# ORIGINAL

# Treatment results of two-stage operation for the patients with esophageal cancer concomitant with liver dysfunction

Mitsuhiro Yasuda[1], Hiroshi Saeki[2], Yuichiro Nakashima[2], Takafumi Yukaya[1,2], Satoshi Tsutsumi[2], Hirotada Tajiri[2], Yoko Zaitsu[2], Yasuo Tsuda[2], Yuta Kasagi[2], Koji Ando[2], Yu Imamura[2], Kippei Ohgaki[2], Tomohiko Akahoshi[1,2,3], Eiji Oki[2], and Yoshihiko Maehara[1,2]

[1]Emergency and Critical Care Center, Kyushu University Hospital, Fukuoka, Japan, [2]Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, [3]Department of Disaster and Emergency of Medicine, Kyushu University, Fukuoka, Japan

**Abstract : Purpose : The aim of this study was to clarify the usefulness of two-stage operation for the patients with esophageal cancer who have liver dysfunction. Methods : Eight patients with esophageal cancer concomitant with liver dysfunction who underwent two-stage operation were analyzed. The patients initially underwent an esophagectomy, a cervical esophagostomy and a tube jejunostomy, and reconstruction with gastric tube was performed after the recovery of patients' condition. Results : The average time of the 1st and 2nd stage operation was 410.0 min and 438.9 min, respectively. The average amount of blood loss in the 1st and 2nd stage operation was 433.5 ml and 1556.8 ml, respectively. The average duration between the operations was 29.8 days. The antesternal route was selected for 5 patients (62.5%) and the retrosternal route was for 3 patients (37.5%). In the 1st stage operation, no postoperative complications were observed, while, complications developed in 5 (62.5%) patients, including 4 anastomotic leakages, after the 2nd stage operation. Pneumonia was not observed through two-stage operation. No in-hospital death was experienced. Conclusion : A two-stage operation might prevent the occurrence of critical postoperative complications for the patients with esophageal cancer concomitant with liver dysfunction. J. Med. Invest. 62 : 149-153, August, 2015**

## INTRODUCTION

Although the treatment and management of esophageal cancer have evolved in recent years, with advances in diagnostic techniques and the development of chemoradiotherapy, surgery remains the cornerstone therapy of localized esophageal cancer (1-3). However, the surgical procedure is associated with an extremely high mortality rate as well as morbidity rate. Our previous study showed, not only a remarkable improvement in the patients' prognosis after esophageal surgery but also a marked decrease in the mortality and morbidity rates (4), whereas, a significant number of severe postoperative complications developed and some of them caused in-hospital death (5).

In patients with liver disease, there is high operative mortality and morbidity after gastrointestinal and portal hypertension surgery (6-8). Because of the etiologic relationship between alcohol consumption and both liver dysfunction and esophageal cancer, liver dysfunction occasionally is encountered in candidates for esophageal cancer surgery (9). Due to the attendant risk of liver dysfunction, extensive esophageal resections sometimes are contraindicated. In cases indicated for operation for esophageal cancer coexisting liver dysfunction, a thorough preoperative evaluation including the assessment of liver function is required along with selection of an appropriate procedure and perioperative phase management.

A two-stage operation was particularly applied for high-risk patients in the late 20th century (10, 11). Esophageal cancer usually occurs in elderly patients who often have coexisting diseases, and these co-morbidities can impair the tolerance of patients to the invasiveness of esophageal surgery. Therefore, we have recently readopted a two-stage operation for such high-risk patients (12).

In this study, we have evaluated our experience of 8 two-stage operations performed for the patients with esophageal cancer concomitant with liver dysfunction. We herein show the usefulness of this procedure for such high risk candidates.

## PATIENTS AND METHODS

### Patients

Two hundred sixty nine patients underwent esophagectomy for esophageal cancer between April, 2005 and December, 2013, at the Department of Surgery and Science, Kyushu University Hospital in Japan. Among them, 8 patients with thoracic esophageal squamous cell carcinoma underwent a two-stage operation by reason of liver dysfunction. The surgical results after the two-stage operation for those patients were analyzed in this study.

