

Case
Report

Esophageal Cancer Surgery in Dialyzed Patients: A Single Institution Case Series

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We sought to evaluate the feasibility of esophageal carcinoma (EC) surgery in cases requiring dialysis. Among 250 consecutive patients undergoing surgical resection for EC, three on maintenance dialysis were identified. We retrospectively analyzed their clinical characteristics. The three dialyzed patients were all males, 39–77 years old at EC surgery. The operations were thoracoscopic esophagectomy with nodal clearance (Case 1), cervical esophageal resection without thoracic procedures (Case 2), and thoracoscopic esophagectomy without reconstruction, emergently conducted for tumor bleeding (Case 3). Reoperation had been required for postoperative abdominal hematoma in Case 1. Postoperative tracheostomy had been performed due to severe pneumonia in Case 2. EC surgery for dialyzed patients, despite appearing to be feasible, might be associated with a high risk of life-threatening morbidities. To minimize surgical risk, therapeutic decision-making for such cases should be based on the balance between radicality and safety.

Keywords: chronic kidney disease, dialysis, esophageal carcinoma, outcome, surgery

Introduction

Chronic kidney disease (CKD), the cause of nearly two million deaths worldwide to date, is an important public health problem.¹⁾ Globally, the burden of end-stage CKD requiring dialysis is growing markedly.²⁾ It is

thus anticipated that clinicians, not limited to nephrologists, will have increasing opportunities to treat CKD patients on maintenance dialysis therapy. Therefore, it is of importance to prepare and implement therapeutic strategies for dialysis-dependent patients in each clinical department.

As regards surgery, however, sufficient data concerning management and outcomes of major operations in dialyzed patients are as yet lacking. This is presumably due to the inclination of surgeons to avoid performing aggressive procedures for CKD patients on regular dialysis, who have far higher risks of postoperative death and cardiovascular events than those with normal renal function.^{3–5)} In particular, there are only a few reports on surgical resection of esophageal carcinoma (EC), one of the most invasive and challenging procedures,⁶⁾ for the dialyzed CKD population.^{7,8)}

We retrospectively reviewed clinical characteristics and surgical outcomes of patients with CKD requiring dialysis who had undergone surgical resection for EC.

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Case Series

In total, 250 consecutive patients had undergone surgical resection for pathologically confirmed EC between October 2015 and December 2019 in Toranomon Hospital. Among these 250, three CKD cases receiving maintenance dialysis were identified (1.2%). Clinicopathological information and postoperative outcomes of these three dialysis cases and those of the other 247 cases were retrospectively analyzed. Tumor staging was determined based on the eighth edition of the TNM system.⁹ The Institutional Review Board of Toranomon Hospital approved this study protocol (No. 2128). Informed consent from the subjects was not necessary because this was a retrospective study.

The clinical presentations and perioperative courses of the three CKD patients on long-term dialysis are described below. In all the cases, perioperative management of CKD included dialysis within 24 hours prior to the operation and resumption of dialysis on the first postoperative day. To avoid the risk of heparin-associated bleeding, nafamostat mesylate was used for anticoagulation for hemodialytic treatment after the surgery. Meticulous monitoring of serum potassium levels and fluid balance was also performed postoperatively in the intensive care unit, under a nephrology consultation. In each case, postoperative hemodynamic condition was stable and hemodialysis was successfully carried out without introduction of continuous hemodiafiltration.

Case 1

A 63-year-old man visited the hospital, where he had been receiving maintenance hemodialysis for CKD caused by glomerulonephritis for 9 months, with a complaint of dysphagia. Esophagogastroduodenoscopy (EGD) revealed a protruding tumor at the lower esophagus, histologically diagnosed as adenocarcinoma. Computed tomography (CT) and ¹⁸F-fluorodeoxyglucose positron-emission tomography (¹⁸F-FDG PET) showed extensive nodal metastases. He subsequently underwent 11 courses of FOLFOX chemotherapy, which can be safely administered even to CKD patients.¹⁰ After radiological confirmation of complete tumor regression in all of the metastatic lesions, with the primary tumor persisting in the lower esophagus, he was referred to our hospital for surgical treatment.

Thoracoscopic esophagectomy with two-field nodal dissection, gastric conduit reconstruction via a retrosternal route, and cervical esophagogastrostomy were performed.

Cervical lymph node dissections were omitted because the absence of recurrent nerve nodal metastases was confirmed by intraoperative pathological examination.¹¹ Histopathological examination of the resected specimen demonstrated adenocarcinoma limited to the submucosal layer without regional lymph node metastasis (pT1bN0).

