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Clinical evaluation of the aberrant left hepatic artery arising from the left gastric artery in esophagectomy

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Abstract

Purpose The left gastric artery (LGA) is commonly severed when the gastric tube is made for esophageal reconstruction. Sacrifice of the LGA can cause liver ischemic necrosis in patients with an aberrant left hepatic artery (ALHA) arising from the LGA. We experienced a case of life-threatening hepatic abscess after severing the ALHA. Therefore, the purpose of this study is to evaluate clinical outcomes of severing the ALHA.

Methods We retrospectively enrolled 176 consecutive patients who underwent esophagectomy with gastric tube reconstruction. They were classified into the ALHA ($N=16$, 9.1%) and non-ALHA ($N=160$, 90.9%) groups. Univariate analysis was performed to compare the clinicopathological variables. Long-term survival was analyzed using the Kaplan–Meier method in matched pair case–control analysis.

Results The postoperative morbidities were not statistically different between the two groups, although serum alanine aminotransferase levels on postoperative days 1 and 3 were significantly higher in the ALHA group (36 IU/L, 14–515; 32 IU/L, 13–295) than in the non-ALHA group (24 IU/L, 8–163; 19 IU/L, 6–180), respectively ($p=0.0055$; $p=0.0073$). Overall survival was not statistically different between the two groups ($p=0.26$).

Conclusions Severe hepatic abscess occurred in 6.3% of the patients with the ALHA after esophagectomy, even though the results presented here found no statistical differences in morbidity or mortality with or without the ALHA. Surgeons should probably attempt to preserve the ALHA especially in patients with altered liver function while making a gastric tube for esophageal reconstruction.

Keywords Aberrant left hepatic artery · Esophagectomy · Esophageal cancer · Hepatic abscess

Abbreviations

LGA	Left gastric artery
ALHA	Aberrant left hepatic artery
CT	Computed tomography
AST	Serum aspartate aminotransferase level
ALT	Serum alanine aminotransferase level
T.Bil	Serum total bilirubin level
COPD	Chronic obstructive pulmonary disease

Introduction

As of 2012, esophageal cancer is the eighth most common cancer and the sixth leading cause of cancer-related mortality worldwide. Its 5-year survival rate is reported to be 15–20% [1, 19]. Esophagectomy with lymphadenectomy is the best curative therapy for localized esophageal cancer; however, postoperative mortality and mobility of esophagectomy are still high [18]. To reduce the mobidity rate, anastomosis of the esophageal remnant to the stomach could be the most suitable method of digestive tract reconstruction with respect to blood supply [21]. A gastric tube constructed from the greater curvature is commonly selected for digestive tract reconstruction, and the left gastric artery (LGA) must be severed when the gastric tube is made.

The most common anatomical variant of concern in constructing the gastric tube is aberrant left hepatic artery (ALHA) arising from the LGA [8]. ALHA includes both

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the replaced left hepatic artery and the accessory left hepatic artery [16]. The ALHA runs within the gastrohepatic ligament through the left sagittal groove, anterior to the caudate lobe and into the left lateral lobe of the liver. The frequency of this anatomical abnormality has been reported to be 4.3–22.4% [15]. Sacrifice of the LGA in a patient with ALHA can result in abnormal liver function. Lethal hepatic ischemia or left lobe hepatic necrosis caused by ligation of the ALHA in gastrectomy have been reported [10].

