Peer Review File

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Reviewer A

Comment 1: The study is of interest summarizing the studies reporting diagnoses, operative outcomes/stage at presentation and outcomes of esophageal cancer during the pandemic. Although the study is relatively simple and basically provides a list of studies assessing these afore mentioned outcomes, the literature search is extensive and the text is really ease to follow. Tables are clear.

I have no suggestions for improve. The study provides useful data regarding the effect of COVID-19 on esophageal cancer.

Reply 1: Thank you for this kind comment.

Reviewer B

Interesting and potentially useful manuscript for guiding esophageal cancer management in next pandemic.
Please address:
1. Abstract Conclusions: add constructive suggestions for which resources should be reallocated or suggest a specific plan on what area to focus on to prepare for next pandemic.

Reply 1: Thank you for this important comment.

First and foremost, we sought to highlight that with the reorganization of oncologic care administration, strict adherence to COVID-19 protective measures, and reallocation of health care resources towards the same, EC surgery was able to continue safely during the COVID-19 pandemic. Furthermore, we simply sought to note that although healthcare systems did well to triage care and prioritize the care of those acutely ill, this may potentially have late ramifications for patients with progressive, indolent diseases such as esophageal cancer. Therefore, our recommendations lie in what was successfully applied during this intense, overwhelming period in global health. We have revised the abstract conclusion accordingly, which now reads as follows:

“Amidst resource scarcity during the COVID-19 pandemic, the multidisciplinary management of patients with EC was affected at multiple stages in the care pathway. Although the complete ramifications of reductions in EC diagnosis and delays in care remain unclear, esophageal cancer surgery was able to safely continue as a result of collaboration between centers, strict adherence to COVID-19 protective measures, and reallocation of healthcare resources towards the same. Ultimately, when healthcare systems are pushed to the brink, the downstream consequences of resource reallocation require judicious analysis to optimize overall patient

outcomes."

2. Highlight Box: under bullet about implication and change, add specific details/suggestions (albeit brief) for resources to be allocated.

Reply 2: Thank you for this pertinent comment.

Please see the response to comment 1. We have added the following bullet point in the highlight box:

"Effective care triage, implantation and strict adherence to public health isolation guidelines and allocation of resources towards the same, as well as collaboration between centers permit the continuation of esophageal cancer surgery when healthcare infrastructure is overwhelmed."

3. Introduction/Background: change "complication" to morbidity."

Reply 3: Thank you for this comment.

The term "complication" has been revised to "morbidity" in the introduction and background.

The "Background" subsection of the introduction now reads as follows:

"Afflicting over 500,000 individuals globally and accounting for 3.2% of all cancer diagnoses, esophageal cancer (EC) is the eighth most common cancer type worldwide. With an average 5-year survival of 19.9%, esophageal cancer has a very poor prognosis. Surgical resection in the form of esophagectomy is the mainstay of management for patients with resectable disease (1,2). Esophagectomy is a complex procedure with an overall morbidity rate greater than 50% (3). Due to the nature of this operation, significant risk of complications, and prolonged recovery time, esophageal cancer and its treatments necessitate the utilization of significant healthcare resources to allow for surgical intervention and patient support for postoperative recovery. Estimated to account for approximately 3% of cancer diagnoses, the prevalence of esophageal cancer is significant (2)."

4. Results: you have a Table of studies, so revise this section so you don't just list each study in its own paragraph. Refer to Table and make Results section more concise.

Reply 4: Thank you for noting this.

In an effort to make the results section more concise without comprising its scope, we have reorganized the individual paragraphs in each of the results subsections. In subsection 3.1 we have grouped individual studies based on their results and the geographic location of the study. In subsection 3.2 we have grouped individual studies based on the outcomes of focus (access to preoperative investigations/endoscopy, Barrett's esophagus screening, delays in surgical treatment). In subsection 3.3 we have grouped individual studies based on their analysis of

alterations in esophageal cancer surgical volume, perioperative mortality, perioperative morbidity, and late surgical outcomes. Finally, in subsection 3.5 we have reviewed all population-based modeling studies concurrently. Furthermore, we have largely removed the statistical data from the results section as this is included in Table 2.

