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REVIEW ARTICLE

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COVID-19 infection and its consequences among surgical oncology patients: A systematic analysis, meta-analysis and meta-regression

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Abstract

We conducted this meta-analysis to address the outcomes in cancer patients after oncologic surgery during COVID-19 pandemic. The primary endpoint was the COVID-19–related mortality rate. Higher body mass index was significantly and negatively associated with higher all-cause mortality and in-hospital COVID-19 infection rates. Male sex, preoperative respiratory disease, and smoking history were positively and significantly associated with increased all-cause mortality rates. Furthermore, male sex was positively and significantly associated with the COVID-19 infection rate.

KEYWORDS
cancer, COVID-19, meta-analysis, mortality, surgery

1 | INTRODUCTION

During the global COVID-19 pandemic, elective surgical procedures have frequently been rescheduled, mainly to preserve medical resources as well as minimize the exposure of patients and health care providers to COVID-19.[1] As a result, maintaining the surgical oncology workflow has been a clinical challenge.[2] Thus, researchers and clinicians have shared and reported institutional experiences, global recommendations, suggestions for adjusted workflows, and international guidelines to optimize cancer care without compromising oncologic surgery outcomes during the COVID-19 pandemic.[3,4] However, one size does not fit all, as travel restrictions, national infection and vaccination rates, availability of medical infrastructure, accessibility to medical resources, and numbers of available providers mandate personalized surgical oncology workflows that follow international guidelines for minimizing the transmission of COVID-19 infection and maintaining patient and workforce safety. Consequently, collaborative work and timely feedback on the feasibility and efficiency of the adjusted surgical workflows are critically needed.

Surgical oncology strategies take into account the need for timely and optimized treatment modalities for downstaging and systemic control, preoperative (nononcologic) interventions to minimize negative perioperative outcomes such as wound complications and length of hospital stay,[5–7] and the presence of comorbidities that

cannot be modified to determine the patient's readiness for oncologic surgery.[8] Additional factors must be considered during the COVID-19 pandemic: uncertain COVID-19 infection trajectory, actual infection risk among health care providers, and expected vaccine protection rates.[3,9] Moreover, some surgical procedures may require interventional radiologic or endoscopic procedures and/or admission to an intensive care unit (ICU) postoperatively or emergency room (ER) perioperatively. Furthermore, virtual perioperative appointments, limited numbers of caregivers and visitors, and additional barriers designed to protect patients and health care providers from infection may further complicate interventions and patient advocacy.[2,10,11]

The available published data on, international recommendations for, and global experience with infections in cancer patients may help overcome the challenges described above.[2,12–14] Nevertheless, our understanding of the COVID-19 pandemic is evolving, and the oncologic surgery workflow must be revisited, updated, and optimized as a result to account for the range of institutional, local, and national conditions during the pandemic. Therefore in this systematic review, meta-analysis, and meta-regression, we analyzed the measurable reported outcomes and identified potential predictors of poor outcome in cancer patients who had oncologic surgery during the COVID-19 pandemic.

2 | METHODS

2.1 | Literature search

A systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[15] The Ovid MEDLINE, Ovid Embase, Clarivate Analytics Web of Science, PubMed, and Wiley-Blackwell Cochrane Library databases were searched for articles published in English from December 1, 2019, to September 21, 2020. The databases were searched for the following terms: COVID-19, severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, coronavirus infections, novel coronavirus, cancer, neoplasms, tumor, leukemia, lymphoma, melanoma, carcinoma, sarcoma, oncology, surgery, surgical, neurosurgery, resection, perioperative care, perioperative period, and postoperative complications. The search terms were combined with "or" if they represented similar concepts and with "and" if they represented different concepts. The complete search strategies are detailed in Tables S1–S4.

2.2 | Study selection

Comparative studies eligible for this systematic review and meta-analysis consisted of those with reported outcomes of patients who were scheduled for oncologic surgery during the COVID-19 pandemic. Studies with fewer than five patients were excluded. For duplicate published studies from the same institution, only the most complete reports were included. In addition, the bibliographies of all studies and meta-analyses were searched to identify additional articles (i.e., backward snowballing). Abstracts, conference presentations, reviews, and expert opinions were excluded.

