ORIGINAL ARTICLE

Short-term postoperative complications and prognostic factors in patients with adenocarcinoma of the esophagogastric junction

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Abstract

Background: The study was conducted to investigate the short-term complications and prognostic factors in patients with esophagogastric junction adenocarcinoma (EGJA).

Methods: This retrospective study included 110 EGJA patients who underwent surgery from January 2010 to November 2012 at The First Affiliated Hospital of BengBu Medical College. The overall survival and short-term complications were analyzed according to the patients' clinical characteristics.

Results: The incidence of postoperative cardiopulmonary complications was significantly higher in patients with preoperative cardiopulmonary disease or elderly patients ($P < 0.05$). Four cases of upper margin cancer residue were detected using the abdominal approach and three using the thoracic approach, which indicated that the cancer residue margin was related to surgical approach. The overall five-year survival rate was 34.3% and statistically differed according to pathological stage and en block resection ($P_{all} < 0.05$). Cox regression analysis showed that lymph node metastasis ($P < 0.05$) and the extent of tumor invasion ($P < 0.05$) were independent prognostic factors.

Conclusion: Elderly patients with preoperative cardiopulmonary disease had an increased risk of developing postoperative cardiopulmonary complications. Lymph node status and depth of tumor invasion were independent factors related to patient prognosis.

Introduction

Esophagogastric junction adenocarcinoma (EGJA) is a malignant carcinoma located at the junction of the thorax and abdomen.[1,2] The surgical scope for this malignancy includes the thoracic and abdominal cavity.[3]Surgical duration is usually long and the trauma is severe; many patients also suffer from preoperative lung and heart disease.[4]The postoperative risk of complication from the procedure is higher than for gastric cancer surgery.[5]With advancements in surgical techniques and medical equipment, surgical indications for gastroesophageal and other digestive tract surgeries have been expanded, and risks of complication and mortality have been significantly decreased.[6] Concurrently, the complication spectrum has gradually changed, and the prognosis of EGJA has considerably improved. We retrospectively reviewed our

department's surgical treatment of EGJA patients from 1 January 2010 to 31 December 2012, analyzed the postoperative complications and follow-up data, conducted a summary analysis, and explored short-term complications and prognosis after EGJA surgery.

Methods

Patients

This retrospective study included the clinical and pathological data of 110 EGJA patients who underwent surgery from 1 January 2010 to 31 December 2012 at the Department of Oncology Surgery, First Affiliated Hospital of Bengbu Medical College. All patients, including 86 men and 24 women, were diagnosed with adenocarcinoma. The male to female

ratio was 3.58:1. The average age of the patients was 62.30 $\pm$ 6.33 years (range 35–79). Thirty-two patients (29.10%) were aged > 70 years. Sixty-five patients underwent surgery via left thoracic, 40 via transabdominal, and 5 via abdominothoracic incision. Siewert types I, II, and III were found in 28, 55, and 27 cases, respectively (Table 1).

A total of 30 patients presented preoperative complications; 16 patients had COPD, 15 had pulmonary dysfunction, 6 had heart diseases, and 4 had diabetes (Table 2). Postoperative cardiopulmonary complications occurred in 14 cases, including: 6 cardiac complications, 11 pulmonary complications, 3 anastomotic fistulas, 1 stomach cramp, 3 chest infections, and 1 stroke. Among the seven cases of residual resection of cancer, four were in the upper and three in the lower margins. Bleeding-induced hemorrhagic shock occurred in one case, which was alleviated by a secondary surgery. One patient died postoperatively after being discharged (Table 3).

Eleven (10.0%) patients were lost to follow-up. A total of 79 men and 20 women were followed up, with a male to female ratio of 3.95:1. The average age of the patients was 62.50 $\pm$ 4.38 years (range 36–75). Among the 99 cases with complete data, 75 cases were type I or II, and 24 were type III. Six, 30, 59, 4, 33, and 66 cases presented with pT1, pT2, pT3, pT4, pN0, and pN+ stages, respectively. Furthermore, 13, 33, and 53 cases were in stages I, II a+b, and III a+b+c, respectively. Among these cases, 67 underwent R0 resection, and 32 R1 + R2 resections. The R0 resection rate was 67.7%.

