Esophagectomy Combined With Aortic Segment Replacement for Esophageal Cancer Invading the Aorta

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Background. **Surgical treatment for patients with esophageal carcinoma that invades the aorta locally (stage IIIc) remains a considerable challenge. This study aimed to introduce radical esophagectomy combined with off-pump descending aorta replacement in these patients and to assess the effects on both short-term and long-term outcomes.**

Methods. **The clinical data of 47 patients who had esophageal carcinoma invading the descending aorta and who underwent radical esophagectomy combined with off-pump aortic replacement between January 2001 and March 2012 in Jinling Hospital were retrospectively reviewed. The intraoperative, early postoperative, and follow-up results were analyzed.**

Results. **Overall, 80.9% and 19.1% of the patients had histopathologically confirmed aortic tunica adventitia invasion and media invasion, respectively. All patients received complete resection (R0) with an average intraoperative blood loss of 227.6 ± 63.3 mL. The mean operative time and aortic cross-clamping time were 4.9 ± 1.3 hours and 17.0 ± 3.2 minutes, respectively. Complications were observed in 59.6% of patients, with no hospital mortality, and all patients resumed an oral diet 1 month after the procedure. The overall 1-, 3-, and 5-year survival rates were 80.9%, 44.7%, and 21.3%, respectively, with a median survival time of 33.6 months.**

Conclusions. **In patients with esophageal carcinoma invading the aorta, it is feasible and safe to perform radical esophagectomy combined with off-pump descending aorta replacement to improve nutritional status and achieve satisfactory survival.**

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The invasion of esophageal carcinoma (EC) into adjacent mediastinal structures occurs easily and usually indicates a poor prognosis and highly advanced stage [1]. The local invasion into the aorta, categorized as stage T4b in the most current staging system, constitutes 33% to 60% of all adjacent invasions in patients with EC and represents the most common site of tumor invasions [2–6].

The present therapeutic strategy for EC that locally invades the aorta remains controversial and presents a challenge. Considering high risks and unclear outcomes of radical surgical intervention, chemoradiotherapy (CRT) is considered the standard treatment for EC with aortic invasion, with or without a palliative surgical procedure [7–10]. However, the prognosis after CRT in EC with aortic invasion is not satisfactory. The median survival time is 10.6 months, and arterioesophageal fistulas related to CRT were observed in 14.7% of the patients with EC and aortic invasion, which might cause massive bleeding and sudden death [4].

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Until now, few surgical trials in patients with EC invading the aorta have been reported and advocated [11–13]. Therefore, the outcomes of patients with EC with aortic invasion after radical operations have not been evaluated. This study aimed to introduce radical esophagectomy combined with off-pump descending aorta replacement in these patients and assess the effects on both short-term and long-term outcomes. A total of 47 patients with locally advanced EC invading the descending aorta were enrolled in the present study. All the patients underwent radical esophagectomy combined with off-pump aortic segment replacement, and their clinical features, complications, and prognoses were retrospectively evaluated.

Patients and Methods

Patients

From January 2001 to March 2012, a total of 49 patients underwent radical esophagectomy combined with off-pump descending aorta replacement in Jinling Hospital, based on a preoperative evaluation and intraoperative exploration, using the following eligibility criteria: (1) pathologically proven squamous cell carcinoma of the

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thoracic esophagus, (2) clinical evidence of invasion into the descending aorta (clinical stage T4b) by thoracic computed tomography (CT) (Fig 1) or intraoperative exploration, (3) no distant organ metastasis (clinical M0), (4) no concomitant advanced cancer, (5) no previous history of upper gastrointestinal operations, and (6) adequate organ function.

Postoperative pathologic examination confirmed local invasion into the descending aorta in 47 of 49 patients (95.9%); these patients were selected for the present study. Demographic data, clinical preoperative assessments, intraoperative features, early postoperative results (1 month), and follow-up results were collected.

Written informed consent was obtained from the patients enrolled in this study or from their authorized relatives, and the study protocols were approved by the Ethics Committee of Jinling Hospital, Medical School of Nanjing University.

Preoperative Evaluation

Upper gastrointestinal series, gastroscopy with biopsy specimen, and thoracoabdominal CT were routinely performed for preoperative evaluation. When the angle of direct contact of the aortic circumference with the tumor (Picus' angle) exceeded 90 degrees or the triangular fat space between the esophagus, aorta, and spine adjacent to the primary tumor was seen to be obliterated on CT, aortic invasion was clinically diagnosed [14, 15].

