Original Article

Diaphragmatic dysfunction is associated with postoperative pulmonary complications in the aged patients underwent radical resection of esophageal cancer: a prospective observational study

Fuqiang Liu[1#]^, Qian Wen[1#], Yiwen Yang[2], Jiahui Chen[2], Guangshan Jin[2], Ling Yu[3], Jianhua He[1,2]

[1]Department of Anesthesiology, The Affiliated Cancer Hospital of Nanjing Medical University, Nanjing, China; [2]School of Anesthesiology, Xuzhou Medical University, Xuzhou, China; [3]Department of Ultrasound, Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine, Nanjing, China

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[#]These authors contributed equally to this work as co-first authors.

Correspondence to: Jianhua He, MD. Department of Anesthesiology, The Affiliated Cancer Hospital of Nanjing Medical University, No. 42, Baizi Pavilion, Xuanwu District, Nanjing 210000, China; School of Anesthesiology, Xuzhou Medical University, Xuzhou, China. Email: hejianhua_73@163.com; Ling Yu, MD. Department of Ultrasound, Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine, No. 100, Cross Street, Hongshan Road, Nanjing 210000, China. Email: Heyiyi2002@126.com.

Background: Diaphragmatic dysfunction escalates the susceptibility to postoperative pulmonary complications (PPCs). Currently, no study reports the occurrence of diaphragmatic dysfunction correlated with PPCs following radical resection of esophageal cancer in aged patients. We aimed to diagnose diaphragmatic dysfunction via ultrasonography and analyze diaphragmatic dysfunction's relation with PPCs after radical resection of esophageal cancer surgery in aged patients.

Methods: This prospective observational study comprised 86 aged patients undergoing radical resection of esophageal cancer. Patient characteristics data and intraoperative details were collected. Ultrasonography was performed before (preoperative) and after (first, third, and fifth day postoperatively) surgery. Outcome measures included PPCs within seven days postoperative, occurrence of diaphragmatic dysfunction, and short-term prognosis.

Results: After excluding 14 patients, we finally analyzed clinical data from 72 patients. The prevalence of PPCs was higher in the patients with diaphragmatic dysfunction than those without (19 of 23, 83% *vs.* 21 of 49, 43%, P=0.004). Postoperative diaphragmatic dysfunction was positively correlated with PPCs in patients who underwent elective radical esophageal cancer surgery (r=0.37, P=0.001). Persistent diaphragmatic dysfunction, furthermore, was positively correlated with the development of multiple PPCs (r=0.43, P<0.001). The logistic regression analysis revealed that age, total open procedure, and postoperative diaphragmatic dysfunction were identified as significant risk factors for PPCs, while total open procedure was an independent risk factor for diaphragmatic dysfunction.

Conclusions: Postoperative diaphragmatic dysfunction positively correlates with developing PPCs. Continuous monitoring of postoperative diaphragmatic function can screen high-risk patients with PPCs, which has specific clinical significance. Age, total open procedure, and diaphragmatic dysfunction are identified as risk factors for developing PPCs, while total open procedure specifically increases the risk for postoperative diaphragmatic dysfunction.

^ ORCID: 0009-0009-3255-8432.

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Introduction

Esophageal cancer is a common malignant tumor of the digestive tract. Epidemiological surveys have shown a significantly high prevalence of esophageal cancer in China, with the incidence sharply increasing after age 60 years (1). Surgical intervention is one of the primary modalities employed for managing esophageal cancer. However, it should be noted that the surgery entails significant trauma and presents a higher incidence of complications than other thoracic surgeries. Additionally, due to the decline in multi-system physiological function in aged patients, there is a substantial risk of adverse pulmonary outcomes following surgery (2,3). The development of postoperative pulmonary complications (PPCs) following radical resection of esophageal cancer exacerbates the financial burden on patients and hospitals, elevates the risk of postoperative mortality, and affects long-term patient survival (4-6).

As the primary respiratory muscle, the diaphragm contributes over 60% of thoracic volume changes during respiration. However, the diaphragmatic function gradually diminishes with advancing age (7). Point-of-care ultrasound is a superior tool for diagnosing diaphragmatic dysfunction in postoperative patients compared with computed tomography and magnetic resonance imaging due to its convenience, ability to provide dynamic observations, and verified accuracy (7-9). The adverse impact of diaphragmatic dysfunction on PPCs has been consistently reported in several studies after thoracic surgery (9-11). Nevertheless, no studies are currently exploring the changing trends in diaphragmatic function after radical resection for esophageal cancer. Most patients with esophageal cancer are elderly, and surgical procedures often involve damage to the chest and abdomen. The impact on diaphragmatic function and its relationship with PPCs is unknown.