The results section now reads as follows:

"3.1 Impact of COVID-19 on Esophageal Cancer Rates & Presentation

Morias et al. conducted an epidemiological analysis of patients with malignancy in Portugal between 2019-2020. A 30.8% decrease in newly diagnosed EC cases was noted, along with a 40% absolute reduction of new cancer cases overall and an increased diagnosis of cancer at an advanced stage (10). Similarly, a German study of patients with GI cancers between 2019-2020 indicated a 3.2% decrease in newly diagnosed gastrointestinal (GI) cancers during the pandemic along with a 25.5% decrease in newly diagnosed EC during the first lockdown (11). Also, an analysis of patients with esophagogastric cancer between 2019-2020 in the United Kingdom (UK) indicated a significant increase in acute hospital admissions and a decline in urgent clinic referrals after the first government-issued lockdown during the pandemic. After the lockdown, increased metastatic disease at presentation was noted (7).

A single-center analysis of 133 patients between 2019-2020 in the United States (US) reported no significant difference in preoperative pathologic tumor stage between pandemic and pre-pandemic patient populations (12). An analogous study of 70 patients undergoing surgical intervention for EC across multiple centers in Italy reported equivalent results, with no significant difference in pathological stage at presentation between pre-pandemic and pandemic groups (13).

In their retrospective study consisting of 556 patients at a single center in Japan from 2018-2021, Miyawaki et al. reported a significant decrease in the number of newly diagnosed EC cases during the first wave of the pandemic. Additionally, they noted an increased proportion of patients diagnosed with distant metastases (14). Another Japanese study reported 1.9% and 3.1% decreases in overall new cancer diagnoses and new EC diagnoses during the pandemic as compared to the average rates from 2016-2019. Of note, greater reductions in early-stage EC were observed (6). However, a separate multicenter study consisting of 5,167 patients in Japan did not report any significant difference in the number of patients with newly diagnosed EC during the pandemic as compared to the pre-pandemic baseline (15).

3.2 Delays in Esophageal Cancer Diagnosis and Care During the COVID-19 Pandemic

In a survey sent to 225 centers across 49 countries, Kamarajah et al. reported limited or delayed availability of diagnostic endoscopy, therapeutic endoscopy, spiral computed tomography (CT) scans, endoscopic ultrasound, positron-emission tomography (PET) scans, and staging laparoscopy in up to 60.7%, 57.3%, 35.0%, 52.2%, 36.8%, and 41.0% of responses, respectively. The same staging modalities were unavailable during the pandemic in up to 9.4%, 10.9%, 2.1%, 23.1%, 13.7%, and 23.7% of cases, respectively (16). Referral delays for diagnostic gastroscopy were also noted in a UK analysis of patients with esophagogastric cancer between 2019-2020 (7). Additionally, Huang et al. noted a 69% decrease in overall endoscopic case volume during the pandemic in China (17).

Consistent with this delayed access to endoscopy, a large multicenter analysis in the US, Trindade et al. reported significant decreases in newly diagnosed Barrett's esophagus (BE) in addition to reductions in newly diagnosed EC cases (18). Analogous results were published in a study utilizing the Northern Ireland Cancer Registry from 2017-2020 (19).

In a survey of 12 Society for Study of Esophageal Diseases (SISME) institutions in Italy between 2019-2020, surgical delays were reported at 50% of centers (20). A single-center analysis of 133 patients between 2019-2020 in the US noted no significant difference in surgical wait time between pandemic and pre-pandemic patient populations (12). Similarly, an Italian multicenter analysis of 70 patients reported no significant difference in surgical wait times between pre-pandemic and pandemic groups (13). Furthermore, in a retrospective, single-center study of 98 patients with EC undergoing surgical intervention in Ireland, Bolger et al. reported no difference in median time to surgery from neoadjuvant therapy during the pandemic as compared to the pre-pandemic baseline (21).

