OPEN

Esophageal cancer operation in the COVID-19 era: are the outcomes different from its past in an observational cohort study?

Mohammad Shirkhoda, MD^a, Monem Basravi, MD^{a,*}, Amirmohsen Jalaeefar, MD^c, Mehdi Farhangian, MD^b, Fereydoun Memari, MD^d, Mohsen Meidani, MD^e

Background: COVID-19 spread rapidly and potentially affected every medical profession, including surgery. This study aims to compare the postoperative outcomes of oesophageal cancer surgeries in COVID-19 age and a year before.

Methods: This retrospective cohort study was performed as a single-centred study from March 2019 to March 2022 at Cancer institute, Tehran, Iran. Demographic data, cancer type, surgical procedures, and postoperative outcomes and complications were compared between the two groups pre-COVID-19 and during the COVID-19 pandemic.

Results: Totally, 120 patients enroled in the study, of which 57 underwent surgery before the COVID-19 pandemic, and 63 during the COVID-19 pandemic. The mean age in these groups was 56.9 (\pm 12.49) and 58.11 (\pm 11.43), respectively. Females included 50.9% and 43.5% of individuals who underwent surgery before and during the COVID-19 pandemic. The interval between admission and surgery was significantly shorter in patients underwent surgery during the COVID-19 pandemic (5.17 vs. 7.05; P=0.013). However, there was no significant difference between time interval between surgery and discharge [11.68 (7.81) vs. 12 (6.92); P=0.689]. Aspiration pneumonia was the most common complication in both groups. There was no significant difference between postoperative complications in both groups.

Conclusion: Outcomes of oesophageal cancer surgeries in COVID-19 age in our institution were comparable with the year before the pandemic. The decrease in the time interval between surgery and discharge did not lead to an increase in postoperative complications and could be noted for post-COVID-19 era policymaking, too. This study suggests not postponing any of the surgical treatments for oesophageal cancer in the COVID-19 era.

Keywords: aspiration pneumonia, COVID-19, oesophageal cancer, respiratory complications, surgical treatment

Introduction

The latest global health threat is a new respiratory disease outbreak known as COVID-19. This novel coronavirus known as SARS-CoV-2 was first recognized in December 2019^[1,2]. The COVID-19 situation was declared a pandemic on 11 March

^aCancer Research Center, Departments of ^bGeneral Surgery, ^cSurgical Oncology, Cancer Institute of Iran, ^dDepartment of General Surgery, Subdivision of Surgical Oncology, Cancer Institute of Iran and ^eDepartment of Infectious Diseases, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

M.B., M.F. and A.J. contributed equally.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Cancer Research Center, Cancer Institute of Iran, Tehran University of Medical Sciences, Tehran, Iran. Tel.: +983135654843; fax: +983135654743. E-mail address: Monem_basravi@yahoo.com (M. Basravi).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Annals of Medicine & Surgery (2023) 85:3303-3307

Received 17 February 2023; Accepted 15 May 2023

Published online 25 May 2023

http://dx.doi.org/10.1097/MS9.000000000000923

HIGHLIGHTS

- This study compares postoperative outcomes of oesophageal cancer surgeries before and during the COVID-19 pandemic at a cancer institute in Tehran, Iran.
- The study found that there was no significant difference in postoperative complications between the two groups, and outcomes were comparable with the year before the pandemic.
- The time interval between admission and surgery was significantly shorter during the COVID-19 pandemic, but this did not lead to an increase in postoperative complications.

 $2020^{[3]}$. Iran has one of the highest reported infection rates worldwide^[4].

As a consequence of the pandemic, the practice of medicine was disturbed in almost all fields in Iran, including cancer and surgical centres^[5,6]. The complexities of the multidisciplinary approach to oesophageal cancer patients, as well as the high morbidity rates of oesophageal surgery, posed challenges to these patients' treatment pathways. Several recommendations and strategies were released to assist surgeons in their decision-making process and to improve the outcomes for these patients^[7].