We also experienced a life-threatening complication in a patient with ALHA who suffered from hepatic abscess after esophagectomy with gastric tube reconstruction. The patient was a 70-year-old man. He underwent endoscopic submucosal dissection for early esophageal squamous cell carcinoma located in the upper esophagus. The size of the tumor was 50 mm × 38 mm. Its depth was to the level of the muscularis mucosae (T1a) and the vertical margin was negative. However, the horizontal margin could not be evaluated and the tumor was positive for lymphovascular invasion. Therefore, the esophagectomy was performed 7 weeks after endoscopic submucosal dissection. Video-assisted thoracic surgery was followed by hand-assisted laparoscopic surgery. The ALHA was severed using a bipolar vessel sealing device (LigaSure™ Maryland Jaw 37 cm, Medtronic, MN, USA.) during dissection of the lesser omentum (Fig. 1a, b). After subtotal esophagectomy, the anastomosis of the esophageal remnant with the gastric tube was conducted via the posterior mediastinal route as usual. On postoperative day 6, the patient's temperature increased to 40 °C. Contrast CT showed multiple hepatic abscesses localized in the left lobe of the liver (Fig. 1c). Each abscess was too small to puncture. Administration of 1.5 g/day of doripenem hydrate was initiated; however, a diagnosis of disseminated intravascular coagulation was made on postoperative day 9. The patient was then transferred to the intensive care unit. 30 mg/day of prednisolone therapy was added as well because the patient also suffered from acute exacerbation of chronic obstructive pulmonary disease (COPD). After the hepatic abscesses and COPD symptoms improved, the patient left the intensive care unit on postoperative day 17. The patient was discharged on the postoperative day 45. Pathological findings on postoperative day 15 revealed a residual tumor 6 mm in size and no lymph node metastasis. The patient has been followed up without recurrence for 12 months.

We hypothesize that to severe the ALHA may increase postoperative morbidity or mortality. However, clinical outcomes have not been fully evaluated in patients with ALHA in whom a gastric tube was constructed following esophagectomy. Therefore, the aim of this retrospective study was to evaluate the clinical implications of severing the ALHA in esophagectomy with gastric tube reconstruction.

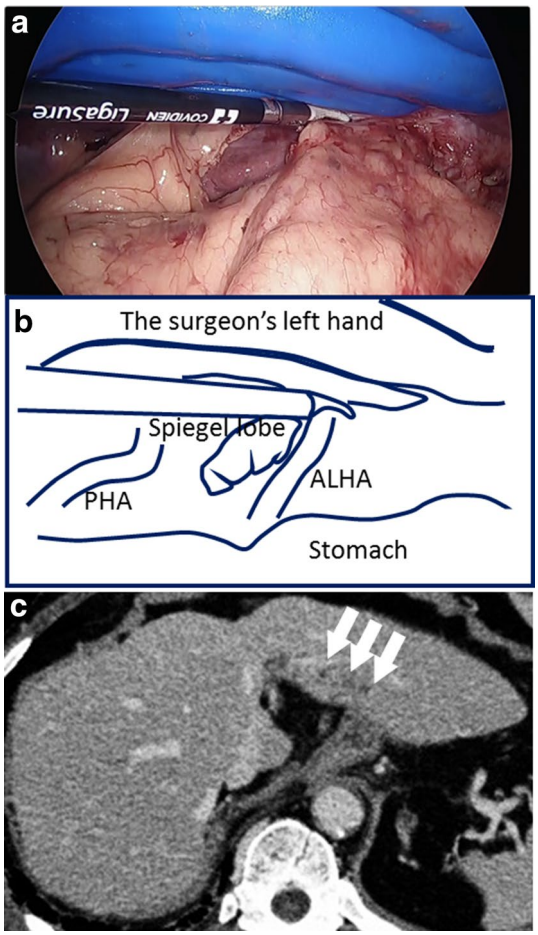

Fig. 1 Case presentation. **a** Intraoperative endoscopic photograph of the presented case during hand-assisted laparoscopic surgery. The ALHA was cut using a bipolar vessel-sealing device, while the lesser omentum was dissected to make the gastric tube. The edge of the Spiegel lobe of the liver was dull. **b** Schema of the endoscopic image. PHA; proper hepatic artery. **c** Postoperative CT revealed multiple hepatic abscesses localized in the left lobe (arrows). The edge of the liver was dull

