



Contents lists available at ScienceDirect

## International Journal of Surgery Case Reports

journal homepage: [www.casereports.com](http://www.casereports.com)

# Salvage photodynamic therapy accompanied by extended lymphadenectomy for advanced esophageal carcinoma: A case report



Takahiro Nishida<sup>a,\*</sup>, Shinsuke Takeno<sup>a</sup>, Koji Nakashima<sup>b</sup>, Masato Kariya<sup>b</sup>, Haruhiko Inatsu<sup>b</sup>, Kazuo Kitamura<sup>b</sup>, Atsushi Nanashima<sup>a</sup>

<sup>a</sup> Division of Gastrointestinal, Endocrine and Pediatric Surgery, Department of Surgery, University of Miyazaki Faculty of Medicine, Miyazaki, Japan

<sup>b</sup> Division of Circulation and Body Fluid Regulation, University of Miyazaki Faculty of Medicine, Miyazaki, Japan

## ARTICLE INFO

## Article history:

Received 11 April 2017

Received in revised form 22 May 2017

Accepted 22 May 2017

Available online 26 May 2017

## Keywords:

Esophageal cancer

Definitive chemoradiotherapy

Salvage surgery

Appleby operation

Photodynamic therapy

## ABSTRACT

**INTRODUCTION:** Salvage surgery for locoregional failures after definitive chemoradiotherapy (dCRT) for esophageal cancer is widely practiced, but treatment options complementing it are also needed due to the high morbidity and mortality and low rate of curative resection.

**PRESENTATION OF CASE:** A 58-year-old man with a surgical history of right upper lobectomy for lung cancer was diagnosed as having esophageal squamous cell carcinoma. Computed tomography revealed swelling of the lesser curvature lymph node, and it had invaded the stomach, the body and tail of the pancreas and the left gastric artery, splenic artery and celiac artery. The patient underwent definitive-dose radiation with chemotherapy. Complete response was attained for the primary tumor, but the metastatic lymph node infiltrating the stomach, pancreas and major vessels remained. Therefore, the Appleby operation was proposed to the patient and subsequently performed aiming at curability. However, the primary tumor recurred 38 months after surgery, so the novel modality of photodynamic therapy using talaporfin sodium and a diode laser was performed, and a complete response was attained for this lesion. The patient is alive at 50 months after the salvage Appleby operation.

**DISCUSSION AND CONCLUSION:** Salvage lymphadenectomy for esophageal cancer may be insufficient as a curative treatment because of regrowth of the primary lesion. However, photodynamic therapy may be applicable as a curative treatment option for recurrence of the primary lesion after salvage lymphadenectomy.

© 2017 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Definitive chemoradiotherapy (dCRT) for esophageal cancer is one of the options for curative treatment. dCRT tends to be performed not only for advanced lesions but also early-stage lesions for the purpose of radical cure, organ preservation, and functional preservation. However, the rate of recurrence or persistence of carcinoma after dCRT still remains high with rates ranging from 12 to 55% [1–4]. Salvage surgery for locoregional failures after dCRT is widely practiced, but its high morbidity, high mortality and the low rate of curative resection need to be improved. In some cases, only

lymph node metastasis remained, although a complete response could be obtained for the primary tumor. Salvage lymphadenectomy can be an option for local disease control, but its clinical efficacy is controversial.

The authors report a case of esophageal cancer for which photodynamic therapy (PDT) was performed for recurrence of the primary tumor after a salvage Appleby operation for post-dCRT remnant lymph node metastasis. The presented case has been reported in line with the SCARE criteria [5].

## 2. Presentation of case

A 58-year-old man with a surgical history of right upper lobectomy for lung cancer complained of difficulty swallowing and weight loss of 6 kg in one month and was admitted to hospital. Routine laboratory tests showed increased levels of tumor markers such as squamous cell carcinoma (SCC) and CYFRA. Endoscopic examination showed a slightly elevated-type and flat-type tumor about 60 mm in diameter in the middle thoracic esophagus (Fig. 1A)

