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Right gastroepiploic artery length determined anastomotic leakage after minimally invasive esophagectomy for esophageal cancer: a prospective cohort study

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Background: This prospective cohort study, conducted at a high-volume esophageal cancer center from July 2019 to July 2022, aimed to investigate the link between the right gastroepiploic artery (RGEA) length and anastomotic leakage (AL) rates following minimally invasive esophagectomy (MIE). Real-world data on stomach blood supply in the Chinese population were examined.

Materials and Methods: A total of 516 cases were enrolled, categorized into two groups based on the Youden index-determined optimal cut-off value for the relative length of RGEA (length of RGEA/length of gastric conduit, 64.69%) through ROC analysis: Group SR (short RGEA) and Group LR (long RGEA). The primary observation parameter was the relationship between AL incidence and the ratio of direct blood supply from RGEA. Secondary parameters included the mean length of the right gastroepiploic artery, greater curvature, and the connection type between right and left gastroepiploic vessels. Patient data were prospectively recorded in electronic case report forms.

Results: The study revealed median lengths of 43.60 cm for greater curvature, 43.16 cm for the gastric conduit, and 26.75 cm for RGEA. AL, the most common postoperative complication, showed a significant difference between groups (16.88 vs. 8.84%, $P=0.01$). Multivariable binary logistic regression identified Group SR and LR (odds ratio: 2.651, 95% CI: 1.124–6.250, $P=0.03$) and Neoadjuvant therapy (odds ratio: 2.479, 95% CI: 1.374–4.473, $P=0.00$) as independent predictors of AL.

Conclusions: The study emphasizes the crucial role of RGEA length in determining AL incidence in MIE for esophageal cancer. Preserving RGEA and fostering capillary arches between RGEA and LGEA are recommended strategies to mitigate AL risk.

Keywords: anastomotic leakage, esophageal cancer, minimally invasive esophagectomy, right gastroepiploic artery

Introduction

Minimally invasive esophagectomy (MIE) with lymphadenectomy is considered the cornerstone of treatment, providing a radical cure for both early and locally advanced esophageal cancers. Among thoracic surgeons, minimally invasive McKeown esophagectomy has emerged as the preferred technique and gained widespread acceptance as the standard approach for esophageal resection[1,2]. Anastomotic leakage (AL), a complication that heightens postoperative morbidity and mortality, increases healthcare costs and prolongs hospital stays, is recognized as a significant challenge[3–5]. The reported incidence of AL ranges from 12.8 to 19%, with an associated mortality rate of 3.8%[2,6,7]. Despite numerous reported risk factors for AL development, such as a higher BMI, comorbidities, and procedural factors[5,7,8], the primary contributor is believed to be compromised tissue perfusion of the gastric conduit.

The right gastroepiploic vessels exclusively supply blood to the gastric conduit and are commonly utilized for reconstruction in

HIGHLIGHTS

- The first published prospective observational study demonstrated that right gastroepiploic artery length determined anastomotic leakage after minimally invasive esophagectomy for esophageal cancer.
- This study uses a large sample of in vivo data to provide novel and strong support for the anatomical data of the stomach and offers insightful information about anastomotic leakage risk factors for the first time.
- Provide potential and valuable insights into preventive measures and improve patient care during minimally invasive esophagectomy procedures.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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minimally invasive McKeown esophagectomy. They are believed to influence blood supply directly. While several studies have highlighted the utility of indocyanine green fluorescence in evaluating blood flow within the gastric conduit[9–11], limited research has focused on the correlation between the entire gastroepiploic vessel and AL.

Therefore, we conducted a single-center prospective observational study to explore the relationship between the length of the right gastroepiploic artery and the incidence of AL in patients undergoing minimally invasive McKeown esophagectomy. Additionally, our investigation aimed to provide detailed insights into the characteristics of the stomach in Chinese individuals, leveraging the resources of our specialized esophageal cancer center. This comprehensive analysis included an examination of factors such as the size of the gastroepiploic vessels, types of vessel arches, and other pertinent details.