### Indications of two-stage operation

The two-stage operation was indicated either mainly for the "patient factor" when the patients' general condition was not retained to tolerate conventional esophagectomy and one-stage reconstruction, or for the "operation factor" when the operation itself was complicated and invasive for patients or that an unexpected event happened during esophagectomy (12). In a patient with chronic liver disease, the degree of liver damage was evaluated according to the Child-Pugh classification and the classification presented by the Liver Cancer Study Group of Japan (13), which consists of the factors such as the presence of controllable ascites, a serum bilirubin level, a serum albumin level, an indocyanine

green retention rate at 15 min, and a prothrombin activity. The two-stage operation was applied when the patient fit at least two categories among the presence of controllable ascites, a serum bilirubin level of 2.0-3.0 mg/dl, a serum albumin level of 3.0-3.5 g/dl, an indocyanine green retention rate of 15-40% at 15 min, and a prothrombin activity of 50-80% and/or a typical liver cirrhosis pattern (irregular or nodular surface and/or dull edge of the liver) was presented by CT scan. Other criteria were described in the previous paper (12).

Table 1 summarizes the patients' backgrounds. The average age of the patients was 65.3 years old (range : 59-74 years old). All patients were male. The underlying liver disease was alcoholic liver damage in 7 patients and hepatitis type C in 1 patient. One patient was categorized into Child-Pugh B, while other 7 patients into Child-Pugh A. Three patients were categorized into liver damage grade B by classification of the Liver Cancer Study Group of Japan, while other 4 patients into grade A. The average of the indocyanine green retention rate at 15 min was 20.9% (range : 7.2-33.5%). The preoperative chemoradiotherapy was performed for 3 patients including definitive chemoradiotherapy for 1 patient. For case #7, the definitive chemoradiotherapy (total of 70 Gy) was indicated for the synchronous hypopharyngeal cancer, on the other hand the preoperative chemoradiotherapy (total of 41.4 Gy) was simultaneously performed for the cStage I esophageal cancer in order to avoid disease progression while definitive chemoradiotherapy for the hypopharyngeal cancer.

### Methods of two-stage operation

The 1st stage operation consists of a resection of the thoracic esophagus, cervical esophagostomy and tube jejunostomies. A right thoracotomy was followed by esophagectomy as well as mediastinal lymphadenectomy. The distal part of the esophagus was dissected and cut with a linear stapler at the level of the esophago-cardial junction. The upper thoracic esophagus was also cut with the stapler. A tube for nutrition is inserted into distal part of jejunum after minimal laparotomy, while another tube is also inserted into the proximal jejunum to avoid excessive pressure in the distal margin of the esophagus. We prefer jejunostomy to gastrostomy for nutrition, because gastrostomy may be disadvantageous for reconstruction with gastric tube. We usually start the enteral nutrition on the 3rd postoperative day after the 1st stage operation. The cervical esophagostomy was made. Cervical lymphadenectomy was performed at the 1st stage operation if indicated. The timing of the 2nd operation is based on the time when the performance status recovered to the same level as that before the 1st stage operation. Laparotomy was followed by abdominal lymph node dissection. A narrow gastric tube, 3.5 cm in width was made (14). The gastric tube was pulled via either the subcutaneous or retrosternal route to the neck. Cervical anastomosis was performed with either hand sutures or the triangular stapling method (15). The splenectomy was performed for 3 patients ; for the purpose of portal decompressing effect for case #1 (16), and to control bleeding the splenic hilum for case #5 and #6.

### Post-operative complications

Surgical complications, such as anastomotic leakage, pyothorax or chylothorax, and wound infection which required for drainage were evaluated. Regarding medical complications, not only pulmonary complications such as pneumonia and hypoxia requiring re-intubation, but also cardiac complications, such as severe arrhythmia, myocardial infarction, and pulmonary embolism were examined.

### Staging of the tumor

The clinicopathological factors were evaluated according to the guidelines for clinical and pathologic studies on carcinoma of the esophagus (17). The staging of the tumor was based on the TNM classification defined by UICC (18) and depth of invasion and lymph node metastasis were defined by clinical findings.