Surgical Technique

The operation was performed using bilumen tracheal intubation and balanced anesthesia. The chest was opened through a left posterolateral incision in the sixth intercostal space to achieve sufficient exposure of the esophagus and aorta in a single field. After exhaustive exploration, the esophagus was encircled by tape at the proximal and distal sites of the tumor and bluntly separated from adjacent structures up to the clavicle level and down to the diaphragmatic hiatus. Notably, the tumor and invaded segment of the aorta could not be separated.

The second step was to isolate and replace the descending aortic segment. After ligating several branches of intercostal arteries and bluntly separating the aorta, a 1 mg/kg dose of heparin was given in a transvenous manner, and the systolic pressure was controlled at approximately 90 mm Hg. Next, the aorta was intercepted by aortic forceps between the distal and proximal sites of the tumor-invading aorta (Fig 2A), followed by resection of the aortic segment 1 cm off the tumor-invading site. Subsequently, an artificial thoracic vascular graft (TERUMO, Shanghai, China) of appropriate diameter was sutured in a continuous manner with 4-0 Prolene (Ethicon, Somerville, NJ) to the margins of the descending aorta (Fig 2B). After finishing the anastomosis, heparin was neutralized with protamine sulfate. The aortic forceps were then alternately removed for aortic patency with the air exhausted, followed by tightening the stitch (Fig 2C). Afterward, the systolic pressure was increased to 110 to 120 mm Hg, and it was confirmed that was no bleeding from the sutured sites.

Additional procedures were performed according to the general principles of esophagectomy. After incision of the diaphragm between the liver and spleen, the stomach was entirely mobilized distal to the pylorus by ligating the gastrolienal ligament, gastrocolic ligament, and left gastric artery. Specifically, the right gastric artery was preserved. The cardia was then excised with a linear cutter (Panther, Beijing, China) and the mobilized stomach was lifted to the esophageal bed below the aortic arch (Fig 2D). Subsequently, the thoracic esophagus was dragged out through the prepared cervical incision. The thoracic esophagus and the tumor-bearing aorta were resected en bloc (Fig 2E). A cervical anastomosis between the stomach and the cervical esophagus was then performed with a circular stapler (Panther, Beijing, China), and the sutures were reinforced. Nasogastric and duodenal tubes were placed across the anastomosis under direct visualization and secured. Prophylactic mass ligation of the thoracic duct was performed in most patients, as described previously [16]. Eventually, mediastinal lymph node and para–left gastric artery lymph node dissections were routinely performed.

After the operation, the specimens were examined histopathologically (Fig 2F), and all patients stayed in the intensive care unit (ICU) to receive parenteral alimentation for the first 3 days. Enteral nutrition was then given on days 4 to 9 postoperatively, and a liquid diet was allowed on postoperative day 7. A semifluid diet was acceptable in most patients on day 9 after the operation.

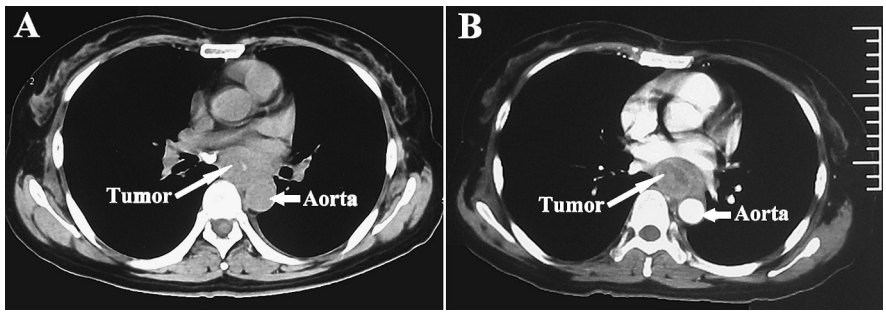

Fig 1. (A) Plain and (B) enhanced chest computed tomographic scans of same patient, suggestive of clinical invasion of esophageal carcinoma (EC) into aorta.