2.3 | Data extraction and endpoints

Excel software (Microsoft Corporation) was used for extraction of data from the studies we identified. Continuous variables were reported as mean (±*SD*) values, and categorical variables were expressed as frequencies. Data on study period, study center, country, type of cancer, type of study, and sample size were retrieved. The following patient characteristics were abstracted: age, male sex, body mass index (BMI), diabetes, renal insufficiency, coronary artery disease, acute kidney injury, peripheral artery disease, smoking history, pre-existing pulmonary disease, and dyslipidemia. Of note, smoking history data were not consistent across studies. Some authors reported this variable as "history of smoking," whereas other authors added more details, such as "former" versus "current" smoker. Comorbidities (e.g., pre-existing pulmonary disease, dyslipidemia), smoking history, BMI, and sex were examined as separate variables, although the possible collinearity could not be assessed or ignored.

The primary endpoint was the COVID-19–related mortality rate, which was calculated for the entire patient population. The secondary endpoints were length of hospital stay and the rates of in-hospital COVID-19 infection, postponed or delayed surgery because of COVID-19 infection, overall COVID-19 infection, all-cause mortality, hospital readmission, postoperative complications, ER visits, surgical recovery, COVID-19 infection recovery (rate was calculated relative to the COVID-19 infected patients), ICU admission, need for a ventilator, and pulmonary complications.

2.4 | Statistical analysis

For the short-term categorical and continuous outcomes, pooled event rates (PERs) and pooled means with their 95% confidence intervals (CIs) were calculated using the DerSimonian-Laird (inverse variance) method. Subgroup analysis was conducted to evaluate the primary endpoint according to the type of cancer.

Univariable meta-regression was performed to explore the relationship of the endpoints with preoperative characteristics. Each study was weighted according to the inverse of the variance of the estimate of that study, and between-study variance was estimated using a DerSimonian-Laird estimator. The meta-regression results were reported using regression coefficients (i.e., β), SEs, and p values.

Hypothesis testing for equivalence was two-tailed with a 0.05 significance level except for the subgroup analysis. A significance level of 0.06 was adopted. Heterogeneity assessment was performed based on the Cochran *Q* test with I^2 values. Individual study inference analysis was performed via leave-one-out sensitivity analysis for the primary endpoint. Funnel plots by graphical inspection and Egger

regression testing were used for assessment of publication bias regarding the primary endpoint.

All statistical analyses were performed using the R computing language (version 3.6.2) and RStudio software with the meta and metafor packages.

3 | RESULTS

3.1 | Overall results

We identified a total of 1936 studies in our database search. After exclusion of duplicates and irrelevant articles, we screened 1026 potentially relevant articles. We then assessed 72 full-text articles for eligibility. Twenty-eight studies with a total of 3508 patients met our inclusion criteria. The sample sizes ranged from 5 to 621. An outline of the systematic review process performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines is shown in Figure S1. The characteristics and demographics of the patients in the included studies are summarized in Table 1 and Table S5. We used the Newcastle-Ottawa Quality Assessment Scale for cohort studies to critically appraise the quality of the included studies (Table S6).[16]

3.2 | Meta-analysis of the outcomes

Figure 1 shows a forest plot of the primary endpoint of COVID-19–related mortality. The PER for this endpoint was 27.15% (95% CI: 18.38%–38.16%). A funnel plot of the results of publication bias assessment and leave-one-out analysis is shown in Figure 2.

The PER for in-hospital COVID-19 infection was 3.00% (95% CI: 1.88%–4.73%) (Figure S2). The PER for all-cause mortality was 2.68% (95% CI: 1.23%–5.72%) (Figure 3A), and that for surgery postponement because of COVID-19 infection was 2.80% (95% CI: 1.49%–5.18%) (Figure 3B). The PER for overall COVID infection was 3.49% (95% CI: 2.34%–5.17%) (Figure S3). The PER for length of hospital stay was 7.26 days (95% CI: 5.03–10.48 days) (Figure S4). The PER for hospital readmission was 2.74% (95% CI: 1.93%–3.88%) (Figure S5). The PER for postoperative complications was 11.44% (95% CI: 7.30%–17.48%) (Figure S6). The PER for ER visits was 2.18% (95% CI: 0.38%–11.51%) (Figure S7). The PER for surgical recovery was 92.03% (95% CI: 73.86%–97.92%) (Figure S8). The PER for COVID-19 infection recovery was 72.85% (95% CI: 61.84%–81.62%) (Figure S9). The PER for ICU admission was 3.82% (95% CI: 1.28%–10.87%) (Figure S10). The PER for need for a ventilator was 9.85% (95% CI: 1.98%–37.20%) (Figure S11). The PER for pulmonary complications was 5.96% (95% CI: 3.24%–10.71%) (Figure S12). The patient outcomes are summarized in Table 2.