## RESULTS

### Surgical results

Table 2 shows the surgical results and postoperative complications. The average time of the 1st stage operation was 410.0 min (range, 204-625 min), while that of the 2nd stage operation was 438.9 min (range ; 362-557 min). The average amount of blood loss in the 1st stage operation was 433.5 ml (range, 125-720 ml), while that in the 2nd stage operation was 1556.8 ml (range ; 319-5086 ml). The average duration between 1st stage operation and the 2nd stage operation was 29.8 days (range, 10-90 days). The gastric tube was used as the reconstructed organ for all patients. The antesternal route was selected for 5 patients (62.5%) and the retrosternal route was for 3 patients (37.5%).

### Postoperative complications

After the 1st stage operation, no postoperative complications were observed. On the other hand, postoperative complications developed in 5 (62.5%) patients after the 2nd stage operation. Anastomotic leakage developed in 4 patients (50.0%) and it was successfully treated by a repair operation with the major pectoral muscle in two patients (19). Left pleural effusion occurred in 1 patient. The transverse colon perforation occurred after 2nd stage operation and the temporal ileostomy was made on 15th postoperative day in case #8. In the 2nd stage operation of case #8, the adhesion was observed in the peritoneal cavity. We suggested that the late phase

Table 1. Clinical backgrounds

| Case # | Age | Sex | Location | cStage | Type | Child-Pugh | Liver damage* | ICGR15 | Preoperative therapy |
|--------|-----|-----|----------|--------|------|-----------|---------------|--------|----------------------|
| 1 | 61 | Male | Mt | cT1b N0 M0 Stage I | Alcoholic | B | B | 33.5 | dCRT |
| 2 | 74 | Male | Mt | cT3 N0 M0 Stage IIA | Alcoholic | A | B | 27.4 | none |
| 3 | 59 | Male | Mt | cT3 N1 M0 Stage III | HCV | A | A | 17.9 | none |
| 4 | 65 | Male | Mt | cT3 N1 M0 Stage III | Alcoholic | A | A | 18.0 | NACRT |
| 5 | 68 | Male | Lt | cT1a N0 M0 Stage I | Alcoholic | A | A | 7.2 | none |
| 6 | 64 | Male | Mt | cT1b N0 M0 Stage I | Alcoholic | A | B | 29.4 | none |
| 7 | 67 | Male | Lt | cT1b N0 M0 Stage I | Alcoholic | A | A | 12.9 | NACRT |
| 8 | 64 | Male | Lt | cT1b N0 M0 Stage I | Alcoholic | A | A | 15.0 | none |

HCV : hepatitis type C ; dCRT : definitive chemoradiotherapy ; NACRT : neoadjuvant chemoradiotherapy
*The classification presented by the Liver Cancer Study Group of Japan.

Table 2.   Surgical results and postoperative complications

| Case # | 1st, OT (min) | 1st, BL (ml) | 1st, complications | Interval (days) | Reconstruction | 2nd, OT (min) | 2nd, BL (ml) | 2nd, complications |
|---|---|---|---|---|---|---|---|---|
| 1 | 204 | 125 | none | 90 | gastric tube/AS | 362 | 2068 | none |
| 2 | 625 | 691 | none | 21 | gastric tube/AS | 486 | 1420 | leak |
| 3 | 354 | 400 | none | 10 | gastric tube/RS | 407 | 518 | none |
| 4 | 566 | 720 | none | 21 | gastric tube/AS | 404 | 855 | leak |
| 5 | 420 | 624 | none | 27 | gastric tube/AS | 436 | 1610 | none |
| 6 | 356 | 400 | none | 18 | gastric tube/AS | 557 | 5086 | leak, pleural effusion |
| 7 | 347 | 250 | none | 28 | gastric tube/RS | 376 | 578 | leak |
| 8 | 408 | 258 | none | 23 | gastric tube/RS | 483 | 319 | colon perforation |

OT : operation time ; BL : blood loss ; AS : antesternal ; RS : retrosternal

colon perforation occurred due to injury of marginal artery of transvers colon resulted from adhesiolysis during the 2nd stage operation. Pneumonia was not observed through 1st and 2nd stage operation. We evaluated the degree of ascites and the increase of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) after the 1st and 2nd stage operation, using Common Terminology Criteria for Adverse Events (CTCAE) ver.4.0 grading scale. As a result, no major complications (CTCAE grade$\geqq$3) were observed both after the 1st and 2nd stage operation. No in-hospital death was experienced in this series.

