Case report

Difficult to treat esophageal perforation after endoscopic balloon dilation for stenosis due to endoscopic submucosal dissection followed by chemoradiotherapy: A case report

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ABSTRACT

Introduction and importance: There is no clear consensus on a specific treatment for esophageal perforation. The surgical approach is deemed necessary for local severe infection and pleural contamination requiring debridement.

Presentations of case: We have reported herein the case of a patient with esophageal perforation with severe mediastinal and thoracic abscess after endoscopic balloon dilation for stenosis due to endoscopic submucosal dissection and chemoradiotherapy. A surgical approach with primary closure was performed, but not found effective; while conservative treatment with mediastinal drainage via posterior neck and recovery of nutritional status was found to be effective. For the recovery of nutritional status, enteral nutrition was assessed using a polymeric formula through a percutaneous endoscopic gastrojejunostomy tube.

Discussion: Esophageal perforation is a life-threatening condition. Iatrogenic injuries are the frequent cause of esophageal perforation. For esophageal perforation, not only surgical interventions but also conservative treatments including various endoscopic approaches have been performed. If the inflammation is not localized, surgical intervention is often needed; however, if the patient's general condition is stable, conservative treatment with drainage, antibiotics, and nutritional management may be considered, even in cases of esophageal perforation.

Conclusions: Esophageal perforation with a large perforation site with widespread inflammation can be improved with proper thoracic and mediastinal drainage and adequate nutrition support if the patient's condition is mild.

1. Introduction

Both endoscopic resection (ER) and chemoradiotherapy (CRT) are standard treatment approaches for esophageal cancer [1,2]. Several adverse events (AE) such as bleeding, stenosis, perforation, and pneumonitis may occur during and after ER and CRT [3,4]. For stenosis, which is a common AE in both ER and CRT, endoscopic balloon dilation (EBD) is generally performed [5]. Perforation during EBD has been reported to occur in 0.4%–1.1% of all cases and 4.1%–9.2% of all patients treated for esophageal stenoses after ER [6,7]. The treatment of

esophageal perforation associated with endoscopic treatment is decided based on the respective experience of each facility. Nonoperative management has been recommended to be reserved for patients with contained esophageal perforations, limited extraluminal soilage, and no evidence of systemic inflammation [8]. The surgical approach (i.e., resection, suture, and debridement) is considered necessary for patients with considerable pleural contamination requiring thoracic debridement [9]. The choice of a suitable surgical approach depends on the patient's condition at that time. In addition, nutritional management is an important factor contributing toward the wound healing process in

gastrointestinal perforation [10].

In this report, we present the case of a patient with esophageal perforation with mediastinal and thoracic abscess after EBD who required several long-term treatments. This case report has been reported in line with the SCARE 2020 criteria [11].

2. Case presentation

This study was approved by the ethics committee of our institution (approval number: J2021-110). Written informed consent was obtained from the patient.

A 59-year-old woman underwent endoscopic submucosal dissection (ESD) for upper thoracic esophageal cancer located 19–21 cm from the incisor teeth, where the lesion covered half of the circumference. Histopathological findings indicated squamous cell carcinoma and (T1b-SM (500 μm), ly1, v0, HM(−), and VM(−), hematoxylin and eosin, desmin, D2-40, and Elastica van Gieson staining were used for diagnosis). Additional treatment was considered because of the high risk for recurrence suggested by tumor depth and lymphatic involvement. The breast cancer was incidentally detected in the patient during a preoperative examination, and she accordingly underwent chemoradiation (CRT) (41.4Gy/23fr) 6 months after ESD. After ESD and before CRT, she underwent EBD and endoscopic triamcinolone injection for postprocedural stenosis. After CRT, she continued to undergo EBD and triamcinolone injection, totaling 30 times. Immediately after the last EBD, she showed no symptoms; however, after 7 days of the last EBD (the day before admission), she complained of heartburn and pain in her neck, chest, and back. After 8 days of her last EBD, she was referred to our hospital (Shizuoka cancer center hospital, Shizuoka, Japan) for complaints of pain and a high fever of 37.8 °C. Complete blood cell count as well as coagulation and serum chemistry studies revealed severe inflammation, with white blood cell count and C-reactive protein elevated to 14,240/μL and 33.3 mg/dL, respectively. Chest radiographs revealed an enlargement of the upper mediastinum, suspecting mediastinitis. Contrast-enhanced computed tomography (CT) revealed only a small amount of mediastinal abscess (Fig. 1-a). Physicians diagnosed her with mediastinal abscess associated with EBD, but they did not suspect any remarkable esophageal perforation. Therefore, they managed her