Subgroup analysis of the primary endpoint showed a non-significant trend of higher COVID-19–related mortality rates in patients with thoracic or lung cancer than in those with other cancers (subgroup difference, $p = 0.30$) (Figure S13).

3.3 | Meta-regression

BMI was significantly and negatively associated with all-cause mortality ($p < 0.001$) and in-hospital COVID-19 infection ($p = 0.0064$) rates. Also, male sex was positively and significantly associated with the COVID-19 infection rate ($p = 0.0479$) and an increased all-cause mortality rate ($p < 0.001$). Finally, preoperative respiratory disease ($p = 0.0079$) and smoking history ($p = 0.0151$) were positively and significantly associated with an increased all-cause mortality rate. Meta-regression outcomes are summarized in Table 3.

4 | DISCUSSION

This meta-analysis addresses the impact of COVID-19 infection on oncologic surgical outcomes and identifies the factors that may influence these outcomes during the COVID-19 era. We report rates of COVID-19–related mortality, in-hospital COVID-19 infection, surgery postponement because of COVID-19 infection, all-cause mortality, hospital readmission, postoperative complications, ER visits, surgical recovery, COVID-19 infection recovery, ICU admission, need for a ventilator, and pulmonary complications as well as length of hospital stay in cancer patients who underwent surgery during the pandemic. The studies in this meta-analysis also comprehensively examined the patient factors (age, sex, BMI, comorbidities, and smoking history) that may influence oncologic surgical outcomes.

In these cohorts of cancer patients scheduled for oncologic surgery during the COVID-19 era, the calculated early mortality rate after COVID-19 infection was 27%. This aligns with published data demonstrating that the mortality rate may reach 20% in general surgical patients[17] and even higher (25%) in cancer patients who undergo surgical intervention.[18] The investigators in the latter study reported that the high mortality rate was attributed to COVID-19 infection in the patients.[18] Over time, the mortality rate during the COVID-19 pandemic has improved, likely due to improved understanding of the infection trajectory and implementation of more optimal care algorithms.[18]

Furthermore, we report herein the PER for all-cause mortality which was 2.68%. These rates are similar to the COVID-19 mortality rate of 3.6% that was reported by Rajasekaran et al.[19] and Brar et al.,[20] who reported no deaths. Indeed, outcome rates vary by country and even by institution within the same country due to the use of personalized COVID-19 protocols adapted according to accessibility to medical care, availability of medical resources, vaccination rates, and the national rate of spread.

At the beginning of the COVID-19 pandemic, despite the use of preoperative assessment, Lei et al.[17] reported a 100% postoperative COVID-19 infection rate, 44% ICU admission rate, 20.5% mortality rate, and 38% complex surgical difficulty rate after elective surgical procedures for 34 cancer patients. Some authors have commented on these reported rates and stated that such a high postoperative COVID-19 infection rate could be a result of prolonged oncologic operation times during the COVID-19 era due to increased use of