Figure 1 shows the images of representative case (case #5). The patient was 68 year-old male. He had a history of heavy alcohol drinking and smoking. The endoscopy examination revealed the multiple Lugol-voiding lesions on middle and lower thoracic esophagus. The pathological examination from biopsy specimen revealed moderately squamous cell carcinoma. His liver function was evaluated as Child-Pugh A and grade A by the classification of the Liver Cancer Study Group of Japan. However, the findings from CT scan indicated typical liver cirrhosis pattern. He underwent a two-stage operation and had uneventful clinical course.
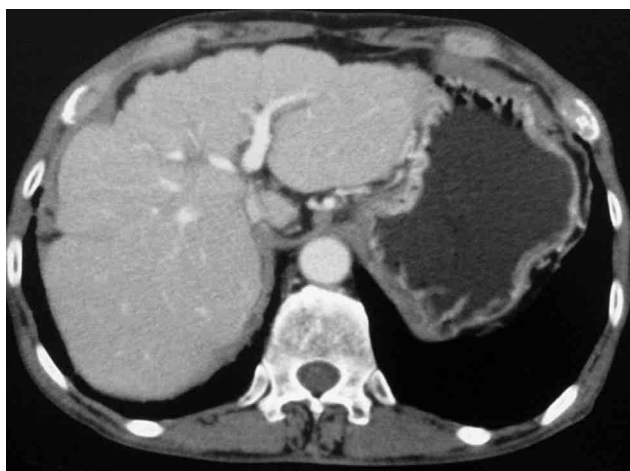


Figure 1.   The CT findings of representative case who underwent the two-stage operation.

## DISCUSSION

The patients with esophageal cancer are often accompanied with chronic hepatitis or cirrhosis, since alcohol abuse could be a common etiological risk of both diseases. Although the major cause of chronic liver disease in Japanese patients is viral infection, most of the patients in this study were alcoholics. This may be attributable to the carcinogenic property of alcohol in esophageal squamous cell carcinoma, which is the dominant histological type of esophageal cancer in Japan (20-23). In general, there are the various postoperative complications likely occurred in the patients with liver dysfunction : impairment of hepatic function, increased ascites, increased susceptibility to infection and hemorrhagic tendency. Besides these, anastomotic leakage occurs as frequently as 13% to 83% in operations involving reconstruction of the gastrointestinal tract and has been reported to be associated with a fatal outcome if accompanied by pyothorax and sepsis (9). It has indicated that depressed hemoglobin oxygen saturation consequent to reduced arterial blood inflow, increased shunt blood flow caused by congestion of the reconstructed gastric tube and delay of wound healing possibly account for the high incidence of anastomotic leakage in those patients (24). Therefore, special attentions are required when we establish the treatment strategy for those patients.

In previous study, Fekete *et al.* (9) reported the treatment results of esophagogastrectomy for carcinoma of the esophagus or cardia performed for 23 patients with liver cirrhosis. They demonstrated that 6 patients (26%) died after operation and the only significant preoperative predictor of mortality was a prothrombin time less than or equal to 60% of normal. Tachibana *et al.* (25) reported that 3 (16.7%) out of 18 patents with esophageal cancer concomitant with liver cirrhosis died of postoperative complications. They also showed that patients who had both weight loss and hypoalbuminemia had a significantly higher mortality rate than those who did not. In the current study, no in-hospital death due to postoperative complications occurred in any patients, which suggests the safety of two-stage operation for the patients with esophageal cancer concomitant with liver dysfunction.