conservatively with antibiotics (ampicillin at 8 g/day and sulbactam at 4 g/day [SULBACILLIN®, Meiji Seika] for days 1–10 and tazobactam/piperacillin [ZOSYN®, TAIHO] at 18 g/day after day 11) and no oral intake. However, her fever of ≥38 °C and pain persisted. On day 12 of admission, her endoscopic examination revealed a large 15-mm-sized defect located 1 cm at the anal side of the dilation (Fig. 2-①), and the mediastinal abscess had spread into the right thoracic cavity, resulting in a pyothorax (Fig. 1-b, c). At this point, the physicians in charge consulted us (surgeons). The next day, the patient's general condition was found to be stable, and the mediastinal abscess of 90 × 15 mm in size spreading to Th1-5 was technically approachable with an interventional procedure by radiologists; therefore, a surgical procedure was not planned at this point. Mediastinal drainage via the right posterior neck and thoracic drainage was successfully performed (Fig. 1-d, e). To improve her nutritional status, a percutaneous endoscopic gastrojejunostomy (PEG-J) tube was installed. From day 13 of admission, enteral nutrition using a polymeric formula (Enevo®, Abbott Japan) was initiated. Her calorie dose was started at 386 kcal and then gradually increased. Finally, she was administered with a diet worth 1850 kcal (the dose was reduced because diarrhea was observed at doses of ≥2000 kcal). Thereafter, the inflammation and nutrition markers gradually improved (Fig. 2), but esophagogastroduodenoscopy (EGD) on day 21 of the admission revealed that the perforation site did not shrink at all (Fig. 2-②). Not expecting any further improvement with conservative treatment alone, we decided to perform surgical treatment.

On day 31 of admission, we performed a right thoracotomy under general anesthesia. The patient's intraoperative findings included fibrotic tissue in the pleural cavity and mediastinum and inflammation around the perforation site rigidly adhering to the surrounding tissues. After dissecting adhesion, the point of esophageal perforation was identified in the posterior wall of the upper esophagus, with a deficit of 1.5-cm diameter. Because no findings of necrosis were recorded at the perforation site, primary closure for the esophagus defect was performed (Fig. 3). Due to severe adhesion and the lack of a sufficient amount of surrounding space, repair by using a harvesting flap was difficult. The thoracic cavity and mediastinum were washed with saline, and a thoracic drain and an additional mediastinal drain were then inserted.