Table 1 Clinical pathological features of Siewert I–III EGJA (*n*, [%])

Index	Type I/II	Type III	*P*
Differentiation			< 0.05
I	9 (10.8)	5 (18.5)	
II	47 (56.6)	7 (25.9)	
III	27 (32.5)	15 (55.6)	
Tumor length			
< 3 cm	18 (21.7)	6 (22.2)	> 0.05
3–5 cm	39 (47.0)	10 (37.0)	
> 5 cm	26 (31.3)	11 (40.7)	
Pathological stage			
PT1	5 (6.0)	1 (3.7)	> 0.05
PT2	26 (31.3)	7 (25.9)	
PT3	45 (54.2)	17 (63.0)	
PT4	7 (8.4)	2 (7.4)	
PN0	27 (32.5)	7 (25.9)	
PN+	56 (67.5)	20 (74.1)	
Clinical stage			> 0.05
I	13 (15.7)	3 (11.1)	
IIa+b	23 (27.7)	13 (48.1)	
IIIa+b+c	47 (56.6)	11 (40.8)	
En bloc resection			> 0.05
R0	54 (65.1)	17 (63.0%)	
R1 + R2	29 (34.9)	10 (37.0%)	

EGJA, esophagogastric junction adenocarcinoma.

Table 2 Preoperative complications of different surgical approaches (*n*, [%])

Factors	Abdominal approach (*n* = 40)	Thoracic approach (*n* = 65)	Thoracoabdominal approach (*n* = 5)
Age ≥ 70 (years)	14 (35.0%)	20 (30.8%)	0 (0)
Preoperative complication	14 (32.5%)	16 (24.6%)	0 (0)
Hypertension	7 (17.5%)	8 (12.3%)	0 (0)
Lung disease	7 (17.5%)	9 (13.8%)	0 (0)
Type 2 diabetes	2 (5.0%)	4 (6.2%)	0 (0)
Two or more complications	2 (5.0%)	2 (3.1%)	0 (0)

Disease classification

The tumors were grouped on the basis of the Siewert classification as follows:[7] type I, the tumor center is located within 1–5 cm above the anatomical EGJ; type II, the tumor center is situated 1 cm above the anatomical EGJ and within 2 cm below; type III, the tumor center is located 2–5 cm below the anatomical EGJ and infringed EGJ from below. Siewert types I and II were classified according to the American Joint Committee on Cancer (AJCC) 7th edition Staging Criteria for Esophageal Cancer, and type III according to the AJCC 7th edition Staging Criteria for Gastric Cancer.

Surgical procedure

The surgical approaches used included low left chest improved, transabdominal, and abdominothoracic incisions. Patients who underwent left thoracic incision received general anesthesia with double lumen tracheal intubation. During surgery, right lateral single-lung ventilation was selected, and the right lateral position was assumed. A surgical cut was created through the skin, subcutaneous tissue, muscular layer, and intercostal muscle of the chest through a left posterolateral incision through the

Table 3 Postoperative complications of EGJA

Complication	No.	Percentage (%)
Heart and lung	14	12.7
Heart	6	5.5
Lung	11	10.0
Anastomotic fistula	3	2.7
Gastroparesis	1	0.9
Chest infection	3	2.7
Hemorrhagic shock	1	0.9
Residual carcinoma on margin	7	6.4
Upper edge	4	3.6
Lower edge	3	2.7
Stroke	1	0.9
Death	1	0.9

EGJA, esophagogastric junction adenocarcinoma.