The mortality rates from leakage and from sepsis in cirrhotic patients were reported to be 50-66% and 60-67%, respectively (9, 25). One possible reason for the high mortality rate due to septic complications is that cirrhotic patients are under severe immunosuppressive conditions to tolerate infectious attack (26). Anastomotic leakage developed in 4 patients in this study. However, we have never experienced the fetal complications following anastomotic leakage. Pulmonary infection also is a well-known cause of in-hospital death after esophageal surgery (4, 27). We previously reported that postoperative pneumonia might be associated with subsequent anastomotic insufficiency (28). In this study, pneumonia was not observed both after 1st and 2nd stage operation. Especially for patients associated with severe liver dysfunction, the surgical stress of esophagectomy followed by reconstruction might be too excessive to overcome. The liver dysfunction can result in increasing blood loss especially in the 2nd stage operation due to portal hypertension. In fact, the amount of blood loss (including ascites)

in the 2nd stage operation was larger than that in the 1st operation in this study. When the gastric tube was made, the right (No. 1) and left (No. 2) cardiac, along the lesser curvature (No. 3), and along the left gastric artery (No. 7) lymph nodes were usually dissected. However, we think that abdominal lymph nodes dissection could be minimized to avoid large amount of blood loss for the patients with portal hypertension.

Regarding therapeutic strategy for high-risk patients, it seems to be a reasonable idea that definitive chemoradiotherapy should be initially indicated since it may be effective and less invasive. In patients with liver cirrhosis, nevertheless, it is common that pancytopenia and esophageal varices due to hypersplenism are present even prior to treatment of the cancer. Eventually, worsening of these complications occurs owing to adverse events associated with radiation therapy combined with chemotherapy such as myelosuppression, esophagitis and liver dysfunction, and hence to failure in accomplishing the treatment. There is also a risk of rupture of esophageal varices. Furthermore, salvage esophagectomy for either remnant or recurrent disease would be difficult in such extremely high-risk patients due to the severe general risk and long term toxicity (29-32). As a result, such patients would lose the chance for the cure of the disease. Therefore, we have principally indicated two-stage operation for high risk patients who fulfill the criteria of organ function (12), while carefully taking account on the patients' general status and social background as well as the overall predicted surgical stress.

The prolonged hospital stay is a disadvantage of two-stage operation. It may not only induce mental stress and be an economic burden to the patient, but also results in the delay of treatment if the patient has either abdominal lymph node metastasis. When a staged operation is indicated, special attention should be paid to such possible disadvantages. The duration between the 1st and 2nd stage operation varies between the patients. Early and adequate recovery from surgical stress of the esophagectomy is warranted ; however, high-risk patients often took a long time to recover. Full recovery of nutrition as well as performance status is essential for the 2nd stage operation. Early enteral feeding is superior to parenteral nutrition for the recovery after esophagectomy (33). We, therefore, establish tube jejunostomy and adopt enteral nutrition as soon as possible after the 1st stage operation.

We have readopted the two-stage operation, with the goal of achieving increased resectability as well as in order to perform a safer operation in high risk patients. We believe that a two-stage operation would be less invasive surgery and it should be aggressively performed for the patients with esophageal cancer concomitant with liver dysfunction. Further investigations concerning two-stage operation for such poor risk patients are required.