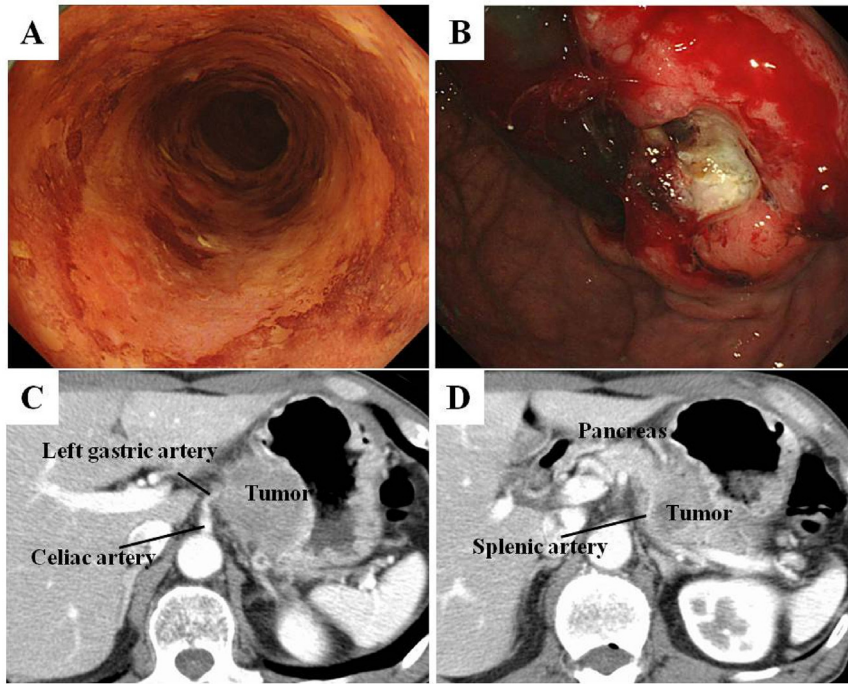
**Abbreviations:** CA, celiac artery; CHA, common hepatic artery; dCRT, definitive chemoradiotherapy; LGA, left gastric artery; PDT, photodynamic therapy; SCC, squamous cell carcinoma; SpA, splenic artery.

\* Corresponding author at: Division of Gastrointestinal, Endocrine and Pediatric Surgery, Department of Surgery, University of Miyazaki Faculty of Medicine, 5200 Kihara Kiyotake, Miyazaki, 889-1692, Japan.

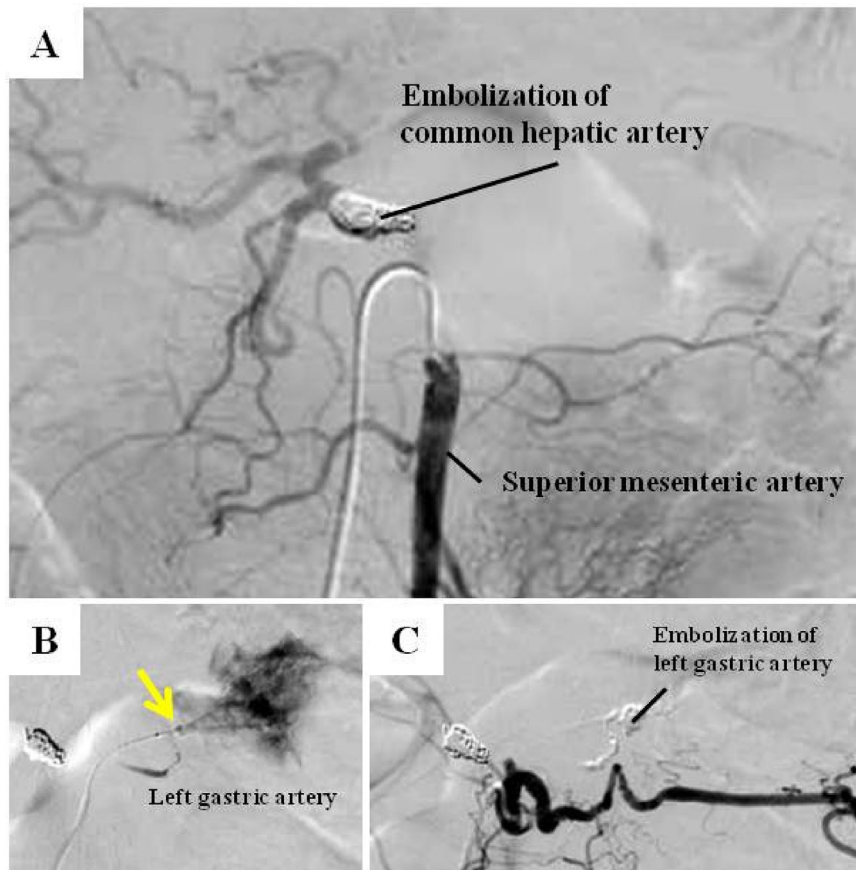
E-mail address: [takahiro.nishida@med.miyazaki-u.ac.jp](mailto:takahiro.nishida@med.miyazaki-u.ac.jp) (T. Nishida).