eighth and ninth ribs. The incision to the thoracic rib joint in front of the incision was extended to the upper abdomen to increase exposure to the surgical field. The pleura of the lower thoracic esophagus was opened and then dissociated. The resection range was bound by the pericardium, descending aorta, and right pleura. The integrity of the abovementioned structures not invaded by the tumor was protected. When these structures were invaded by a tumor, partial excision of these structures was performed for enbloc resection. The lymph nodes beside the lower esophagus, inferior pulmonary veins, and diaphragmatic muscles were also removed. The phrenic nerve branches at the diaphragmatic hiatus should be protected. The abdomen was explored to determine the presence of ascites, planted nodules on the omental pelvic floor, and liver metastasis. Local external invaders and part of the diaphragm were removed. The ligamentum hepatogastricum, splenogastric ligament, and ligamentum gastrolicum into the abdomen were successively disconnected. The right gastric lining blood vessels were protected to ensure blood supply to the distal stomach. The subphrenic, left and right, small curved stomach, celiac artery (including the left of the gastric artery, in the hepatic artery, and beside the celiac artery), and large curved stomach lymph nodes were also removed. The upper and lower margins were > 5 cm from the tumor. The distal stomach was anastomosed to the esophageal stapler through the esophagus bed. The anastomotic site was located below the aortic arch.

In patients who underwent the abdominal approach, an upper abdominal incision was made, and the skin, subcutaneous tissue, and abdominal line into the abdomen were successively cut. The presence of implanted nodules was determined from the farthest to the closest locations in the pelvic floor of Douglas's fossa, the planting omentum, and the liver. The ligaments of the stomach were severed along the transverse colon, and the right vascular area of the gastro-omentum was protected. The free gastric curvature was broken on the side of the ligamentum of the spleen and stomach. The branches of the gastric omentum and the short vessels of the stomach were ligated, and the lesser omentum was cut. During surgery, the diaphragmatic hiatus and free distal thoracic esophagus were opened. Lymph nodes at the subphrenic, left and right, small and large curved stomach, celiac artery, and left gastric artery adjacent to the hepatic artery were removed. The upper and lower margins were > 5 cm from the tumor. The distal stomach was anastomosed to the esophageal stapler, and the anastomotic site was located in the split hole (Fig 1).

In patients who underwent the thoracoabdominal joint approach, the rib arch was cut obliquely to the left through a midline abdominal incision, which was advanced into the chest along the seventh intercostal space. The remaining surgical procedures were similar to those of the left thorax-

low incision. Lymph nodes were grouped during surgery and sent for pathological examination.

Follow-up

All patients were followed-up by telephone or outpatient department visit. The patients who were not followed-up by telephone were sent letters and visited at the contact addresses provided at patient registration.

Statistical analysis

Data analysis was conducted using SPSS version 19.0 (IBM Corp., Armonk, NY, USA). Measurement data were expressed with $\overline{x} \pm s$ and the comparison between groups was made based on a t-test of the sample mean. Enumeration data were expressed as a percentage, and comparison between groups was made based on the χ^2 test of Fisher's exact test. Kaplan–Meier curves were drawn for overall survival (OS) and compared between groups. Cox's proportional regression analyses were performed to analyze the independent factors relevant to prognosis. Two tailed P values < 0.05 were considered statistically significant.

Results

Association between clinical pathological features and postoperative cardiopulmonary complications

Twenty-eight preoperative patients presented with cardiopulmonary diseases. Postoperative cardiopulmonary complications occurred in eight patients (29.6%) with and six patients (7.2%) without preoperative cardiopulmonary disease. The incidence of postoperative heart and lung complications in patients with preoperative cardiopulmonary diseases was significantly higher than in patients without ($P < 0.01$): 34 cases occurred in elderly ($\geq$ 70 years) patients, 8 (23.5%) of whom presented with postoperative cardiopulmonary complications. A total of 76 patients were aged > 70 years, six (7.9%) of whom suffered from postoperative cardiopulmonary complications. The incidence of postoperative cardiopulmonary complications in elderly patients was higher than in patients aged < 70 years ($P < 0.05$). The proportions of postoperative cardiopulmonary complications according to surgical approach were: 8 (12.2%) after left thoracic incision, 5 (7.5%) after transabdominal incision, and 1 (20.0%) after abdominothoracic incision. No statistical difference was found in the incidence of postoperative heart and lung complications among the different surgical approaches.