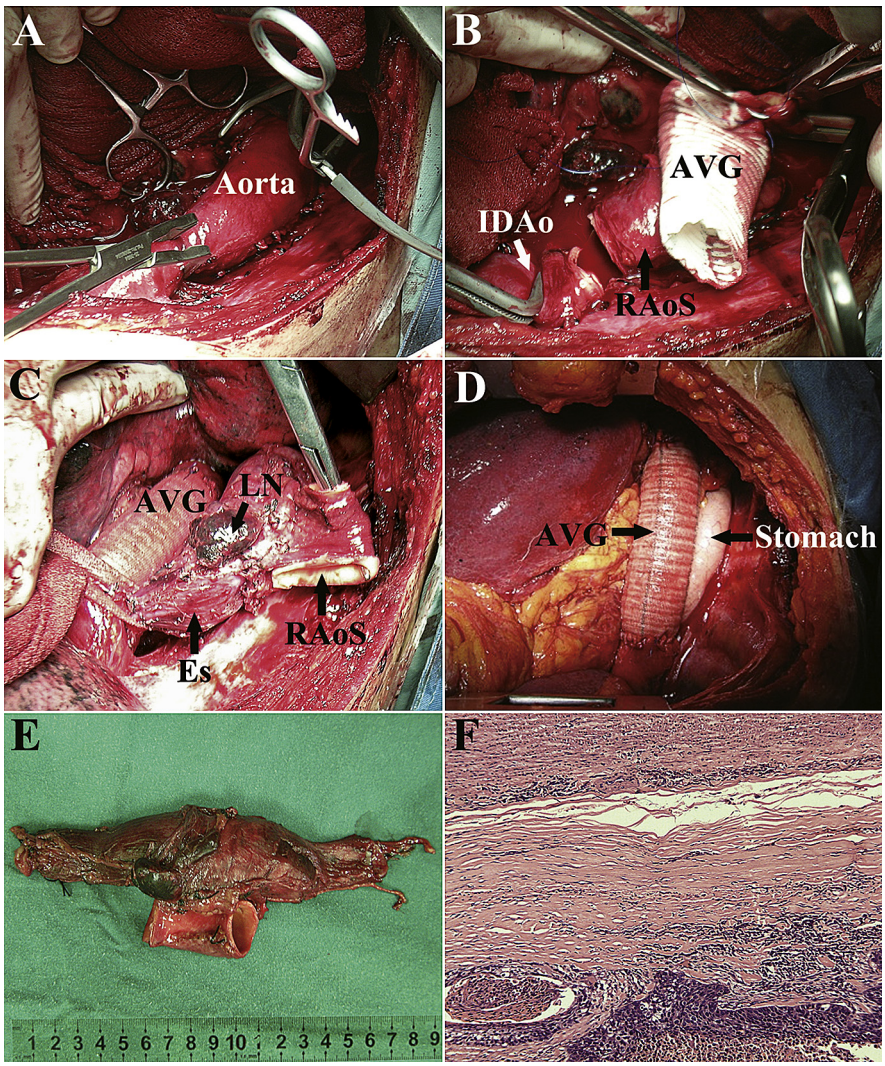

Fig 2. Overview of operation. (A) Descending aorta was intercepted by aortic forceps between distal and proximal sites of tumor-invading aorta. (B, C) Artificial thoracic vascular graft was sutured to margins of aorta, with tight adhesion between tumor and aortic segment not separated. (D) Mobilized stomach was lifted to esophageal bed, and cervical anastomosis was performed. (E) Esophagus and tumor-bearing aortic segment were resected en bloc. (F) Histopathologic invasion of EC into aortic tunica adventitia (hematoxylin and eosin staining, ×200 magnification). (AVG = artificial vascular graft; Es = esophagus; IDAo = intercepted distal aorta; LN = lymph node; RAoS = resected aortic segment.)

Postoperative Chemotherapy

Postoperative adjuvant chemotherapy was recommended to patients approximately 1 month after the operation. The advised regimen consisted of 5-fluorouracil (400 mg/m^2/d as a continuous intravenous infusion for 24 hours from day 1 to day 5 and from day 8 to day 12), and cisplatin (40 mg/m^2/d on days 1 and 8, as an intravenous drip infusion for 2 hours).