Six days after the esophagectomy, the patient complained of intense abdominal pain of sudden onset. CT exhibited a low-density oval mass with peripheral higher density in the intrapancreatic area, raising suspicion of a rapidly growing hematoma (**Fig. 1**). We conducted an emergent laparotomy and detected massive mesenteric hematoma without active bleeding. Hematomectomy with hemorrhagic drainage was successfully carried out and the course after reoperation was uneventful. Postoperative surveillance examinations have shown no evidence of recurrence for 27 months, to date.

Case 2

A 77-year-old man, who had a 3-year history of peritoneal dialysis for CKD due to purpura nephritis, underwent EGD in the hospital where he had experienced subtotal esophagectomy with ante-sternal gastric conduit reconstruction for EC (T1bN0M0) 15 years earlier and 66.0 Gy irradiation for laryngeal cancer 14 years earlier. The endoscopy revealed a protruding tumor in the remnant cervical esophagus, pathologically diagnosed as squamous cell carcinoma (SCC). CT and ¹⁸F-FDG PET detected no metastatic lesions. He was referred to our hospital for radical surgical treatment.

Cervical esophageal resection with free jejunal flap transfer was successfully performed with preservation of the laryngopharynx. This procedure was conducted without thoracic manipulations. The entire tumor, which had invaded the adventitia, was resected with microscopically negative margins (pT3N0M0). Removal of the peritoneal dialysis catheter, cannulation of the femoral vein for temporary vascular access, and creation of an arteriovenous fistula in the non-dominant arm were also performed as preparation for postoperative hemodialysis.

Four days postoperatively, intubation and mechanical ventilation were carried out for urgent management of progressive pneumonia without marked edematous findings. Tracheostomy was performed 20 days after the cervical esophagectomy. The respiratory dysfunction gradually improved thereafter. However, his severe deglutition disorder was deemed to be incurable and, 119 days after the cervical esophagectomy, simple laryngectomy was carried out for the purpose of regaining oral



Fig. 1 CT (coronal section) revealed a low-density abdominal mass, compatible with postoperative hematoma (arrow). CT: computed tomography

ingestion. His subsequent course has been uneventful for 17 months, to date, with no evidence of EC relapse.

Case 3

A 39-year-old man underwent screening EGD in the hospital where he had received maintenance hemodialysis for CKD due to hypertensive nephrosclerosis for 3 years. A large ulcerative tumor at the lower esophagus was biopsied, yielding a diagnosis of adenocarcinoma. CT and ¹⁸F-FDG PET showed extensive nodal metastases along with sternal metastasis (M1). He was referred to our hospital for further systemic treatment.

After 10 courses of FOLFOX chemotherapy, he suddenly developed copious hematemesis and was emergently transported to our hospital. Laboratory tests indicated marked anemia with a hemoglobin level of 6.3 g/dL and CT revealed a massive intraluminal hematoma expanding inside the esophagus, apparently originating from tumor bleeding. As endoscopic hemostasis was not considered to be feasible, emergency surgery was performed.

Under thoracoscopic view, the esophagus was remarkably distended due to the intraluminal hemorrhage (**Fig. 2**). Subtotal esophagectomy without nodal clearance was undertaken using a thoracoscopic approach. Cervical esophagostomy and jejunal feeding tube placement were also performed, without esophageal replacement construction.

After a 40-day stable postoperative course with enteral feeding, the second stage surgery for retrosternal gastric conduit reconstruction was successfully carried out. He

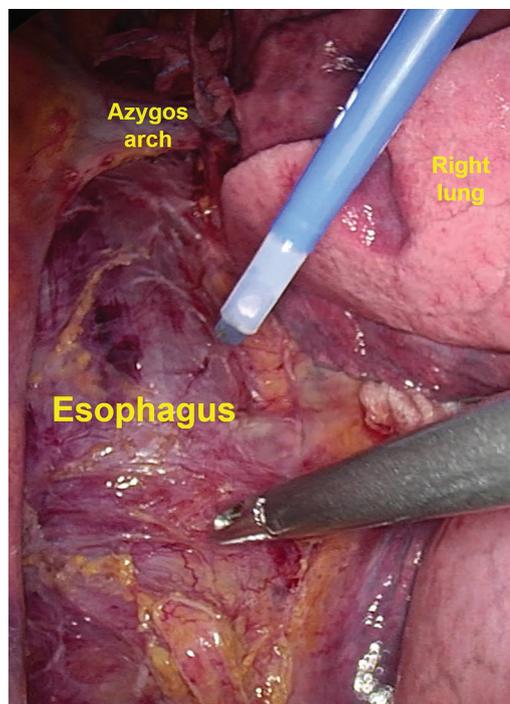


Fig. 2 Intraoperative view. Dissection around the esophagus, markedly distended due to the intraluminal hemorrhage, was performed during emergent thoracoscopic esophagectomy.