Materials and methods

Study design

The current study adopts a single-center, prospective cohort (UNI: ChiCTR2300071691 and hyperlink to the registration: https://www.chictr.org.cn/) design to identify the length of the right gastroepiploic artery as the primary determinant of anastomotic fistula incidence in MIE for esophageal cancer. The study period spans from July 2019 to July 2022, during which the Department of Thoracic Surgery at Daping Hospital, Army Military Medical University in Chongqing, China, performed minimally invasive esophagectomies on 539 patients diagnosed with esophageal carcinoma. All surgeries were conducted by a single surgical team led by Professor Guo W. Postoperative TNM stage classification followed the 8th edition of the American Joint Committee on Cancer staging protocol[12]. Perioperative variables, relevant patient features, and postoperative death (defined as death within 30 days of surgery) were assessed. The Ethics Committee of Daping Hospital, Army Military Medical University approved the evaluation (Ethics Committee Number: 2019-65). The reporting of this work adheres to the strengthening the reporting of cohort, cross-sectional, and case–control studies in surgery (STROCSS) criteria[13] (Supplemental Digital Content 1, http://links.lww.com/JS9/B909).

Inclusion criteria encompassed histologically confirmed esophageal cancer, minimally invasive McKeown esophagectomy, and complete clinicopathological data, with tumors and lymph nodes being radically resected (R0). Exclusion criteria comprised noncurative (R1 or R2) resection (tumor-free margin <1 mm) and incomplete data.

A total of 516 patients met the inclusion criteria and were enrolled in the study. The patient selection and group classification processes are delineated in Figure 1. The two groups, short right gastroepiploic artery (SR) and long right gastroepiploic artery (LR) were defined based on the optimal cut-off value of the relative length of the right gastroepiploic artery (length of the right gastroepiploic artery/length of the gastric conduit, 64.69%). This cut-off value was determined using the Youden index method through receiver operating characteristic (ROC) analysis, as illustrated in Figure S1 (Supplemental Digital Content 2, http://links.lww.com/JS9/B910), to differentiate between the AL and non-AL groups.

Surgical procedures

The primary surgical technique for esophageal procedures is Thoracoscopic McKeown esophagectomy[14,15]. In this procedure, the thoracic esophagus is mobilized from the hilum and pericardium to the cervicothoracic area, with mediastinal lymphadenectomy extending to stations No. 2 L, 2R, 7, 8U/M/L, and 15. In the subsequent stage, either laparotomy or laparoscopy is performed with the patient in a supine position, and celiac lymph nodes are dissected, including at least No. 16, 17, 18, 19, and 20. The preferred esophageal substitute is a gastric conduit, and the final step involves creating a cervical esophagogastric anastomosis using a circular stapler.

Types of vessel arches between the right and left gastroepiploic vessels and the measurement methods of R/L

In Figure 2, the classification of connections between the right and left gastroepiploic vessels followed the criteria outlined by Kumagai *et al.*[9]. Consistent with their study, we visually assessed the connection between the right and left gastroepiploic vessels after constructing the gastric tube, categorizing them into three types: Type I (good), Type II (sparse), and Type III (absent)[9]. The procedure for measuring the R/L ratio is

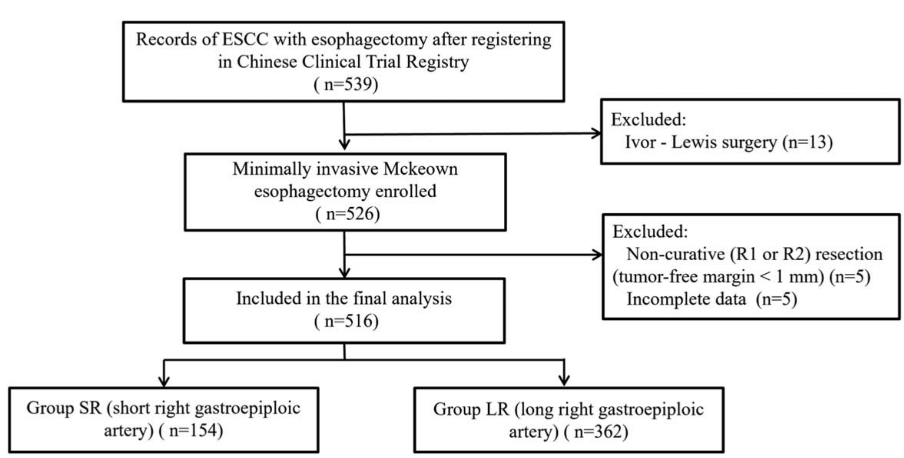

Figure 1. Flowchart of patient inclusion, allocation, and analysis, 516 patients were enrolled in this study.