Follow-Up and Statistical Analysis

Early postoperative data were collected at the outpatient clinic. Follow-up data were obtained by telephone interview. Survival time was defined as the period from the date of operation until death or the most recent follow-up investigation (March 2012), with no patients lost to follow-up. All statistical analyses were performed using IBM SPSS Statistics, version 21 (SPSS Inc, Chicago, IL). Continuous data were expressed as means ± standard deviation. Categorical data were expressed as percentages. Survival analysis was performed with the Kaplan-Meier method, and the log-rank test was used for comparisons. Paired *t* tests or Wilcoxon signed-rank tests were used to compare preoperative and postoperative differences with no adjustment. $p < 0.05$ was considered statistically significant.

Results

Patient Characteristics

The characteristics of the 47 patients enrolled in this study are summarized in Table 1. The patients included 32 (68%) men and 15 (32%) women, with a mean age of 54.3 ± 9.0 years. The major preadmission symptoms were progressive dysphagia (100%) and weight loss (87.2%). Most patients had a passable Eastern Cooperative Oncology Group performance status [17]. All 47 patients had histopathologically confirmed squamous cell carcinoma, with aortic tunica adventitia invasion in 38 (80.9%) patients and aortic tunica media invasion in 9 (19.1%) patients. All patients had complete

Table 1. Characteristics of 47 Patients with Esophageal Carcinoma Invading the Aorta

Variable	Value
Sex	
Male	32 (68%)
Female	15 (32%)
Age (y)	54.3 ± 9.0
Tumor location	
Upper thoracic	2 (4.2%)
Middle thoracic	24 (51.1%)
Lower thoracic	21 (44.7%)
Tumor size (cm)	7.1 ± 1.7
4–8	33 (70.2%)
>8	14 (29.8%)
Preoperative nodal stage	
cNx	10 (21.3%)
cN0	16 (34.0%)
cN1–N3	21 (44.7%)
Postoperative pathologic analysis	
Depth of aortic invasion	
Tunica adventitia	38 (80.9%)
Tunica media	9 (19.1%)
Pathologic nodal stage	
pN0	29 (61.7%)
pN1	2 (4.3%)
pN2	11 (23.4%)
pN3	5 (10.6%)
ECOG PS	
0–1	19 (40.4%)
2–3	28 (59.6%)

ECOG PS = Eastern Cooperative Oncology Group performance status.

resection (R0 resection), and regional nodal metastasis was found in 18 (38.3%) patients. Most tumors were located in the middle or lower thoracic esophagus, and the tumor size was 4 to 8 cm in 33 (70.2%) patients but greater than 8 cm in 14 (29.8%) patients, with a mean size of 7.1 ± 1.7 cm. Twenty-two (46.8%) patients received postoperative adjuvant chemotherapy for 2.1 ± 1.3 cycles, following our regimen.

Conspicuously enlarged mediastinal lymph nodes were observed in 21 patients (cN1–3) on preoperative computed tomographic images, and positron emission tomography/CT was performed in 3 patients, with positive findings. However, because of the difficulty in determining the number of metastatic lymph nodes [2], the clinical N stage by CT was accurate in only 14 (29.8%) patients with cN0 disease, compared with the accuracy of the pathologic N stage.

Operative Outcomes

The operative and postoperative data are listed in Table 2. The mean operative time and aortic cross-clamp time were 4.9 ± 1.3 hours and 17.0 ± 3.2 minutes, respectively. The mean length of the resected aortic segment was 7.0 ± 2.1 cm, and the average intraoperative blood loss was 227.6 ± 63.3 mL. The mean ventilation period and duration of chest tube drainage were 21.8 ± 4.7 hours and 7.2 ± 2.3 days, respectively. The average drainage volume on the first postoperative day was 220.6 ± 43.2 mL. The mean ICU stay was 3.2 ± 1.8 days. The mean hospital stay and postoperative hospital stay were 23.8 ± 7.7 and 14.3 ± 5.1 days, respectively. The highest postoperative lactic acid and creatinine levels were 1.3 ± 0.27 mmol/L and 51.2 ± 9.4 μmol/L, respectively.

Table 2. Operative Features of Patients Undergoing Radical Esophagectomy Combined With Off-Pump Descending Aorta Replacement

Variable	Value
Operative time (h)	4.9 ± 1.3
Aortic cross-clamp time (min)	17.0 ± 3.2
Resected aortic segment (cm)	7.0 ± 2.1
Ligated intercostal arteries (pair)	2.2 ± 0.9
Intraoperative blood loss (mL)	227.6 ± 63.3
Postoperative ventilation (h)	21.8 ± 4.7
Chest tube drainage (d)	7.2 ± 2.3
Drainage on the first postoperative day (mL)	220.6 ± 43.2
ICU stay (d)	3.2 ± 1.8
Postoperative LOS (d)	14.3 ± 5.1
Highest postoperative lactic acid (mmol/L)	1.3 ± 0.27
Highest postoperative creatinine (μmol/L)	51.2 ± 9.4

ICU = intensive care unit; LOS = length of stay.