Methods

Patient selection

In this study, we retrospectively enrolled 197 consecutive patients who underwent esophagectomy for esophageal cancer from January 2005 to December 2016 in our institute. Informed consent was obtained from each patient. Five patients were excluded because preoperative abdominal computed tomography (CT) had not been performed. The ileum and the right-sided colon were used as a digestive conduit in 12 patients and the jejunum was used in 4 patients. They were also excluded. Finally, a total of 176 patients with gastric tube were included. Sixteen of these had ALHA (ALHA group) and the other 160 patients

(non-ALHA group) did not. In only one patient of the ALHA group, the ALHA was preserved during operation at the surgeon's discretion (Fig. 2).

Data collection of the ALHA group and the non-ALHA group

Pre- and post-operative demographics, laboratory and radiographic data were collected and analyzed. We performed univariate analysis to compare clinicopathological variables and surgical outcomes between the ALHA group and the non-ALHA group. The diameter of the LGA was measured on contrast CT images, because Kim et al. [8] pointed out the correlation between the ALHA and the diameter of the LGA. TNM classification and pathological stage were based on the 10th edition of the Japanese Classification of Esophageal Cancer [7]. Minimally invasive surgeries consisted of video-assisted thoracic surgery or hand-assisted laparoscopic surgery. Anastomotic leakage was diagnosed clinically or by CT images and anastomotic stricture was defined from endoscopic findings. Postoperative morbidity was classified by Clavien–Dindo classification [2]. Serum aspartate aminotransferase level (AST), serum alanine aminotransferase level (ALT) and total bilirubin level (T.Bil) were measured on preoperative day 1, the day of the operation, and on postoperative days 1, 3, 7, and 14, respectively.

Statistical analysis

We used EZR 1.33 statistical software (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphic user interface for R software (The R Foundation for Statistical Computing, Vienna, Austria) [6]. Categorical variables were analyzed with the χ^2 test or Fisher's exact test. Continuous variables were expressed as medians and ranges and compared with Wilcoxon signed-rank test. Long-term survival was analyzed by matched pair case–control analysis and log-rank test by using the Kaplan–Meier method. All results were judged as significant when p values were less than 0.05.

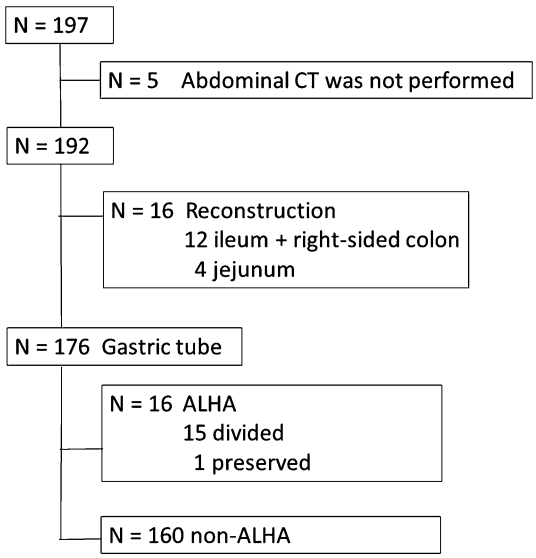

Fig. 2 Patient selection

Ethics

This study was approved by the ethics committee of NTT Medical Center Tokyo (Approval number: 16–87).

Results

Univariate analysis of clinicopathological variables

Comparisons of clinicopathological variables between the ALHA group and the non-ALHA group are shown in Table 1. ALHA was detected in 16/176 patients (9.1%). There were no significant differences in the preoperative clinical settings. The median diameter of the LGA in the ALHA group was statistically different from that in the non-ALHA group, at 3.3 mm (range 2.1–5.7 mm) and 2.4 mm (range 1.1–4.0 mm), respectively ($p = 0.000051$). The cutoff value of the LGA diameter was determined to be 2.9 mm from the receiver operating characteristic curve (Fig. 3). The area under the curve was 0.863. ALHA was detected in 13 of 37 patients (35%) whose LGA was ≥2.9 mm in diameter. As for pathological factors, a statistical difference was observed in the grade of lymph node metastasis ($p = 0.017$).

