

Treatment options for synchronous lung and esophagus tumors: A difficult decision to make

Senkron akciğer ve özofagus tümörleri için tedavi seçenekleri: Zor karar

Yasemin Büyükkarabacak¹, Mehmet Gökhan Pirzirelli¹, Selçuk Gurz¹, Ayşen Taslak¹,
Yurdanur Sullu², Burçin Çelik¹, Ahmet Başoğlu¹

¹Department of Thoracic Surgery, Ondokuz Mayıs University Faculty of Medicine, Samsun, Türkiye

²Department of Pathology, Ondokuz Mayıs University Faculty of Medicine, Samsun, Türkiye

ABSTRACT

Synchronous lung and esophageal carcinomas are rare clinical entities. Curative resection with lymph node dissection is the most optimal treatment approach for both tumors. However, due to the high potential risk of postoperative complications, the right approach is to make a patient-specific decision via a multidisciplinary approach at all stages. In this article, we present three cases of synchronous lung and esophageal tumors treated with different approaches due to their specific circumstances and discuss their pre-, intra-, and postoperative stages.

Keywords: Esophageal cancer, lung cancer, multidisciplinary approach, synchronous.

Synchronous lung and esophageal carcinomas are rare clinical conditions. Their incidence has been reported as 0.54 to 3.2%.^[1] Morbidity and mortality significantly increase after esophagectomy + esophagogastrotomy and pulmonary anatomic resection and lymph node dissection (LND) for synchronous tumors in the same session.^[1]

The most important step in these cases is correct staging. A synchronous mass detected in the lung is likely to be the metastasis of esophageal malignancy; synchronous esophageal and lung tumors have a better prognosis than metastatic esophageal tumors.^[1,2]

The right approach is to take a patient-specific, multidisciplinary approach after accurate and detailed staging before deciding on the choice of treatment.^[2] As

ÖZ

Senkron akciğer ve özofagus tümörleri nadir klinik durumlardır. Lenf nodu diseksiyonu ile küratif rezeksiyon, her iki tümör için de en uygun tedavi yaklaşımıdır. Ancak, ameliyat sonrası muhtemel komplikasyon riskinin yüksek olması nedeniyle, doğru yaklaşım tüm evrelerde multidisipliner yaklaşım ile hastaya özgü karar alınmasıdır. Bu yazıda, farklı koşullar nedeniyle farklı yaklaşımlar ile tedavi edilen senkron akciğer ve özofagus tümörlü üç olgu sunuldu ve olguların ameliyat öncesi, ameliyat sırası ve ameliyat sonrası aşamaları tartışıldı.

Anahtar sözcükler: Özofagus kanseri, akciğer kanseri, multidisipliner yaklaşım, senkron.

synchronous lung and esophageal carcinomas can be accompanied by high-risk postoperative complications.

In this article, we present three cases of synchronous lung and esophageal tumors treated with different approaches due to their specific circumstances and discuss their pre-, intra-, and postoperative stages.

CASE REPORT

Case 1- A 54-year-old male patient with a history of tuberculosis 29 years ago presented with dysphagia. In his endoscopic examination, an ulcerated lesion was detected in the esophagus between 30 cm and 35 cm from the incisors. The histopathological examination result was reported as a well-differentiated squamous cell carcinoma

Corresponding author: Yasemin Büyükkarabacak.
E-mail: yaseminbuyukkarabacak@gmail.com

Doi: 10.5606/tgkdc.dergisi.2023.21233

Received: December 09, 2020

Accepted: January 13, 2021

Published online: January 30, 2023

Cite this article as: Büyükkarabacak Y, Pirzirelli MG, Gurz S, Taslak A, Sullu Y, Çelik B, et al. Treatment options for synchronous lung and esophagus tumors: A difficult decision to make. Turk Gogus Kalp Dama 2023;31(1):136-142. doi: 10.5606/tgkdc.dergisi.2023.21233.

©2023 All right reserved by the Turkish Society of Cardiovascular Surgery.



This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes (<http://creativecommons.org/licenses/by-nc/4.0/>).