Postoperative cardiopulmonary complications by differentiation were: 3 (21.4%) grade I, 7 (13.0%) grade II, and
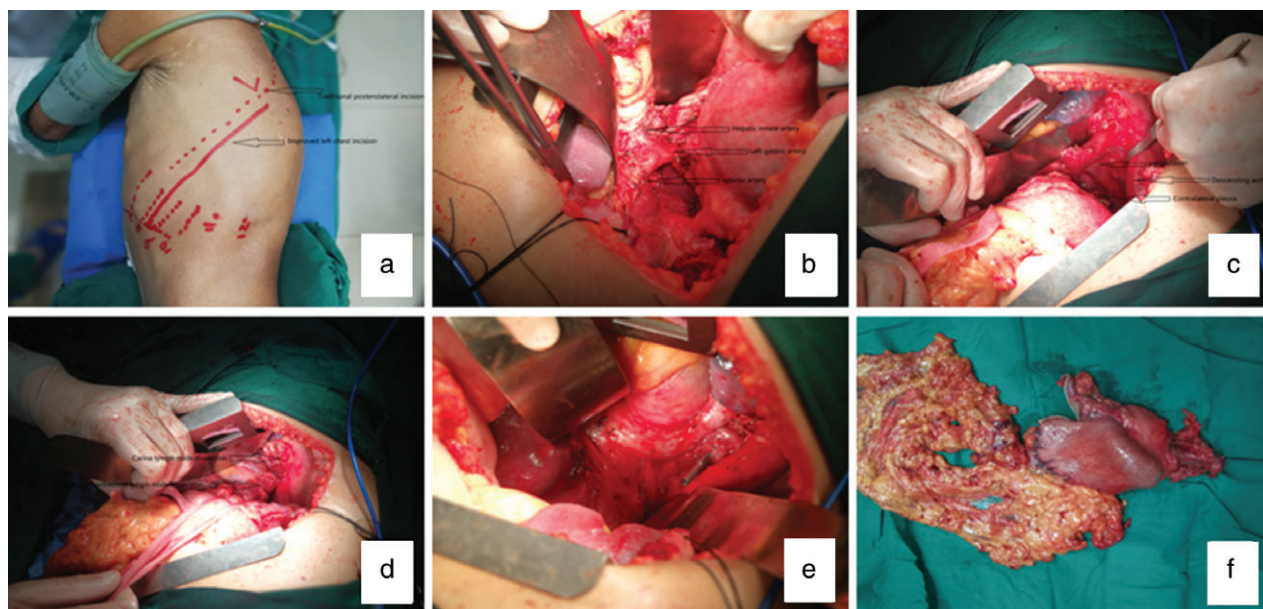
Figure 1 Surgical procedure for the treatment of adenocarcinoma of the esophagogastric junction.(**a**) The left thoracotomy incision was made between the eighth and ninth costal spaces. (**b**) Lymph nodes around the celiac artery were removed (group 7, 8, 9, and 12a lymph nodes). (**c,d**) Mediastinal lymph node dissection was performed. The descending aorta, contralateral pleura, and pericardium were used as the edge to clear the middle lower esophageal side and the supraphrenic and subcarinal lymph nodes. (**e**) Anastomosis located below the aorta and above the pulmonary vein. (**f**) The specimen was removed.

4 (9.5%) grade III. No statistical difference was found among the different differentiation groups. Additionally, 7 (18.0%) patients with pathological stage T1 + T2 and 7 (11.5%) with pathological stages T3 + T4 presented with postoperative cardiopulmonary complications; however, no significant difference was observed between these groups. Four (11.8%) patients with pathological stage N0 and 10 (13.2%) with pathological stage N+ showed postoperative heart and lung complications, with no significant difference between groups. Table 4 shows the relationship between clinical pathological indexes and postoperative cardiac and pulmonary complications.