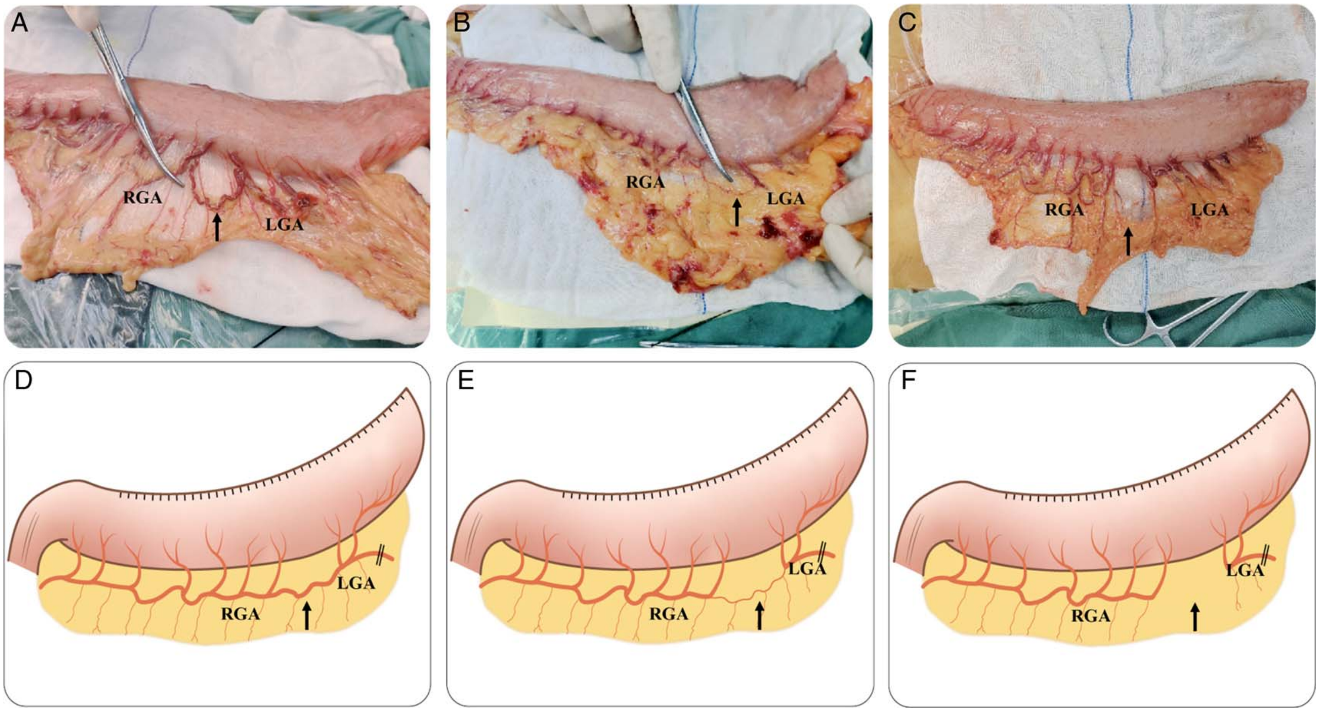

Figure 2. The type of connection between the right and left gastroepiploic vessels: (A) and (D) Type I (Good): the right and left gastroepiploic vessels are connected continuously, and there is no clear border between them. (B) and (E) Type II (Sparse): The vessel that connects the right and left gastroepiploic vessels is frail. (C) and (F) Type III (Absent): any connection between the right and left gastroepiploic vessels is completely absent. LGA, left gastroepiploic artery; RGA, right gastroepiploic artery[9].

illustrated in Figure 3. The R/L ratio represents the length of the right gastroepiploic artery in relation to the distance between its anastomosis and the pylorus. This measurement may provide insights into the extent of the blood supply to the gastric conduit.

Observational parameters

The primary focus of the study was to examine the correlation between the incidence of AL and the proportion of direct blood supply from the RGEA following McKeown esophagectomy. AL is defined as the escape of luminal contents from a surgical joint connecting the esophagus and gastric conduit. Secondary observational parameters included the average length of the right gastroepiploic artery, the greater curvature, and the type of connection between the right and left gastroepiploic vessels within the Chinese population. All patient data were systematically recorded through electronic case report forms prospectively.