<http://dx.doi.org/10.1016/j.ijscr.2017.05.025>

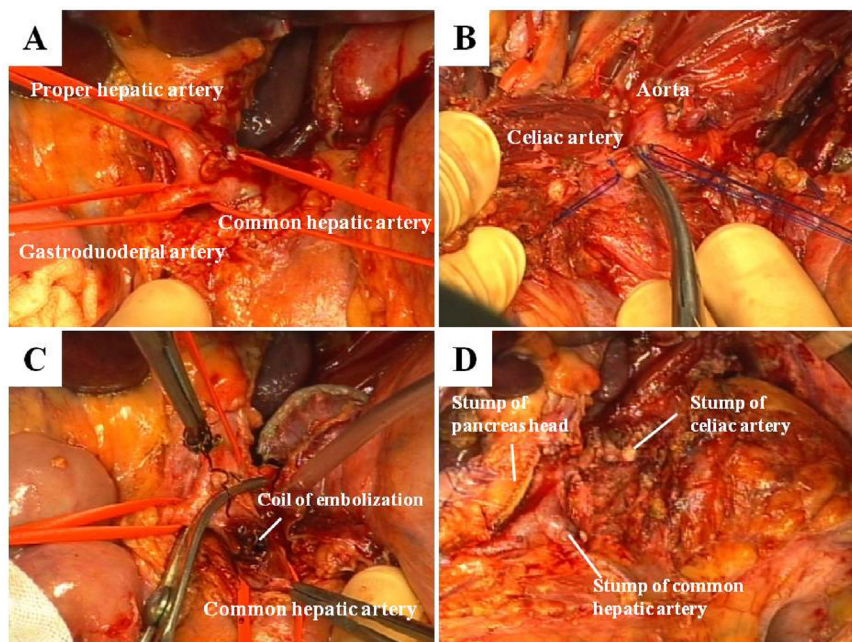
2210-2612/© 2017 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



**Fig. 1.** Endoscopic examination shows a slightly elevated-type and flat-type tumor in the middle thoracic esophagus (A) and an ulcerative-type tumor in the cardia of the stomach (B). Contrast-enhanced abdominal computed tomography reveals swelling of the lesser curvature lymph node, which invades the stomach, the body and tail of the pancreas and the left gastric artery, splenic artery and celiac artery (C, D).



**Fig. 2.** Preoperative angiography. Conversion of hepatic blood flow by coil embolization of the common hepatic artery (A). On day 7 after embolization, urgent hemostasis via interventional radiology was performed (C) due to major bleeding (arrow) from the LGA (B).



**Fig. 3.** Intraoperative findings. Taping of the common hepatic artery, proper hepatic artery and gastroduodenal artery (A). Cutting of the celiac artery (B). Removal of the embolization coil and cutting of the common hepatic artery (C). Condition after total gastrectomy, distal pancreatectomy, splenectomy, cholecystectomy, and D2 lymph node dissection (D).