TABLE 1 Demographics of the patients in the included studies

First Author	Year	Country	No. of patients	Age (years)	Male sex, n (%)	BMI, kg/m^2	HTN, *n* (%)	DM, *n* (%)	Previous cancer treatment, *n* (%)	Type of cancer
Vanni	2020	Italy	37	Mean (±*SD*), 61.20 ± 7.88	0	Mean (±*SD*), 22.40 ± 5.13	–	–	NeoAdj CTH, 7 (18.9)	Breast cancer
MacInnes	2020	UK	202	Mean, 57 (range: 48–65)	0	Mean: 29.1 (IQR: 17.5–55.2)	–	–	NeoAdj CTH, 27 (14.0)	Breast cancer
Fregatti	2020	Italy	85	–	–	–	–	–	NeoAdj CTH, 5 (5.9)	Breast cancer
Lisa	2020	Italy	51	Mean: 53.4	–	–	–	2 (3.9)	Previous RTH, 11 (21.6); NeoAdj CTH, 3 (5.9)	Breast cancer
Gautam	2020	India	118	–	–	–	–	–	–	GI tract cancer
Bogani	2020	Italy	355	Mean: 65 (range: 49–84)	0	–	–	–	–	Ob/Gy cancer
Galli	2020	Italy	27	Mean: 67.2	19 (70.4)	–	16 (77.7)	7 (25.9)	–	Head and neck cancer
Peng	2020	China, New Zealand	11	Mean: 61 (range: 51–69)	8 (72.7)	–	2 (18.2)	0	–	Thoracic cancers
Gonfiotti	2020	Italy	5	Mean: 74 (range: 67–80)	1 (20%)	Mean (±*SD*), 21.94 ± 2.96	1 (20%)	0	CTH + RTH, 1	Lung cancer
Pai	2020	India	184	Mean: 47 (range: 1–79)	78 (42.4)	Mean: 23.8 (range: 12.5–43.5)	24 (13.0)	12 (6.5)	NeoAdj, 68 (37.0)	Mixed cancers
Cai	2020	China	7	Mean: 60 (range: 57–66)	5 (71.4%)	–	1 (14.3%)	–	–	Lung cancer
de Santiago	2020	Spain	126	Mean: 60 (range: 29–89)	0	–	42 (33.3)	11 (8.7)	NeoAdj, 24 (19)	Gynecologic tumors
Filipe	2020	Netherlands	217	Mean (±*SD*), 62.2 ± 13.1	0	Mean: 23.3 (range: 23.0–30.4)	–	–	NeoAdj, 61 (28.1)	Breast cancer
Sorrentino	2020	Italy	54	Mean (±*SD*), 67.0 ± 13.7	26 (48.1%)	–	–	–	NeoAdj, 11	Colon cancer
Di Martino	2020	Spain	15	Mean (±*SD*), 66.00 ± 15.55	7 (46.7%)	–	11 (73.3%)	1 (6.7%)	–	General surgery oncology
Santambrogio	2020	Italy	11	Mean (±*SD*), 71.60 ± 8.65	9 (81.8%)	–	–	–	–	Hepatocellular carcinoma
Changzheng	2020	China	71	Mean (±*SD*), 59.77 ± 12.35	46 (64.8%)	Mean (±*SD*), 24.8 ± 10.7	–	–	NeoAdj, 1	GI cancer
Bakkar	2020	Jordan	12	Mean: 56 (range: 33–80)	3 (25%)	–	–	–	–	Thyroid cancer
Laccourreye	2020	France	106	Median: 63 (range: 29–85)	79 (74.5%)	Median: 25 (range: 13–39)	–	–	–	Head and neck cancer
Ji	2020	UK	621	Mean: 63.5 (range: 28.0–91.0)	–	–	–	–	–	Many types of cancer

TABLE 1 (Continued)

First Author	Year	Country	No. of patients	Age (years)	Male sex, n (%)	BMI, kg/m^2	HTN, *n* (%)	DM, *n* (%)	Previous cancer treatment, *n* (%)	Type of cancer
Covas Moschovas	2020	USA	147	Median: 68 (IQR[a]: 8)	147 (100%)	Median: 27.8 (IQR[a]: 6.1)	–	–	–	Prostate cancer
Stevenson	2020	UK	100	Mean: 52.4 (range: 16.0–94.0)	65 (65%)	–	–	–	NeoAdj, 5	Orthopedic cancer
Brar	2020	UK	47	–	31 (66%)	–	–	–	–	Head and neck cancer
Shrikhande	2020	India	494	Mean: 48 (range: 27–85)	173 **(35%)**	–	–	–	–	Multiple cancer types
Rajasekaran	2020	UK	56	Mean: 57 (range: 18–87)	30 (53.6%)	–	–	–	–	Bone, soft tissue cancer
Dursun	2020	Turkey	200	Mean: 56 (range: 24–85)	0	Mean: 31 (range: 18–49)	43 (21.5)	20 (10)	–	Gynecologic cancer
Abdalla	2020	UK	130	Median: 57.6 (range: 33.0-88.0)	0	–	–	–	–	Breast cancer
Wahed	2020	UK	19	Median: 70 (range: 43–81)	15	Median: 27.1 (range: 21.1–41.9)	–	3	NeoAdj, 12	Esophagogastric cancer

Abbreviations: BMI, body mass index; CTH, chemotherapy; DM, diabetes; GI, gastrointestinal; Gy, gynecologic; HTN, hypertension; IQR, interquartile range; NeoAdj, neaoadjuvant; Ob, obstetric; RTH, radiotherapy.

[a]The paper expresses IQR as the result of the difference between the two limits.