3.3 Surgical Intervention for Esophageal Cancer During the COVID-19 Pandemic

Rebecchi et al. surveyed 12 SISME institutions in Italy between 2019-2020. 50% of centers experienced significant restrictions in EC surgery. Of these centers, 25% reported general reductions in EC resections, 16.7% limited resections to patients without severe comorbidities, and 8.3% completely ceased all surgical activity. However, there was no significant difference in the overall number of EC resections during the pandemic (20). A separate Italian analysis of 70 patients across multiple centers noted a 64% decrease in esophagectomy volume during the pandemic, with no significant difference in 30-day mortality or hospital LOS between pre-pandemic and pandemic groups, as well as a 0% rate of postoperative COVID-19 infection (13). Retrospective studies conducted in India (22), Ireland (21), and the US (12), reported equivalent perioperative mortality between pre-pandemic and pandemic groups undergoing EC surgery, along with a 0% rate of postoperative COVID-19 infection. Similarly, a multicenter study of 307 patients in Holland, Germany, Sweden, and Belgium reported no differences in 30-day mortality or postoperative morbidity, as well as a 0% rate of postoperative COVID-19 infection (23). In a prospective analysis of 731 patients undergoing thoracic oncologic surgery in France, Germany, Italy, and Canada, Seitlinger et al. also reported low perioperative mortality (3%) and COVID-19 infections (1.2%).

Regarding postoperative morbidity, a prospective, single-center analysis of 20 patients undergoing Ivor Lewis esophagectomy (ILO) in the US a 35% rate of postoperative pneumonia, a 5% rate of postoperative anastomotic leak, and the median length of hospital stay was 9 days (24). The aforementioned multicenter analysis of 731 across Europe and North America noted a 0.5% rate of hospital readmission during the follow-up period. In terms of late surgical outcomes, Doyle et al. reported a 2-year disease-free and overall survival for EC resection of 70.8% and 72.9%, respectively (25).

3.4 Esophageal Cancer Outcomes During the COVID-19 Pandemic

Khan et al. conducted a retrospective analysis of 349 patients being treated for esophagogastric cancer between 2019-2020 in the UK and found a 6-month decrease in overall median survival for patients presenting with EC after the first UK national lockdown (7 vs 13 months, P=0.001). There was a 3-month decrease in survival in patients not treated with

surgical resection (5 vs 8 months, P=0.004). In addition to the aforementioned increased rates of acute hospital admissions (28.0% vs 12.5%, P=0.001) and metastatic disease at presentation (47.8% vs 33.3%, P=0.008), significantly higher rates of palliative treatment were noted after the lockdown in this patient population (71.3% vs 55.7%, P=0.003) (7).

3.5 Modeling of the Impact of Pandemic-Related Delays in Esophageal Cancer Care

In their model of cancer survival and economic impact after pandemic-induced delays in cancer care, Gheorghe et al. estimated overall losses of 32,700 quality-adjusted life years (QALYs) and £103.8 million over the next five years. Regarding EC, they estimated 2700 QALYs lost and productivity losses of £6.6 million over the next five years (27). A population-based modeling study addressing the estimated impacts of immediate vs delayed surgical resection in a T1b esophageal adenocarcinoma was performed by Shipe et al. Immediate esophagectomy resulted in an insignificant improvement in 5-year overall survival compared to delaying surgery by 3 months. However, in a sensitivity analysis, delayed esophagectomy (>3 months) resulted in a superior 5-year overall survival when the probability of COVID-19 infection was > 7% (28). Sud et al. modeled cancer progression during the pandemic as a result of pandemic-induced delays solely in surgical care. They estimated a 24.7%-35.9% reduction in 5-year net survival for EC as a consequence of a 6-month delay to surgery depending on tumor stage and age at diagnosis (29).”