Therefore, the objectives of our study were: (I) to assess diaphragmatic function in aged patients who underwent radical resection of esophageal cancer by measuring diaphragmatic excursion via point-of-care ultrasound; (II) to investigate the association between diaphragmatic dysfunction and PPCs in aged patients following radical resection of esophageal cancer; (III) to identify potential perioperative risk factors for PPCs and diaphragmatic dysfunction. We hypothesized that the incidence of PPCs would be higher in patients with postoperative diaphragmatic dysfunction and that diaphragmatic dysfunction was a significant risk factor for PPCs. The insights gained from this study will provide valuable strategies for predicting PPCs after radical resection of esophageal cancer in the elderly. It will help clinically screen high-risk patients with PPCs, provide evidence for decision-making on clinical intervention strategies, and improve patient prognosis. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-197/rc).

Highlight box

Key findings
- We evaluated for the first time postoperative diaphragmatic function in elderly patients after radical esophageal cancer surgery.
- Patients with diaphragmatic dysfunction, especially persistent diaphragmatic dysfunction, are susceptible to postoperative pulmonary complications.

What is known and what is new?
- Ultrasound is an effective tool for assessing diaphragmatic function after surgery, and diaphragmatic dysfunction is one of the causes of pulmonary complications after thoracic or abdominal surgery.
- Persistent diaphragmatic dysfunction may contribute to multiple pulmonary complications.

What is the implication, and what should change now?
- Monitoring diaphragm function after surgery has clinical significance, and early recovery training of diaphragm function may improve pulmonary outcomes in surgical patients.

Methods

Study designs

The study was performed at the Affiliated Cancer Hospital of Nanjing Medical University, Jiangsu, China. All patients receiving elective radical resection of esophageal cancer between August 2023 and November 2023 were included. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Affiliated Cancer Hospital of Nanjing Medical University (2023 R-Rapid-024), with informed consent obtained from all patients. We registered the protocol in the Chinese Clinical Trials Registry as an observational study (ChiCTR2300074827).

The inclusion criteria were age 65 years or more, American Society of Anesthesiology (ASA) physical status classification score of II or III, and body mass index (BMI) within the range of 18.5 to 30 kg/m^2. The exclusion criteria were the following: (I) scheduled for Sweet procedure; (II) respiratory infection within four weeks before surgery; (III) history of moderate to severe restrictive or obstructive respiratory dysfunction; (IV) history of neuromuscular junction diseases or associated pharmacotherapy; (V) liver or kidney insufficiency, malnutrition; (VI) New York Heart Association (NYHA) grade II, III, or IV; (VII) cardiothoracic surgery history; (VIII) diaphragmatic surgery history; (IX) preoperative diaphragmatic dysfunction (diaphragmatic excursion <10 mm); (X) tumor invades phrenic nerve.

Patients who experienced the following situations after enrollment were excluded from the final analysis: (I) persistent intraoperative hypoxemia (intraoperative preoperative transcutaneous oxygen saturation (SpO_2) <90%, requiring pulmonary recruitment maneuvers); (II) unable to be extubated after surgery; (III) confirmed or suspected phrenic nerve injury during surgery; (IV) reintubated for mechanical ventilation within seven days after surgery; (V) intensive care unit (ICU) readmission within seven days after surgery; (VI) development of anastomotic leak within seven days after surgery; (VII) failure to obtain satisfactory imaging during postoperative ultrasonography; (VIII) the patient refused follow-up during the course of study.

Data collection

Data were collected from patient interviews, electronic medical record systems, and surgical anesthesia management systems.

Patients' characteristics

We recorded the patients' preoperative characteristics: age, gender, BMI, ASA physical status, comorbidities, smoking history, history of abdominal operation, and history of neoadjuvant therapy. Additionally, we recorded the surgical characteristics: preoperative transcutaneous oxygen saturation (SpO_2), type of procedure, duration of operation, the volume of fluid therapy, blood loss, the use of propofol and rocuronium, duration of one-lung ventilation, and mechanical ventilation.

The primary and secondary outcomes

The primary outcome was the occurrence of PPCs within seven days after surgery. The PPCs were diagnosed by the patient's attending doctor, who was unaware of the patient's diaphragmatic functional status. The PPCs were defined as the occurrence of at least one of the following conditions: hypoxemia, respiratory infection, pleural effusion, atelectasis, pneumothorax, bronchospasm, and aspiration pneumonitis (12).

The secondary outcomes were the occurrence of diaphragmatic dysfunction and persistent diaphragmatic dysfunction. Ultrasonography was performed before (preoperative) and after (first, third, and fifth days postoperatively) surgery. Diaphragmatic dysfunction was defined as a diaphragmatic excursion less than 10 mm (13). Persistent diaphragmatic dysfunction was defined as the occurrence of diaphragmatic dysfunction on two consecutive ultrasonography of the same patient. The indicators that reflected short-term prognosis were also recorded, including the time of chest tube removal, the length of the hospital, and the first defecation.