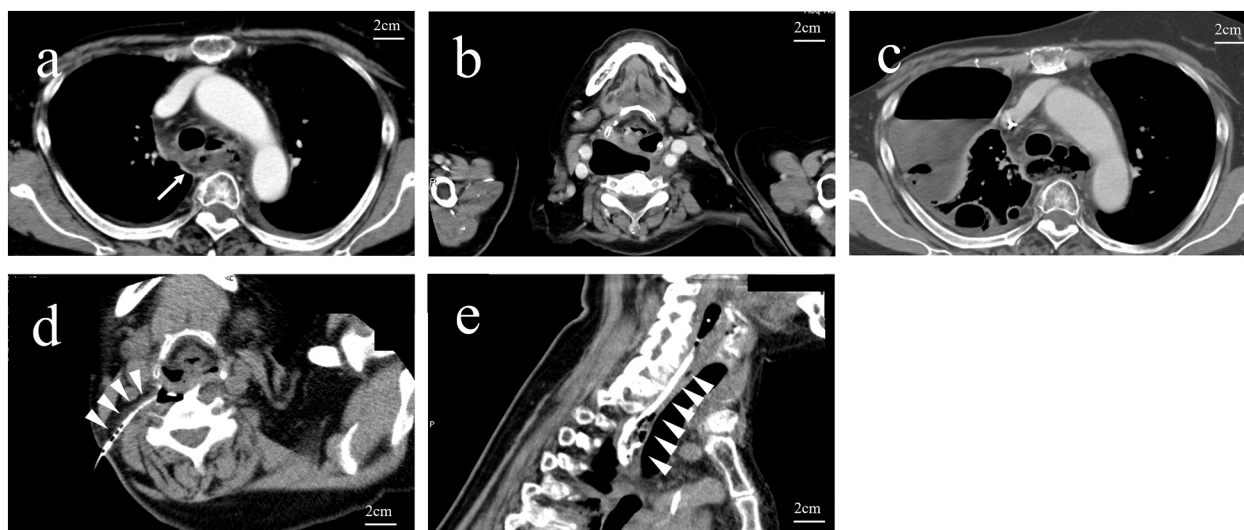After the surgery, the patient's general condition was stable, but her

Fig. 1. Computed tomography and mediastinal drainage.

a: Computed tomography on the day of admission, b, c: CT on day 10 of admission, d, e: CT-guided mediastinal drainage on day 13 of admission.

a: White arrow indicates mediastinal abscess. No disruption in the continuity of the esophageal wall was noted.

b: CT view showing the spread of the abscess into the retropharyngeal space.

c: White arrow indicates a break in the continuity of the esophageal wall, which was considered to be a perforation site.

d: We reached the posterior mediastinal space from the dorsal side of the right neck. White arrowheads indicate the drainage tube.