Postoperative Complications

Postoperative complications are listed in Table 3. Complications were observed in 59.6% of our patients, with no hospital mortality. Esophageal anastomotic leaks occurred in 4 (8.5%) patients, in whom continuous douching and negative pressure drainage using a homemade double cannula, accompanied with fasting, were performed to facilitate stomal healing. Reoperations were conducted in 3 (6.4%) patients, including reinforced sutures with polytetrafluoroethylene felt patches in the aorta-graft margins in 1 (2.1%) patient with continuous bleeding into the drainage fluid, and ligating the thoracic duct in 2 (4.3%) patients with massive chylopleura. Neither massive bleeding nor arterioesophageal fistula was observed in the postoperative course. Furthermore, wound

Table 3. Postoperative Complications (N = 47)

Complications	Number (%)
Esophageal anastomotic leak	4 (8.5)
Aorta-graft anastomotic bleeding	1 (2.1)
Chylopleura	2 (4.3)
Pneumonia	6 (12.8)
Arrhythmia	6 (12.8)
Wound infection	2 (4.3)
Diarrhea	7 (14.9)
Total	28 (59.6)

infection was found in 2 (4.3%) patients but was controlled after dioxogen irrigation and gauze drainage for approximately 5 days. As the most common complication, diarrhea occurred in 7 (14.9%) patients caused by the adaptation to enteral nutrition, whereas pneumonia and arrhythmia occurred in 6 (12.8%) patients each. None of the 47 patients experienced postoperative paralysis or renal failure.

Comparison Between Preoperative and Early Postoperative Nutritional Status

The comparison between the preoperative and early postoperative (1 month) nutritional status is listed in Table 4. All patients resumed oral nutrition in the early postoperative period, and this dietary mode elicited significant amelioration ($p < 0.001$). There were significant increases in hemoglobin level and the short-form Mini-Nutritional Assessment (MNA-SF) scores [18], which indicated a significant improvement in nutritional status. Early postoperative serum albumin level and body mass index were higher than preoperative values, but the differences did not achieve statistical significance.

Survival Rate

No patients were lost to follow-up. The overall 1-, 3- and 5-year survival rates for 47 patients were 80.9%, 44.7%, and 21.3%, respectively, with a median survival time of 33.6 months (Fig 3A). The 1-, 3- and 5-year survival rates for the 29 patients without regional nodal metastasis were 79.3%, 48.3%, and 27.6%, respectively, with a median survival time of 34.8 months, whereas the corresponding rates for the 18 patients with regional nodal metastases were 83.3%, 38.9%, and 11.1%, respectively, with a median survival time of 20.4 months (Fig 3B). There was a significantly better survival rate in the T4bN0M0 group ($p < 0.05$). Moreover, more patients survived beyond 5 years among those receiving postoperative chemotherapy than those receiving surgical intervention alone (6 versus 4). However, there was no significant difference between the 2 groups ($p = 0.544$) (Fig 3C).

Table 4. Comparison Between Preoperative and Early Postoperative Nutritional Status (N = 47)

Variable	Preoperative	Early Postoperative	*p* Value
Diet mode			<0.001[a]
Jejunostomy	3 (6.4%)	0	
Liquid diet	22 (46.8%)	1 (2.1%)	
Semifluid diet	17 (36.2%)	17 (36.2%)	
Normal diet	5 (10.6%)	29 (61.7%)	
Hemoglobin (g/L)	101.7 ± 8.9	114.1 ± 7.5	0.001[a]
Serum albumin (g/L)	31.4 ± 3.9	39.8 ± 2.4	0.346
BMI (kg/m^2)	18.2 ± 0.94	20.3 ± 0.75	0.078
MNA-SF score	4.6 ± 0.9	8.5 ± 1.1	<0.001[a]

[a] Statistically significant

BMI = body mass index; MNA-SF = Mini-Nutritional Assessment, short-form.