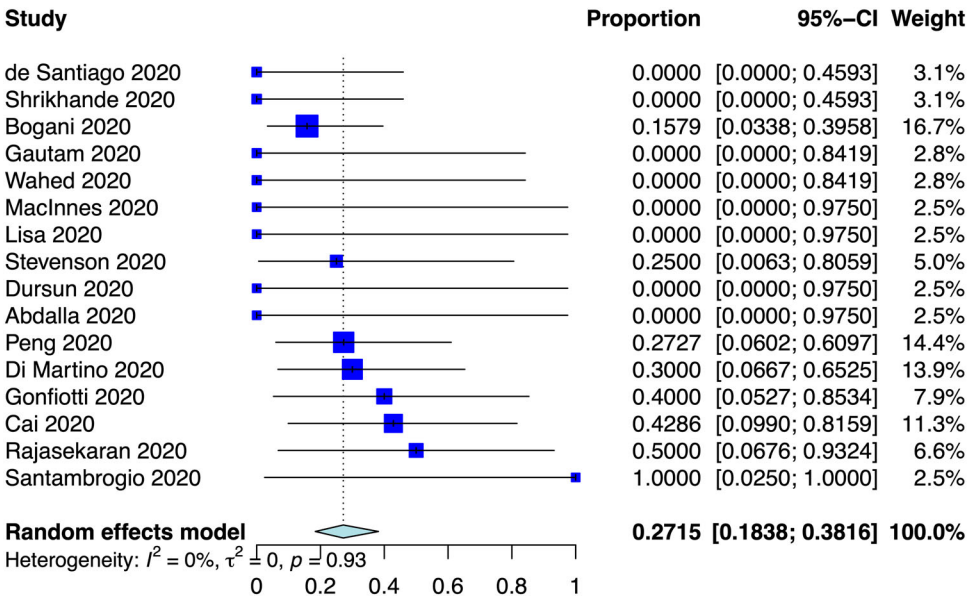

FIGURE 1 Forest plot of the primary endpoint of COVID-19–related mortality

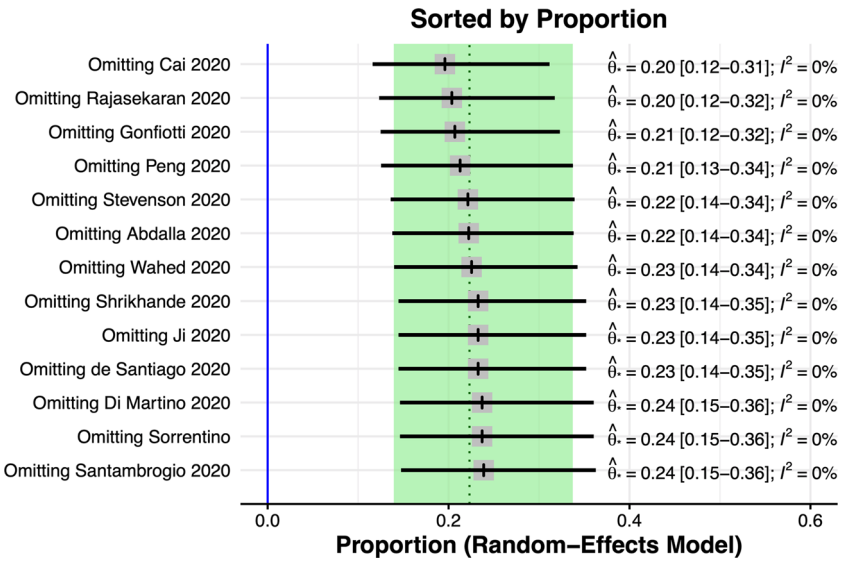

FIGURE 2 Leave-one-out analysis: funnel plot for publication bias assessment

safety measures along with the subsequent increase in the need for postoperative ICU admission, which may increase the likelihood of contracting COVID-19 infections and increase mortality rates in cancer patients who undergo surgery.[21] Nevertheless, the observed rates of COVID-19 infection in these patients have improved and are reported to be low in oncologic surgical settings, and recovery rates have been high after surgery during the COVID-19 pandemic.[21] Due to improved understanding of the COVID-19 infection trajectory and optimized care, our data demonstrate that cancer patients are still at risk (although low) for COVID-19 infection during hospitalization, with a PER of 3%. This rate is very similar to the infection rate of 5% reported by Bogani et al.[22] Furthermore, authors reported that the COVID-19 infection rate was only 1% in a cohort of gynecologic cancer patients during preoperative assessment.[23] Our data also demonstrated that the PER for oncologic surgical recovery was 92.03% and the PER for COVID-19 infection recovery was 72.85%.