Surgery techniques

Tumor location is often the main reason for the choice of operation methods. Middle and lower esophageal cancer always choose the Ivor Lewis method, while upper esophageal cancer chooses McKeown. In addition, there are no absolute indications for open or minimally invasive surgery. The surgeon will decide on the surgical access method based on comprehensive considerations such as tumor stage and risk for postoperative anastomotic leakage.

Ivor Lewis: the surgical approach includes the right thorax and the middle of the upper abdomen. First, gastric dissection and tubular stomach formation were performed transabdominally in the supine position. Then, change to the left lateral position and disinfect the surgical field again. After the esophagus was dissected and resected, the tubular stomach and the upper end of the esophagus were anastomosed intrathoracically.

McKeown: two postural changes were performed intraoperatively, with two surgical field disinfections. In the left lateral decubitus position, the esophagus was freed through the right chest, and the mediastinal lymph nodes were dissected. Then, in the supine position, the stomach was dissociated through the abdomen to create a tubular stomach, and the gastroesophageal anastomosis was completed through the left neck incision.

Anesthesia and postoperative analgesia

After patients were admitted to the operating room, vital signs were monitored, including non-invasive arterial blood pressure, SpO_2, and electrocardiogram. After that, invasive arterial blood pressure monitoring via the radial artery was established following infiltration anesthesia with 1% lidocaine.

Midazolam, propofol, and sufentanil citrate were used for anesthesia induction. Rocuronium was used to achieve neuromuscular blockade and facilitate tracheal intubation. A single-lumen endotracheal tube and a bronchial blocker were selected to facilitate one-lung ventilation, with their positioning guided by fiberoptic bronchoscopy. The performance of one-lung ventilation occurred when the patient transitioned into the left lateral decubitus position. The parameters for mechanical ventilation were as follows: mechanical ventilation mode, pressure-controlled ventilation-volume guaranteed; tidal volume, 6–8 mL/kg (ideal weight); inspiratory-to-expiratory ratio, 1:2; positive end-expiratory pressure, 5 mmHg; and the end-tidal carbon dioxide partial pressure was maintained at 35 to 45 mmHg by changing the respiratory rate. The anesthesiologist removed the bronchial blocker after the surgeon closed the chest and restored two-lung ventilation following full suction of the sputum. The pulmonary recruitment strategy was implemented upon the patient's transition to the supine position following the procedure. The recruitment maneuver strategy involved the application of continuous positive airway pressure, with the pressure level between 30 and 45 mmHg for a duration of 20 to 30 seconds. Sugammadex (2 mg/kg) was used intravenously to antagonize rocuronium upon patients' arrival in the post-anesthesia care unit, and the timing of administration was determined by senior anesthesiologists on duty. The same anesthesiologist in the post-anesthesia care unit performed the extubation procedure, relying on their extensive clinical experience. The attending anesthesiologist determined the volume of intraoperative fluid therapy, primarily utilizing crystalloid fluids and administering 500 mL of colloid to treat hemodynamic disorders as deemed appropriate.

Patient-controlled intravenous analgesia was used for postoperative analgesia. The analgesic pump formula was as follows: dezocine, 0.4–0.8 mg/kg; dexmedetomidine, 0.6–1.0 μg/kg; and diluted to 100 mL with 0.9% normal saline. The analgesic pump settings were as follows: no loading dose, a background dose of 1.0–1.5 mL/h, a single patient-controlled additional dose of 1.5–2.0 mL, and a locking time of 15 min. A dedicated postoperative analgesia follow-up team performed the pain state assessment using the numeric rating scale (NRS). The analgesic pump settings were adjusted according to the patient's complaints and NRS score. Morphine (5–10 mg) subcutaneous injection was used for remedial analgesia when the NRS score was >3.

Ultrasonography

Before induction, we performed the first diaphragm examination to exclude preoperative diaphragmatic dysfunction in patients. After surgery, the NRS score was administered before each ultrasonography, and if the NRS score was ≤3, the evaluation was performed. The same anesthesiologist (F.L.) consistently conducted the diaphragmatic function assessments according to expert consensus guidance who had undergone extensive training in this area for over six months (14).

Ultrasonography was performed via a diagnostic ultrasound system (Mindray, TE7, Shenzhen, China), and diaphragmatic excursion was shown using a 1- to 5-MHz convex ultrasound probe. The patient was lying in a semi-recumbent position with the head elevated at 30° to 45°. The patients maintained spontaneous tidal breathing during the ultrasonography. For the right diaphragm excursion: The probe was placed with an inward, cephalad, and dorsal orientation between the right subcostal midclavicular line and the anterior axillary line, using the liver as the acoustic window. For the left diaphragm excursion: The probe position was placed with a cephalic side-oriented, dorsal orientation between the left anterior axillary line and the midaxillary line, using the spleen as the acoustic window. B-mode was initially selected for diaphragm exploration, and the sound beam was positioned perpendicularly to the posterior third of the diaphragm. The diaphragm appeared as a continuous hyperechoic bright line clinging to the surface of the liver or spleen, exhibiting synchronized movement with respiration. The M-mode was subsequently selected, and the cursor was positioned perpendicular to the diaphragm motion to record a sine wave containing three respiratory movements. The distance between the peak and trough of this sine wave was measured, then calculated, and recorded the mean value.