Statistical analysis

Numeric data were presented using median values and ranges. The Kruskal–Wallis test, Fisher's exact test, or the χ^2 test was employed to compare continuous and categorical variables

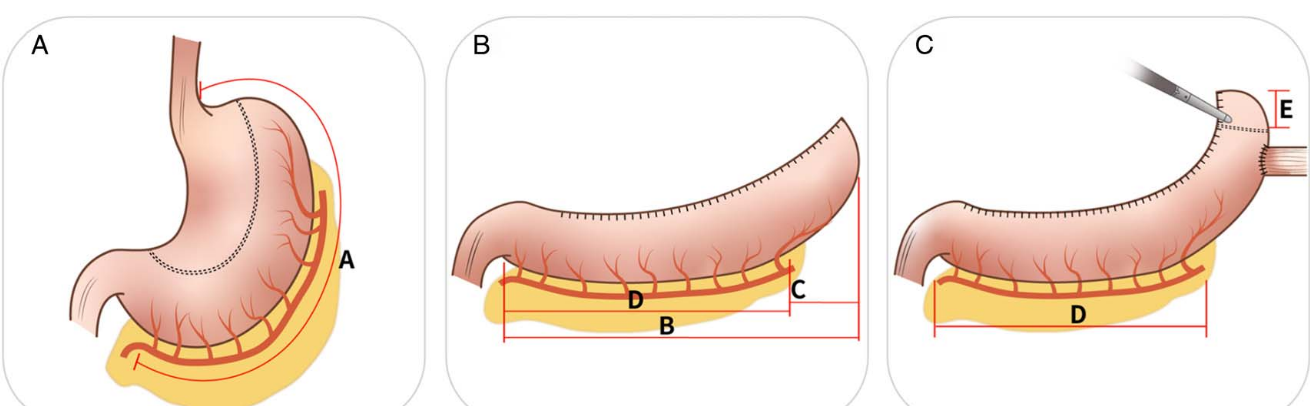

Figure 3. Measurement methods of R/L: R/L = D/(B-E). (A) A: the length of greater curvature. (B) B: the length of the gastric conduit, C: the length between the top of the RGEA and gastric conduit, D: the length of the RGEA. (C) E: the length of resected part (linear stapler close to the common opening). L, LAP (length between anastomosis and pylorus); R, RGEA (right gastroepiploic artery).

between groups. RL was divided into SR and LR groups based on the Youden index derived from ROC analysis, distinguishing between AL and non-AL groups. Due to the rarity of AL occurrence, a rare event logistic regression, implemented through the R package 'Zelig' with a tau value of 0.128, assessed the association of RL and other clinical factors with AL[16]. For case–control correction, multivariable binary logistic regression analyses were conducted, encompassing independent variables such as Group SR and LR, intraoperative blood loss, operative duration, age, BMI, preoperative serum albumin level, Length of RGEA, pathological stage (pStage), type of vessel arches, smoking history, comorbidities, and neoadjuvant therapy. Statistical analyses were performed using IBM SPSS statistical software (version 22.0; IBM Corp.). All reported *P*-values are two-sided, with statistical significance set at $P < 0.05$.

Results

Relevant patient characteristics

In the study, 516 patients were included, comprising 423 males and 93 females, with a median age of 65.00 years (range: 41.00–91.00) and a median BMI of 22.96 (range: 16.38–34.23). Among them, 216 received neoadjuvant chemotherapy or chemoradiotherapy, and 159 had no history of smoking. Baseline patient characteristics are presented in Table 1. Importantly, there were no differences in postoperative TNM stages between the two groups.

Real-world data from our medical center pertaining to the stomach

In this study, the median length of the greater curvature was 43.60 (range: 20.00–54.50), with no significant difference observed between Group SR and Group LR. Table 2 highlights notable differences in the mean length of the gastric conduit, RGEA, and R/L ratio between the two groups. Specifically, the RGEA measured 23.20 (range: 6.00–29.60) cm and the gastric conduit exhibited a mean length of 27.95 (range: 20.40–40.80) cm. The median R/L (%) was 68.61 (range: 35.30–95.60). Regarding the connection between the RGEA and LGEA, Type I (good) was the predominant type, accounting for 209 of the 516 cases (40.5%). Additionally, 178 cases (34.5%) were classified as Type III (absent), indicating a significant difference between the groups (Table 2).