and an ulcerative-type tumor about 35 mm in diameter in the cardia of the stomach (Fig. 1B). Biopsy of these tumors revealed moderately differentiated SCC. The depth of esophageal tumor invasion was estimated to be in the submucosal layer. Computed tomography revealed swelling of the lesser curvature lymph node, and it involved the stomach, the body and tail of the pancreas and the left gastric artery (LGA), splenic artery (SpA) and celiac artery (CA) (Fig. 1C, D). Positron emission tomography-computed tomography showed significant 18F-fluorodeoxyglucose accumulation in the swollen lymph node. The patient underwent definitive-dose radiation (50.4 Gy) concurrently with chemotherapy consisting of standard-dose cisplatin and 5-fluorouracil (2 courses, cisplatin at 70 mg/m<sup>2</sup> on days 1 and 29 + 5-fluorouracil at 700 mg/m<sup>2</sup> on days 1–4 and 29–32). Complete response was obtained the primary tumor, but the metastatic lymph node infiltrating the stomach, pancreas and major vessels remained. The Appleby operation was proposed to the patient as curative lymphadenectomy after conversion of blood flow by coil embolization of common hepatic artery (CHA) (Fig. 2A). On day 7 after embolization, urgent hemostasis via interventional radiology was performed due to major bleeding from the LGA (Fig. 2B, C), followed by surgery. Total gastrectomy, distal pancreatectomy, splenectomy, cholecystectomy and D2 lymph node dissection were performed by the Appleby procedure (Fig. 3), followed by reconstruction using the jejunum (Roux-en-Y method). The resected specimen showed a mass 63 × 46 mm in diameter on the serosal surface of the gastric cardia involving the pancreas, SpA and LGA (Fig. 4). The histopathological diagnosis was SCC, which was node metastasis derived from the esophageal carcinoma. The resected surface was free of cancer cells. Endoscopic examination and biopsy at 38 months after surgery revealed recurrence of the primary lesion in the middle thoracic esophagus (Fig. 5A, B). The depth of tumor invasion was estimated to be in the submucosal layer. Because the patient refused another highly invasive procedure, i.e., salvage endoscopic submucosal dissection and salvage esophagectomy, minimally invasive PDT using talaporfin sodium and a diode laser was attempted (Fig. 5C). Complete response was obtained for the

primary lesion (Fig. 5D), and the patient is alive at 50 months after the salvage Appleby operation.

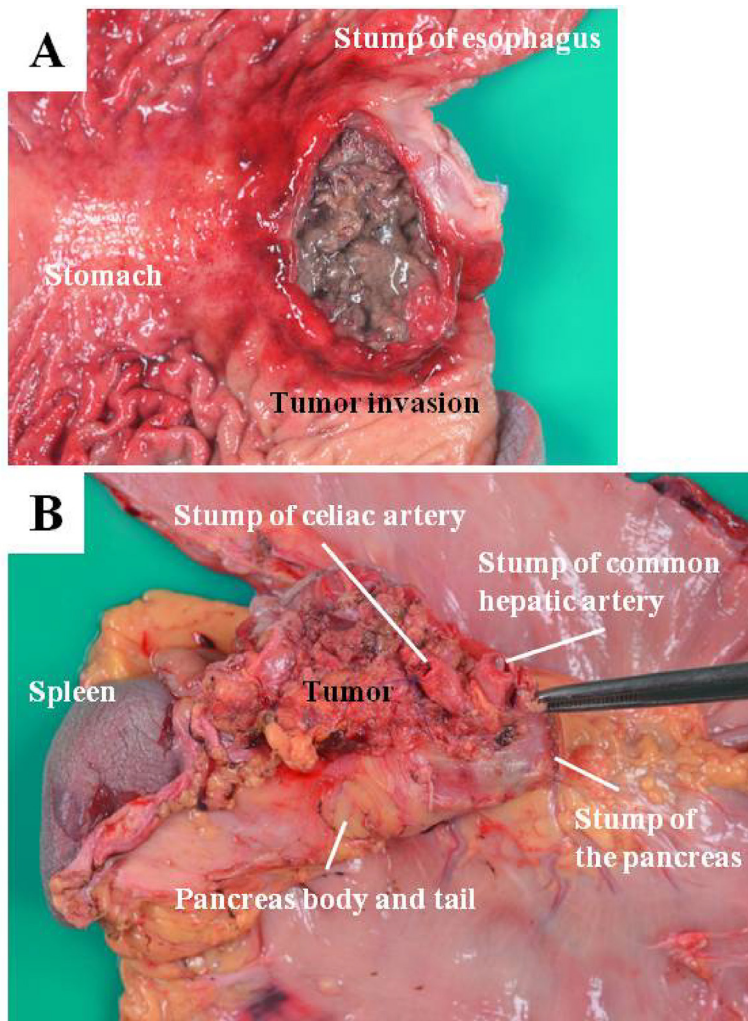
### 3. Discussion

Salvage esophagectomy after dCRT for esophageal cancer has been reported for which the morbidity and mortality are high and the rate of curative resection is still low. The factors of high morbidity, high mortality and a low rate of curative resection negatively affect long-term patient survival [6]. Some studies have reported respective rates of morbidity and mortality of 63–89% and 7.9–22.2%, and the rate of curative resection in cT4 patients is approximately 20% [6–8]. In contrast, salvage lymphadenectomy for local recurrence or persistence after dCRT has been reported that is safe compared to salvage esophagectomy and is an effective treatment option [9–11]. Matono et al. [9] reported that patient survival after salvage lymphadenectomy is not worse than that after salvage esophagectomy.