Our data demonstrated that the PERs for ICU admission, need for a ventilator, and pulmonary complications were 3.82%, 9.85%, and 5.96%, respectively. Careful screening for symptoms and sick contacts as well as selection of eligible cancer patients for surgery[2] may explain the low ICU admission rate in cancer patients after surgery during the COVID-19 pandemic. Nevertheless, institutions have postponed many oncologic surgeries in response to the pandemic.[2,24] Our data also demonstrated that the PER for surgery postponement because of COVID-19 infection was 2.79%. Others reported COVID-related changes in 10% of gynecologic patients who underwent oncologic surgery.[23] In deciding whether to delay or perform surgical procedures, physicians aim to maintain safety for

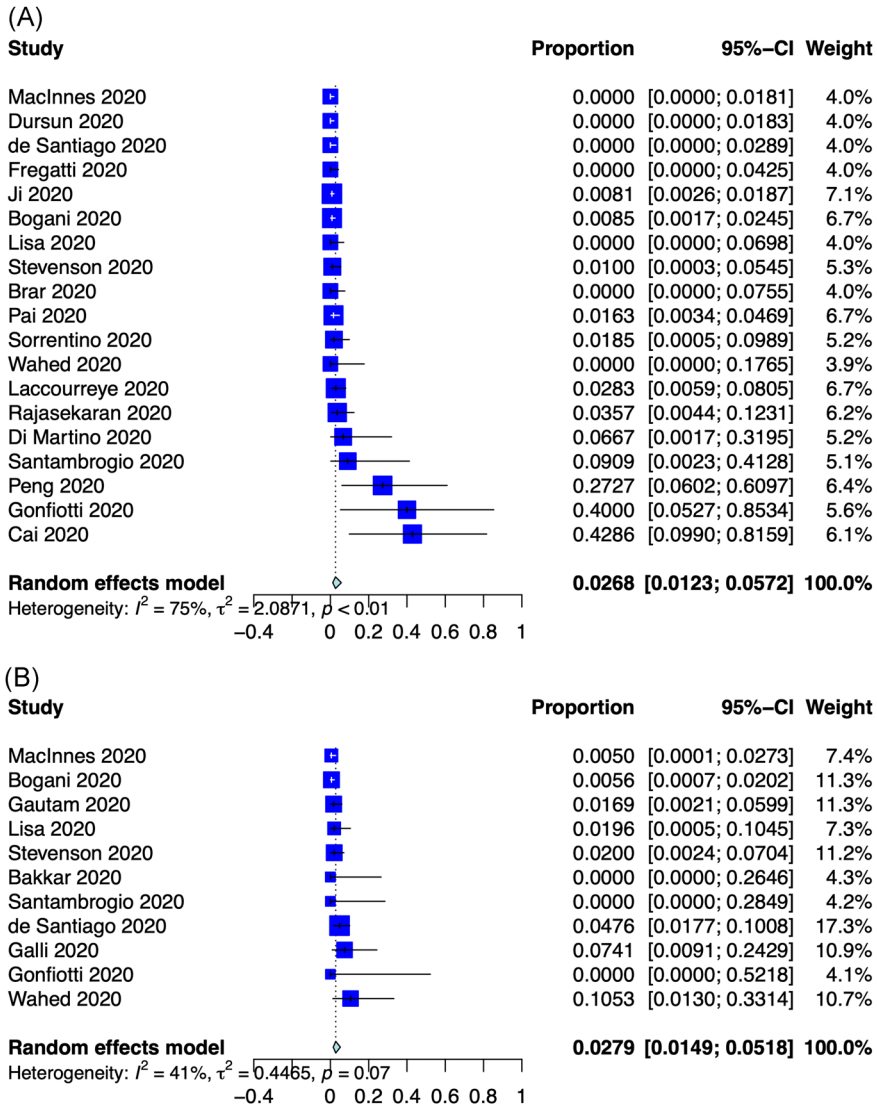

FIGURE 3 Forest plots of (A) all-cause mortality and (B) surgery postponement because of COVID-19 infection

patients and health care providers while weighing the risks and benefits of proceeding with surgery. However, delaying oncologic interventions may negatively impact cancer patient outcomes.[25,26] Therefore, authors have suggested following international guidelines and implementing recommended adjustments to the surgical workflow for the purpose of overcoming the pandemic-related restrictions on the workflow.[27] We agree that safety should come first, so surgical scheduling may have to be adjusted according to the national situation and medical resources. Still, maintenance of safety should not compromise patient outcomes. We must also remember that cancer patients require special considerations and extra measures.[28]

In our meta-analysis, the PER for postoperative complications was 11%. Authors reported a postoperative complication rate of 12% in patients with gynecologic cancer,[23] and Lisa et al.[29] reported a lack of a significant difference in the complication rate after breast reconstruction before and after the start of the COVID-19 pandemic. The authors contributed such success (no increase in complication rates during the pandemic) to adapting robust protocols, multidisciplinary teamwork, and the use of telehealth options. Filipe et al.[30] reported a very similar success story, observing no increase in the number or severity of postoperative complications in cancer patients after the start of the pandemic.