Surgical approach recommendations were not certain during the pandemic; at first, the International Society for Diseases of the Esophagus (ISDE)^[8] suggested against the use of laparoscopy

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www. annalsjournal.com.

unless there were special conditions due to the risk of an increase in virus aerosolization during minimally invasive surgery, but they changed back^[9]. However, there were no major changes in Iran's surgical protocols other than personal protective guidelines^[5].

This survey was performed on oesophageal cancer patients treated surgically in order to compare the surgical outcomes and management strategies employed before and during the COVID-19 pandemic in Iran. We present the findings on this topic here, with a focus on the impact of the COVID-19 pandemic on surgical techniques and short-term outcomes.

Methods

Design

This study was conducted as a retrospective cohort study from March 2019 to March 2022 in Cancer institute, Tehran, Iran. Since the study was performed on human subjects, ethical approval was required. The ethics committee of Cancer institute, Tehran, Iran approved the study protocol with the ethics code: IR.TUMS. IKHC.REC.1400.364. Written informed consent was obtained from the patient for the publication of this study. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. This study was reported based on the STROCSS guideline^[10].

Participants

All patients with oesophageal cancer who had undergone surgery for it in the cancer institute of IKHC were included in this study. The patients were divided into two groups those who had undergone surgery during the COVID-19 pandemic and those who had gone surgery before the COVID-19 pandemic. The exclusion criteria were as follows: (1) oesophageal perforation due to a tumour or other causes, (2) urgent or emergent surgery for an oesophageal tumour and (3) clinical or radiological signs suggesting COVID-19 infection before the surgery.

Procedures and outcomes

Documents of all patients with oesophageal cancer who had undergone surgery for it from March 2019 to March 2022 were retrieved. Four group of variables were evaluated in this study. First, we recorded the basic and demographic characteristics of participants, including age and sex. Second, characteristics of oesophageal cancer and history of its treatment, including tumour type (squamous-cell carcinoma, adenocarcinoma and adenoid cystic carcinoma), the distance of the tumour from incisor and its location (middle or lower third of oesophagus), stage of tumour according to the Tumor, Nodes, Metastasis staging, neoadjuvant therapy and its type, and the interval between last session of neoadjuvant therapy and surgery were recorded. Third, characteristics of surgical procedure performed for the patients were recorded, including the interval between admission and surgery, interval between surgery and discharge, type of surgery (Transhiatal, McKeown, Ivor Lewis and colon interposition), surgical approach (open, thoracoscopic and thoracoscopic & laparoscopic), chest tube placement, duration of surgery and intubation and ICU admission after surgery. Finally, complications due to the surgery, including surgical site infection, salivary fistula, tracheal injury, gastropleural fistula, anastomosis leak, deep vein thrombosis, pulmonary thromboembolism, chylothorax, aspiration pneumonia, conduit necrosis and mortality after surgery were recorded. For patients who had undergone surgery during the COVID-19 pandemic, we recorded the incidence of COVID-19–related symptoms, such as fever and dyspnoea. Also, the diagnosis of COVID-19 based on computed tomography scan findings or reverse transcription polymerase chain reaction test was recorded.

Statistical analysis

Mean and SD were calculated for continuous variables, and number and percentage were calculated for categorical variables. We used the χ^2 test or Fisher exact test to compare the categorical variables between groups. The Kolmogorov–Smirnov test was used to determine whether the continuous variables are distributed normally or not. As none of the continuous variables were distributed normally (P > 0.05), we used the Mann– Whitney test to compare the continuous variables between groups. We calculated the relative risk of complications and mortality after surgery for patients who had undergone surgery during the COVID-19 pandemic. *P* less than 0.05 was considered statistically significant. We used SPSS version 22 for all analyses.

Results

In total, 120 individuals enroled in the study, of which 57 underwent surgery before the COVID-19 pandemic, and 63 underwent surgery during the COVID-19 pandemic. The mean age of participants was 56.9 (SD = 12.49) and 58.11 (SD = 11.43) in those who underwent surgery before and during the pandemic, respectively. Also, 50.9% and 43.5% of individuals who underwent surgery before and during the COVID-19 pandemic were females. The basic and demographic characteristics of participants are shown in Table 1. There were no significant differences between the groups regarding age, sex, tumour characteristics, tumour stage and tumour treatment (P > 0.05). In both groups, T4 and N1 were the most common stages according to the Tumor, Nodes, Metastasis staging. Also, most patients had received neoadjuvant therapy, with Chemoradiation being the most commonly used neoadjuvant therapy.