e: Coronal image CT-guided drainage. We placed the drainage tube from the cranial side to the perforation site. White arrowheads indicate the drainage tube.
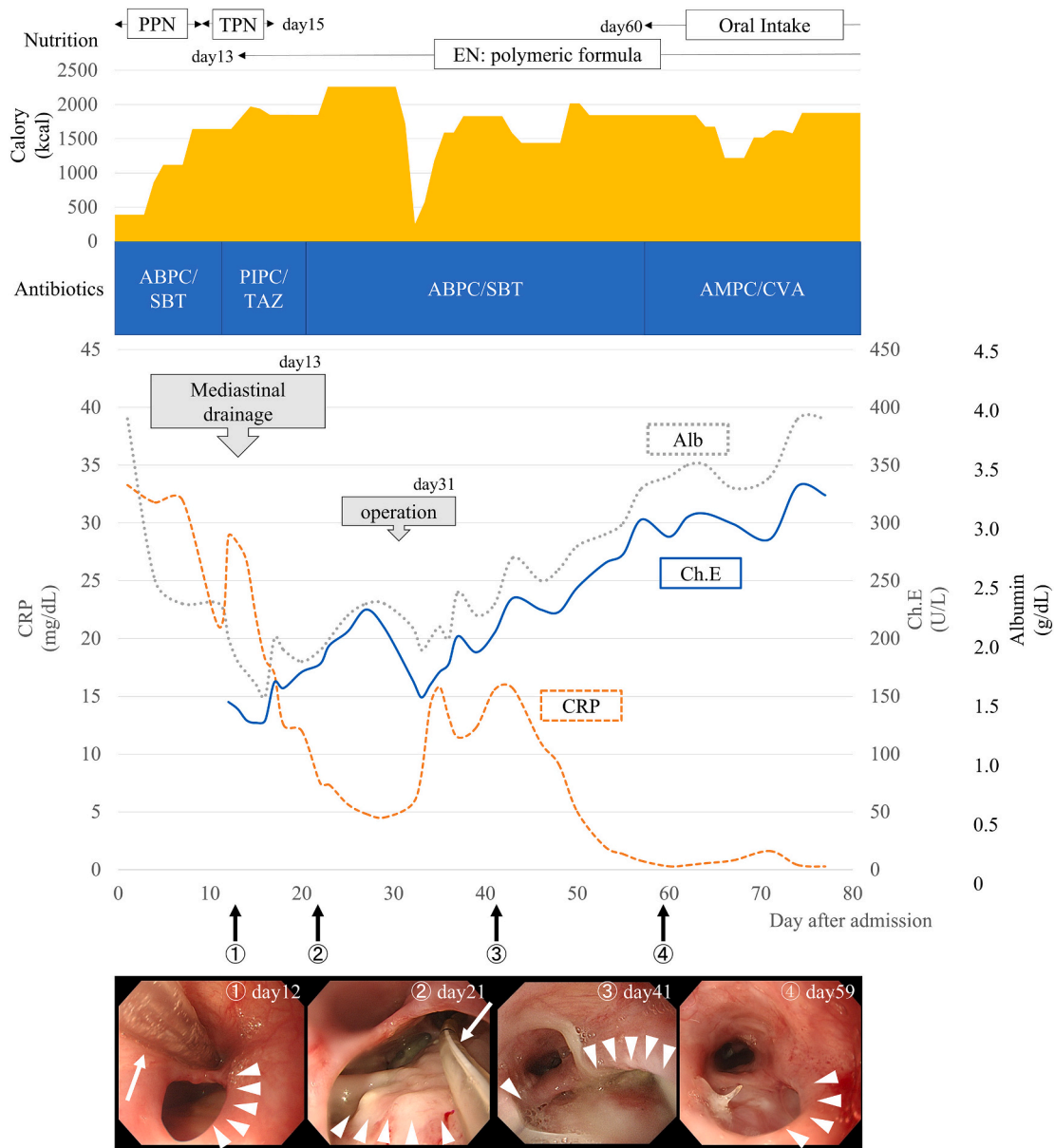
Fig. 2. Clinical course and endoscopic findings.

① Endoscopy revealed a large 15-mm defect (white arrow heads) on the posterior wall at the 1-cm-distal side of the dilation site. The nasogastric tube (white arrow) was placed in the appropriate esophagus space on day 12 of admission.

② Endoscopy revealed the growth of some granulation tissue (white arrow heads), but the size of the perforation site did not shrink. Drainage tube (white arrow) in the mediastinal space was visible in the cavity on day 21 of admission.

③ The perforation site that had been closed surgically was re-opened (white arrow heads) on day 41 of admission, day 28 after mediastinal drainage, and day 10 after primary closure. More granulation tissue was growing.

④ The large esophageal defect (white arrow heads) nearly completely closed on day 59 of admission and day 46 after mediastinal drainage.

ABPC: ampicillin, AMPC: amoxicillin, Alb: albumin, ChE: cholinesterase, CRP: C-reactive protein, CVA: clavulanate, OI: oral intake, PPN: peripheral parenteral nutrition, SBT: sulbactam, TPN: total parenteral nutrition.

mediastinal drainage continued to drain the contaminated fluid. On day 41 of admission (the 10th postoperative day), EGD revealed that the perforation site had re-opened and a lot of granulation tissues were growing (Fig. 2-③). On the basis of these findings, we considered that the drainage with the tube inserted through the cervical site was extremely effective and no additional surgical procedures were required. Mediastinal drainage, antibiotic therapy (ampicillin at 8 g/day and sulbactam at 4 g/day [SULBACILLIN®, Meiji Seika] for days 19–59 and amoxicillin at 1.5 g/day and clavulanate at 375 mg/day [Augmentin®, GlaxoSmithKline] after day 60), and adequate enteral nutrition were accordingly continued. The patient's general condition and

CRP gradually improved. On day 59 of admission, her EGD revealed that the perforation site had almost completely closed (Fig. 2-④). Her oral intake was resumed on day 60 of admission, and the patient became drain-free on day 75 of admission and was then discharged on day 77 of admission. After 14 months, the patient presently maintains a normal state of daily life.