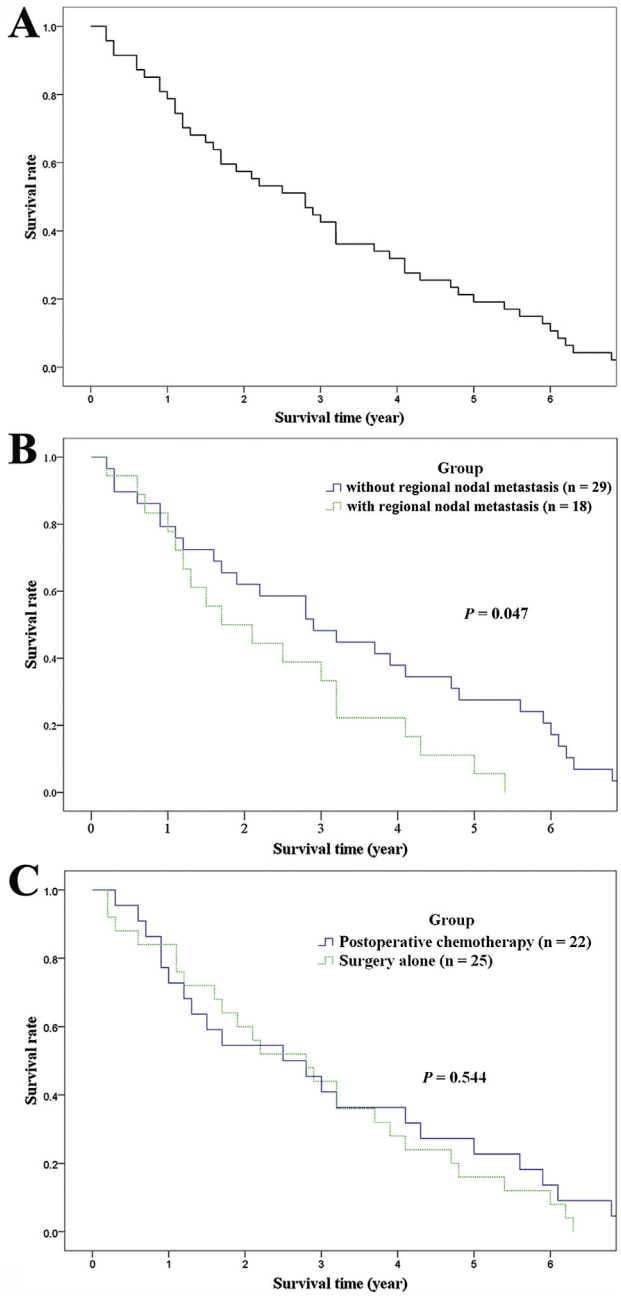

Fig 3. Survival rate (A) for all 47 patients, (B) according to pathologic N status, and (C) according to postoperative therapies.

Comment

In the present study, we demonstrated the feasibility and safety of radical esophagectomy combined with off-pump descending aortic segment replacement in 47 patients with EC invading the aorta. The operation satisfactorily improved the short-term nutritional status and long-term survival of the patients.

In past decades, several surgical trials have been reported in patients with EC invading the aorta. In 1985, Kawahara and associates [11] described a 2-stage operation consisting of an annular resection of the thoracic aorta with an aorta-aorta bypass graft through the left thoracic approach, followed by a subtotal esophagectomy through the right thoracic approach in 1 patient with invasion of EC into the aorta. The patient died of hepatic failure and right pyothorax 4 months after the operation. In 1999, Kabuto and colleagues [12] performed combined resection of the aortic wall using a temporary aorta-aorta bypass together with an upper mediastinal lymph node dissection through a right thoracotomy in 4 patients with EC invading the thoracic aorta. This operation provided a longer survival time with no particular complications in the postoperative course. Ayabe and coworkers [13] proposed that an extended operation with combined resection of the invaded neighboring organs for stage T4b EC could be considered a curative operation for very selected patients to improve their survival.