5. Discussion: Where were the Hub and Spoke models utilized. maybe I missed but not clear when I got to this portion of manuscript.

Reply 5: Thank you for this important comment.

The Hub and Spokes model was described and primarily utilized in Italian centers during the initial stages of the COVID-19 pandemic. This consisted of “spoke” centers where patients were initially evaluated followed by referral to a central “hub” which is specialized in the multidisciplinary management of thoracic cancer. There is additional evidence of its use in the management of lung cancer during the COVID-19 pandemic. We have added the following references in support of this model:

Ciriaco P, Carretta A, Bandiera A, Muriana P, Negri G. Perspective: Did Covid-19 Change Non-small Cell Lung Cancer Surgery Approach? Front Surg. 2021;8(May):1–5.

Bertolaccini L, Spaggiari L. Reorganization of thoracic surgery activity in a national high-volume comprehensive cancer centre in the Italian epicentre of coronavirus disease 2019. European Journal of Cardio-thoracic Surgery. 2020;58(2):210–2.

The revised subsection 4.4 now reads as follows:

“Surgical resection is a critical aspect of the management algorithm for patients with EC. Delays in EC surgery can have a significant impact on patient outcomes (30). Therefore, proper management of EC patients requiring surgery amidst resource scarcity was paramount during the pandemic. At the height of the pandemic, there was considerable variation in EC surgical practice globally, likely secondary to differential COVID-19 case burden, continuation of

oncology care recommendations, and existing pathways of care (31–35). Despite heterogeneous practice, outcomes of EC surgery were excellent, with delays rarely reported (12,13,21) and equivalent rates of morbidity and mortality surgery to pre-pandemic baselines (12,13,21–23). There were several factors critical to the global success of EC surgery during the pandemic. Implementation of Hub-and-Spoke models, characterized by care triage at "Spoke" centers followed by redirection of patients free of infection requiring surgical management to designated "Hub" centers, was essential and highlighted the importance of collaboration between centers (36,37). The establishment and strict adherence to COVID-19 protective measures, including preoperative and postoperative self-isolation, questionnaires, testing, imaging, as well as thorough multidisciplinary review and utilization of personal protective equipment by hospital staff were also central to the success of institutional modifications in EC care provision. Additional aspects of EC surgery that were not as highly emphasized in the current literature include minimally invasive techniques and enhanced recovery after surgery protocols (1). Given the effectiveness of these interventions both independently and combined, moving forward they should be utilized to hasten patient recovery and optimize healthcare resource utilization."

6. Conclusions: same as suggestion for Abstract Conclusion.

Reply 6: Thank you for this comment.

As previously noted in our response to comments 1 and 2, we sought to highlight that with the reorganization of oncologic care administration, strict adherence to COVID-19 protective measures, and reallocation of health care resources towards the same, EC surgery was able to continue safely during the COVID-19 pandemic. Furthermore, we simply sought to note that although healthcare systems did well to triage care and prioritize the care of those acutely ill, this may potentially have late ramifications for patients with progressive, indolent diseases such as esophageal cancer. Therefore, our recommendations lie in what was successfully applied during this intense, overwhelming period in global health. We have revised the conclusion accordingly, which now reads as follows:

The Conclusion now reads:

"Pushing healthcare systems well beyond their capacity, the COVID-19 pandemic necessitated resource reallocation away from non-COVID patients to meet the escalating disease burden. Amidst resource scarcity, the multidisciplinary management of patients with EC was affected at multiple stages in the care pathway. The was an overall reduction in the detection of esophageal cancer and significant variability in the presenting disease stage. EC patients experienced delays in diagnostic and preoperative staging investigations. However, EC surgery was able to safely continue and patients experienced excellent short-term outcomes likely secondary to revised guideline recommendations, effective care triage, institutional modifications, and collaboration between centers. Ultimately, the complete ramifications of reductions in EC diagnosis and delays in care remain unclear. When healthcare systems are pushed to the brink, the downstream consequences of resource allocation away from patients

with chronic disease require judicious analysis to optimize overall patient outcomes."