Surgical outcomes and postoperative complications

As detailed in Table 3, the median duration of surgery, intraoperative blood loss, and the number of retrieved nodes were 205.00 (135.00–395.00) minutes, 50.00 (10.00–600.00) ml, and 30.00 (10.00–77.00), respectively. No significant differences were observed between the two groups. The overall incidence of postoperative complications was 31.9% (165/516) of the summarized patients (Table 2).

Notably, AL emerged as the most prevalent complication, with a significant difference between the two groups (26/154, 16.88% vs. 32/362, 8.84%; $P = 0.01$). The next four common postoperative complications—pleural effusion, pulmonary infection, pneumothorax, and ARDS—did not differ significantly between the groups ($P > 0.05$). Vocal cord palsy, ranked sixth in frequency, showed a significant difference between the groups (7/154, 4.55% vs. 5/362, 1.38%; $P = 0.03$). Additional details are provided in Table 2.

Predictive factors analyzed by multivariate binary logistic regression

As depicted in Table S1 (Supplemental Digital Content 3, http://links.lww.com/JS9/B911), we employed the rare-event logistic regression method with the tau value as the correction factor. Multivariate binary logistic regression was utilized to identify the risk factors for AL, as shown in Figure 4. Our analysis revealed that SR and LR (odds ratio: 2.651, 95% CI: 1.124–6.250, $P = 0.03$) and neoadjuvant therapy (odds ratio: 2.479, 95% CI: 1.374–4.473, $P = 0.00$) independently predicted the occurrence of AL. Specifically, the presence of a short right gastroepiploic artery (SR group) was associated with a higher likelihood of AL, while neoadjuvant therapy emerged as a significant risk factor for AL. Conversely, the long right gastroepiploic artery acts as a protective factor, reducing the incidence of AL.

Discussion

The current MIE involves repositioning the gastric conduit to substitute the esophagus, relying on 60% of the blood supply from the REGA and its branches[17,18]. The dimensions of the human stomach and gastric conduit after esophagectomy lack a standardized description; their shapes and sizes vary among individuals and are additionally influenced by gastric contents. Several cadaver studies have reported a mean greater curvature ranging from 38 to 49.6 cm, and the average length of the RGEA is 25.9 cm[17–19]. Ferrua and Singh[20] designed a simplified 3-D model depicting the stomach with a greater curvature of 34 cm. In this prospective study, we examined the stomachs of 516 patients devoid of gastric content and determined that the average length of the greater curvature is 43.60 (20.00–54.50) cm in individuals of Chinese descent, according to our extensive esophageal cancer database. The average length of the gastric conduit created during MIE is 43.16 (19.00–55.60) cm, and the actual length of the RGEA is 26.75 (6.00–40.8) cm, with an R/L ratio (%) of 68.61 (35.30–95.60). Consistent with prevailing literature, the long arch is the predominant configuration of the REGA, contributing between 2/3 and 3/4 of the length of the greater curve[19], consistent with our observation that 40.5% of cases fall into Type I (Good). However, types II (sparse) and III (absent) were evident in 25.0 and 34.5% of the patients, respectively, where the REGA blood supply did not reach the 2/3 threshold, as reported in most cases.

While there is a consensus that the anastomotic technique, tension within the anastomosis, and the location of the anastomosis are considered important risk factors in the development of AL[17], it is noteworthy that ischemia of the gastric conduit is the most decisive and direct cause of AL occurrence[21]. Buunen *et al.*[22] found that in human specimens, the incorporation of LGEA in the construction of a gastric tube could increase the length of the arterial arcade along the greater curvature by 18.7%. The present study revealed that 65.5% (comprising Types I and II) of the individuals exhibited branches between the RGEA and LGEA, with capillary arches observed in Type III. During the operation, the entire course of the RGEA was preserved while dissecting the gastrocolic and gastrosplenic ligaments to release the stomach. However, the terminal branch of

Table 1

Clinical and other relevant patient characteristics.