was discharged on the 14th day after the second operation without serious complications. Systemic chemotherapy was subsequently resumed and he remains alive, with control of tumor progression (13 months).

Comparison with 247 non-dialytic EC cases

With regard to operative procedures, three-field lymph node dissection was not conducted in the dialysis group, though it was carried out in 154 cases of the non-dialysis group (62%). Two-stage operations were conducted in only three of the 247 non-dialysis cases (1.2%), while being performed in one of the three dialysis cases (33%) (Case 3). There was no emergency surgery performed in 247 non-dialyzed subjects.

Discussion

We conducted a retrospective investigation of clinico-pathological features and outcomes of three dialyzed CKD patients undergoing surgery for EC. Despite steady growth in the utilization of long-term dialysis in almost all areas of the world,²⁾ little is known about outcomes following EC surgery for dialysis-dependent patients due to the lack of published data. There are two possible background factors explaining why EC surgery for CKD

patients on maintenance dialysis has rarely been discussed. First, risks for developing EC are reported to be significantly lower in patients with end-stage CKD than in the normal healthy population, although the mechanism remains unknown.¹²⁾ Second, CKD requiring regular dialysis markedly contributes to postoperative morbidity and mortality associated with major surgery, regardless of the type of operation.^{3–5)} Concerning EC, in fact, esophageal resection itself often has a dismal surgical outcome, with a mortality rate of 4–10% and a morbidity rate of 26–41%.¹³⁾ Therefore, surgeons may well avoid such risks by not performing aggressive esophageal surgery.⁶⁾ In particular, esophageal SCC is highly associated with respiratory and otolaryngologic morbidities, and harbors higher surgical risks than adenocarcinoma of the esophagus.¹⁴⁾ This might explain why SCC was rare in our dialysis cases (1/3), despite accounting for over 90% of EC in Japan.¹⁵⁾

In our series of three dialyzed patients, other non-surgical therapies might have been an option. For instance, irradiation for the primary tumor might have been an option in Case 1. However, radiotherapy carries a possible risk of severe infectious adverse effects especially in chronically dialyzed individuals.¹⁶⁾ Safety and efficacy of chemoradiation or radiation therapy for EC in dialytic patients has yet to be established, as it has been described only in a limited number of reports.^{16,17)} In the other two cases, radiation had been contraindicated due to the history of definitive radiotherapy (Case 2) and an emergent situation (Case 3), respectively. It is feasible for dialysis patients to receive chemotherapy, with appropriate dosage adjustment to assure safety.¹⁸⁾ Nevertheless, its radicality remains uncertain as compared to surgical removal.¹⁹⁾ Consequently, we opted for surgical treatment for each of these dialysis patients.

In an attempt to reduce surgical stress, two-field nodal dissection or a two-stage operation was selected in our dialysis cases. All three patients remain alive after overcoming serious morbidities. Our results, despite being anecdotal, raise the possibility that (i) EC surgery for dialysis-dependent cases is feasible with selection of less invasive approaches and that (ii) postoperative comorbidity risks are still relatively high. Dialyzed population are highly susceptible of anastomotic leakage, surgical site infection, cardiopulmonary disorder, and hemorrhage, owing to their impaired wound healing, unstable hemodynamic condition and platelet dysfunction.^{1–5)} Given these difficulties, therapeutic decision-making tailored to each patient on the basis of pretreatment

meticulous assessment may be of importance to minimize the risk of severe complications. Considering that dialysis itself is known to be associated with a high mortality rate,²⁰⁾ we must carefully maintain a balance between curability and safety when choosing therapeutic approaches for EC patients on maintenance dialysis. Without such a prudent policy, EC would not be amenable to surgical resection in dialyzed patients.

Conclusion

We retrospectively analyzed the characteristics of three EC surgery cases on maintenance dialysis. Esophageal resection was achieved in all three cases, with specialized approaches such as a two-stage operation. However, these procedures involved serious postoperative morbidities. When treating EC patients receiving regular dialysis, surgeons should select therapeutic modalities considering both tumor curability and patient tolerance to challenging EC surgery.