3. Discussion

Esophageal perforation is a life-threatening condition [12,13]. A meta-analysis of 75 studies including 2971 patients reported a pooled
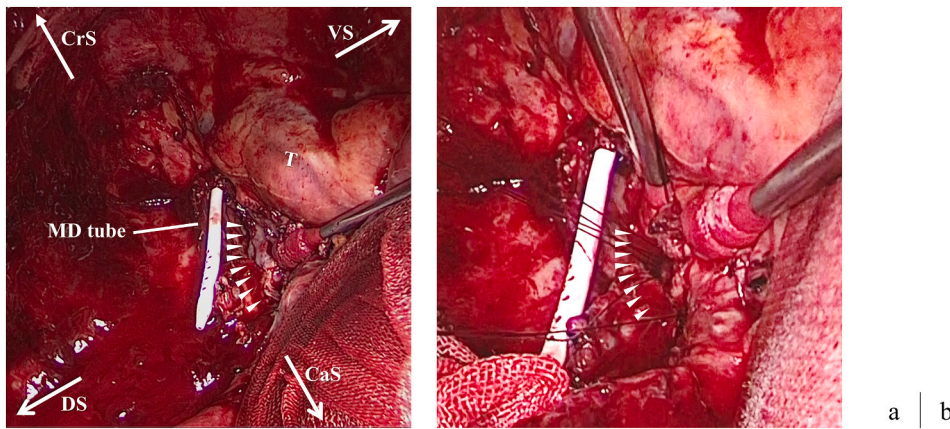
Fig. 3. Surgical findings. Our approach via right posterior lateral thoracotomy. CaS: caudal side, CrS: cranial side, DS: dorsal side, MD tube; mediastinal drainage tube, T: trachea, and VS: ventral side.

(a) A 15-mm perforation site was identified in the posterior wall of the upper thoracic esophagus (white arrowheads). The white tube behind the perforation site indicates a mediastinal drainage tube placed preoperatively.

(b) We conducted primary closure (white arrow head). Due to the lack of a sufficient amount of surrounding space, repair by using a harvesting flap was difficult.

mortality rate of 11.9% [14]. The highest mortality rate was reported in patients with spontaneous perforation (14.8%), followed by in those with iatrogenic (13.2%) and foreign body (2.1%) perforations [14]. On the other hand, another report indicated that iatrogenic injuries are the most common cause of esophageal perforations, accounting for 59% of all cases [12]. Generally, esophageal perforation during EBD occurs at the site of balloon dilation because the most pressure is applied at that site. In the present case, the rupture occurred not at the site of balloon dilation, but at approximately 1 cm to the anal side. The esophageal wall was fragile owing to the sequelae of ESD, CRT, and local steroid injection, and guidewire manipulation before EBD and the balloon tip might have triggered the later perforation.

The criteria for selecting the nonsurgical treatment of esophageal perforation have been reported previously [13]. Endoscopic treatments for esophageal perforation have, however, been evolving [15–19]. Various options have been reported such as clips [17], over-the-scope clips (OTSC) [16], polyglycolic acid (PGA) sheet with fibrin glue [18], self-expandable metallic stent (SEMS) [15], and endoscopic vacuum-assisted closure (E-VAC) [19]. In contrast, a surgical approach (such as resection, suture, and debridement) becomes necessary for patients with severe local infection [20] and considerable pleural contamination requiring thoracic debridement [9].