Characteristics	Total ($n=516$, %)	Group SR ($n=154$, %)	Group LR ($n=362$, %)	*P*
Sex				0.66[a]
Males	423 (82.0)	128 (83.1)	295 (81.5)	
Females	93 (18.0)	26 (16.9)	67 (18.5)	
Age (years, median (range))	65.00 (41.00–91.00)	65.00 (46.00–85.00)	65.00 (41.00–91.00)	0.56[b]
Smoking history				0.76[a]
No	159 (30.8)	46 (29.9)	113 (31.2)	
Yes	357 (69.2)	108 (70.1)	249 (68.8)	
BMI (kg/m2, median (range))	22.96 (16.38–34.23)	23.02 (16.66–34.23)	22.86 (16.38–31.59)	0.69[b]
Comorbidity				
No	373 (72.3)	118 (76.6)	255 (70.4)	0.15[a]
Yes	143 (27.7)	36 (23.4)	107 (29.6)	
Neoadjuvant therapy				0.29[a]
No	300 (58.1)	95 (61.7)	205 (56.6)	
Yes	216 (41.9)	59 (38.3)	157 (43.7)	
Preoperative serum albumin (g/l)	39.40 (29.20–52.80)	39.40 (29.20–52.80)	39.100 (30.40–50.60)	0.55[b]
pT				0.63[a]
T0	58 (11.2)	18 (11.7)	40 (11.0)	
T1	152 (29.5)	42 (27.3)	110 (30.4)	
T2	102 (19.8)	36 (23.4)	66 (18.2)	
T3	181 (35.1)	53 (34.4)	128 (35.4)	
T4	23 (4.4)	5 (3.2)	18 (5.0)	
pN				0.90[a]
N0	298 (57.7)	90 (58.4)	208 (57.5)	
N1	115 (22.3)	35 (22.7)	80 (22.1)	
N2	81 (15.7)	24 (15.6)	57 (15.7)	
N3	22 (4.3)	5 (3.3)	17 (4.7)	
Distant metastasis (M)				> 0.99[a]
M0	516 (100)	154 (100.0)	362 (100.0)	
M1	0	0	0	
Tumor location				0.51[a]
Upper thoracic	113 (21.9)	31 (20.1)	82 (22.6)	
Middle thoracic	244 (47.3)	78 (50.6)	166 (45.9)	
Lower thoracic	159 (30.8)	45 (29.3)	114 (31.5)	
Tumor differentiation				0.347[a]
G1	33 (6.4)	14 (9.1)	19 (5.2)	
G2	309 (59.9)	88 (57.1)	221 (61.1)	
G3	93 (18.0)	30(19.5)	63 (17.4)	
GX	81 (15.7)	22 (14.3)	59 (16.3)	
pStage				0.68[a]
0	12 (2.3)	4 (2.6)	8 (2.2)	
I	188 (36.4)	55 (35.7)	133 (36.7)	
II	111 (21.5)	32 (20.8)	79 (21.8)	
III	167 (32.4)	55 (35.7)	112 (31.0)	
IV	38 (7.4)	8 (5.2)	30 (8.3)	

[a]χ2 test.

[b]Kruskal–Wallis test.

LGEA, the left gastroepiploic artery; N, lymphatic dissemination stage (based on the American Joint Committee on Cancer (AJCC), 7th edition 13; N0, no positive lymph nodes; N1, 1–2 positive lymph nodes; N2, 3–6 positive lymph nodes; N3, > 6 positive lymph nodes); R/L, the ratio of the length of the right gastroepiploic artery and the length between anastomosis to the pylorus; RGEA, the right gastroepiploic artery; T, tumor stage (depth of invasion).

the greater curvature (the Demel point) is released. Our findings indicate the presence of capillaries extending beyond Demel's point, potentially elongating the feeding arterial arcades and contributing to ischemic conditions at the apex of the gastric conduit.

The anastomosis is strategically positioned within this ischemic region, necessitating consideration of methods to enhance blood supply. This study was prompted by the inadequate graft perfusion observed at the tip of the gastric conduit. Our findings revealed that both SR and LR were independent predictors of AL. Specifically, the elongated right gastroepiploic artery (with a ratio of the length of RGEA to gastric conduit ≥64.69%) emerged as a protective factor associated with a reduced incidence of AL. Our findings also provide insights into why Ivor-Lewis esophagectomy has a lower incidence of AL compared to McKeown esophagectomy[23–25]. When all other influencing factors were kept constant, a higher proportion of blood vessels was associated with a reduced incidence of AL. Although AL is an inevitable complication of MIE, preserving the blood supply range from the RGEA may lower the prevalence of AL, especially by maintaining more arcades of small vessels. Importantly, our study suggests that early detection of inadequate

Table 2

Real-world data related to the stomach.