Statistical analysis

The Shapiro-Wilk Normality Test was used to analyze the normal data distribution. Data were reported as mean ± SD or median (interquartile range), as appropriate. Student's *t*-tests or Mann-Whitney U tests was used to test the differences between groups for data with normal or non-normal distribution, respectively. Pearson's Chi-square or Fisher exact test was used to compare categorical data. A 2×2 chi-square was computed from a phi coefficient, the Pearson correlation between diaphragmatic dysfunction and PPCs. The Spearman correlation analysis was used to examine the association between postoperative diaphragmatic dysfunction (or persistent diaphragmatic dysfunction) and multiple PPCs.

The association between PPCs and perioperative variables was modeled using binary logistic regression analysis and was reported as the estimated crude odds ratio (OR) and relative 95% confidence interval (CI). Similarly, binary logistic regression analysis was applied to investigate the possible perioperative risk factors for diaphragmatic dysfunction. The interactive effect of surgical procedure and diaphragmatic dysfunction on PPCs was tested using likelihood ratio test. A two-tailed P value less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS Statistics for Windows, Version 26.0 (IBM, Armonk, New York, USA).

The sample size was determined based on the study conducted by Spadaro *et al.* (9), which reported an incidence of diaphragmatic dysfunction of approximately 60% following thoracic surgery. Furthermore, the incidence of PPCs in patients with postoperative diaphragmatic dysfunction and those without postoperative diaphragmatic dysfunction were found to be 65% and 25%, respectively. Considering a statistical power of 0.9, a two-tailed significance level (alpha) of 0.05, and accounting for a loss to follow-up of 20%, the study required a total of 75 patients. The sample size was calculated using PASS, Version 15.0 (NCSS, Kaysville, Utah, USA).

Results

A total of 86 patients were enrolled in the study, with 14 patients excluded (two patients refused surgical intervention, seven patients were unable to be extubated after surgery, one patient experienced anastomotic leakage on the third day after surgery, and four patients could not obtain satisfactory imaging during ultrasonography), a total of 72 patients completed all ultrasonography were ultimately included in the final analysis. The study flow chart is shown in *Figure 1* and ultrasonography results are shown in Table S1.

Diaphragmatic dysfunction and PPCs

Twenty-three of 72 patients (32%) experienced postoperative diaphragmatic dysfunction, and 10 of 23 patients (44%) diagnosed with diaphragmatic dysfunction were persistent. Specifically, on the first postoperative day, 21 patients experienced diaphragmatic dysfunction, with bilateral involvement observed in 4 patients and unilateral involvement exclusively on the right side in 17 patients. On the third postoperative day, diaphragmatic dysfunction was observed in 11 patients, including 9 persistent diaphragmatic dysfunction and 2 newly diagnosed patients solely involving the right side. On the fifth postoperative day, diaphragmatic dysfunction was still observed in 3 patients, with 2 of 3 showing persistent diaphragmatic dysfunction from the first postoperative day, and no new development of diaphragmatic dysfunction was detected. The results are shown in *Figure 2*.

PPCs were developed in 19 of 23 patients with diaphragmatic dysfunction and 21 of 49 without diaphragmatic dysfunction (83% *vs.* 43%; P=0.004). Concretely speaking, patients with postoperative diaphragmatic dysfunction showed a higher propensity for developing hypoxemia, respiratory infection, pleural effusion, and atelectasis. The results are shown in *Table 1*. Additionally, diaphragmatic dysfunction patients demonstrated an increased likelihood of developing multiple PPCs {2; interquartile range [1, 3] *vs.* 0; interquartile range [0, 2]; P=0.001}, whereas the observed correlation was relatively weak (r=0.38, P=0.001). Nevertheless, further