Characteristics of surgical treatment of the participants in both groups are shown and compared in Table 2. The interval between admission and surgery was significantly shorter in patients who underwent surgery during the COVID-19 pandemic (5.17 vs. 7.05; P = 0.013). However, there were no significant differences between groups regarding the surgery type, surgical approach, chest tube placement, surgery duration, intubation period and ICU admission (P > 0.05). McKeown surgery was the most common type in both groups, and most patients had undergone open surgery.

Outcomes and complications of surgery in both groups are shown in Table 3. 42.1% and 34.9% of patients who underwent surgery before and during the COVID-19 pandemic had at least one complication, respectively. Also, Aspiration pneumonia was the most common complication in both groups. The mean interval between surgery and discharge was 11.68 (SD = 7.81) and 12 (SD = 6.92) in patients who underwent surgery before the COVID-19 pandemic and those who underwent surgery during the COVID-19, respectively, and there was no significant difference between groups in this regard (P=0.689). The 30-day

Basic and demographic characteristics of participants							
Variable	Before COVID-19 pandemic (N=57)	During COVID-19 pandemic (N=63)	Р				
Sex							
Female	29 (50.9)	27 (43.5)	0.465				
Male	28 (49.1)	35 (56.5)					
Age (year)	59.6 (12.49)	58.11 (11.43)	0.362				
Tumour type							
Squamous-cell carcinoma	38 (77.6)	48 (78.7)	0.533				
Adenocarcinoma	10 (20.4)	13 (21.3)					
Adenoid cystic carcinoma	1 (2)	0					
Tumour site							
Middle third	21 (40.4)	16 (27.6)	0.165				
Lower third	31 (59.6)	42 (72.4)					
Tumour distance from incisor	30.92 (4.74)	31.93 (4.95)	0.278				
(cm)							
Tumour stage according to TNN	1 staging						
In situ	1 (1.8)	0	0.534				
1	0	2 (3.4)					
2	12 (21.8)	11 (18.6)					
3	32 (58.2)	36 (61)					
4	10 (18.2)	10 (16.9)					
Nodes stage according to TNM	staging						
0	10 (18.2)	5 (8.5)	0.213				
1	24 (43.6)	33 (55.9)					
2	16 (29.1)	19 (32.2)					
3	5 (9.1)	2 (3.4)					
Neoadjuvant therapy							
No	3 (5.7)	1 (1.6)	0.333				
Yes	50 (94.3)	61 (98.4)					
Type of neoadjuvant therapy							
CRT	38 (84.4)	55 (96.5)	0.041				
Chemotherapy	7 (15.6)	2 (3.5)					
The interval between last	8.46 (3.3)	8.93 (3.38)	0.444				
neoadjuvant therapy and							
surgery (week)							

Values are reported as number (percentage), except for age, turnour distance from incisor and the interval between last neoadjuvant therpy and surgery, which are reported as mean (SD). CRT indicate chemoradiation; TNM, turnor nodes metastasis.

mortality rate was 17% and 22.2% in patients who underwent surgery before and during the COVID-19 pandemic. There were no significant differences between groups regarding the complications and mortality between groups (P > 0.05). In patients who underwent surgery during the COVID-19 pandemic, 26 individuals (41.3%) developed fever or dyspnoea with a mean interval of 3.73 (SD=2.33) days after the surgery. Also, computed tomography scan findings in 11 individuals (17.5%) were compatible with COVID-19, and nine individuals (14.3%) had positive reverse transcription polymerase chain reaction tests for COVID-19 after the surgery.