7. Table 1: a) break into two tables - retrospective and prospective; b) add column for n; c) move country to be in parentheses after study name.

Reply 7: Thank you for this comment.

Given that there is only 1 prospective study included in this review, we have subdivided Table 1 into retrospective studies, prospective studies, and population-based modeling studies. Additionally, we have added a column for the study sample size (n) and revised the study name to include the country in parentheses.

The revised Table 1 now reads as follows:

Table 1. Characteristics of included studies.

Study name	**Study Type**	**Study Organization**	**Years Data Collected**	**Study Population**	**Sample Size (n)**	**Outcomes**
Retrospective						
Bolger et al. 2022 (Ireland)	Retrospective, single center	Group 1: Baseline (April 2019-June 2019) – 45 patients Group 2: Pandemic (April 2020-June 2020) – 53 patients	2019-2020	Patients undergoing surgery for EC	98 patients	EC surgical outcomes
Borgstein et al. 2021 (Netherlands, Germany, Sweden, Belgium)	Retrospective, multi-center	Group 1: Baseline (October 2019-February 2019) – 168 patients Group 2: Pandemic (March 2020-May 2020) – 139 patients	2019-2020	Patients undergoing surgery for EC	307 patients	Rate of respiratory failure requiring mechanical ventilation
Dolan et al. 2021 (United States)	Retrospective, single center	Group 1: Baseline (March 2019-June 2019) – 96 patients Group 2: Pandemic (March 2020-June 2020) – 37 patients	2019-2020	Patients undergoing surgery for EC	133 patients	EC surgical outcomes
Doyle et al. 2022 (United Kingdom)	Retrospective, single center	231 patients	2020-2021	Patients with upper GI cancer undergoing surgical resection	231 patients	Upper GI cancer surgical outcomes
Huang et al. 2021	Retrospective,	Group 1: Baseline	2019-2020	Patients	7,711	Endoscopic case

(China)	single center	(February 2019-May 2019) – 5903 cases Group 2: Pandemic (February 2020-May 2020) - 1,808 cases		undergoing diagnostic/therapeutic endoscopy	patients	volume, GI cancer diagnosis
Kamarajah et al. 2020 (International; 49 countries	Retrospective, multi-center, survey-based	Online survey sent to 225 centers	2020	Patients with EG cancer	234 survey respondents	EC initial investigations, oncological and surgical therapy
Khan et al. 2022 (United Kingdom)	Retrospective, single center	Group 1: Pre-lockdown Group 2: Pandemic lockdown	2019-2020	Patients with EG cancer	506 patients	EC diagnosis, stage, treatment, and outcomes
Kirchberg et al. 2021 (Germany)	Retrospective, single center	Group 1: Baseline (March 2019-May 2019) Group 2: Pandemic (March 2020-May 2020)	2014-2020	Patients with GI cancer	15,995 patients	EC diagnosis
Kuzuu et al. 2021 (Japan)	Retrospective, multi-center	Group 1: Baseline (January 2017-February 2020) – 4218 patients Group 2: Pandemic (March 2020-December 2020) – 949 patients	2016-2020	Patients with GI cancer	5167 patients	EC diagnosis and stage
Milito et al. 2022 (Italy)	Retrospective, multi-center	Group 1: Baseline (2019) – 41 patients Group 2: Pandemic (March 2020-March 2021) – 29 patients	2019-2021	Patients undergoing surgery for EC	70 patients	EC surgical outcomes
Miyawaki et al. 2022 (Japan)	Retrospective, single center	Group 1: Baseline (April 2018-March 2020) – 378 patients Group 2: Pandemic (April 2020-June 2020) – 178 patients	2018-2021	Patients with EC	546 patients	EC diagnosis, stage, treatment, and outcomes
Morias et al. 2020 (Portugal)	Retrospective, single center	Group 1: Baseline (March-July 2019) Group 2: Pandemic (March-July 2020)	2019-2020	Patients with malignancy	2,072 patients	Cancer-related screening and diagnosis