Surgical treatment for esophageal perforation includes primary suture closure at the perforation site, additional coverage with a harvesting flap or esophagectomy with two-stage reconstruction. Primary suture closure is possible at approximately 24 h of the onset. If >24 h have passed, depending on the degree of contamination, it is preferable to use a harvesting flap owing to the high rate of suture failure [21]. In fact, in the present case, approximately 20 days had passed since the onset, making it necessary to fill and cover the perforation site using a latissimus dorsi muscle flap or an intercostal muscle flap. However, this procedure could not be performed because of the distance between the perforation site and the harvesting flaps, and the lack of space caused by the strong adhesion. Considering that the simple suture closure resulted in re-opening in the present case, simple surgical closure might not be necessary if the drainage is effective and the general condition is improved. Of course, surgery may be an effective method when the infection and general condition are uncontrollable because it is possible to clean and drain the abscess under direct vision. The choice of a suitable surgical approach depends on the patient's condition at that time. Therefore, we need to make appropriate decisions based on the situation.

In this patient, no apparent perforation was observed immediately after EBD. However, the pain was noted on the 7th day after EBD, and the CT scan on the 8th day after EBD (the day of admission) confirmed mediastinal abscess. Because upper gastrointestinal endoscopy was not performed at that moment, we cannot be sure. However, in retrospect, we believe that esophageal perforation had occurred at that point. On the day of admission, the inflammation was confined to the mediastinum around the perforation site. If the diagnosis of esophageal perforation had been appropriately made by upper gastrointestinal endoscopy at the time of admission, percutaneous tube insertion or endoscopic transesophageal abscess drainage [22] could have been performed to achieve improvement in a shorter period. This could have been a good situation for the indication of E-VAC; however, in Japan, E-VAC is unusable. As a result of conservative treatment without mediastinal drainage until day 13 of admission, the mediastinal abscess spread from the upper to lower mediastinum and into the right thoracic cavity.

Nutrition and wound healing are closely associated [23]. Nutrition deficiencies impede the normal processes of wound healing due to the prolongation of the inflammatory phase, decrease of fibroblast proliferation, and alteration of the collagen synthesis [10]. In critically ill patients, it is, therefore, recommended that enteral feeding be started as early as possible [24]. In the present case, the perforation site shrank with improvement in the nutritional status. Conservative treatment for esophageal perforation requires not only proper drainage but also proper nutritional management. At our institution, we mainly use Enevo® (Abbott Japan) for patients with normal digestive and absorptive functions. Enevo® is a polymeric formula designed to meet the nutritional requirements of Japanese postoperative, older, and malnourished patients who require tube feeding. In addition to carbohydrates, proteins, and fats, Enevo® contains dietary fiber, essential vitamins, and trace elements such as selenium and molybdenum [25].

In the present case, mediastinal drainage via the posterior neck was found to be extremely effective and became the therapeutic main axis; however, it may not be a feasible technique in all facilities. In the case of the absence of a technically sound interventional radiologist, surgery may be necessary for proper drainage. Moreover, if the infection is uncontrolled and the patient is in poor general condition, surgery should be planned as soon as possible. For example, if the perforation site extends to the anterior wall, a tracheoesophageal fistula may form. This is a more critical and challenging condition to treat [26]. Inappropriate decisions can rapidly worsen the patient's condition, which makes it important to make an accurate diagnosis and select an effective treatment plan.

4. Conclusion

Esophageal perforation with a large perforation site with widespread inflammation can be possibly improved with appropriate thoracic and mediastinal drainages and adequate nutrition support if the patient's condition is not unstable or complicated with sepsis or tracheoesophageal fistula.

CRediT authorship contribution statement

TK performed data acquisition and drafted the manuscript. KI, RH, MI, SM, TA, and YT were involved in drafting the manuscript and revising it critically for important intellectual content. KI reviewed and provided the final approval for the version of the manuscript to be submitted for publication. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no competing interests.

Ethical approval

This study was approved by the ethics committee of our institution (approval number: J2021-110). Written informed consent was obtained from our patient.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research registration

N/A.

Guarantor

Kenjiro Ishii.