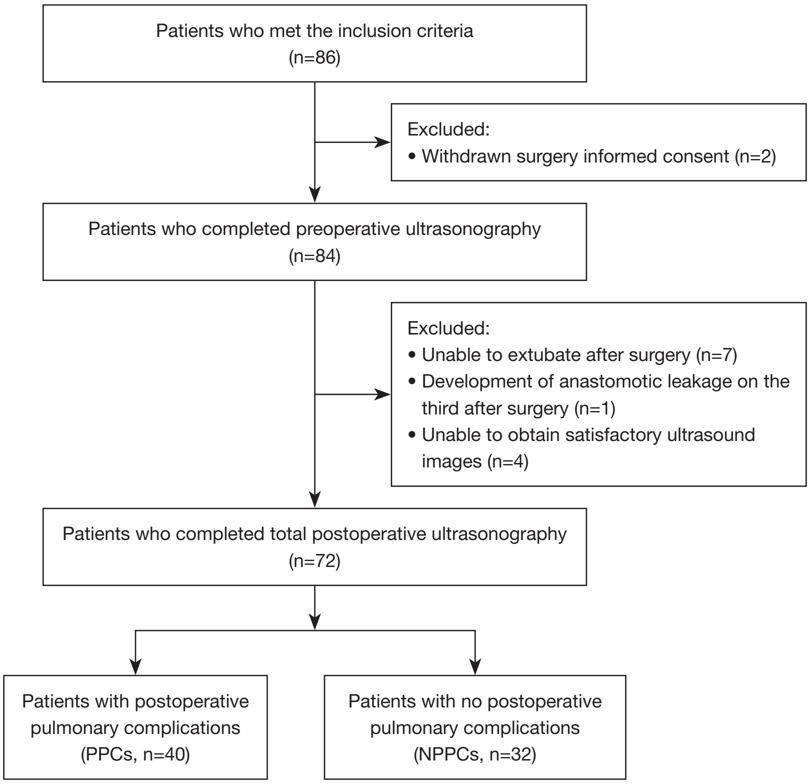
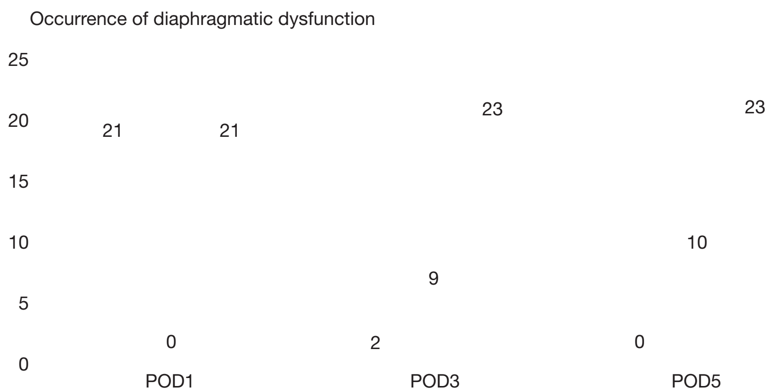


Figure 1 Flowchart of the study. PPCs, postoperative pulmonary complications; NPPCs, no postoperative pulmonary complications.



	POD1	POD3	POD5
Newly diagnosed number of patients with diaphragmatic dysfunction	21	2	0
Cumulative number of patients with persistent diaphragmatic dysfunction	0	9	10
Cumulative number of patients with diaphragmatic dysfunction	21	23	23

Figure 2 Occurrence of postoperative diaphragmatic dysfunction. A total of 23 patients with diaphragmatic dysfunction were observed postoperatively, of which 21 were diagnosed on the first postoperative day and 2 were newly diagnosed on the third postoperative day. POD1, first postoperative day; POD3, third postoperative day; POD5, fifth postoperative day.

Table 1 Impact of diaphragmatic dysfunction on postoperative pulmonary complications

Variables	DD			Persistent DD		
	Yes (n=23)	No (n=49)	P value	Yes (n=10)	No (n=62)	P value
At least of 1 PPC (n=40)	19 (83%)	21 (43%)	0.004	9 (90%)	31 (50%)	0.04
Individual PPCs						
Hypoxemia (n=15)	10 (43%)	5 (10%)	0.002	5 (50%)	10 (16%)	0.03
Respiratory infection (n=36)	16 (70%)	20 (41%)	0.04	9 (90%)	27 (44%)	0.01
Pleural effusion (n=19)	10 (43%)	9 (18%)	0.04	7 (70%)	12 (19%)	0.002
Atelectasis (n=10)	7 (30%)	3 (6%)	0.01	6 (60%)	4 (6%)	<0.001
Pneumothorax (n=3)	0	3 (6%)	0.55	0	3 (5%)	1.0
Bronchospasm (n=0)	0	0	–	0	0	–
Aspiration pneumonitis (n=0)	0	0	–	0	0	–
No. of PPC(s)	2 [1–3]	0 [0–2]	0.001	3 [2–4]	0.5 [0–2]	<0.001

Values are presented as n (%) or mean [IQR]. DD, diaphragmatic dysfunction; PPC(s), postoperative pulmonary complication(s); IQR, interquartile range.

analysis revealed a moderate correlation between persistent diaphragmatic dysfunction and the development of multiple PPCs (r=0.43, P<0.001).

Preoperative characteristics

Forty of 72 patients (56%) developed PPCs within one week after surgery. Patients in the PPCs group were older than those in the no PPCs (NPPCs) group (72±4 *vs.* 70±3 years; P=0.03). The other preoperative characteristics did not show any statistically significant differences. The results are shown in *Table 2*.