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Disclosure Statement

The authors have no conflicts of interest to declare.

References

- 1) GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2020; **395**: 709–33.
- 2) Thomas B, Wulf S, Bikbov B, et al. Maintenance dialysis throughout the world in years 1990 and 2010. *J Am Soc Nephrol* 2015; **26**: 2621–33.
- 3) Mathew A, Devereaux PJ, O'Hare A, et al. Chronic kidney disease and postoperative mortality: a systematic review and meta-analysis. *Kidney Int* 2008; **73**: 1069–81.
- 4) Shinkawa H, Yasunaga H, Hasegawa K, et al. Mortality and morbidity after pancreatoduodenectomy in patients undergoing hemodialysis: analysis using a national inpatient database. *Surgery* 2019; **165**: 747–50.
- 5) Matsumoto S, Takayama T, Wakatsuki K, et al. Short-term and long-term outcomes after gastrectomy for

- gastric cancer in patients with chronic kidney disease. *World J Surg* 2014; **38**: 1453–60.
- 6) Abdelsattar ZM, Habermann E, Borah BJ, et al. Understanding failure to rescue after esophagectomy in the United States. *Ann Thorac Surg* 2020; **109**: 865–71.
 - 7) Kitamura M, Hiraga S, Takamiya T, et al. Radical esophagectomy on a maintenance hemodialysis patient. *Nephron* 1990; **56**: 103–4.
 - 8) Zaza M, Gaur P, Chan EY, et al. Minimally invasive esophagectomy in a patient with end-stage renal disease. *BMJ Case Rep* 2016; **2016**: bcr2016214551.
 - 9) Brierley JD, Gospodarowicz MK, Wittekind C. TNM classification of malignant tumours. 8th ed. Oxford, UK: Wiley-Blackwell, 2017.
 - 10) Takimoto CH, Remick SC, Sharma S, et al. Dose-escalating and pharmacological study of oxaliplatin in adult cancer patients with impaired renal function: a National Cancer Institute Organ Dysfunction Working Group Study. *J Clin Oncol* 2003; **21**: 2664–72.
 - 11) Nagatani S, Shimada Y, Kondo M, et al. A strategy for determining which thoracic esophageal cancer patients should undergo cervical lymph node dissection. *Ann Thorac Surg* 2005; **80**: 1881–6.
 - 12) Liang JA, Sun LM, Yeh JJ, et al. The association between malignancy and end-stage renal disease in Taiwan. *Jpn J Clin Oncol* 2011; **41**: 752–7.
 - 13) Wright CD, Kucharczuk JC, O'Brien SM, et al. Predictors of major morbidity and mortality after esophagectomy for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk adjustment model. *J Thorac Cardiovasc Surg* 2009; **137**: 587–95; discussion 596.
 - 14) Mariette C, Finzi L, Piessen G, et al. Esophageal carcinoma: prognostic differences between squamous cell carcinoma and adenocarcinoma. *World J Surg* 2005; **29**: 39–45.
 - 15) Kitagawa Y, Uno T, Oyama T, et al. Esophageal cancer practice guidelines 2017 edited by the Japan Esophageal Society: part 1. Esophagus 2019; **16**: 1–24.
 - 16) Hirota H, Ito K, Kageyama SI, et al. Safety of radiotherapy for hemodialysis patients with cancer. *Int J Clin Oncol* 2020; **25**: 978–83.
 - 17) Rebibou JM, Chauffert B, Dumas M, et al. Combined chemotherapy and radiotherapy for esophageal carcinoma in a hemodialyzed patient. Long-term survival. *Nephron* 1996; **74**: 611–2.
 - 18) Janus N, Thariat J, Boulanger H, et al. Proposal for dosage adjustment and timing of chemotherapy in hemodialyzed patients. *Ann Oncol* 2010; **21**: 1395–403.
 - 19) Ter Veer E, Haj Mohammad N, van Valkenhoef G, et al. The efficacy and safety of first-line chemotherapy in advanced esophagogastric cancer: a network meta-analysis. *J Natl Cancer Inst* 2016; **108**: djw166.
 - 20) Robinson BM, Zhang J, Morgenstern H, et al. Worldwide, mortality risk is high soon after initiation of hemodialysis. *Kidney Int* 2014; **85**: 158–65.