Univariate analysis of surgical outcomes

Surgical outcomes of the ALHA group and the non-ALHA group are described in Table 2. Operative time was significantly longer in the ALHA group than in the non-ALHA group ($p = 0.043$). The number of dissected lymph nodes was not statistically different between the ALHA group and the non-ALHA group. There were no significant differences in morbidities.

Comparison of perioperative serum hepatobiliary enzyme level

Median ALT on postoperative day 1 was higher in the ALHA group than in the non-ALHA group at 36 (range 14–515) and 24 (range 8–163), respectively ($p = 0.0055$). Median ALT on postoperative day 3 was 32 (range 13–295) and 19 (range 6–180) in the ALHA and non-ALHA groups, respectively ($p = 0.0073$). The trend of the median value of each is shown graphically in Fig. 4. Both

Table 1 Comparison of clinicopathological variables between the ALHA and non-ALHA groups

	ALHA group ($n=16$)	Non-ALHA group ($n=160$)	p value
Sex			
Male/female	13/3	133/27	0.74
Age (year)	63 (49–77)	66 (44–87)	0.41
BMI (kg/m^2)	22.2 (14.5–28.6)	21.0 (12.7–29.3)	0.18
Smoking			
Yes (%)	11 (69%)	18 (83%)	0.18
Alcohol			
Yes (%)	13 (81%)	146 (91%)	0.19
Diabetes mellitus			
Yes (%)	1 (6.2%)	24 (27%)	0.25
Hypertension			
Yes (%)	1 (6.2%)	18 (11%)	1.0
COPD			
Yes (%)	3 (19%)	35 (22%)	1.0
Neoadjuvant chemotherapy			
Yes (%)	2 (13%)	15 (9.4%)	0.66
Diameter of LGA (mm)	3.3 (2.1–5.7)	2.4 (1.1–4.0)	0.000051*
Tumor location			
Ce	1	6	0.36
Ut	4	17	
Mt	6	76	
Lt	5	51	
Ae	0	10	
T factor			
T1	6	67	0.24
T2	4	14	
T3	6	70	
T4	0	9	
N factor			
N0	9	62	0.017*
N1	0	51	
N2	7	37	
N3	0	9	
N4 (M1)	0	1	
Pathological stage			
0	3	15	0.74
I	3	30	
II	3	42	
III	7	66	
IVa	0	7	

ALHA aberrant left hepatic artery, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *LGA* left gastric artery, *Ce* cervical esophagus, *Ut* upper thoracic esophagus, *Mt* middle thoracic esophagus, *Lt* lower thoracic esophagus, *Ae* abdominal esophagus

*$p<0.05$

AST and ALT tended to be higher in the ALHA group than in the non-ALHA group (Fig. 4a, b). ALT on postoperative day 7 was higher than on postoperative day 3 in both groups (Fig. 4b). There was no significant difference in

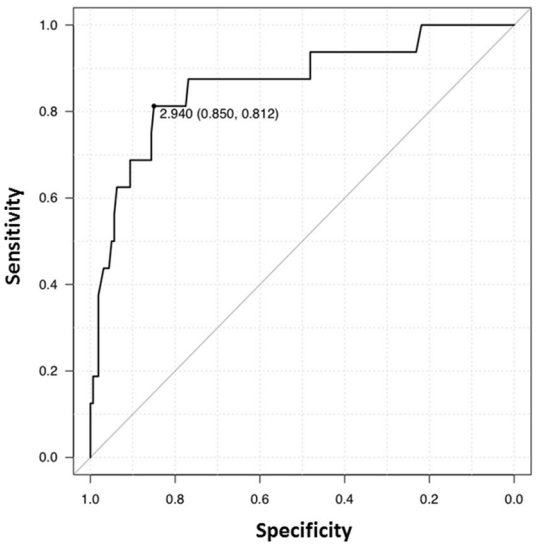

Fig. 3 Receiver operating characteristic curve showing the relation between ALHA and LGA diameter. The cutoff value for LGA diameter was determined to be 2.9 mm. The area under the curve was 0.863

T.Bil (Fig. 4c). Values of perioperative AST, ALT and T.Bil are shown in Online Resource 1.