(Figure 1a-f). Computed tomography (CT) of the thorax detected a diffuse lesion of malignant appearance extending to the paraesophageal and subcarinal fatty tissue in the middle part of the esophagus approximately 5 cm in the segment, reaching up to 15 mm in thickness; alveolar densities and calcific nodules with chronic sequelae bilaterally in the lung parenchyma due to previous tuberculosis; and a 20×25 mm malignant nodular lesion with irregular borders in the anterior of the lower lobe of the right lung (Figure 1a, b). In addition, fluorodeoxyglucose positron emission tomography (FDG-PET) imaging showed a hypermetabolic focus in the right supraclavicular area (maximum standardized uptake value [SUV_{max}]: 3.98); a hypermetabolic mass lesion in the esophagus starting from the carina level and continuing as a concentric

wall thickening in a 55 mm segment on the coronal axis (SUV_{max}: 11.20); diffuse, calcific, FDG-negative tuberculous sequela lesions bilaterally in the lung parenchyma and mediastinum; a hypermetabolic parenchymal nodular lesion with lobulated contours in the anterobasal segment of the lower lobe of the right lung showing heterogeneous metabolic activity (late SUV_{max}: 9.99) (Figure 1c, d).

There was no metastasis evident in the cranial magnetic resonance imaging (MRI). It was decided to perform supraclavicular lymphadenopathy (LAP) biopsy and transthoracic aspiration biopsy (TTAB) from the lung mass, as agreed in the Multidisciplinary Tumor Council (MTC). The supraclavicular lymph node biopsy was negative for malignancy, but an adenosquamous cell carcinoma was revealed in the TTAB of the mass