In the present report, the patient had a surgical history of right lobectomy for lung cancer, and complete response had been obtained for the primary tumor after dCRT; thus, an esophagectomy was not performed. Because the remnant metastatic lymph nodes involved the stomach, pancreas, SpA and CA, the Appleby operation was required for radical resection.

The Appleby operation was first described by Appleby in 1953 for the purpose of controlling retroperitoneal invasion of gastric carcinoma and clearance of lymph nodes along the celiac axis [12]. Recently, the procedure has been performed not only for gastric cancer but also for pancreatic cancer [13], but there are few reports of its use in esophageal carcinoma. In general, the morbidity of the Appleby operation is high. Specific complications include liver necrosis (4.8%), gallbladder necrosis (9.2%), duodenal necrosis, anastomotic leakage (10.8%) and pancreatic fistula (7.2%) [14]. These complications are based on the ischemia related to ligation of the CHA, and securing the blood flow of the proper hepatic artery supplied by the superior mesenteric artery is essential. Therefore, we performed preoperative angiography to secure hepatic blood flow through the pancreaticoduodenal arcade from the superior





**Fig. 4.** Macroscopic findings. The resected specimen shows a mass of 63 × 46 mm in diameter on the gastric cardia (A) that infiltrates the pancreas, splenic artery and left gastric artery (B).

mesenteric artery with balloon occlusion of the CHA, and then embolized the CHA. During the operation, a cholecystectomy was added to prevent gallbladder necrosis. The bleeding that occurred from the LGA after embolism may have been affected by an increase in the blood flow of the LGA due to the conversion of blood circulation. The effect of tumor self-destruction was also considered, and the cause of the bleeding remains unclear. In cases in which R0 resection is possible, the Appleby operation, which prevent complications as much as possible, is considered to be one option for salvage surgery.

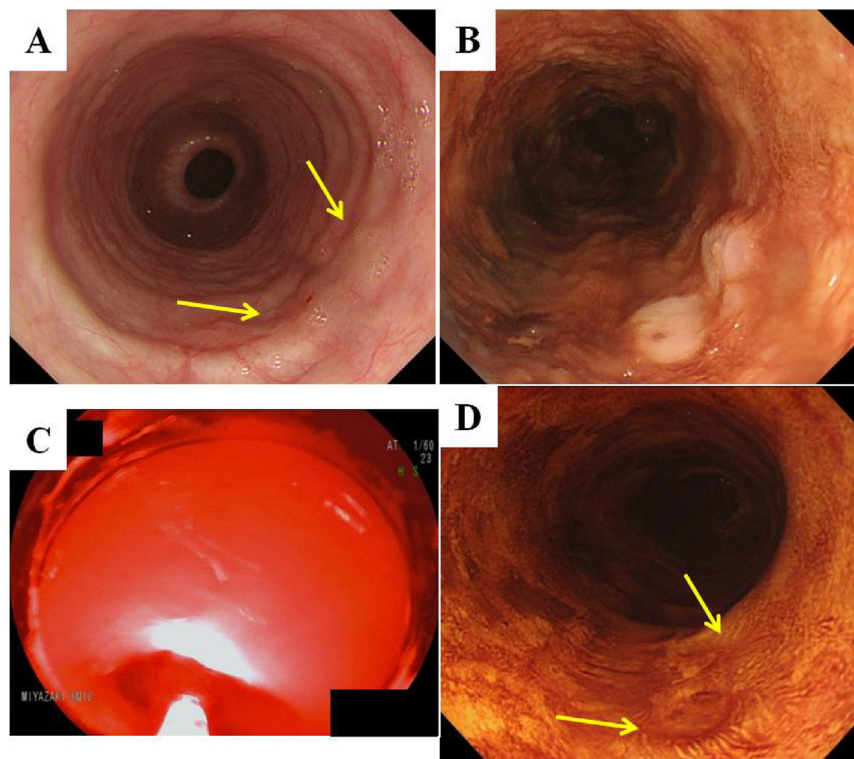
Among reports of effective salvage lymphadenectomy, recurrence from the primary tumor for which a complete response was once obtained after dCRT is observed [11]. Watanabe et al. [15] reported that salvage lymphadenectomy after dCRT may not have benefits for patients although secondary lymphadenectomy after esophagectomy offers a favorable long-term outcome. In our case, the esophageal primary tumor recurred at 38 months after the salvage Appleby operation. Salvage lymphadenectomy may be insufficient as a curative treatment because of regrowth of the primary lesion, although it might be effective in prolonging survival. As an additional therapy, the authors performed PDT for the primary tumor.