Long-term outcomes in the ALHA and non-ALHA groups

Matched pair case–control analysis was performed to compare long-term outcomes because the grade of lymph node metastasis, one of the prognostic factors in esophageal cancer [7], was significantly different between the ALHA group and the non-ALHA group (Table 1). Sixteen patients were extracted from the non-ALHA group for matched pair case–control analysis according to the grade of lymph node metastasis. There was no statistical difference in overall survival between the ALHA group and the non-ALHA group ($p = 0.26$) (Fig. 5).

Discussion

This study revealed that dividing the ALHA in making gastric tube for esophageal reconstruction could result in postoperative transient elevation of hepatobiliary enzyme levels. However, sacrificing the ALHA did not statistically confer postoperative morbidity or mortality, while life-threatening hepatic abscess occurred in 1 of 16 patients with ALHA.

The findings of Kim et al. [8] indicated that the ALHA should be preserved during laparoscopic gastrectomy when the diameter of the LGA is ≥ 5 mm. They determined a cutoff value for LGA diameter by comparing an ALHA-ligated group with an ALHA-preserved group. ALHA was detected in 35% of patients whose LGA was ≥ 2.9 mm in diameter in our study. Our results suggest that there is a risk of postoperative liver infarction even when the LGA is less than 5 mm in esophagectomy patients.

In previous studies on gastrectomy, ALT often peaked on postoperative day 1 and decreased by postoperative day 7, and lethal complications were extremely rare [5, 8, 14, 17]. However, in our study, ALT on postoperative day 7 was higher than that on postoperative days 1 and 3. This might be because esophagectomy is more invasive than gastrectomy.

Other possible reasons for postoperative elevation of liver enzymes can be assumed. Miyayama et al. mentioned extrahepatic collateral pathways supplying hepatocellular carcinoma in the left lobe of the liver [13]. That is, we could sacrifice the left inferior phrenic, right and left internal mammary, right and left gastric, cystic, and omental arteries in esophagogastrectomy. In addition, previous studies on laparoscopic surgery have reported that direct liver retraction and elevation of peritoneal pressure by the pneumoperitoneum can reduce portal venous blood flow and cause liver injury. One case of postoperative necrosis of the left lobe of the liver was reported in whom the necrosis was related to the use of a liver retractor during laparoscopic-assisted total gastrectomy [9]. The time to press the left lobe of the liver using a liver retractor during operation may tend to be longer in esophagectomy than in gastrectomy. The amount of intraoperative anesthetic agents and postoperative analgesics may also cause hepatic toxicity. The effect on postoperative liver function of sacrificing the ALHA in esophagectomy should be carefully estimated.

Preoperative liver disease is not rare in patients with esophageal cancer because esophageal cancer and liver dysfunction share the etiology of excessive alcohol consumption. Valmasoni et al. [19] reported in their single-center study that pulmonary and infectious complications had occurred in 24.7 and 31.5% of cirrhotic patients, respectively, and both rates were significantly higher than those of non-cirrhotic patients. Yasuda et al. [20] introduced a two-stage operation for patients with esophageal cancer concomitant with liver dysfunction. Huang et al. [5] reported that when the accessory left hepatic artery, which is a subtype of ALHA, was severed during radical gastrectomy, the postoperative increase of AST and ALT was more accelerated in patients with chronic liver disease than in those without chronic liver disease. Extra caution may be needed before dividing the ALHA in patients with chronic liver disease during radical esophagectomy.