Our analysis also showed that BMI is negatively associated with all-cause mortality and COVID-19 infection rates in cancer patients. This aligns with published data demonstrating that higher BMI or obesity contributes to higher morbidity and mortality rates after COVID-19 infection.[31–35] The detrimental effect of obesity after COVID-19 infection may be attributed to the observed negative effects of obesity of impaired immune function and decreased lung capacity and reserve.[31,34–36]

Smoking is another major risk factor for poor oncologic surgery outcomes after COVID-19 infection as demonstrated by our data. Lung damage from tobacco use increases infection susceptibility due to tobacco-induced and immunologically induced structural modifications that include but are not limited to changes in peribronchiolar homeostasis and inflammation, epigenetic modifications, and the immune response required for infection clearance.[37–40]

TABLE 2 Patient outcomes summary

Outcome	No. of studies	Estimate	95% CI	Heterogeneity: I^2, p value
COVID-19–positive at hospitalization	24	3.00%	1.88%–4.73%	47.3%, $p = 0.0058$
Postponed because of COVID infection[a]	11	2.79%	1.49%–5.18%	41.4%, $p = 0.0732$
COVID infection rate	21	3.49%	2.34%–5.17%	60.3%, $p = 0.0002$
Length of hospital stay, days	14	7.26	5.03%–10.48	99.8%, $p < 0.0001$
All-cause mortality	19	2.68%	1.23%–5.72%	74.8%, $p < 0.0001$
Hospital readmission	9	2.74%	1.93%–3.88%	11.4%, $p = 0.3400$
Postoperative complications	17	11.44%	7.30%–17.48%	85.7%, $p < 0.0001$
ER visits	4	2.18%	0.38%–11.51%	72.3%, $p = 0.0126$
Surgical recovery	6	92.03%	73.86%–97.92%	75.5%, $p = 0.0010$
COVID infection recovery	16	72.85%	61.84%–81.62%	0%, $p = 0.9336$
COVID-related mortality[b]	16	27.15%	18.38%–38.16%	0%, $p = 0.9336$
ICU admission	10	3.82%	1.28%–10.87%	85.9%, $p < 0.0001$
Need for a ventilator	5	9.85%	1.98%–37.20%	81.5%, $p = 0.0002$
Pulmonary complications	3	5.96%	3.24%–10.71%	8.1%, $p = 0.3369$

Abbreviations: CI, confidence interval; ER, emergency room; ICU, intensive care unit.

[a]The denominator was all included patients, not the infected patients only.

[b]The denominator was the infected patients only, not the entire population.

TABLE 3 Meta-regression of different variables according to COVID-19 positivity at hospitalization, the COVID-19 infection rate, COVID-19–related mortality, and all-cause mortality

Variable	COVID-19–positive at hospitalization		COVID infection rate		COVID-19–related mortality		All-cause mortality	
	β (±*SE*)	*p* value	*β* ± *SE*	*p* value	*β* ± *SE*	*p* value	*β* ± *SE*	*p* value
Mean age (years)	0.0708 ± 0.0407	*0.0820*	0.0066 ± 0.0330	0.8411	0.0291 ± 0.0453	0.5210	0.0896 ± 0.0575	0.1190
Male sex (%)	0.0048 ± 0.0044	0.2737	0.0064 ± 0.0032	**0.0479**	0.0003 ± 0.0043	0.9495	0.0426 ± 0.0104	**<0.0010**
Mean BMI (kg/m^2)	−0.4353 ± 0.1596	**0.0064**	−0.1570 ± 0.2482	0.5271	−0.1064 ± 0.1639	0.5163	−0.5987 ± 0.1507	**<0.0010**
Respiratory disease (%)	0.0108 ± 0.0205	0.5988	0.0005 ± 0.0237	0.9824	−0.0276 ± 0.0459	0.5471	0.0889 ± 0.0335	**0.0079**
Smoking history (%)	0.0236 ± 0.0121	*0.0507*	−0.0303 ± 0.0447	0.4976	−0.0216 ± 0.0610	0.7231	0.0444 ± 0.0183	**0.0151**
Hypertension (%)	−0.0014 ± 0.0236	0.9522	−0.0182 ± 0.0148	0.2206	−0.0534 ± 0.0427	0.2109	−0.0153 ± 0.0453	0.7360
Chronic kidney disease (%)	−0.0090 ± 0.2863	0.9750	−0.0241 ± 0.2731	0.9297	Not enough studies		Not enough studies	
Coronary artery disease (%)	0.0238 ± 0.0373	0.5236	0.1768 ± 0.1743	0.3104	−0.0432 ± 0.3604	0.9045	0.0211 ± 0.0307	0.4919
Neoadjuvant therapy (%)	0.0129 ± 0.0507	0.7989	0.0133 ± 0.0254	0.6012	−0.0197 ± 0.0285	0.4896	0.0188 ± 0.0386	0.6252