Relationship between clinical pathological indicators and survival

The overall five-year survival rate of the patient cohort was 34 months (34.3%). Twenty-two (35.5%) patients aged ≥ 60 years and 12 (32.4%) aged < 60 achieved five-year survival; however no significant difference was observed between the groups. Twenty-six (34.7%) Siewert type I and II and 8 (33.3%) type III patients survived five years, with no significant difference between the groups. The five-year survival rates according to surgical approach were: 21 (35.6%) via left thoracic incision, 13 (34.2%) via transabdominal incision, and 0 (0%) 2 via abdominothoracic

Table 4 Relationship between postoperative cardiac pulmonary complications and clinical pathological features (*n*, [%])

Features	Postoperative cardiac pulmonary complications		*P*
	Positive	Negative	
Age (years)			
≥ 70	26 (76.5)	8 (23.5)	< 0.05
< 70	70 (92.1)	6 (7.9)	
Preoperative cardiopulmonary disease			< 0.01
Positive	20 (71.4)	8 (29.6)	
Negative	76 (92.7)	6 (7.2)	
Surgical approach			> 0.05
Thoracic	57 (87.7)	8 (12.2)	
Abdominal	37 (92.5)	3 (7.5)	
Abdominothoracic	4 (80.0)	1 (20.0)	> 0.05
Differentiation			
I	11 (78.6)	3 (21.4)	
II	47 (87.0)	7 (13.0)	
III	38 (90.5)	4 (9.5)	
Pathological T stage			> 0.05
T1 + T2	32 (82.0)	7 (18.0)	
T3 + T4	54 (88.5)	7 (11.5)	
Pathological N stage			> 0.05
N0	30 (88.2)	4 (11.8)	
N+	66 (86.8)	10 (13.2)	

incision. No statistical difference was observed between the left thoracic and transabdominal approaches. In the T stage, 22 (61.1%) patients with T1 + T2 stage and 12 (19.1%) with T3 + T4 stage survived five years, and a statistical difference was observed between the groups. In the N stage, 22 (60.0%) patients with N0 stage and 12 (23.2%) with N+ stage survived five years, and a significant difference was observed between the groups. The five-year survival rates according to pathological stage were: stage I, 8 cases (61.5%); stage II, 14 (42.4%); and stage III, 11 (20.8%). The statistical differences were significant among these groups. Among 67 cases of R0 resection and 32 cases of R1 + R2 resection, 28 (41.8%) and 6 (18.8%) patients survived five years, respectively, with a significant difference observed between the two groups (Table 5).

The survival curves of the different age groups (Fig 2) and survival rates according to Siewert types III and I/II within five years showed no statistical differences (Fig 3). The five-year survival rates of the different surgical approaches were significantly different (Fig 4). The five-year survival rate of R0 resection was significantly better than that of the R1 + R2 group (Fig 5). The five-year survival rates of the different T and N stages significantly differed from one another (Figs 6–7). Cox regression analysis showed that lymph node metastasis ($P < 0.05$) and the
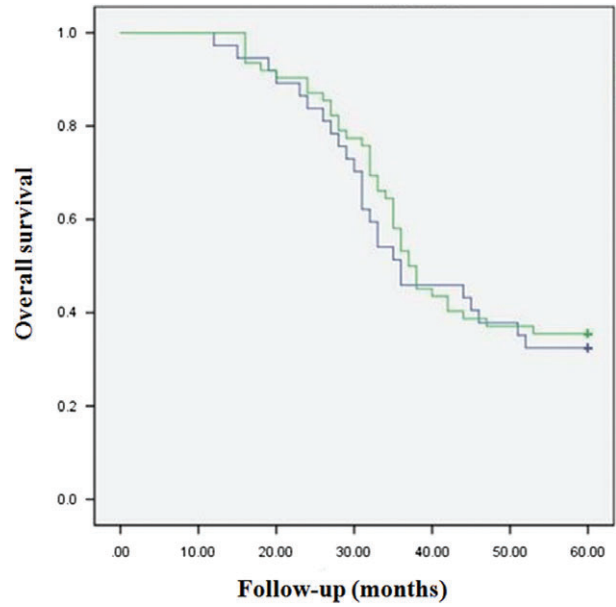

Figure 2 Survival curves of different ages. ——, <60; ——, ≥60.

extent of tumor invasion ($P < 0.05$) were independent prognostic factors.