Provenance and peer review

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References

[1] Y. Kitagawa, T. Uno, T. Oyama, K. Kato, H. Kato, H. Kawakubo, et al., Esophageal cancer practice guidelines 2017 edited by the Japan esophageal society: part 1, Esophagus 16 (2019) 1–24, https://doi.org/10.1007/s10388-018-0641-9.

[2] Y. Kitagawa, T. Uno, T. Oyama, K. Kato, H. Kato, H. Kawakubo, et al., Esophageal cancer practice guidelines 2017 edited by the Japan esophageal society: part 2, Esophagus 16 (2019) 25–43, https://doi.org/10.1007/s10388-018-0642-8.

[3] S. Ono, M. Fujishiro, K. Niimi, O. Goto, S. Kodashima, N. Yamamichi, et al., Long-term outcomes of endoscopic submucosal dissection for superficial esophageal squamous cell neoplasms, Gastrointest. Endosc. 70 (2009) 860–866, https://doi.org/10.1016/j.gie.2009.04.044.

[4] 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, https://doi.org/10.1016/j.ijrobp.2010.06.033.

[5] S. Hashimoto, M. Kobayashi, M. Takeuchi, Y. Sato, R. Narisawa, Y. Aoyagi, The efficacy of endoscopic triamcinolone injection for the prevention of esophageal stricture after endoscopic submucosal dissection, Gastrointest. Endosc. 74 (2011) 1389–1393, https://doi.org/10.1016/j.gie.2011.07.070.

[6] Y. Kishida, N. Kakushima, N. Kawata, M. Tanaka, K. Takizawa, K. Imai, et al., Complications of endoscopic dilation for esophageal stenosis after endoscopic submucosal dissection of superficial esophageal cancer, Surg. Endosc. 29 (2015) 2953–2959, https://doi.org/10.1007/s00464-014-4028-2.

[7] H. Takahashi, Y. Arimura, S. Okahara, S. Uchida, H. Ishigaki, H. Tsukagoshi, et al., Risk of perforation during dilation for esophageal strictures after endoscopic resection in patients with early squamous cell carcinoma, Endoscopy 43 (2011) 184–189, https://doi.org/10.1055/s-0030-1256109.

[8] S. Lampridis, S. Mitsos, M. Hayward, D. Lawrence, N. Panagiotopoulos, The insidious presentation and challenging management of esophageal perforation following diagnostic and therapeutic interventions, J. Thorac. Dis. 12 (2020) 2724–2734, https://doi.org/10.21037/jtd-19-4096.

[9] T. Hauge, O.C. Kleven, E. Johnson, B. Hofstad, H.O. Johannessen, Outcome after iatrogenic esophageal perforation, Scand. J. Gastroenterol. 54 (2019) 140–144, https://doi.org/10.1080/00365521.2019.1575464.

[10] J.K. Stechmiller, Understanding the role of nutrition and wound healing, Nutr. Clin. Pract. 25 (2010) 61–68, https://doi.org/10.1177/0884533609358997.

[11] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, S.C.A.R.E. Group, The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines, Int J Surg 84 (2020) 226–230, https://doi.org/10.1016/j.ijsu.2020.10.034.

[12] C.J. Brinster, S. Singhal, L. Lee, M.B. Marshall, L.R. Kaiser, J.C. Kucharczuk, Evolving options in the management of esophageal perforation, Ann. Thorac. Surg. 77 (2004) 1475–1483, https://doi.org/10.1016/j.athoracsur.2003.08.037.

[13] H.A. Shaffer, G. Valenzuela, R.K. Mittal, Esophageal perforation: a reassessment of the criteria for choosing medical or surgical therapy, Arch. Intern. Med. 152 (1992) 757–761, https://doi.org/10.1001/archinte.152.4.757.

[14] F. Biancari, V. D'Andrea, R. Paone, C. Di Marco, G. Savino, V. Koivukangas, et al., Current treatment and outcome of esophageal perforations in adults: systematic review and meta-analysis of 75 studies, World J. Surg. 37 (2013) 1051–1059, https://doi.org/10.1007/s00268-013-1951-7.