Discussion

The purpose of this study was to compare the outcomes of oesophageal cancer surgeries in patients before and after COVID-19 era. The findings were thought to help surgeons all over the world better understand what they would face and how to deal with it in similar situations. The review of the literature revealed

Variable	Before COVID-19 pandemic ($N = 57$)	During COVID-19 pandemic (N=63)	Р
Interval between admission and surgery (day)	7.05 (3.98)	5.17 (2.03)	0.013
Type of surgery			
Transhiatal	19 (33.3)	26 (41.3)	0.257
McKeown	31 (54.4)	35 (55.6)	
Ivor Lewis	5 (8.8)	1 (1.6)	
Colon interposition	2 (3.5)	1 (1.6)	
Surgical approach			
Open	42 (73.7)	41 (65.1)	0.203
Thoracoscopic	15 (26.3)	19 (30.2)	
Thoracoscopic and laparoscopic	0	3 (4.8)	
Chest tube placement			
No	0	1 (1.7)	0.381
One-sided	35 (67.3)	33 (48.5)	
Two-sided	17 (32.7)	24 (41.4)	
Surgery duration (min)	5.76 (1.42)	5.97 (1.47)	0.454
Intubation duration (h)	34.9 (46.58)	38.04 (62.84)	0.886
ICU admission duration (day)	4.15 (4.82)	4.29 (5.8)	0.15

The values are reported as mean (SD), except for type of surgery, surgical approach and chest tube placement, which are reported as number (percentage).

that there is little real-world experience with oesophageal cancer surgeries on COVID-19 patients^[11].

Demographic characteristics were similar in both groups, and they were nearly identical in male and female groups. This finding should be noted for further research on the role of sex in oesophageal cancer in the Iranian population, as it has been previously reported that the highest male-to-female incidence rate ratios of oesophageal cancer was seen in the age group of 50–59 in other races^[12]. According to the Tumor, Nodes, Metastasis staging, the most common stages of the tumours were T4 and N1, and most patients received neoadjuvant therapy, which is compatible with the previous studies^[13].

The time interval between surgery and discharge was significantly shorter in patients who underwent surgery during the COVID-19 pandemic. This may be due to the cancellation of other elective surgeries or the decision of surgeons to discharge the patient to protect them against the probable nosocomial COVID-19 transmission^[14].

McKeown surgery was the most common type of surgery in our study, which is among the most common oesophageal surgeries^[15]. Most of the patients were operated on in an open method both before and during the pandemic, which reflects the impact of our institutional policy on our surgeons, which was not necessarily based on the ISDE recommendations and their uncertainties^[8,16].

Surgical outcomes of the pandemic age were comparable to those of the time before. This finding is in line with the previous studies^[11,17,18]. Aspiration pneumonia was the most common complication, which is a notable predictor of mortality^[19,20], so it should be noted that no change in its rate was so noticeable finding in this survey.

The postoperative complication rates in both groups were nearly the same. Shorter hospital stays in previous studies resulted in more complications^[18]. Although, Chemoradiation had

Table 3

Outcomes and complications of surgery in both groups

Variable	Before COVID-19 pandemic ($N = 57$)	During COVID-19 pandemic ($N = 63$)	Relative risk (95% Cl)	Р
Any complication	24 (42.1)	22 (34.9)	0.829 (0.527-1.306)	0.456
Surgical site complication	0	1 (1.6)	_	1
Salivary fistula	6 (10.5)	5 (7.9)	0.754 (0.243-2.337)	0.755
Tracheal injury	2 (3.5)	1 (1.6)	0.452 (0.042-4.857)	0.604
Gastropleural fistula	1 (1.8)	3 (4.8)	2.667 (0.285-24.908)	0.621
Anastomosis leak	4 (7)	1 (1.6)	0.226 (0.026-1.965)	0.189
Deep vein thrombosis/ Pulmonary thromboembolism	4 (7)	2 (3.2)	0.452 (0.086- 2.377)	0.422
Chylothorax	0	2 (3.2)		0.497
Aspiration pneumonia	10 (17.5)	9 (14.3)	0.814 (0.356-1.86)	0.803
Conduit necrosis	0	1 (1.6)	_	1
AF	6 (10.5)	2 (3.2)	0.302 (0.063-1.435)	0.148
Mortality during hospitalization	9 (16.1)	14 (22.2)	1.383 (0.649–2.954)	0.488
30-day mortality	9 (17)	14 (22.2)	1.309 (0.616–2.78)	0.641

The values are reported as number (percentage).