Discussion

Epidemiological studies have indicated that EGJA incidence has increased in recent years.[8,9] Most cases of EGJA are adenocarcinoma, which is difficult to diagnose in early stages. At diagnosis, most patients are already at advanced

Table 5 Relationship between clinical pathological features and survival of EGJA (*n*, [%])

| Characteristics	Five-year survival		
	Positive (*n* = 34)	Negative (*n* = 65)	*P*
Age (years)			0.76
≥ 60	22 (35.5)	40 (64.5)	
< 60	12 (32.4)	25 (67.6)	
Siewert type			0.90
I/II	26 (34.7)	49 (65.3)	
III	8 (33.3)	16 (66.7)	
Surgical approach			0.89
Thoracic	21 (35.6)	38 (64.4)	
Abdominal	13 (34.2)	25 (65.8)	
Thoracoabdominal	0 (0)	2 (100)	
Pathological T stage			< 0.01
T1 + T2	22 (61.1)	14 (38.9)	
T3 + T4	12 (19.1)	51 (80.9)	
Pathological N stage			< 0.01
N0	22 (60.0)	11 (40.0)	
N+	12 (23.2)	54 (76.8)	
Clinical			< 0.01
I	8 (61.5)	5 (38.5)	
IIa+b	14 (42.4)	19 (57.6)	
IIIa+b+c	11 (20.8)	42 (79.2)	
Resection			
R0	28 (41.8)	39 (58.2)	< 0.05
R1 + R2	6 (18.8)	26 (81.2)	