Okuyama et al. 2022 (Japan)	Retrospective, multi-center	Group 1: Baseline (2016-2019) Group 2: Pandemic (2020)	2016-2020	Patients with cancer	22,556 patients	EC diagnosis and stage
Rebecchi et al. 2021 (Italy)	Retrospective, multi-center, survey-based	Online questionnaire sent to 12 SISME institutions	2019-2020	Patients with EC	12 Italian Society for Study of Esophageal Diseases esophageal surgery units	EC initial investigations, oncological and surgical therapy
Schandl et al. 2021 (Sweden)	Retrospective, single-center, interview and survey-based	134 patients	2013-2019	Patients with EC	134 patients	Impact of social distancing on HRQL in EC patients
Seitlinger et al. 2021 (France, Germany, Italy, Canada)	Retrospective, multi-center	731 total patients (17 esophagectomies)	2020	Patients undergoing thoracic oncologic surgery	731 patients	Thoracic oncologic surgical outcomes
Soni et al. 2022 (India)	Retrospective, single center	Group 1: Baseline (April 2019-April 2020) Group 2: Pandemic (May 2020-May 2021)	2019-2021	Patients undergoing oncologic surgery	1576 patients	Oncologic surgical outcomes
Trindade et al. 2022 (United States)	Retrospective, multi-center	Group 1: Baseline (April 2019-March 2020) Group 2: Pandemic (April 2020-March 2021)	2018-2021	Patients with Barrett's esophagus or EC	-	EC and Barrett's esophagus diagnosis, treatment
Turkington et al. 2021 (Northern Ireland)	Retrospective, multi-center	Group 1: Baseline (March 2017-September 2019) Group 2: Pandemic (March 2020-September 2020)	2017-2020	Patients with Barrett's esophagus or EC; NICR database	-	EC and Barrett's esophagus diagnosis
Prospective						
Chan et al. 2021	Prospective,	20 patients	2020	Patients	20	EC surgical outcomes

(United Kingdom)	single center			undergoing ILO for EC	patients	
Population-based Modeling Studies						
Gheorghe et al. 2021 (United Kingdom)	Population-based modeling study	Model of cancer survival and economic impact after COVID-19-induced delays in care	-	Patients with EC; NHS database	-	Health losses (QALYs), lost economic productivity (HC)
Maringe et al. 2020 (United Kingdom)	Population-based modeling study	Model of cancer survival after COVID-19-induced delays in care	-	Patients with EC; NHS database	-	Estimated additional deaths, YLLs
Shipe et al. 2021 (United States)	Population-based modeling study	Model of immediate vs delayed surgical resection in a T1b esophageal adenocarcinoma	-	Patients with T1b esophageal adenocarcinoma	-	5-year overall survival
Sud et al. 2020 (United Kingdom)	Population-based modeling study	Model of cancer progression during COVID-19-induced delays in care	2013-2017	Patients with malignancy	-	Hazard ratios of cancer progression, 5-year reduction in survival

EC, esophageal cancer; EG, esophagogastric; HRQL, health-related quality of life; NICR, Northern Ireland Cancer Registry; National Health Service; QALYs, quality-adjusted life years; HC, human capital; YLLs, years lost of life; ILO, Ivor-Lewis esophagectomy; GI, gastrointestinal; SISME, Society for Study of Esophageal Diseases

8. Table 2: define level of evidence in Table legend.

Reply 8: Thank you for this comment.

The level of evidence utilized in Table 2 (now Table 3) is the Quality Rating Scheme for Studies and Other Evidence based on the Oxford Centre of Evidence-Based Medicine. We have included the same in the Table legend.