Values	Total	Group SR	Group LR	*P*
Length of greater curvature (cm, median (range))	43.60 (20.00–54.50)	43.60 (20.00–53.10)	43.00 (33.50–54.50)	0.59[a]
Length of gastric conduit (cm, median (range))	43.16 (19.00–55.60)	42.65 (19.00–52.30)	43.45 (31.40–55.60)	0.01[ab]
Length of RGEA (cm, median (range))	26.75 (6.00–40.8)	23.20 (6.00–29.60)	27.95 (20.40–40.80)	0[ab]
R/L (%, median (range))	68.61 (35.30–95.60)	60.90 (35.30–64.60)	71.10 (64.70–95.60)	0[ab]
Type of connection between RGEA and LGEA				0[bc]
Type I (Good) (*n*, %)	209 (40.5)	15 (9.7)	194 (53.6)	
Type II (Sparse) (*n*, %)	129 (25.0)	32 (20.8)	97 (26.8)	
Type III (Absent) (*n*, %)	178 (34.5)	107 (69.5)	71 (19.6)	

[a]Kruskal–Wallis test

[b]Statistically significant at $P \leq 0.05$.

[c]χ^2 test

LGEA, the left gastroepiploic artery; R/L, the ratio of the length of the right gastroepiploic artery and the length between anastomosis to the pylorus; RGEA, the right gastroepiploic artery.

perfusion can guide clinical decision-making regarding additional surgical interventions. These include determining the anastomotic level, utilizing the greater omentum to cover the anastomotic site, and considering primary anastomotic repair, all of which may lead to improved postoperative outcomes.

This study employed a large cohort of in vivo data to provide novel and robust support for the anatomical aspects of the stomach, offering insightful information about AL risk factors. However, it is important to note that there is a possibility that measurement errors may have affected the accuracy of our findings. We attempted to minimize such errors by employing trained personnel to perform measurements with standardized protocols, ensuring that the same surgical team performed the procedures, and enrolling a substantial number of patients to enhance statistical power. Additionally, we took precautions such as avoiding excessive traction, compression, or twisting, and ensuring the

Table 3

Intraoperative data and postoperative complications.

Characteristics	Total (*n* = 516, %)	Group SR (*n* = 154, %)	Group LR (*n* = 362, %)	*P*
Operation duration (min, median (range))	205.00 (135.00–395.00)	200.00 (145.00–330.00)	205.00 ((135.00–395.00)	0.713[a]
Intraoperative blood loss (ml, median (range))	50.00 (10.00–600.00)	50.00 (10.00–600.00)	50.00 (10.00–350.00)	0.533[a]
Number of retrieved nodes (median (range))	30.00 (10.00–77.00)	30.00 (10.00–76.00)	30.00 (12.00–77.00)	0.559[a]
Postoperative complications				
Anastomotic complications				
Anastomotic leakage	58 (11.24)	26 (16.88)	32 (8.84)	0.01[b]
Anastomotic hemorrhage	2 (0.39)	0	2 (0.55)	0.49[c]
Respiratory complications				
Pulmonary infection	24 (4.7)	5 (3.25)	19 (5.25)	0.32[b]
ARDS	15 (2.91)	6 (4.00)	9 (2.49)	0.38[b]
Pleural complications				
Pneumothorax	21 (4.07)	5 (3.25)	16 (4.42)	0.54[b]
Pleural effusion	28 (5.43)	8 (5.19)	20 (5.52)	0.88[b]
Chylothorax	2 (0.38)	1 (0.65)	1 (0.28)	0.53[c]
Cardiac complications				
Heart disfunction	4 (0.78)	0	4 (1.10)	0.32[c]
Atrial fibrillation	2 (0.39)	1 (0.28)	1 (0.65)	0.51[c]
Embolism				
Phlebothrombosis	3 (0.58)	0	3 (0.83)	0.56[c]
Superior mesenteric artery embolus	4 (0.78)	2 (1.30)	2 (0.55)	0.59[c]
Left atrial thrombus	1 (0.19)	1 (0.65)	0	0.30[c]
Others				
Wound infection	6 (1.16)	1 (0.65)	5 (1.38)	0.67[c]
Vocal cord palsy	12 (2.32)	7 (4.55)	5 (1.38)	0.03[b]
Incisional hernia	2 (0.39)	0	2 (0.55)	0.49[c]
Ileus	2 (0.39)	1 (0.28)	1 (0.65)	0.51[c]
Cerebral infarction	2 (0.39)	1 (0.28)	1 (0.65)	0.51[c]
Hiatus hernia	1 (0.19)	0 (0.00)	1 (0.28)	0.70[c]
Pancreatitis	2 (0.39)	1 (0.28)	1 (0.65)	0.51[c]