EGJA, esophagogastric junction adenocarcinoma.
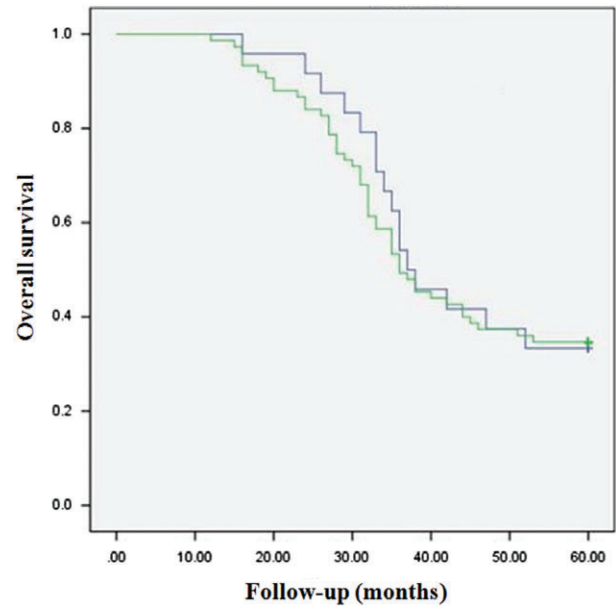
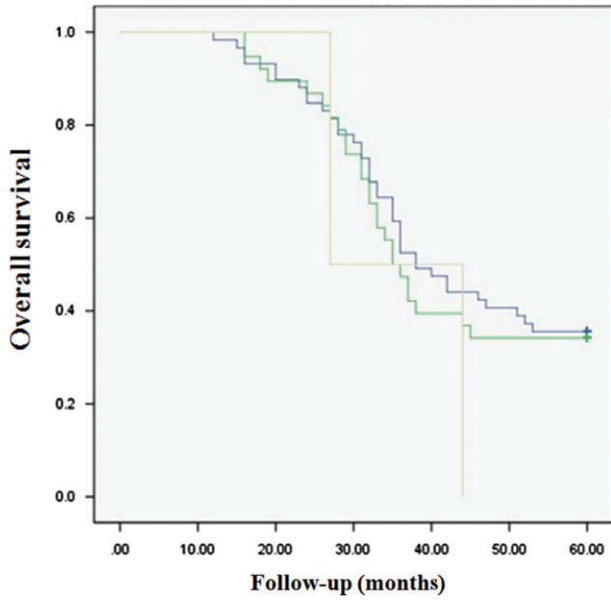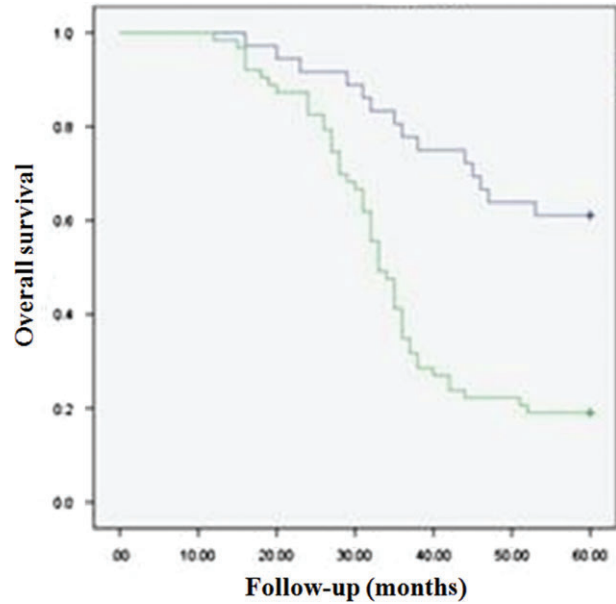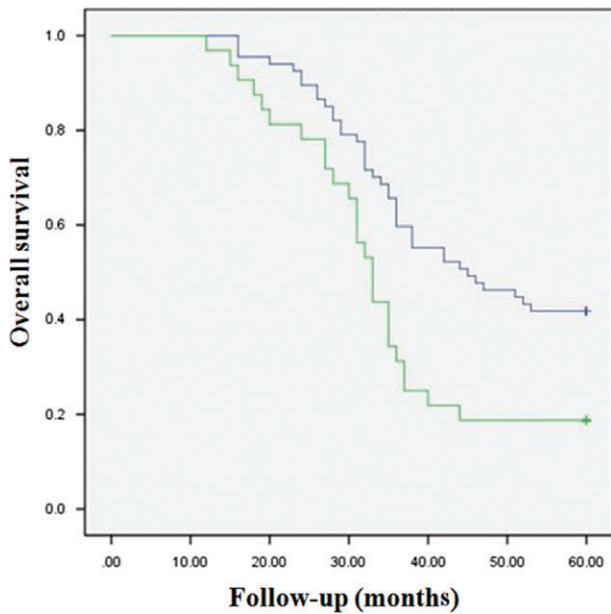**Figure 3** Survival curves of different Siewert types. ——, III; ——, I/II.
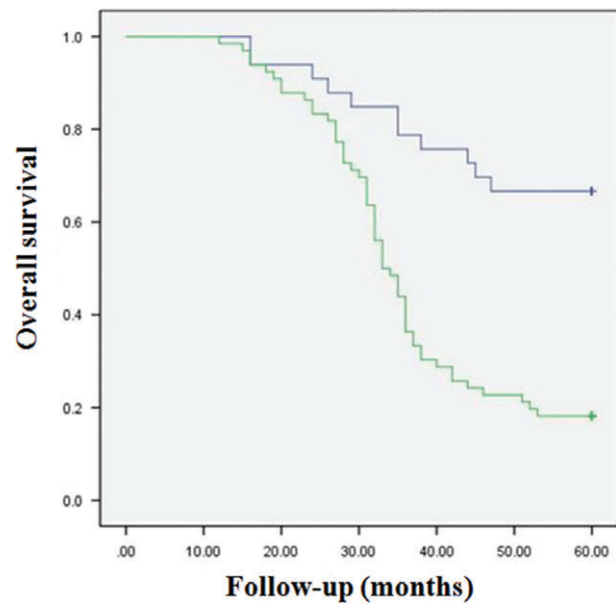
Figure 4 Survival curves of different operative approaches. ——, Thoracic; ——, abdominal; ——, thoracoabdominal.