Surgical data

Twenty-nine of 32 patients (91%) in the NPPCs group and only 18 of 40 (45%) in the PPCs group received the total minimally-invasive procedure (the combined video-assisted thoracoscopic and laparoscopic surgery) (P<0.001). The other surgical data did not show any statistically significant differences. Additionally, diaphragmatic dysfunction was detected in 19 of 40 patients (48%) in the PPCs group and only 4 of 32 (13%) in the NPPCs group (P=0.004). The short-term prognosis of the PPCs group was comparatively unfavorable, with a significantly prolonged duration of hospitalization {23; interquartile range [21, 27] *vs.* 20; interquartile range [17, 23] days; P=0.01}. However, no statistically significant disparities were observed between the two groups in terms of the time of chest tube removal and the first time of defecation. The results are shown in *Table 3*.

Variables associated with PPCs

We incorporated the independent variables with a significance level of P<0.2 resulting from one-way ANOVA into the logistic regression analysis. Moreover, we also included age and smoking history, two widely reported risk factors. Among them, the growth of age (OR: 1.23, 95% CI: 1.01 to 1.49; P=0.04), total open procedure (OR: 10.42, 95% CI: 2.47 to 44.01; P=0.001), and diaphragmatic dysfunction (OR: 4.15, 95% CI: 1.04 to 16.62; P=0.04) were identified as significant risk factors PPCs. The results are shown in *Table 4*.

The type of procedure did not significantly affect the association between diaphragmatic dysfunction and PPC development (likelihood-ratio test for interaction term: P=0.18).

Variables associated with postoperative diaphragmatic dysfunction

Similarly, we included the independent variables that showed a significance level of P<0.2 from one-way ANOVA in the logistic regression analysis. The controversial perioperative variables of age and smoking history were also

Table 2 Preoperative characteristics

Variables	PPCs group (n=40)	NPPCs group (n=32)	P value
Male	27 (68%)	25 (78%)	0.32
Age (years), mean [SD]	72 [4]	70 [3]	0.03
BMI (kg/m^2)	23 [3]	22 [2]	0.27
ASA physical status			0.58
II	25 (63%)	22 (69%)	
III	15 (37%)	10 (31%)	
Comorbidities			
Hypertension	15 (38%)	14 (44%)	0.59
Diabetes	3 (8%)	5 (16%)	0.48
Silent cerebral infarction	4 (10%)	4 (13%)	>0.99
Smoking history			0.86
Smoking cessation	13 (33%)	12 (38%)	
Currently smoking	5 (13%)	3 (9%)	
Preoperative hemoglobin levels (g/L)	135 [14]	139 [15]	0.34
Preoperative albumin levels (g/L)	44 [3]	45 [3]	0.53
History of abdominal surgery	5 (13%)	5 (16%)	0.97
History of neoadjuvant therapy	9 (23%)	11 (34%)	0.26

Age range of PPCs group, median [IQR]: 70 [68, 72] years; age range of NPPCs group, median [IQR]: 71 [70, 76] years. Values are presented as n (%) or mean [SD]. PPCs, postoperative pulmonary complications; NPPCs, no postoperative pulmonary complications; BMI, body mass index; ASA, American Society of Anesthesiologists; IQR, interquartile range; SD, standard deviation.

incorporated similarly. Only the total open procedure (OR: 4.09, 95% CI: 1.34 to 12.43; P=0.01) was a risk factor for developing postoperative diaphragmatic dysfunction. The results are shown in *Table 5*.

Discussion

The study showed that 40 of 72 (56%) patients who underwent radical resection of esophageal cancer developed PPCs, with the most common being respiratory infection (36 of 72, 50.0%). Postoperative diaphragmatic dysfunction was associated with PPCs within seven days after surgery, while persistent diaphragmatic dysfunction showed a moderate correlation with multiple types of PPCs.

Previous studies have shown that the incidence of PPCs after radical resection of esophageal cancer is about 20–50% (4,15-18). Compared with video-assisted endoscopic surgery and robot-assisted surgery, the incidence of PPCS in patients who accepted total open procedures is higher, and this study also confirmed the above conclusions (9,16-19). The radical resection of esophageal cancer is primarily categorized into three surgical methods based on the tumor's location: Ivor Lewis (via right thoracic and abdominal approach), McKeown (via the abdomen and left neck approach), and Sweet (via left thoracic approach). Ding *et al.* have suggested that the incidence of PPCs is similar among those three methods (17). We did not choose to include only patients who underwent Ivor Lewis or McKeown surgery, but excluded the Sweet procedure from our study to mitigate potential interference caused by direct damage to the diaphragm associated with this method. The surgical method may impact postoperative diaphragmatic dysfunction and PPCs, but no differences were found between the two groups in our study.

The development of diaphragmatic dysfunction following radical resection of esophageal cancer in this study was observed in 23 of 72 patients (32%), demonstrating a lower prevalence than previous research studies (68%) (9,10).