Normally, EC invading the aorta has been considered a dismal prognosis with a high postoperative mortality risk. The current standard treatment for EC invading aorta includes definitive CRT and a salvage operation with neoadjuvant CRT [4, 6, 10, 19–21]. Taniguchi and associates [4] reported a retrospective analysis of 48 patients with EC with pathologic invasion into the aorta who were treated with concurrent CRT. The 1- and 2-year survival rates were 44% and 25%, respectively, and CRT-related arterioesophageal fistulas were observed in 7 patients (14.6%). Similarly, Shimada and colleagues [6] demonstrated overall 3- and 5-year survival rates of 10% and 5%, respectively, in 268 patients who underwent esophagectomy with adjuvant therapy for stage T4b EC, and the R0 resection rate was only 8% in patients with aortic invasion. However, our present study showed better overall 3- and 5-year survival rates of 44.7% and 21.3%, respectively, with an R0 resection rate of 100%. Consistent with our findings, Matsubara and coworkers [3] reported similar satisfactory survival rates in 34 patients with stage T4b EC who received R0 resections—approximately 47% and 30% for the 3- and 5-year survival rates, respectively. These data suggest that an excellent R0 resection rate with no residual cancer could be achieved by surgical procedures, leading to improved survival.

Interestingly, postoperative chemotherapy did not show any significant benefit in our study (Fig 2C). The lack of a complete regimen in enough patients might partially affect the mentioned results. Conversely, Zenda and coworkers [22] demonstrated that complete response rate in patients with a pre-CRT hemoglobin level of 130 g/L or less was only 24%, whereas the early postoperative hemoglobin level was just 114.1 ± 7.5 g/L in our patients. Therefore, a poor complete response rate may lower the intention of postoperative chemotherapy, not to mention the balance between toxicity and utility [23, 24].

As in advanced stages, patients with EC with aortic invasion generally have large tumors (7.1 ± 1.7 cm) (Table 1), which usually lead to progressive dysphagia and even malnutrition. However, all our patients resumed oral nutrition in the early postoperative period. In particular, 61.7% of patients resumed a normal diet compared with 10.6% before the operation, owing to the successful reconstruction of the upper gastrointestinal region. The increase in MNA-SF scores indicated the success of our surgical procedure in ameliorating the nutritional status of patients.

During the operation, we opened the chest through a left posterolateral incision to expose the esophagus and descending aorta in the same visual field, which might ease the operation in the esophagus and aorta. Unlike other reports [11, 12], all the operations in our study were conducted without the presence of a cardiopulmonary pump or aorta-aorta bypass, which might greatly reduce the extra lesions for patients and simplify the operation. In our experience, the procedure is safe with aortic cross-clamp time less than 30 minutes and average arterial pressures of the lower limbs no less than 60 mm Hg to prevent renal and spinal injuries. The highest postoperative creatinine level was 51.2 ± 9.4 μmol/L in this study (Table 2), indicating healthy postoperative renal function. In addition, the intercostal arteries should be ligated in less than 3 pairs, if possible, to prevent spinal cord ischemia.

Furthermore, chylopleura occurred in 2 patients in the early stages of this study but was cured after urgently ligating the thoracic duct. Based on this, we routinely conducted prophylactic mass ligation of the thoracic duct at the T8–9 vertebral plane for all patients that followed, and no chylopleura was found in the postoperative course, which was in agreement with a previous randomly controlled study [16]. However, we must be aware of the possible occurrence of arterioesophageal fistulas, a fatal complication. To avoid the fistulas, Kawahara and colleagues [11] described a 2-stage operation using bilateral thoracic approaches, whereas we routinely performed cervical anastomosis between the lifted stomach and cervical esophagus in all 47 patients, regardless of the tumor location. With adequate distance between the esophageal stoma and the aortic suture margins, if esophageal anastomotic leaks were to occur, they would not easily implicate the aortic stoma. In fact, neither esophageal anastomotic leaks nor aorta-graft anastomotic bleeding in our patients resulted in arterioesophageal fistulas.

The present study has several limitations. Several comparisons were made with multiple p values with no adjustment, although the clinical data were not normally distributed. Moreover, 5 (10.6%) patients received preoperative CRT, and only 22 (46.8%) patients received postoperative adjuvant chemotherapy in local hospitals. Thus, it is necessary to comprehensively evaluate the effects of adjuvant CRT with follow-up studies. Additionally, we set strict indications for surgical treatment, and consequently, only a small cohort of patients was admitted. Further large-scale study, prospectively if possible, is required to determine whether the surgical indications could be broadened.

In summary, in highly selected patients with locally advanced EC invading the aorta, it is feasible and safe to conduct radical esophagectomy combined with descending aorta replacement without any cardiopulmonary pump or aorta-aorta bypass. This operation can improve nutritional status and survival rates of the patients satisfactorily.

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