AF indicates Atrial fibrillation.

been performed more frequently after the COVID-19 pandemic, it has been shown that chemotherapy can also have the same effects on patients with oesophageal cancer outcome^[21]. Our findings show that our policy—not discharging the patients earlier—was in contrast with their findings and did not lead to further complications in our patients during the pandemic.

To our best knowledge, this is the first original study on oesophageal cancer surgery in COVID-19 patients in iran that have evaluated the various aspects of management and postoperative outcomes. This study, conducted in a country with a high infection rate, attempted to shed light on the role of the COVID-19 pandemic on surgeries. The study was also designed in a cohort method, which allowed us to compare the results in two different groups with homogeneity in basic variables in the samples.

We implemented strict personal protective equipment (PPE) protocols during all patient visits and in the operation room. Additionally, we provided PPE for all patients and conducted educational sessions to ensure effective use of PPE. Our results indicate that when PPE is utilized correctly by both the medical team and patients, along with adherence to protective measures guidelines, the rate of infectious and surgical complications during oesophageal cancer surgery is comparable to the pre-COVID-19 era^[22].

We excluded high-risk patients with oesophageal perforation or requiring urgent/emergent surgery, as well as those with clinical and radiological signs of COVID-19 before surgery, due to the associated higher rates of morbidity and mortality and pulmonary complications, respectively^[23].

One of the limitations of this study is that the patients had not been followed for a long time at the time of reporting this survey, and the sample size could have been larger. However, the emergence of the outbreak and the lack of real-world experiences in the reviewed literature were the most important reason for us to share this experience to be useful to other surgeons, and healthcare providers. Also, as this study was a retrospective cohort, it can be subject to bias, such as selction bias or information bias.

This study was conducted in a single centre in Iran, specifically at the cancer institute, which happens to be the most high-volume centre for oesophageal cancer surgery. Our patient cohort was drawn from 28 different provinces and 95 different cities across the country. Despite the high incidence of COVID-19 infection in both our country and centre, we were able to mitigate the impact of this pandemic on our oncological results by implementing effective protective measures. Therefore, our findings are generalizable and comparable to the pre-COVID-19 era.

More research could be conducted to determine which aspects of surgical management in COVID-19 patients should be prioritized. This could be a call to create a universal or national guideline for performing surgeries during future pandemics.

Conclusion

In conclusion, we believe that this study shows that outcomes of oesophageal cancer surgeries in the COVID-19 era in our institution were comparable with the year before the pandemic. The time interval between surgery and discharge did not change during the COVID-19 pandemic compared to before, and it shows that proper hospital management is possible in such situations without affecting the surgical outcomes, including a 30-day mortality rate. Regarding the findings and the importance of timely cancer management, this study suggests not postponing any of the surgical treatments for oesophageal cancer in the COVID-19 er Ethical approval

Ethical approval

The ethics committee of Tehran University of Medical Sciences approved the study protocole with the ethics code: IR.TUMS. IKHC.REC.1400.364.

Consent

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

Source of funding

No funding to declare.

Authors contributions

M.S. was primarily responsible for the study design. He also supervised the entire project. All authors were equally responsible for data collection. Statistical analysis was mainly performed by M.F. and F.M. M.B., A.J., M.F. and M.M. were involved in the writing of the paper.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

None.

Guarantor

Monem Basravi.

Data availability statement

Datasets generated during and analyzed during the current study are available upon reasonable request from the corresponding author, M.B.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgements

I would like to thank all the people who helped us with this research, especially my beloved wife, Maedeh.

References

- Chowell G, Mizumoto K. The COVID-19 pandemic in the USA: what might we expect? Lancet 2020;395:1093–4.
- [2] Fauci AS, Lane HC, Redfield RR. Covid-19—navigating the uncharted. Mass Med Soc 2020;382:1268–9.
- [3] Bedford J, Enria D, Giesecke J, et al. COVID-19: towards controlling of a pandemic. Lancet 2020;395:1015–8.
- [4] Rassouli M, Ashrafizadeh H, Shirinabadi Farahani A, et al. COVID-19 management in Iran as one of the most affected countries in the world: advantages and weaknesses. Front Public Health 2020;8:510.