Note: A positive β reflected an increase in the outcome with an increase in the variable, whereas a negative β reflected a decrease in the outcome with an increase in the variable when significant ($p < 0.05$).

Abbreviation: BMI, body mass index. Bold values indicates significant *p* value. Italic values indicates statistical significant trend.

Additionally, as expected, pre-existing pulmonary disease increases mortality and morbidity rates after COVID-19 infection as shown herein and by others.[41–43] Furthermore, male sex was an independent factor associated with increased 30-day mortality rates.[44,45] We also found that male sex was positively associated with all-cause mortality and overall COVID-19 infection. Additional risk factors (e.g., age, other comorbidities) require close attention. Wang et al [46] attributed the high incidence of ICU admission after surgery during the COVID-19 pandemic to advanced patient age and comorbidities. Other published data also demonstrate that poor oncologic surgery outcomes after COVID-19 infection may be attributed to advanced age.[11,47]

A vital point worth highlighting is the mental burden on health care providers during the COVID-19 pandemic. Authors have reported that surgeons and other providers face several types of burdens and challenges during the pandemic, including but not limited to the mental strain of not being able to operate, financial loss, social isolation, and burnout.[48–50] Unfortunately, these factors may have contributed to increasing suicide rates among health care providers.[51]

We acknowledge that all results are based on our best knowledge, and data heterogeneity across the studies must be considered when interpreting these results. This heterogeneity is a universal limitation of all published COVID-19 studies, as researchers want to share experiences and present as much data as possible to help others understand the trajectory of COVID-19 infection to optimize the treatment workflow and improve outcomes. All the data come from different institutions and countries, and each institution has its own protocols for collecting and presenting data. We designed this project to include patients who were eligible and scheduled for oncologic surgery. Nevertheless, we still need to include those who had their surgery delayed/canceled as delayed/canceled surgeries are probably due to COVID-19 infection-related workflow changes. Investigators have observed that delaying or canceling surgery for cancer may impact mortality, as well. Also, as we acknowledged earlier, cancer patient characteristics overlap (sex, BMI, comorbidities, smoking history, and even age). We collected and analyzed each of these variables separately, but the overlap of these factors is impossible to ignore and assess. Furthermore, we sought to present as much valuable data as possible, but we were challenged by the heterogeneous definitions of some outcomes in the studies (i.e., recovery rates). Also, a point to consider is the possible impact of missing data on the patients who underwent treatment outside a hospital or were lost to follow-up, especially when it comes to the impact of missing data on recovery rates.

During the first wave of the COVID-19 pandemic, the rate of oncologic surgical procedures decreased by 80%.[8] Furthermore, authors reported that 44% of cancer patients needed ICU admission.[17] These rates have improved greatly since that time. Balancing the competing requirements of safety, timely oncologic care, and optimal use of operation units, ERs, and ICUs is always essential before setting workflows for oncologic surgical care.[2,4,9,11,12,14] We must face the reality that the COVID-19 pandemic may be prolonged, as we are still learning about the course of the disease, and not everyone has access to and/or received the vaccine. Moreover, new strains are emerging, and the vaccine does not provide 100% protection. Data demonstrate that cancer does not appear to be associated with an elevated risk of COVID-19 infection as long as preventive measures are taken for selected patients.[52] However, COVID-19 infection is always a risk for cancer patients during preparation for surgery. Therefore, we extensively reviewed published data to guide effective clinical care for cancer patients who need surgical interventions. As the rates of COVID-19 infection decline and access to vaccines expands, our hope is that this progress enables full oncologic surgical capacity while maintaining the safety of patients and providers and prioritization of the oncologic surgical workflow based on institutional resources and the national situation.[53,54] Our data reported herein constitute a reliable, solid resource to help oncologic surgeons better understand the trajectory and outcomes of COVID-19 infection and identify cancer patients at increased risk for poor surgical outcomes.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

Not available.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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