Figure 6 Survival curves of different T stages. ——, T1 + T2; ——, T3 + T4.

Figure 5 Survival curves of different resection types. ——, R0; ——, R1 + R2.

Figure 7 Survival curves of different N stages. ——, N0; ——, N+.

stage and have developed lymph node metastasis.[10–13] The metastatic lymph node rate of Siewert II and III patients is reported at 64.1% and 74.0% respectively.[14,15]

With developments in technology and equipment, gradual improvements have been made regarding postoperative complications. Common complications such as anastomotic fistula and empyema have decreased; however, the incidence of postoperative cardiopulmonary complications has increased with the number of elderly patients undergoing surgery. Ping *et al.* reported that the incidence of postoperative complications in esophageal patients has decreased from 39.77% to approximately 5.0% during the past 60 years.[16] Koufuji *et al.* reported that the incidence of major postoperative complications is 22%: anastomotic fistula 6%, abdominal hemorrhage 6%, pneumonia 6%,

pancreatitis 4%, and perioperative death 4% (mainly caused by anastomotic fistula and myocardial infarction).[17] Xie *et al.* found that the incidence of postoperative cardiopulmonary complications was related to the surgical approach. Patients who underwent abdominal surgery had the lowest rate of postoperative cardiopulmonary complications compared to the transthoracic and abdominothoracic approaches.[18] In our study, we found that advanced age was no longer an absolute contraindication for surgery. In the 34 patients aged > 70 (30.9%), the incidence of anastomotic fistula was 2.7% and no postoperative death as a result of anastomotic fistula occurred. This result is attributed to the wide application of the stapler, improvements in anastomosis techniques, and postoperative retention of the duodenal nutrition tube, which can provide long-term nutritional support for esophageal cancer patients who have undergone surgery. Residual cancer of the surgical margin is one of the most important factors affecting prognosis. Previous studies have demonstrated that residual cancer is closely related to the surgical approach.[18,19] In our study, four cases of upper margin cancer residue were detected using the abdominal approach and three from the thoracic approach, indicating that the cancer residue margin was related to surgical approach.

Tumor invasion depth was closely related to prognosis and five-year survival rate sin patients with EGJA. Five-year survival rates of T1 and T2 esophageal cancer patients are reported at 82% and 72%, respectively.[20] However, the five-year survival rate is 0 for patients with T3 or T4 disease.[20] Koufuji *et al.* reported five-year survival rates of stage I, II, III, and IV of 86%, 40%, 21%, and 0, respectively.[17] The five-year survival rates for T1/T2 and T3/T4 disease in our study were 61.1% and 19.1%, respectively, with statistical significance. Cox regression analysis showed that lymph node status and tumor invasion depth were independent factors related to prognosis. Ito *et al.* conducted multivariate regression analysis of prognosis in patients with esophageal cancer and found residual tumor and lymph node metastasis were the most important factors relevant to prognosis.[21] We found the five-year survival rate was statistically different between patients who underwent R0 and R1/R2 resection, but was not an independent factor relevant to prognosis by Cox regression analysis. This may be a result of the small sample size used in our study.

In conclusion, elderly patients with preoperative cardiopulmonary disease have an increased risk of developing postoperative cardiopulmonary complications. Preoperative preparation, such as cardiopulmonary exercise and pulmonary infection control, is important to decrease the risk of post cardiopulmonary complications in these patients. Careful consideration of which approach to take is important to prevent postoperative complications.

Disclosure

No authors report any conflict of interest.

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