PDT for esophageal cancer was first reported in the early 1980s [16]. The PDT is expected as a treatment for a lesion in a layer deeper than the submucosal layer which is outside the indication

of endoscopic submucosal dissection. However, PDT using the first-generation photosensitizer, porfimer sodium, and an excimer dye laser caused problems such as severe skin phototoxicity. Recently, Yano et al. [17] reported a multicenter phase II study of salvage PDT using a second-generation photosensitizer, talaporfin sodium, for local failure after dCRT. The local complete response rate was 88.5%, and no skin phototoxicity was observed in their study [17]. We attempted minimally invasive PDT using this second-generation photosensitizer, and we achieved local complete response without complications in our patient. PDT is very effective for recurrent primary lesions to the proper muscularis propria layer, and long-term survival is expected following its use.

#### 4. Conclusion

Generally, salvage lymphadenectomy for locoregional failures after dCRT is a safer procedure than salvage esophagectomy. However, indications for surgery with high risk of complications such as those with the Appleby operation should be carefully considered in salvage surgery. However, salvage lymphadenectomy may be insufficient as a curative treatment. PDT may be able to complement controversial salvage lymphadenectomy as a curative treatment option. Long-term survival is expected from multidisciplinary therapy combined with new therapeutic modalities such as PDT for recurrence of esophageal cancer after dCRT.



**Fig. 5.** Endoscopic examination at 38 months after surgery reveals recurrence (arrows) of the primary lesion in the middle thoracic esophagus (A, B). Photodynamic therapy using talaporfin sodium and a diode laser was performed (C). A complete response was obtained for the lesion (arrows) (D).

#### Conflicts of interest

Takahiro Nishida and other co-authors have no conflict of interest.

#### Funding

There are no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

#### Ethical approval

This is not a research study.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

#### Author contribution

Takahiro Nishida contributed to operation, follow-up and writing the manuscript. Koji Nakashima, Masato Kariya and Haruhiko Inatsu contributed to photodynamic therapy. Shinsuke Takeno, Kazuo Kitamura and Atsushi Nanashima critically reviewed the manuscript.

#### Registration of research studies

This is not a research study.

#### Guarantor

This is not a research study. All authors read and approved the final manuscript. Therefore, all authors are responsible for this article.