We reported one patient with hepatic abscess after esophagectomy with gastric tube reconstruction. Hepatic abscess is most commonly caused via biliary disease, while liver ischemic necrosis after arterial embolization may serve as a nidus for infection and can also cause abscess [11]. In our patient, the hepatic abscess could not be definitively

Table 2 Comparison of surgical outcomes between the ALHA and non-ALHA groups

	ALHA group ($n=16$)	Non-ALHA group ($n=160$)	p value
Operative time (min)	391 (279–502)	355 (189–591)	0.043*
Blood loss (ml)	355 (60–2290)	305 (40–1720)	0.21
Transfused			
Yes (%)	3 (19%)	13 (8.1%)	0.17
Procedure			
Thoracotomy and laparotomy	12	133	0.49
Minimally invasive surgery	4	27	
Reconstruction route			
Posterior mediastinal	11	129	0.34
Retrosternal	1	10	
Antesternal	4	21	
Jejunostomy			
Yes (%)	8 (50%)	51 (32%)	0.17
Lymph node dissection			
Three fields	13	108	0.40
Others	3	52	
Number of dissected lymph nodes	45 (14–91)	49 (0–181)	0.82
Overall morbidity			
Anastomotic leakage	3 (19%)	14 (8.8%)	0.19
Anastomotic stricture	6 (38%)	38 (24%)	0.24
Respiratory disorder	3 (19%)	56 (35%)	0.27
Clavien-Dindo $\geq$ 3a	8 (50%)	50 (31%)	0.16
Time to first flatus (day)	4 (2–7)	4 (1–14)	0.69
Time to first intake food (day)	7 (7–7)	4 (2–49)	0.40
Day to discharge (day)	22 (12–170)	19 (12–214)	0.43
Mortality	0 (0%)	2 (1.2%)	1.0
Overall survival (day)	1601 (187–3236)	975 (9–4279)	0.34

ALHA aberrant left hepatic artery

*$p<0.05$

attributed to the division of the ALHA, because the arterial flow had been maintained on postoperative CT. Previous reports have revealed that three anastomotic pathways were present from the right to the left hepatic artery, namely, hilar anastomoses, translobar vessels and capsular arteries. The arterial flow of the left lobe was restored within no more than 10 h after arterial ligation, and therefore lethal hepatic necrosis would have been prevented [12]. We were able to assume that our patient had had chronic liver disease because the edge of the liver was dull in CT images and intraoperative findings. We might have opted to preserve the ALHA with consideration of preventing postesophagectomy liver infarction. Additionally, the possibility of lymph node metastasis is extremely low in T1a esophageal cancer [18].

Our matched pair case–control analysis showed no significant difference in overall survival between the ALHA group and the non-ALHA group. Moreover, the number of dissected lymph nodes was not statistically different between the ALHA group and the non-ALHA group. Shinohara et al. reported no significant difference in dissected lymph nodes and metastatic lymph nodes around the LGA between ALHA-divided and ALHA-preserved groups who underwent curative gastrectomy [17]. The ALHA could be preserved even in patients with advanced-stage esophageal cancer who required aggressive lymphadenectomy. However, further prospective study will be needed to confirm the oncological neccesity of preservation of the ALHA.

Minimally invasive surgery has been applied to esophagectomy [18]; however, Hemming et al. [3] reported the method of open esophagogastrectomy in the presence of ALHA arising from the left hepatic artery in 1992. Oki et al. [15] described laparoscopic gastrectomy with preservation of the ALHA. Hess et al. [4] reported five cases with replaced left hepatic artery, which is another subtype of ALHA, in whom robotic-assisted minimally invasive esophagectomy was performed. It could be technically feasible to preserve the ALHA to prevent postoperative liver infarction during minimally invasive esophagogastrectomy.