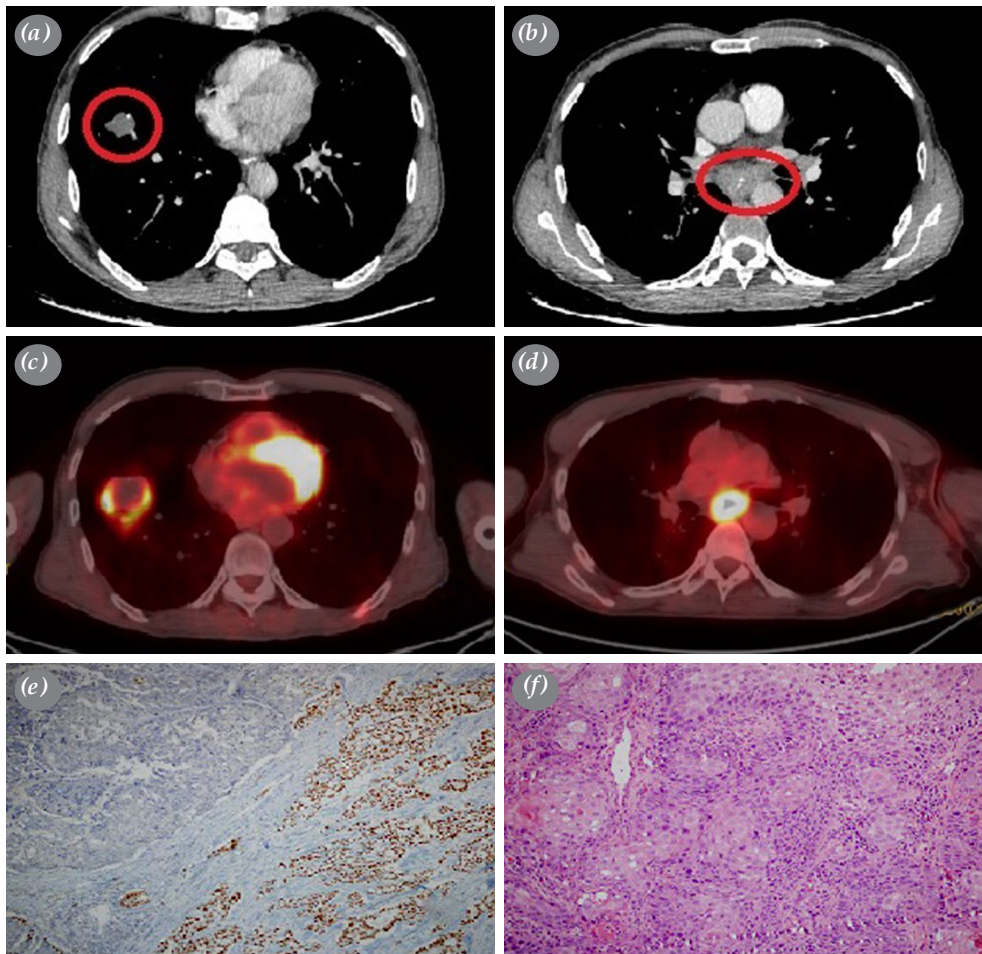


Figure 1. (a, b) Thoracic CT and (c, d) PET-CT showing a diffuse malignant lesion in the middle part of the esophagus and 20 mm ×25 mm malignant nodular lesion in lower lobe of the right lung; adenosquamous carcinoma, (e) lung, ×200, TTF1, squamous cell carcinoma, esophagus, (f) H&E, ×200. PET-CT: Positron emission tomography-computed tomography; TTF1: Thyroid transcription factor-1.

in right lower lobe. The histopathological examination was reported as revealed an adenocarcinoma (Figure 1e). Based on these results, the esophageal tumor T3N?M0 was staged as a lung tumor T3N0M0 and neoadjuvant chemoradiotherapy (CRT) were initiated for the esophageal tumor. A total of 50.4 Gy was administered at 1.8 Gy/Fx during 28 Fx sessions with external intensity-modulated radiation therapy (IMRT) and concurrent and weekly, paclitaxel and carboplatin/AUC2 were administered at 50 mg/m².

Post-treatment control FDG-PET showed that metabolic activity completely disappeared in the esophageal lesion followed at the carina level (complete metabolic response to treatment). However, an increase in the size and metabolic activity of the mass in the right lower lobe's superior segment was detected. The patient's case was discussed again by the MTC regarding the re-staging results after neoadjuvant CRT. Based on the diagnosis of synchronous lung and esophageal tumors, a collective decision was made for curative resection for both tumors. In exploration, a lesion of approximately 5×4 cm mass was detected in the anterobasal segment of the lower lobe of the right

lung. Frozen sections were studied after sampling the lymph nodes station of 2, 4, 9, and 7. The result was reported as tumor-negative.

Based on these results, it was decided to perform a right lower lobectomy initially. Right lower lobectomy and mediastinal LND were, then, performed. Following these procedures, the esophagus was suspended and the surrounding tissues were freed. In the second stage, the abdomen was entered with a median incision over the umbilicus in the supine position. The stomach was skeletonized and tubed and a conduit was prepared. The esophagus was explored on the left side of the neck and the conduit was pulled into the neck. The posterior wall of the stomach and esophagus anastomosis was performed with a 45-mm Endo GIA™ (Medtronic Inc., MN, USA), while the anterior wall was anastomosed manually. After the methylene blue test on the sixth postoperative day, oral nutrition was started. Due to chylous drainage from the chest tube, a special diet for chylothorax was initiated. On Day 5 of follow-up, re-exploration was decided, as the amount of drainage from chest drain reached 1000 mL/day. Thoracic duct was reattached through the diaphragmatic hiatus.

