | 5 (11.4) | 15 (8.3) | 0.719 |
| Do you have regurgitation? | 150 (53.6) | 31 (56.4) | 21 (47.7) | 98 (54.1) | 0.659 |
| Have you woken during the night because of choking? | 17 (6.1) | 4 (7.3) | 5 (11.4) | 8 (4.4) | 0.208 |
| Do you have heartburn? | 31 (11.1) | 8 (14.5) | 9 (20.5) | 14 (7.7) | 0.034 |
| Current medications | 70 (25.0) | 11 (20.0) | 15 (34.1) | 44 (24.3) | 0.261 |
| Do you have shortness of breath? | 57 (20.4) | 20 (36.4) | 9 (20.5) | 28 (15.5) | 0.003 |
| Do you have chronic cough? | 52 (18.6) | 12 (21.8) | 10 (22.7) | 30 (16.6) | 0.516 |
| Do you smoke? | 25 (8.9) | 3 (5.5) | 5 (11.4) | 17 (9.4) | 0.617 |
| How do you rate your overall digestive comfort? (mean score from 0 to 10) | 8 (7–9) | 7 (7–9) | 8 (6–9) | 9 (7–10) | <0.001[a] |

*Chi-squared test or Fisher's exact test unless otherwise indicated

[a]Kruskal–Wallis test among groups

10 years after surgery and did not improved over time, even required long-term medication treatment.

Several previous studies have investigated the relationship between postoperative complications and QoL after esophagectomy. For example, the study by Derogar and associates [19] on 141 patients showed that the occurrence of postoperative complications exerts a long-lasting negative effect on QoL in patients who survive 5 years after esophagectomy for cancer. Another nationwide and prospective cohort study enrolled 616 patients undergoing esophageal cancer surgery with 10 years of follow-up conducted by Kauppila et al. [6] revealed that postoperative medical complications (mainly pneumonia and respiratory failure) were independently associated with considerably impaired global QoL and dyspnea from 3 years onwards, whereas surgical complications (mainly anastomotic problems and surgical infections) were associated with poor QoL and symptoms, most importantly fatigue, nausea and vomiting, dyspnea, and problems related to eating or swallowing up to 5 years postoperatively. In addition, van der Schaaf and associates [20] demonstrated that patients with an intrathoracic anastomotic leak after esophagectomy were at increased risk of eating difficulties and odynophagia 6 months after surgery. Moreover, Jezerskyte and colleagues [21] revealed that grade 2 or 3 anastomotic leakage was associated with more ''chocking when swallowing'' compared with grade 1 or no anastomotic leakage. Similarly, in the current study, patients in the initial learning phase were associated with more pulmonary complications and anastomotic leak after McKeown MIE, and complained more respiratory and digestive symptoms of shortness of breath and dysphagia, which did not improved over time. Undoubtedly, the considerably adverse events occurrence after surgery will lead to long-lasting symptoms.

Furthermore, subgroup QoL analyses for patients without major complications were conducted and revealed that patients in the initial learning phase remained suffering from a deterioration in QLQ-C30 mean scores of functional scales and more symptoms including dyspnea or shortness of breath, which indicated that the surgeon's experience could have a direct impact on the recovery of long-term QoL after MIE. As we all know, accumulated sufficient experience did have beneficial effects on protecting adjacent tissue

and organs (e.g., thoracic duct, recurrent laryngeal nerve, nourishing blood vessels, bronchus, and lung tissue) against intraoperative injury, and would likely be conducive to restoration of the organ function and improvement of QoL. Park and colleagues [22] showed a significantly reduced incidence rate of vocal cord palsy after robotic esophagectomy during the experienced period than during the initial learning phase. In addition, Baba et al. [23] revealed that patients reported severe hoarseness due to permanent recurrent nerve paralysis were associated with restricted daily activity and difficulty in talking at 60 months or more after esophagectomies.

Findings presented herein offer new insight into improvement of long-term health-related QoL and symptoms after esophagectomy for cancer, that is, optimizing the learning process of MIE and preventing learning associated adverse events. The study by Ninomiya et al. [24] showed that MIE can be mastered quickly and safely with a flat learning curve under the direction of an experienced surgeon from another institution. In addition, Lin and associates [25] also revealed that a new attending surgeon can attain the requisite basic skill to perform MIE in a relatively short period of time with supervision from senior experienced surgeons, and no significant difference in the incidence of postoperative complications was identified among all groups. Moreover, Oshikiri et al. [26] demonstrated that the rate of RLN palsy during initial learning period was significantly lower for trainee surgeon using a standardized procedure developed by a mentoring surgeon. Besides, as mentioned above, anastomotic problems after esophagectomy was associated with problems related to eating or swallowing. Therefore, more research focusing on how to prevent anastomotic leakage or stricture during initial learning period for MIE should be encouraged.

Recently, several previous studies had revealed that Da Vinci robot-assisted system or 3D glasses-based video system could be a more viable technique over conventional MIE for patients with esophageal cancer in terms of operative duration, intraoperative blood loss, lymph nodes dissection, and incidence rate of RLN palsy after surgery [27–29]. However, whether radical surgery using Da Vinci robot-assisted system or 3D glasses-based video system to treat esophageal carcer can exert favorable effect on long-term health-related QoL has not previously been studied.

This study has several limitations. It was retrospective and performed at a single center, patient demographics differed among groups in terms of age, gender, hypertension, tumor location and depth of tumor invasion, and the postoperative and long-term QoL outcomes may be affected by selection bias. Moreover, all patients completed above questionnaires at a single time point after surgery, it is therefore not possible to comment on the evolution of health-related QoL and symptoms of patients between different groups. Besides, although our perioperative care strategies had remained largely the same over this time period, inevitably, some potential factors, such as improvements in perioperative management and critical care, may have influenced these findings.

In conclusion, our data suggest that the surgeon's experience did have a direct impact on the long-term health-related QoL and symptoms in survivors after McKeown MIE. Patients operated in initial learning phase tend to suffer from a deterioration in QoL and higher symptomatic burden as compared to experienced phase, which did not improved over time. More research focusing on how to optimize the learning process of MIE and prevent learning associated adverse events should be encouraged.

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**Author contributions** WG, XYZ and TB conceived and designed the experiments. TB, PC, JY, DHC, XDH, YJW, XFX and KKL recorded the follow-up data. TB, PC and JY analyzed the data. TB wrote the manuscript. TB, PC and JY contributed equally to this work and should be considered the co-first authors.

## Declarations

**Disclosures** Tao Bao, Ping Chen, Jun Yu, Dao-Hong Cai, Xian-Dong He, Ying-Jian Wang, Xian-Feng Xie, Kun-Kun Li, Xiao-Ying Zhao and Wei Guo have no conflicts of interest or financial ties to disclose.

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