Table 3 Surgical data and secondary outcomes

Variables	PPCs group (n=40)	NPPCs group (n=32)	P value
Pre-SpO_2	99 [98–100]	99 [98–100]	0.63
Type of procedure			0.59
Ivor Lewis	15 (38%)	14 (44%)	
McKeown	25 (62%)	18 (56%)	
Surgical access			<0.001
Total minimally-invasive	18 (45%)	29 (91%)	
Total open	22 (55%)	3 (9%)	
Duration of operation (min)	254 [218–319]	239 [211–312]	0.57
Duration of OLV (min)	111 [90–143]	94 [82–138]	0.68
Duration of MV (min)	356 [301–490]	350 [266–502]	0.18
The use of propofol (mg)	945 [835–1,158]	1,065 [888–1,335]	0.09
The use of rocuronium (mg)	214 [180–248]	234 [190–277]	0.13
Fluid therapy (mL)	2,500 [2,500–3,000]	2,500 [2,500–3,000]	0.42
Colloid (500 mL)	22 [55%]	16 [50%]	0.67
Blood loss (mL)	150 [100–200]	175 [100–200]	0.44
Diaphragmatic dysfunction	19 [48%]	4 [13%]	0.004
The length of hospital (days)	23 [21–27]	20 [17–23]	0.01
The time of chest tube removal (days)	7 [5–10]	8 [5–10]	0.64
The first time of defecation (days)	4 [3–5]	4 [3–5]	0.60

Values are presented as n (%) or mean [IQR]. PPCs, postoperative pulmonary complications; NPPCs, no postoperative pulmonary complications; Pre-SpO_2, preoperative transcutaneous oxygen saturation; OLV, one-lung ventilation; MV, machinic ventilation; IQR, interquartile range.

Table 4 Variables associated with postoperative pulmonary complications according to logistic regression analysis

Variables	B value	OR (95% CI)	P value
Age	0.20	1.23 (1.01–1.49)	0.04
Pre-SpO_2	0.17	1.19 (0.79–1.78)	0.40
Total open procedure	2.34	10.42 (2.47–44.01)	0.001
Diaphragmatic dysfunction	1.42	4.15 (1.04–16.62)	0.04
Smoking history			
Smoking cessation	–0.34	0.72 (0.20–2.63)	0.61
Currently smoking	0.21	1.24 (0.15–9.93)	0.84

Pre-SpO_2, preoperative transcutaneous oxygen saturation; OR, odds ratio; CI, confidence interval.

Table 5 Variables associated with postoperative diaphragmatic dysfunction according to logistic regression analysis

Variables	B value	OR (95% CI)	P value
Age	0.08	1.09 (0.91–1.30)	0.35
Total open procedure	1.41	4.09 (1.34–12.43)	0.01
Silent cerebral infarction	1.46	4.28 (0.81–22.57)	0.09
Smoking history			
Smoking cessation	–0.68	0.51 (0.15–1.77)	0.29
Currently smoking	–0.20	0.82 (0.14–4.80)	0.82

OR, odds ratio; CI, confidence interval.

The decrease in incidence may be attributed, on the one hand, to advancements in surgical techniques that have reduced surgical trauma. On the other hand, the patients included in this study exhibited better cardiopulmonary function, while preexisting chronic cardiopulmonary conditions before surgery could potentially compromise diaphragmatic function (10,19-23). The incidence of PPCs was significantly higher in patients with diaphragmatic dysfunction than those without diaphragmatic dysfunction, primarily manifested as respiratory infections, hypoxemia, atelectasis, and pleural effusion. Although the combination and definition of PPCs selected by different studies are not the same, it is confirmed that diaphragmatic dysfunction increases the risk of respiratory infection or pneumonia (10,24-26). The patients with diaphragmatic dysfunction had worse pulmonary compliance and sputum retention due to weakened cough ability, which may be a pathophysiological mechanism promoting respiratory infection and pneumonia (27-29). The impairment of pulmonary physiology characterized by reduced tidal volume and postoperative oxygenation index in patients with diaphragmatic dysfunction may be the primary mechanism underlying postoperative hypoxemia (9,19,30). Patients with diaphragmatic dysfunction demonstrate lower inspiratory and transdiaphragmatic pressures, indicating chest wall and respiratory mechanics impairment (9,28). This combination and low tidal volume may contribute to developing postoperative atelectasis (9,30). Finally, we observed a higher incidence of pleural effusion in patients with diaphragmatic dysfunction. We propose that the higher incidence of pleural effusion may be caused by an imbalance between intrathoracic secretion and absorption mediated by chest wall lymphatics due to reduced transdiaphragmatic pressure in patients with diaphragmatic dysfunction (31).