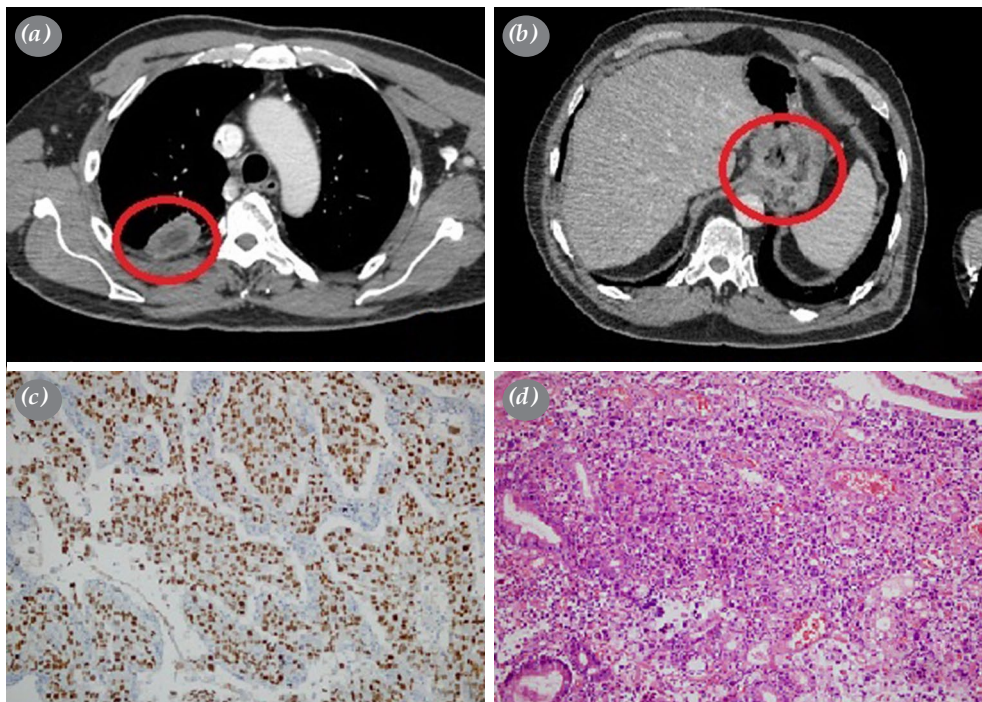


Figure 2. Thoracoabdominal CT showing a pleural-based 35×23 mm mass in posterior segment of the right lung upper lobe and a malignant mass on the small curvatural surface of the esophagocardiac junction and proximal part of the corpus; adenocarcinoma, lung, (c) ×200; TTF1, adenocarcinoma, cardia, (d) H&E, ×200.

CT: Computed tomography; TTF1: Thyroid transcription factor-1.

The patient was discharged on Day 16 of follow-up. The patient, who did not have any additional problems at the first month of follow-up, was consulted to the oncology outpatient clinic.

Case 2- A 75-year-old male patient was examined for reflux, and his endoscopy revealed a malignant mass in the cardia, distal to the esophagogastric junction. The histopathological diagnosis was Siewert type 3 esophagogastric junction adenocarcinoma. Abdominal CT showed wall thickening at the level of the antrum-small curvature of the stomach and multiple lymph nodes in its neighborhood. Subsequently, the patient received six courses of neoadjuvant chemotherapy consisting of docetaxel 50 mg/m², oxaliplatin 85 mg/m², leucovorin 200 mg/m², and 5-FU 2,600 mg/m² (24 h intravenous infusion).

On the PET-CT scan, a pleural-based 35×23-mm mass in posterior segment of the right lung upper lobe (SUV_{max}: 22.5) involving the right lower paratracheal (SUV_{max}: 7.9), left upper paratracheal (SUV_{max}: 6.1), precarinal (SUV_{max}: 4.3), right hilar (SUV_{max}: 7.5), and subcarinal (SUV_{max}: 5.6) lymph nodes, was detected. In TTAB, the mass was reported as a lung adenocarcinoma histopathologically.

Abdominal CT revealed a malignant mass that showed significant infiltration into the adjacent fatty tissue on the small curvatural surface of the esophagocardiac junction and proximal part of the corpus. In the periesophageal area, there were four to five round-shaped lymph nodes, the largest of which was 11 mm in diameter, adjacent to the esophagogastric junction, cardiac and left gastric curvature (Figure 2a, b). The patient was discussed with these results in the MTC. Decisions to proceed with curative resection and LND were made for both tumors, based on the diagnosis of synchronous gastroesophageal junction and lung carcinomas. In the first session, total gastrectomy + esophagojejunostomy and lower mediastinal and D2 LND were performed transhiatally. Postoperative histopathological examination confirmed the diagnosis of adenocarcinoma (Figure 2c, d), with associated perineural and lymphovascular invasion including 11 metastatic lymph nodes (1 splenic artery lymph node, 2 at the tumor periphery, and 8 at the small curvature) (T4aN2M0). Three weeks after this procedure, a mediastinoscopy (the R2 and R4 stations were reported as tumor-negative), followed by a right upper lobectomy and LND, were performed. Histopathological examination resulted in a diagnosis