## SOURCES OF SUPPORT

## REFERENCES

1.  Altorki N, Skinner D : Should en bloc esophagectomy be the standard of care for esophageal carcinoma? Ann Surg 234 : 581-587, 2001
2.  Muller JM, Erasmi H, Stelzner M, Zieren U, Pichlmaier H : Surgical therapy of oesophageal carcinoma. Br J Surg 77 : 845-857, 1990
3.  Earlam R, Cunha-Melo JR : Oesophogeal squamous cell carcinoms : II. A critical view of radiotherapy. Br J Surg 67 : 457-461, 1980
4.  Morita M, Yoshida R, Ikeda K, Egashira A, Oki E, Sadanaga N, Kakeji Y, Yamanaka T, Maehara Y : Advances in esophageal cancer surgery in Japan : an analysis of 1000 consecutive patients treated at a single institute. Surgery 143 : 499-508, 2008
5.  Morita M, Nakanoko T, Fujinaka Y, Kubo N, Yamashita N, Yoshinaga K, Saeki H, Emi Y, Kakeji Y, Shirabe K, Maehara Y : In-hospital mortality after a surgical resection for esophageal cancer : analyses of the associated factors and historical changes. Ann Surg Oncol 18 : 1757-1765, 2011
6.  Mosnier H, Farges O, Vons C, Belghiti J, Fekete F : Gastroduodenal ulcer perforation in the patient with cirrhosis. Surg Gynecol Obstet 174 : 297-301, 1992
7.  Lehnert T, Herfarth C : Peptic ulcer surgery in patients with liver cirrhosis. Ann Surg 217 : 338-346, 1993
8.  Garrison RN, Cryer HM, Howard DA, Polk HC, Jr. : Clarification of risk factors for abdominal operations in patients with hepatic cirrhosis. Ann Surg 199 : 648-655, 1984
9.  Fekete F, Belghiti J, Cherqui D, Langonnet F, Gayet B : Results of esophagogastrectomy for carcinoma in cirrhotic patients. A series of 23 consecutive patients. Ann Surg 206 : 74-78, 1987
10.  Sugimachi K, Kitamura M, Maekawa S, Matsufuji H, Kai H, Okudaira Y : Two-stage operation for poor-risk patients with carcinoma of the esophagus. J Surg Oncol 36 : 105-109, 1987
11.  Saito T, Shimoda K, Shigemitsu Y, Kinoshita T, Miyahara M, Kobayashi M : Extensive lymphadenectomy for thoracic esophageal carcinoma : a two-stage operation for high-risk patients. Surg Today 24 : 610-615, 1994
12.  Morita M, Nakanoko T, Kubo N, Fujinaka Y, Ikeda K, Egashira A, Saeki H, Uchiyama H, Ohga T, Kakeji Y, Shirabe K, Ikeda T, Tsujitani S, Maehara Y : Two-stage operation for high-risk patients with thoracic esophageal cancer : an old operation revisited. Ann Surg Oncol 18 : 2613-2621, 2011
13.  Liver Cancer Study Group of Japan. General rules for clinical and pathological study of primary liver cancer. Second English Edition. Tokyo : Kanehara & Co., Ltd., 2003.
14.  Sugimachi K, Ikeda M, Kai H, Ueo H, Okudaira Y, Inokuchi K : Assessment of the blood flow in various gastric tubes for esophageal substitutes. J Surg Res 33 : 463-468, 1982
15.  Toh Y, Sakaguchi Y, Ikeda O, Adachi E, Ohgaki K, Yamashita Y, Oki E, Minami K, Okamura T : The triangulating stapling technique for cervical esophagogastric anastomosis after esophagectomy. Surg Today 39 : 201-206, 2009
16.  Kawanaka H, Akahoshi T, Kinjo N, Iguchi T, Ninomiya M, Yamashita YI, Ikegami T, Yoshizumi T, Shirabe K, Maehara Y : Effect of laparoscopic splenectomy on portal haemodynamics in patients with liver cirrhosis and portal hypertension. Br J Surg 101 : 1585-1593, 2014
17.  Japanese Society of Esophageal Diseases. Japanese Classification of Esophageal Cancer (Tenth Edition) Tokyo : Kanehara & Co., Ltd., 2008.
18.  UICC International Union Against Cancer. TNM classification of Malignant Tumors (6th Edition). New York : Wiley, 2002.
19.  Morita M, Ikeda K, Sugiyama M, Saeki H, Egashira A, Yoshinaga K, Oki E, Sadanaga N, Kakeji Y, Fukushima J, Maehara Y : Repair using the pectoralis major muscle flap for anastomotic leakage after esophageal reconstruction via the subcutaneous route. Surgery 147 : 212-218, 2010
20.  Morita M, Kumashiro R, Kubo N, Nakashima Y, Yoshida R, Yoshinaga K, Saeki H, Emi Y, Kakeji Y, Sakaguchi Y, Toh Y, Maehara Y : Alcohol drinking, cigarette smoking, and the development of squamous cell carcinoma of the esophagus : epidemiology, clinical findings, and prevention. Int J Clin Oncol 15 : 126-134, 2010