Table 3 now reads as follows:

Table 3. Studies Evaluating the Impact of Resource Allocation During the COVID-19 Pandemic on Esophageal Cancer: Summary of Systematic Review and Findings.

Study name	**Level of Evidence**	**Findings**
EC Rates & Presentation		

Dolan et al. 2021	3	- No significant difference in preoperative pathologic tumor stage between pandemic and control group
Khan et al. 2022	3	- Increase in acute hospital admissions after the lockdown (28.0% vs 12.5%, P=0.001) - Decline in urgent clinic referrals after the lockdown (5.7% vs 12.5%, P=0.042) - Increased metastatic disease at presentation after the lockdown (47.8% vs 33.3%, P=0.008)
Kirchberg et al. 2021	3	- 3.2% decrease in total number or newly diagnosed GI cancers during the pandemic - 25.5% decrease in new EC diagnoses during the first shutdown
Kuzuu et al. 2021	3	- No significant difference in the number of patients with newly diagnosed EC during the pandemic
Morais et al. 2020	3	- 30.8% decrease in new EC diagnoses - 40% absolute reduction of new cancer cases overall - Increased diagnosis of advanced stage cancer
Miyawaki et al. 2022	3	- Decrease in number of newly diagnosed EC during the first wave of the pandemic - Increased proportion of patients diagnosed with distant metastases during the pandemic
Okuyama et al. 2022	3	- 1.9% overall decrease in new cancer diagnoses during the pandemic - 3.1% decrease in new diagnoses of EC during the pandemic - 8.6%, 7.1%, and 10% decrease in new diagnoses of stage I, II, III EC during the pandemic, respectively
Delays in EC Diagnosis/Care		
Bolger et al. 2022	3	- No difference in median time to surgery from neoadjuvant therapy (8 weeks in both groups)
Dolan et al. 2021	3	- No significant difference in surgical wait times
Huang et al. 2021	3	- 69% decrease in endoscopic case volume during the pandemic
Kamarajah et al. 2020	4	- 26.5% and 62.8% availability of endoscopic ultrasound and spiral CT for staging as compared to pre-pandemic baseline
Khan et al. 2022	3	- Increased referral wait time during the pandemic (28 vs 15 days, P=0.021)
Milito et al. 2022	3	- No significant difference in surgical wait time during the pandemic
Rebecchi et al. 2021	4	- Significant restrictions in esophageal cancer surgery at 50% of centers

		- Surgical delays reported at 50% of centers
Trindade et al. 2022	3	- Significant decrease in newly diagnosed BE, BE endoscopic ablation procedures, and newly diagnosed esophageal cancer during the pandemic - No difference in esophagectomy rates during the pandemic
Turkington et al. 2021	4	- 59.3% decrease in newly diagnosed BE during the first 6 months of the pandemic - 26.6% decrease in newly diagnosed EG cancer during the first 6 months of the pandemic
EC Surgical Outcomes		
Bolger et al. 2022	3	- No differences in patient demographics, co-morbidities, or use of neoadjuvant therapy - No significant differences in operative interventions or in-hospital mortality - 0% rate of postoperative COVID-19 infection
Borgstein et al. 2021	3	- No difference in the rate of respiratory failure requiring mechanical ventilation or number of pulmonary complications - No difference in all measures of postoperative morbidity - No difference in 30-day mortality - 0% rate of postoperative COVID-19 infection
Dolan et al. 2021	3	- Reduced rate of overall postoperative complications during the pandemic - 0% rate of perioperative mortality - 0% rate of postoperative COVID-19 infection
Doyle et al. 2022	3	- 3.5% 90-day mortality rate - 0.4% rate of postoperative COVID-19 infection - 2-year disease-free and overall survival for EC resection 70.8% and 72.9%, respectively
Milito et al. 2022	3	- 64% decrease in esophagectomy volume during the pandemic - No significant difference in 30-day mortality or hospital LOS - 0% rate of postoperative COVID-19 infection
Rebecchi et al. 2021	4	- No significant difference in the overall number of EC resections during the pandemic - Increased rate of open EC resections during the pandemic - 1.5% rate of postoperative pneumonia
Seitlinger et al. 2021	3	- 1.2% rate of COVID-19 infection