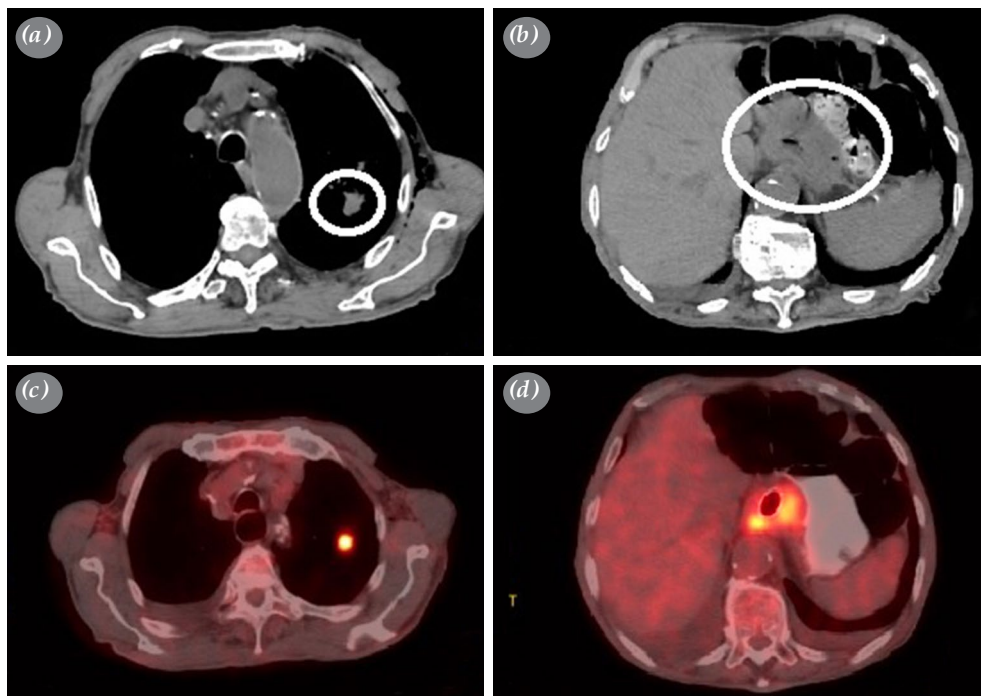


Figure 3. (a, b) Thoracic CT and (c, d) PET-CT showing a mass lesion with a 15-mm spicular extension in the left upper lobe's apicoposterior segment and thickening of the wall at the esophagus-gastroesophageal junction and spreading to the cardia and the lower curvature.

PET-CT: Positron emission tomography-computed tomography.

of solid pattern predominant lung adenocarcinoma (Figure 2c)+ reactive LAPs at stations 10, 4, 2, 7, and 9 (pT3N0M0). The patient was discharged on Day 4 of follow-up and as he did not have any additional problems at the first month of follow-up, and he was referred to the medical oncology clinic.

Case 3- A 75-year-old male patient who presented with dysphagia and weight loss underwent thoracic CT and PET-CT. A mass lesion with a 15-mm spicular extension in the left upper lobe apicoposterior segment (SUV_{max} : 6.52), and thickening of the wall at the esophagus-gastroesophageal junction and spreading to the cardia and the lower curvature (SUV_{max} : 6.43), were detected. During esophagogastroscopy, an ulcerovegetan mass was detected, starting from 36 cm into the esophagus and invading the stomach, cardia and small curvature. Histological assessment of the biopsy specimen confirmed the diagnosis of adenocarcinoma. The TTAB was requested from the mass in the apicoposterior segment of left upper lobe. The histopathological examination was reported as non-diagnostic. A repeat biopsy was recommended; however, the patient refused. The patient's poor performance score according to the Eastern Cooperative Oncology Group (ECOG) performance scale and limited respiratory reserve were discussed in the MTC. The tumor in the lung was evaluated as malignant and second primary based on its radiological and activity characteristics (Figure 3a-d). The patient was evaluated as surgical and medical inoperable Siewert Type III gastroesophageal junction carcinoma+lung carcinoma. A fully-coated nitinol esophageal stent was applied to the distal esophagus for enteral nutrition. The patient, who was discharged on the second day after the procedure, did not have any additional problems at the first month of follow-up.