Like the findings by Spadaro *et al.* (9), our study also observed a higher likelihood for diaphragmatic dysfunction patients to incorporate multiple types of PPCs [2 (1–3) *vs.* 0 (0–2), P=0.001]. Multiple types of PPCs often indicate a poorer prognosis, an extended length of hospital and ICU, and an increased risk of postoperative mortality (6). Moreover, 10 of 72 patients were observed to have persistent diaphragmatic dysfunction, with a stronger association between persistent diaphragmatic dysfunction and incorporating multiple types of PPCs. Related study has demonstrated that persistent diaphragmatic dysfunction exacerbates preexisting chronic obstructive pulmonary disease (10). Laghlam *et al.* also found that patients with persistent diaphragmatic dysfunction on the seventh day after elective cardiac surgery required longer mechanical ventilation and longer ICU stays (24). The above findings suggest that continuous postoperative monitoring of diaphragmatic function holds specific clinical significance. There are few studies on persistent postoperative diaphragmatic dysfunction, and therefore, it is difficult to state a definite cause. The reason may be due to heterogeneity in patient characteristics and varying degrees of oxidative stress due to surgery and anesthesia. In addition, postoperative pain causes patients to breathe shallowly and quickly, aggravating diaphragm fatigue and stress injury. Complete postoperative analgesia and early respiratory muscle rehabilitation training may reduce the occurrence of this condition (32,33). Of course, more relevant research is still needed to explore the exact causes and therapeutic interventions for persistent diaphragmatic dysfunction.

We observed that the risk of PPCs increased by 1.125-fold for each additional year in the age of elderly patients, which is similar to the findings reported by Bevilacqua *et al.* (34). Moreover, stratified studies have revealed a positive correlation between age and the incidence of PPCs (35,36). Additionally, a previous study of healthy volunteers has reported a linear inverse correlation between age and diaphragm function (7). However, our regression analysis did not reveal a significant association between age and diaphragmatic dysfunction, similar to previous studies' findings. The negative result may be attributed to the relatively minor impact of aging on diaphragm function itself and inter-individual variations among study cohorts.

Our findings indicate that preoperative smoking cessation did not mitigate the incidence of PPCs. Considering the duration of smoking cessation in our study was only two weeks before surgery, which is shorter than the minimum requirement of 4 weeks set by Wong *et al.* (37). Our result supports the conclusion that smoking cessation initiated within two weeks before surgery may not significantly improve pulmonary outcomes. However, basic studies have shown that smoking could damage the diaphragm muscle fiber and lead to atrophy of the diaphragm, but whether this damage is reversible is still unclear (38,39). Therefore, further research is also needed.

Our study implemented relatively strict inclusion and exclusion criteria because we wanted to focus on the impact of perioperative factors on diaphragm function. So, we excluded patients with preoperative high-risk factors affecting diaphragmatic function and preoperative diaphragmatic dysfunction. We also terminated follow-up for suspected phrenic nerve injury during surgery, although no patient dropped out of the study for this reason. Therefore, our study was conducted on people with relatively good diaphragmatic function before surgery, and the results only applied to the relevant population. In addition, we found that diaphragm function may not be closely related to early postoperative gastrointestinal function recovery, but this result is inconclusive. Some studies have also found that 5% of patients with esophageal cancer will develop diaphragmatic hernia after surgery (40). The diaphragmatic hernia may be related to poor recovery of diaphragm function. However, this requires long-term follow-up and is not the focus of our research, so this can be one of the directions for future research.

Our study also had certain limitations. First, this study was performed at a single center with a relatively small sample size, which restricts our ability to determine the independent effects of all perioperative variables on PPCs and diaphragmatic dysfunction, as evidenced by the wide confidence intervals observed in the binary logistic regression analysis. Another problem caused by the small sample size is that some of our variables, such as surgical methods, are heterogeneous between groups. This drawback somewhat affects our judgment of the relationship between diaphragm dysfunction and PPCs. Second, the postoperative analgesia regimen employed in our study was patient-controlled intravenous analgesia, and its impact on diaphragm activity remains uncertain. Pu *et al.* suggested that postoperative sedation and analgesia administered intravenously did not influence the occurrence of postoperative diaphragmatic dysfunction (25). Third, we only chose diaphragmatic excursion as a diagnostic index for diaphragmatic dysfunction, while the diaphragmatic thickening fraction also serves as an indicator to evaluate diaphragmatic function (41). However, the diaphragmatic thickening fraction was excluded due to potential amplification of measurement errors during calculation and obstruction of the ultrasonic detection window by the dressing on the right chest wall surgical incision.

Conclusions

This study showed that the aged patients with postoperative diaphragmatic dysfunction were at a higher risk of developing PPCs. Postoperative monitoring of diaphragmatic function is clinically crucial in preventing and treating PPCs, with point-of-care ultrasound as an invaluable assessment tool. Moreover, the total open procedure was associated with increased risks of PPCs and diaphragmatic dysfunction, reflecting the extensive benefits of minimally invasive procedures. However, prospective studies with larger patient populations are needed to confirm perioperative risk factors associated with PPCs and postoperative diaphragmatic dysfunction.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-197/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Affiliated Cancer Hospital of Nanjing Medical University (2023 R-Rapid-024), with informed consent obtained from all patients.

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