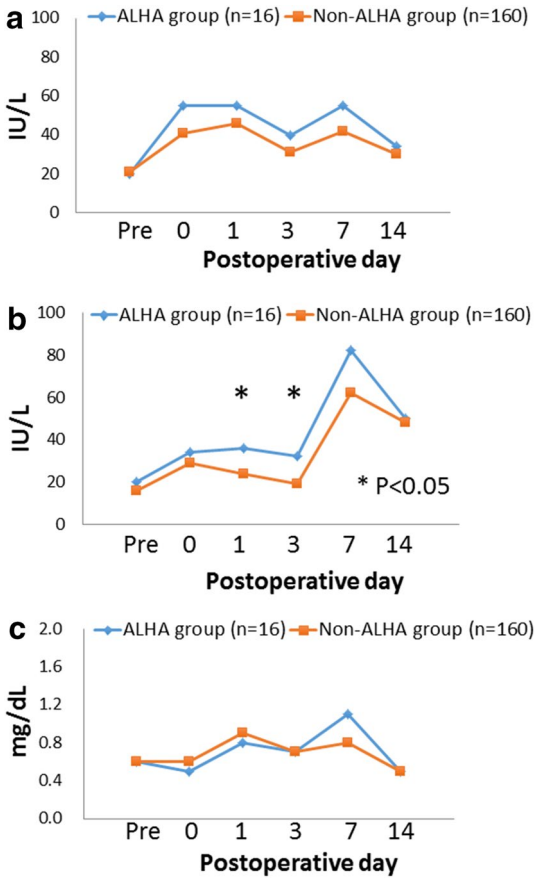

Fig. 4 Trends of perioperative liver function tests. ALHA; aberrant hepatic artery. **a** Aspartate aminotransferase (AST). **b** Alanine aminotransferase (ALT). **c** Total bilirubin (T.Bil)

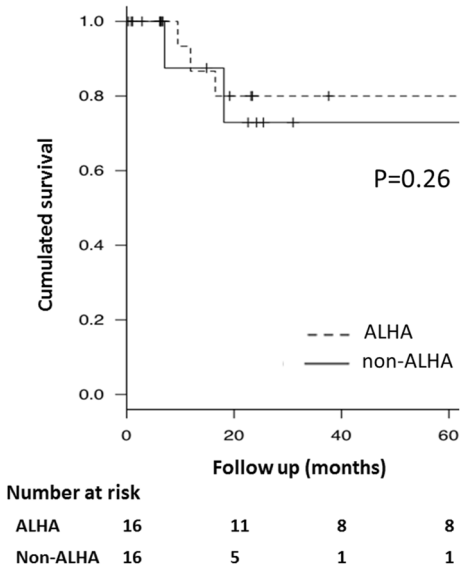

Fig. 5 Kaplan–Meier curve of overall survival in matched pair case–control analysis

Our study has several limitations. First, this was a retrospective study with a limited number of cases. The statistical power of this study is short. We were not able to confirm either the clinical safety of dividing the ALHA or the oncological necessity of preserving the ALHA. Second, ALHA was detected in 9.1% of patients in our study. This rate was relatively low compared with previous investigations of liver transplantation patients and similar to those of preoperative angiography [15]. The incidence of ALHA might be underestimated by CT findings. Further prospective studies in a large number of patients should be conducted to confirm the clinical significance of ALHA in esophagectomy.

Conclusion

Severe hepatic abscess occurred in 6.3% of the patients with the ALHA after esophagectomy, even though the results presented here found no statistical differences in morbidity or mortality with or without the ALHA. Surgeons should probably attempt to preserve the ALHA especially in patients with altered liver function in making a gastric tube for esophageal reconstruction.

Authors' contribution HM: project development, data collection and analysis and manuscript writing. HS: manuscript editing. SS, KN, AN, KW, SN and KF: rounds on patients. YH: manuscript editing.

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Compliance with ethical standards

Conflict of interest We have no conflict of interest to declare.

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