DISCUSSION

Although the most common synchronous tumor in patients with esophageal tumors are head and neck tumors, synchronous esophagus and lung carcinomas are rare pathological entities. They are most frequently encountered in male patients between the ages of 50 and 60, and histopathology is usually evaluated as squamous cell carcinomas.^[3]

Synchronous lung tumor can usually be evaluated as metastasis in the first evaluation. However, after a detailed histopathological evaluation, they can be diagnosed as a second primary tumor, if one or more of the following criteria is fulfilled: (i) If the synchronous lung tumor is of a different histological type; (ii) if there is a lung tumor present before an

esophageal tumor; and (iii) if a solitary lesion with endobronchial spread and/or irregular borders is detected radiologically, then asynchronous primary lung tumor should be mentioned.^[2,4]

In the present report, different histological types were detected in one patient. However, the second patient presented with both an esophagus and lung adenocarcinoma. It was not difficult to diagnose synchronous tumors in the patient with different histopathological types. However, a diagnosis of synchronous tumors was made in other patients on the basis of the radiological features of the lung tumor and, histopathologically, the bronchial invasiveness of the tumor.

For synchronous esophageal and lung tumors, preoperative evaluation requires a very careful and patient-specific approach. Both tumors carry a high risk of postoperative complications, particularly in the elderly and in patients with limited respiratory reserve. An increase in morbidity and mortality rates is inevitable in simultaneous, curative surgical interventions for synchronous tumors.^[1] In the review article of Mukerji and Wolf,^[5] a high percentage of complications was reported for patient groups with esophagus and lung carcinoma. However, in patients undergoing curative surgery, long-term survival is reported to be significantly longer than in other patients. Therefore, multidisciplinary decisions were made for the diagnostic process and treatment selection for all three of our patients. In particular, the pathologist's and radiologist's opinions were of the utmost importance in the selection of the treatment protocol for the patients. Especially in patients with the same histopathological type, the radiological image of the lung tumor was evaluated together with its histopathological features and the diagnosis was a synchronous second primary tumor. In the patient who was considered to be medically inoperable, it was decided to continue with CRT after palliative stenting in MTC.

The second most important decision for patients for whom a decision has been made for curative surgery for both tumors is to decide whether the surgeries would be performed in one or two stages. Although it has been reported that no postoperative complications were encountered in single-stage surgeries, it has also been reported that the postoperative complication rate for single session surgeries is 20 to 50%.^[6-8] If the general condition of the patient suggests intolerance of all surgeries in the same session, then two-stage surgery would be the most appropriate treatment choice.

However, the most important factor is the localization of the esophageal tumor. Total gastrectomy + esophagojejunostomy and lower mediastinal and abdominal D1/D2 LND can be applied in cases of Type II-III gastroesophageal junction tumors, if the tumor extends less than 3 cm proximally along the esophagus. After three weeks of follow-up, lung resection and mediastinal LND were performed in the second session. If the esophageal tumor is not extending more than 3 cm proximally, and the general condition of the patient is appropriate, esophagectomy and esophagogastrostomy and lung resection and LND can be applied in the same session.

For cervical esophageal tumors, esophagectomy and LND and cervical esophagostomy and lung resection are performed in the first stage. In the second session, after the appropriate recovery period, the gastric conduit is reconstructed and the anastomosis is completed by pulling it from the substernal region to the neck.^[6-8]

We performed two-stage surgery (right thoracotomy + laparotomy + cervical esophagogastrostomy) in one session on one of our patients. The patient with Type III gastroesophageal junction tumor underwent two sessions of surgery. In the first session, esophagojejunostomy and LND were performed with laparotomy, leaving a safe surgical margin that was confirmed with frozen-section procedure. Three weeks later, in the second session, the right upper lobectomy and LND were performed. There were no postoperative complications in the patient.