- [5] Ebrahimpour A, Chehrassan M, Hoveidaei AH, et al. Surgical management of extremity fractures in COVID-19 patients. J Orthop Spine Trauma 2021;7:127–33.
- [6] Hoveidaei A. Radiotherapy technology education in iran: a year after the COVID-19 pandemic. J Biomed Phys Eng 2021;2:105–6.
- [7] Tuech J-J, Gangloff A, Di Fiore F, et al. Strategy for the practice of digestive and oncological surgery during the Covid-19 epidemic. J Visc Surg 2020;157:S7–12.
- [8] Yip HC, Chiu P, Hassan C, et al. ISDE guidance statement: management of upper gastrointestinal endoscopy and surgery in COVID-19 outbreak. Dis Esophagus 2020;33:doaa029.
- [9] Barbieri L, Talavera Urquijo E, Parise P, et al. Esophageal oncologic surgery in SARS-CoV-2 (COVID-19) emergency. Dis Esophagus 2020;33:doaa028.
- [10] Agha R, Abdall-Razak A, Crossley E, et al. STROCSS 2019 Guideline: strengthening the reporting of cohort studies in surgery. Int J Surg 2019;72:156–65.
- [11] Rebecchi F, Arolfo S, Ugliono E, et al. Impact of COVID-19 outbreak on esophageal cancer surgery in Northern Italy: lessons learned from a multicentric snapshot. Dis Esophagus 2021;34:doaa124.
- [12] Nordenstedt H, El-Serag H. The influence of age, sex, and race on the incidence of esophageal cancer in the United States (1992–2006). Scand J Gastroenterol 2011;46:597–602.
- [13] Pimiento JM, Weber J, Hoffe SE, et al. Outcomes associated with surgery for T4 esophageal cancer. Ann Surg Oncol 2013;20:2706–12.
- [14] Du Q, Zhang D, Hu W, et al. Nosocomial infection of COVID-19: a new challenge for healthcare professionals. Int J Mol Med 2021;47:31; 1.
- [15] D'Amico TA. Mckeown esophagogastrectomy. J Thorac Dis 2014;6 (Suppl 3):S322.
- [16] Chiu PW, Hassan C, Yip HC, et al. ISDE guidance statement management of upper-GI endoscopy and surgery in COVID-19 outbreak. Dis Esophagus 2020;33:1–4.
- [17] Milito P, Asti E, Resta M, et al. Minimally invasive esophagectomy for cancer in COVID hospitals and oncological hubs: are the outcomes different? . Eur Surg 2022;54:98–103.
- [18] Dolan DP, Swanson SJ, Lee DN, Polhemus E, Kucukak S, Wiener DC, et al. Esophagectomy for esophageal cancer performed during the early phase of the COVID-19 pandemic. Semin Thorac Cardiovasc Surg. Elsevier; 2021.
- [19] Atkins BZ, Shah AS, Hutcheson KA, et al. Reducing hospital morbidity and mortality following esophagectomy. Ann Thorac Surg 2004;78: 1170–6.
- [20] Bailey SH, Bull DA, Harpole DH, *et al.* Outcomes after esophagectomy: a ten-year prospective cohort. Ann Thorac Surg 2003;75:217–22.
- [21] Fan N, Wang Z, Zhou C, et al. Comparison of outcomes between neoadjuvant chemoradiotherapy and neoadjuvant chemotherapy in patients with locally advanced esophageal cancer: A network metaanalysis. EClinicalMedicine 2021;42:101183.
- [22] Agrawal V, Yadav SK, Agarwal P, *et al.* Strategies for optimizing the use of PPE during surgery in COVID-19 pandemic: rapid scoping review of guidelines. Indian J Surg 2021;83:17–27.
- [23] Deng JZ, Chan JS, Potter AL, et al. The risk of postoperative complications after major elective surgery in active or resolved COVID-19 in the United States. Ann Surg 2022;275:242–6.