#### References

- [1] H. Kato, A. Sato, H. Fukuda, Y. Kagami, H. Udagawa, A. Togo, et al., A phase II trial of chemoradiotherapy for stage I esophageal squamous cell carcinoma: Japan Clinical Oncology Group study (JCOG9708), *Jpn. J. Clin. Oncol.* 39 (2009) 638–643.
- [2] K. Kato, K. Muro, K. Minashi, A. Ohtsu, S. Ishikura, N. Boku, et al., Phase II study of chemoradiotherapy with 5-fluorouracil and cisplatin for stage II-III esophageal squamous cell carcinoma: JCOG trial (JCOG 9906), *Int. J. Radiat. Oncol. Biol. Phys.* 81 (2011) 684–690.
- [3] J.S. Cooper, M.D. Guo, A. Herskovic, J.S. Macdonald, J.A. Martenson Jr, M. Al-Sarraf, et al., Chemoradiotherapy of locally advanced esophageal cancer: long-term follow-up of a prospective randomized trials (RTOG 85-01). Radiation Therapy Oncology Group, *JAMA* 281 (1999) 1623–1627.
- [4] B. Minsky, T. Pajak, R. Ginsberg, T.M. Pisansky, J. Martenson, R. Komaki, et al., INT 0123 (Radiation Therapy Oncology Group 94-05) phase III trial of combined- modality therapy for esophageal cancer: high-dose versus standard-dose radiation therapy, *J. Clin. Oncol.* 20 (2002) 1167–1174.
- [5] R.A. Agha, A.J. Fowler, A. Saetta, I. Barai, S. Rajmohan, D.P. Orgill, SCARE Group, The SCARE Statement: consensus-based surgical case report guidelines, *Int. J. Surg.* 34 (2016) 180–186.
- [6] S. Markar, C. Gronnier, A. Duhamel, A. Pasquer, J. Théreaux, M.C. du Rieu, et al., Salvage surgery after chemoradiotherapy in the management of esophageal cancer: is it a viable therapeutic option? *J. Clin. Oncol.* 33 (2015) 3866–3873.
- [7] M. Watanabe, S. Mine, K. Nishida, K. Yamada, H. Shigaki, A. Matsumoto, et al., Salvage esophagectomy after definitive chemoradiotherapy for patients with esophageal squamous cell carcinoma: who really benefits from this high-risk surgery? *Ann. Surg. Oncol.* 22 (2015) 4438–4444.
- [8] Y. Niwa, M. Koike, Y. Fujimoto, H. Oya, N. Iwata, N. Nishio, et al., Salvage pharyngolaryngectomy with total esophagectomy following definitive chemoradiotherapy, *Dis. Esophagus* 29 (2016) 598–602.
- [9] S. Matono, H. Fujita, T. Tanaka, N. Mori, T. Nagano, K. Nishimura, et al., Salvage lymphadenectomy without esophagectomy is an option for recurrent of residual lymph nodes after definitive chemoradiotherapy for esophageal cancer, *Esophagus* 11 (2014) 197–203.
- [10] Y. Doki, T. Yasuda, H. Miyata, Y. Fujiwara, S. Takiguchi, M. Yamasaki, et al., Salvage lymphadenectomy of the right recurrent nerve node with tracheal

- involvement after definitive chemoradiation therapy for esophageal squamous cell carcinoma: report of two cases, *Surg. Today* 37 (2007) 590–595.
- [11] M. Nakajima, Y. Domeki, H. Satomura, M. Takahashi, A. Sugawara, H. Muroi, et al., Salvage lymphadenectomy for recurrent esophageal cancer after chemoradiotherapy, *Int. Surg.* 99 (2014) 452–457.
- [12] L. Appleby, The coeliac axis in the expansion of the operation for gastric carcinoma, *Cancer* 6 (1953) 704–707.
- [13] K. Yamaguchi, K. Nakano, K. Kobayashi, Y. Ogura, H. Konomi, A. Sugitani, et al., Appleby operation for pancreatic body-tail carcinoma: report of three cases, *Surg. Today* 33 (2003) 873–878.
- [14] I. Iizuka, K. Katayama, Y. Tanaka, T. Konishi, Y. Idezuki, Y. Maruyama, et al., Postoperative complications of Appleby's operation: complications due to visceral ischemia and their prevention (in Japanese), *Nihon Shokaki Geka Gakkai Zasshi.* 20 (1987) 40–48.
- [15] M. Watanabe, S. Mine, K. Yamada, H. Shigaki, Y. Baba, N. Yoshida, et al., Outcomes of lymphadenectomy for lymph node recurrence after esophagectomy or definitive chemoradiotherapy for squamous cell carcinoma of the esophagus, *Gen. Thorac. Cardiovasc. Surg.* 62 (2014) 685–692.
- [16] J.S. McCaughan Jr, J.T. Guy, P. Hawley, W. Hicks, W. Inglis, L. Laufman, et al., Hematoporphyrin-derivative and photoradiation therapy of malignant tumors, *Lasers Surg. Med.* 3 (1983) 199–209.
- [17] T. Yano, H. Kasai, T. Horimatsu, K. Yoshimura, S. Teramukai, S. Morita, et al., A multicenter phase II study of salvage photodynamic therapy using talaporfin sodium (ME2906) and a diode laser (PNL6405EPG) for local failure after chemoradiotherapy or radiotherapy for esophageal cancer, *Oncotarget.* 8 (2017) 22135–22144.

#### Open Access

This article is published Open Access at [sciencedirect.com](https://www.sciencedirect.com). It is distributed under the [IJSCR Supplemental terms and conditions](#), which permits unrestricted non commercial use, distribution, and reproduction in any medium, provided the original authors and source are credited.