21. Toh Y, Oki E, Ohgaki K, Sakamoto Y, Ito S, Egashira A, Saeki H, Kakeji Y, Morita M, Sakaguchi Y, Okamura T, Maehara Y : Alcohol drinking, cigarette smoking, and the development of squamous cell carcinoma of the esophagus : molecular mechanisms of carcinogenesis. Int J Clin Oncol 15 : 135-144, 2010

22. Saeki H, Ohno S, Miyazaki M, Araki K, Egashira A, Kawaguchi H, Watanabe M, Morita M, Sugimachi K : p53 protein accumulation in multiple oesophageal squamous cell carcinoma : relationship to risk factors. Oncology 62 : 175-179, 2002

23. Saeki H, Ohno S, Araki K, Egashira A, Kawaguchi H, Ikeda Y, Morita M, Kitamura K, Sugimachi K : Alcohol consumption and cigarette smoking in relation to high frequency of p53 protein accumulation in oesophageal squamous cell carcinoma in the Japanese. Br J Cancer 82 : 1892-1894, 2000

24. Kato T, Motohara T, Kaneko Y, Shikishima H, Okushiba S, Kondo S, Kato H : Two cases of esophageal cancer with portal hypertension : esophagectomy with venous shunt procedure. Hepatogastroenterology 48 : 1656-1658, 2001

25. Tachibana M, Kotoh T, Kinugasa S, Dhar DK, Shibakita M, Ohno S, Masunaga R, Kubota H, Kohno H, Nagasue N : Esophageal cancer with cirrhosis of the liver : results of esophagectomy in 18 consecutive patients. Ann Surg Oncol 7 : 758-763, 2000

26. Caly WR, Strauss E : A prospective study of bacterial infections in patients with cirrhosis. J Hepatol 18 : 353-358, 1993

27. Morita M, Yoshida R, Ikeda K, Egashira A, Oki E, Sadanaga N, Kakeji Y, Ichiki Y, Sugio K, Yasumoto K, Maehara Y : Acute lung injury following an esophagectomy for esophageal cancer, with special reference to the clinical factors and cytokine levels of peripheral blood and pleural drainage fluid. Dis Esophagus 21 : 30-36, 2008

28. Saeki H, Masuda T, Okada S, Ando K, Sugiyama M, Yoshinaga K, Endo K, Sadanaga N, Emi Y, Kakeji Y, Morita M, Yamashita N, Maehara Y : Impact of perioperative peripheral blood values on postoperative complications after esophageal surgery. Surg Today 40 : 626-631, 2010

29. Ishikura S, Nihei K, Ohtsu A, Boku N, Hironaka S, Mera K, Muto M, Ogino T, Yoshida S : Long-term toxicity after definitive chemoradiotherapy for squamous cell carcinoma of the thoracic esophagus. J Clin Oncol 21 : 2697-2702, 2003

30. Saeki H, Morita M, Tsuda Y, Hidaka G, Kasagi Y, Kawano H, Otsu H, Ando K, Kimura Y, Oki E, Kusumoto T, Maehara Y : Multimodal treatment strategy for clinical T3 thoracic esophageal cancer. Ann Surg Oncol 20 : 4267-4273, 2013

31. Oki E, Morita M, Kakeji Y, Ikebe M, Sadanaga N, Egasira A, Nishida K, Koga T, Ohata M, Honboh T, Yamamoto M, Baba H, Maehara Y : Salvage esophagectomy after definitive chemoradiotherapy for esophageal cancer. Dis Esophagus 20 : 301-304, 2007

32. Morita M, Kumashiro R, Hisamatsu Y, Nakanishi R, Egashira A, Saeki H, Oki E, Ohga T, Kakeji Y, Tsujitani S, Yamanaka T, Maehara Y : Clinical significance of salvage esophagectomy for remnant or recurrent cancer following definitive chemoradiotherapy. J Gastroenterol 46 : 1284-1291, 2011

33. Gabor S, Renner H, Matzi V, Ratzenhofer B, Lindenmann J, Sankin O, Pinter H, Maier A, Smolle J, Smolle-Juttner FM : Early enteral feeding compared with parenteral nutrition after oesophageal or oesophagogastric resection and reconstruction. Br J Nutr 93 : 509-513, 2005