[15] M. Omae, M. Konradsson, F. Baldaque-Silva, Delayed perforation after endoscopic submucosal dissection treated successfully by temporary stent placement, Clin. J. Gastroenterol. 11 (2018) 118–122, https://doi.org/10.1007/s12328-017-0808-2.

[16] H. Ono, M. Tanaka, Kohei Takizawa, N. Nakashima, Kenichiro, et al., Utility of the over-the-scope-clip system for treating a large esophageal perforation, Esophagus 12 (2015) 336–339, https://doi.org/10.1007/s10388-014-0462-4.

[17] G.S. Raymer, A. Sadana, D.B. Campbell, W.A. Rowe, Endoscopic clip application as an adjunct to closure of mature esophageal perforation with fistulae, Clin. Gastroenterol. Hepatol. 1 (2003) 44–50, https://doi.org/10.1053/jcgh.2003.50007.

[18] R. Takahashi, T. Yoshio, Y. Horiuchi, M. Omae, Akiyoshi Ishiyama, T. Hirasawa, et al., Endoscopic tissue shielding for esophageal perforation caused by endoscopic resection, ClinJ. Gastroenterol. 10 (2017) 214–219, https://doi.org/10.1007/s12328-017-0738-z.

[19] H.C. Youn, S.H. Kwon, Endoscopic vacuum-assisted closure (E-VAC) treatment in a patient with delayed anastomotic perforation following a perforated gastric conduit repair after an Ivor-Lewis esophagectomy, Ann. Thorac. Cardiovasc. Surg. 22 (2016) 363–366, https://doi.org/10.5761/atcs.cr.15-00305.

[20] N.C. Schizas, D. Paliouras, T. Rallis, A.S. Gogakos, A. Lazopoulos, F. Chatzinikolaou, et al., Successful surgical treatment of a complicated esophageal perforation, by use of primary closure and lung parenchyma reinforcement, Ann. Transl. Med. 4 (2016) 448, https://doi.org/10.21037/atm.2016.11.29.

[21] L.A. Brewer 3rd, R. Carter, G.A. Mulder, Q.R. Stiles, Options in the management of perforations of the esophagus, Am. J. Surg. 152 (1986) 62–69, https://doi.org/10.1016/0002-9610(86)90144-3.

[22] A. Hara, S. Fukunishi, Y. Sasaki, M. Sanomura, K. Higuchi, EUS-FNA can be an effective procedure for the transesophageal drainage of a patient with intraperitoneal abscess, Clin. J. Gastroenterol. 8 (2015) 212–216, https://doi.org/10.1007/s12328-015-0588-5.

[23] M. Arnold, A. Barbul, Nutrition and wound healing, Plast. Reconstr. Surg. 117 (2006) 42–58, https://doi.org/10.1097/01.prs.0000225432.17501.6c.

[24] S.A. McClave, B.E. Taylor, R.G. Martindale, M.M. Warren, D.R. Johnson, C. Braunschweig, et al., Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient, J. Parenter Enteral Nutr. 40 (2016) 159–211, https://doi.org/10.1177/0148607115621863.

[25] R. Fukushima, M. Yano, K. Ikejiri, I. Mochizuki, T. Nomura, S. Nakagawa, et al., Efficacy and safety evaluation of a novel enteral nutrition formula (ENG-J) in postoperative patients who underwent esophagectomy or Total gastrectomy for cancer —a multicenter randomized open-label, unblinded parallel comparative study—, J. Jpn. College Surg. 39 (2014) 840–851, https://doi.org/10.4030/jjcs.39.840.

[26] M.F. Reed, D.J. Mathisen, Tracheoesophageal fistula, Chest Surg. Clin. N. Am. 13 (2003) 271–289, https://doi.org/10.1016/s1052-3359(03)00030-9.