[a]Kruskal–Wallis test.

[b]$\chi 2$ test.

[c]Fisher's exact test.

ARDS, Acute Respiratory Distress Syndrome.

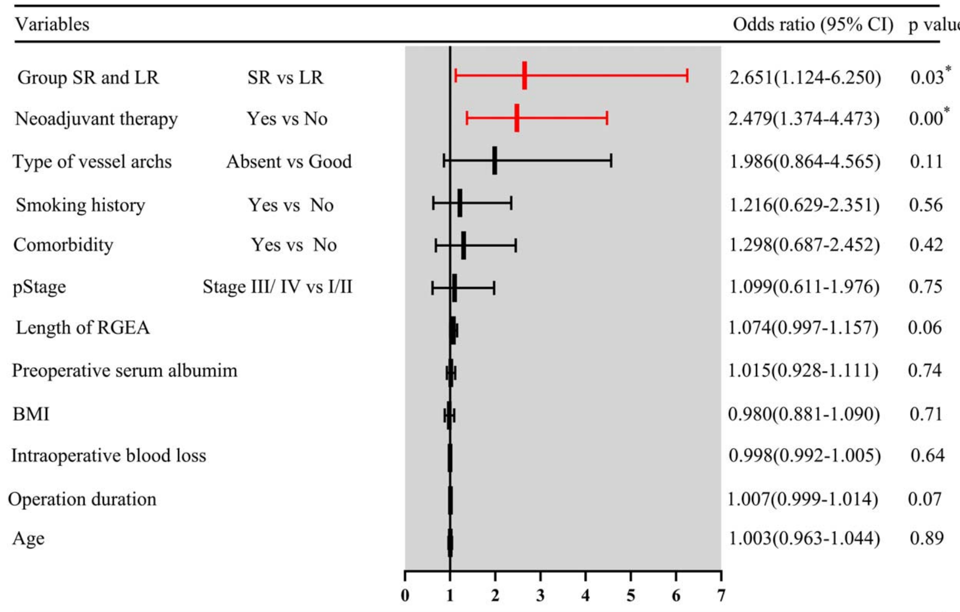

Figure 4. The forest plot depicts the multivariate logistic regression with the AL outcome, values on the right are reported as the odds ratio with the respective 95% CI in parenthesis. *Statistically significant at $P \leq 0.05$.

correct number of sutures and complete donuts in the mechanical anastomosis during the procedures. We believe that these measures were used to minimize bias and the large sample size provided reliable and trustworthy results. Nevertheless, we recognize the need for additional research using more advanced measurement tools to confirm our findings.

In conclusion, this study highlights the pivotal role of the RGEA length in determining the incidence of AL in MIE for esophageal cancer. Preserving the RGEA and fostering capillary arches between the RGEA and the LGEA are advocated strategies for mitigating AL risk.

Ethical approval and consent to participate

This study was approved by the Ethics Committee of Daping Hospital, Army Medical University(2019-65), and written informed consent was obtained from the patient for publication and any accompanying images.

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

K.K.L. and W.G.: carried out the studies, participated in collecting data, and drafted the manuscript; Y.J.W., T.B., and T.M.Z.: performed the statistical analysis and participated in its design; L.Z., S.L.Z., X.F.X., and L.C.: participated in the data collection, analysis, or draft the manuscript. All authors read and approved the final manuscript.

Conflict of interest disclosure

All authors declare that they have no any conflict of interests.

Research registration unique identifying number (UIN)

1. Name of the registry: Chinese clinical trial registration.
2. Unique identifying number or registration ID: ChiCTR 1900026072.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): http://www.chictr.org.cn/edit.aspx?pid=28828&htm=4.

Guarantor

Wei Guo.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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