		- 0.5% rate of readmission for oxygen requirements with 0.3% of these patients requiring ICU admission and mechanical ventilatory support - 3% overall mortality
Soni et al. 2022	3	- 35% reduction in oncological surgical activity during the pandemic - 11% reduction in thoracic oncological surgical activity - No difference in postoperative mortality for thoracic surgery - 0% rate of postoperative COVID-19 infection for thoracic surgery
EC Overall Outcomes		
Khan et al. 2022	3	- 6-month decrease in overall median survival for all new patients with EC after the first lockdown - 3-month decrease in median survival after the first lockdown in patients not treated with surgical resection
Statistical Modelling		
Gheorghe et al. 2021	3	- Overall, an estimated loss of 32,700 QALYs and £103.8 million GBP in the next five years in England alone - An estimated 2700 QALYs lost and productivity losses of £6.6 million GBP in the next five years specific to esophageal cancer
Maringe et al. 2020	3	- Estimated 330-342 additional deaths due to EC with a 5.8-6.0% increase up to 5 years after diagnosis - Overall, an estimated 3291-3621 additional deaths due to all malignancy within 5 years and total YLLs 59,204-63,229 years
Shipe et al. 2021	3	- Slight improvement in 5-year overall survival with immediate esophagectomy - Delayed esophagectomy (>3 months) preferred when the probability of perioperative COVID-19 infection > 7%
Sud et al. 2020	3	- 24.7%-35.9% reduction in 5-year net survival as a consequence of 6-month delay to surgery depending on tumor stage and age at diagnosis

Quality Rating Scheme for Studies and Other Evidence based on the Oxford Centre of Evidence-Based Medicine. EC, esophageal cancer; QALYs, quality-adjusted life years; YLLs, years lost of life; GI, gastrointestinal; BE, Barrett's esophagus; EG, esophagogastric; CT, computed tomography; ICU, intensive care unit.

Reviewer C

This is a systematic review of the literature without meta-analysis on the subject of- resource allocation following the COVID-19 pandemic in the context of esophageal cancer.
Although it is well designed, the variability of data acquired from these articles was big making it hard to compare them and thus to reach a conclusion.
In addition, the authors related just mildly to the effect of the pandemic on the medical and radiational aspects of the treatment of esophageal cancer. This is an important part of the multidisciplinary treatment of this disease and although they mention the delayed diagnosis and late stage of the disease at the time of presentation, they did not relate to the impact on these modalities.
lastly, we don't know what are the long term outcomes of these patients.

Reply 1: Thank you for these important comments.

We agree with the authors the data on this topic is highly heterogeneous and therefore makes it challenging to come to concrete conclusions. As a result, we have not performed an aggregate analysis of the data and have kept our conclusions to more broad observations in the literature. While we also agree that medical treatment and radiation are critical aspects of the multidisciplinary management of esophageal cancer, we sought to focus in greater detail on the surgical management of the same and therefore limited our scope. We have consequently included this as a limitation of the review. Finally, we also agree that there is a paucity of data on long-term outcomes in this patient population and have highlighted the need for further investigation to fully realize the true impact of the COVID-19 pandemic on the outcomes of patients with esophageal cancer.

We have added the following statement to the “Strengths and limitations” subsection of the Discussion:

“Additionally, although the surgical treatment of EC was the primary focus of this review, medical and radiologic therapies also represent critical aspects of EC multidisciplinary management and consequently should be highlighted in future studies.”

Reviewer D

This is an interesting review article on the practice in the COVID-19 Pandemic for esophageal cancer. There is nothing in particular that needs revision.

Reply 1: Thank you for this kind comment.