Although concomitant surgery has a high risk of postoperative complications, several important measures taken during surgery would help to minimize the possibility. To illustrate, muscle-sparing thoracotomy and minimally invasive surgery may be the right approaches. Minimally invasive surgery, particularly in eligible patients, provide significant advantages for synchronous curative surgeries with small incisions, less blood loss and shorter hospital stay. The ideal patient profile for synchronous surgery is defined by normal partial pressure of oxygen (PO₂) and partial pressure of carbon dioxide (PCO₂), forced expiratory volume in 1 sec (FEV1) >70%, and estimated postoperative vital capacity > 50%.^[8] However, it should be kept in mind that even patients meeting all these criteria, or even better situated, may occasionally encounter complications that cannot be foreseen preoperatively.

In conclusion, synchronous lung and esophageal carcinomas can be accompanied by various

postoperative complications. According to the case series in the literature and similarly the results obtained in our series, despite all the complications, curative resection with lymph node dissection is the most optimal treatment approach for such tumors. However, the most appropriate approach is to make decisions on a patient-specific and multidisciplinary basis at all stages. Selection of a treatment strategy for each patient among gastroenterologists, thoracic surgeons, and medical and radiation oncologists may result in a good short-term prognosis and improved quality of life.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conception or design of the experiment(s), or collection and analysis or interpretation of data, drafting the manuscript or revising its intellectual content; and approval of the final version of the manuscript to be published: Y.B.; Conception or design of the experiment(s), or collection and analysis or interpretation of data, drafting the manuscript or revising its intellectual content: M.G.P., Y.S.; Conception or design of the experiment(s), or collection and analysis or interpretation of data, drafting the manuscript or revising its intellectual content; and approval of the final version of the manuscript to be published: S.G., A.T., B.Ç., A.B.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Wang XX, Liu TL, Wang P, Li J. Is surgical treatment of cancer of the gastric cardia or esophagus associated with a concurrent major pulmonary operation feasible? One center's experience. *Chin Med J (Engl)* 2012;125:193-6.
2. Lindenmann J, Matzi V, Maier A, Smolle-Juettner FM. Transthoracic esophagectomy and lobectomy performed in a patient with synchronous lung cancer and combined esophageal cancer and esophageal leiomyosarcoma. *Eur J Cardiothorac Surg* 2007;31:322-4. doi: 10.1016/j.ejcts.2006.11.013
3. Song X, Shen H, Li J, Wang F. Minimally invasive resection of synchronous triple primary tumors of the esophagus, lung, and thymus: A case report. *Int J Surg Case Rep* 2016;29:59-62. doi: 10.1016/j.ijscr.2016.10.048
4. Ishii H, Sato H, Tsubosa Y, Kondo H. Treatment of double carcinoma of the esophagus and lung. *Gen Thorac Cardiovasc Surg* 2008;56:126-30. doi: 10.1007/s11748-007-0200-0
5. Mukerji AN, Wolf A. Synchronous esophageal and lung cancer. *Thorac Surg Clin* 2018;28:97-104. doi: 10.1016/j.thorsurg.2017.09.002

6. Cellini F, Morganti AG, Di Matteo FM, Mattiucci GC, Valentini V. Clinical management of gastroesophageal junction tumors: Past and recent evidences for the role of radiotherapy in the multidisciplinary approach. *Radiat Oncol* 2014;9:45. doi: 10.1186/1748-717X-9-45
7. Kocaman G, Enön S. Özofagogastrik bileşke kanserleri ve cerrahi tedavisi. *Ankara Üniversitesi Tıp Fakültesi Mecmuası* 2016;69. doi: 10.1501/Tipfak_0000000950
8. Matsubara T, Ueda M, Takahashi T, Nakajima T, Nishi M. Surgical treatment of cancer of the thoracic esophagus in association with a major pulmonary operation. *J Am Coll Surg* 1997;185:520-4. doi: 10.1016/S1072-7515(97)00102-6