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original reports

Elective Cancer Surgery in COVID-19–Free Surgical Pathways During the SARS-CoV-2 Pandemic: An International, Multicenter, Comparative Cohort Study

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abstract

PURPOSE As cancer surgery restarts after the first COVID-19 wave, health care providers urgently require data to determine where elective surgery is best performed. This study aimed to determine whether COVID-19–free surgical pathways were associated with lower postoperative pulmonary complication rates compared with hospitals with no defined pathway.

PATIENTS AND METHODS This international, multicenter cohort study included patients who underwent elective surgery for 10 solid cancer types without preoperative suspicion of SARS-CoV-2. Participating hospitals included patients from local emergence of SARS-CoV-2 until April 19, 2020. At the time of surgery, hospitals were defined as having a COVID-19–free surgical pathway (complete segregation of the operating theater, critical care, and inpatient ward areas) or no defined pathway (incomplete or no segregation, areas shared with patients with COVID-19). The primary outcome was 30-day postoperative pulmonary complications (pneumonia, acute respiratory distress syndrome, unexpected ventilation).

RESULTS Of 9,171 patients from 447 hospitals in 55 countries, 2,481 were operated on in COVID-19–free surgical pathways. Patients who underwent surgery within COVID-19–free surgical pathways were younger with fewer comorbidities than those in hospitals with no defined pathway but with similar proportions of major surgery. After adjustment, pulmonary complication rates were lower with COVID-19–free surgical pathways (2.2% *v* 4.9%; adjusted odds ratio [aOR], 0.62; 95% CI, 0.44 to 0.86). This was consistent in sensitivity analyses for low-risk patients (American Society of Anesthesiologists grade 1/2), propensity score–matched models, and patients with negative SARS-CoV-2 preoperative tests. The postoperative SARS-CoV-2 infection rate was also lower in COVID-19–free surgical pathways (2.1% *v* 3.6%; aOR, 0.53; 95% CI, 0.36 to 0.76).

CONCLUSION Within available resources, dedicated COVID-19–free surgical pathways should be established to provide safe elective cancer surgery during current and before future SARS-CoV-2 outbreaks.

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ASSOCIATED CONTENT

See accompanying article 10.1200/JCO.20.02835

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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INTRODUCTION

During the initial phases of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, an estimated 2.3 million cancer operations worldwide were postponed because of the risk of in-hospital transmission.[1] Perioperative SARS-CoV-2 is associated with a high risk of pulmonary complications and death.[2-5] Elective surgical activity was reduced to increase critical care capacity for patients with coronavirus disease 2019 (COVID-19) and to release surgical team members to support wider hospital responses.[6-8] However, some elective surgery for time-sensitive conditions continued, with prioritization of patients with resectable cancers at risk for progression and patients for whom alternative treatment modalities would be ineffective.[9-11]

Before the pandemic, most cancer surgery was performed in hospitals that also supported acute medical services.[12-14] Such hospitals have admitted patients with COVID-19 during the pandemic, increasing the risk of cross infection of elective surgery patients. To avoid this, some health care providers have established dedicated COVID-19–free surgical pathways, which deliver surgery, critical care, and inpatient ward care with no shared areas with patients with COVID-19.

Major reorganization of hospital services to provide COVID-19–free surgical pathways for elective cancer surgery needs to be justified because it will carry significant costs for providers and patients. Information is urgently required to determine whether these pathways reduce adverse postoperative outcomes. This study aimed to compare the rate of postoperative pulmonary complications after elective cancer operations in COVID-19–free surgical pathways and hospitals with no defined pathway.

CONTEXT

Key Objective

Surgical providers have begun to create COVID-19–free surgical pathways in both separate elective hospitals and major acute hospitals in which elective operating room, critical care, and inpatient ward areas are not shared with patients with COVID-19. Major service redesign to provide these pathways is expensive and difficult; evidence is urgently needed to inform clinical practice.

Knowledge Generated

Our data demonstrated that pulmonary complication rates, SARS-CoV-2 infection rates, and mortality rates were consistently lower for patients within COVID-19–free surgical pathways. These findings persisted after risk adjustment, sensitivity analyses of low-risk patients and propensity score–matched groups, and patients who had a negative preoperative SARS-CoV-2 test. Differences in outcomes were observed in both high and low SARS-CoV-2 incidence areas.

Relevance

As health providers restart elective cancer surgery, they should prevent harm by investing in dedicated COVID-19–free surgical pathways tailored to local resources available.

PATIENTS AND METHODS

Study Design and Protocol

This was an international, multicenter cohort study of adults who underwent elective cancer surgery. Local principal investigators were responsible for obtaining clinical audit, institutional review board, or ethical approval in line with local and national regulations. For example, in the United Kingdom, the study was registered as a clinical audit at each participating hospital, whereas in other countries, such as Saudi Arabia, nationwide ethics approval was granted. Data were collected online and stored on a secure data server running the Research Electronic Data Capture web application.[15]

Centers and Settings

Hospitals that performed elective cancer surgery in areas affected by the COVID-19 pandemic were eligible to participate. Enrollment of consecutive patients commenced from the date of admission of the first patient with SARS-CoV-2 to the participating hospital or, in the case of COVID-19–free surgical pathways in hospitals where no cases had been recorded, to the nearest hospital treating patients with COVID-19.

Each patient was classified as having undergone surgery within a COVID-19–free surgical pathway or with no defined pathway. To determine whether a COVID-19–free surgical pathway was used, an assessment was made of the operating room, critical care, and inpatient ward areas where each patient was treated. Patients were classified as being treated within a COVID-19–free pathway if there was a policy of complete segregation in all three areas away from patients with COVID-19. Patients were classified as being treated within no defined pathway if in any one of these areas was shared with patients with COVID-19. The classification was based on whether there was a policy of segregation in place rather than whether individual elective patients came into contact with patients with COVID-19 because asymptomatic SARS-CoV-2 infection is common, so contact with an infectious patient was possible even if this was not known at the time. COVID-19–free surgical pathways could be provided by hospitals that only provided elective care, including specialized units set up during the pandemic. Alternatively, they could be provided by acute hospitals that designated separate COVID-19–free areas and COVID-19 treatment areas to ensuring that there were no shared areas. In any particular hospital, it was possible that some patients were treated within a COVID-19–free surgical pathway, whereas others had no defined pathway (eg, where a COVID-19–free surgical pathway was introduced part way through the study inclusion period), and our patient-level classification captured this. Figure 1 shows examples of COVID-19–free surgical pathways and no defined pathways.

Surgical Pathway Components

To better understand health system responses to the COVID-19 pandemic, additional data points were introduced on April 2, 2020, to capture data on individual components of the surgical pathway (operating room, critical care, inpatient ward). These were completed for consecutive patients after this date.

Patients and Procedures

Adult patients (age $\geq$ 18 years) who underwent elective surgery with curative intent for a suspected cancer were included from emergence of COVID-19 up to April 19, 2020. Patients were identified preoperatively from multidisciplinary team (MDT) meeting (or tumor board) lists and the subsequent operation location identified by the operating surgeon. Patients were followed up to postoperative day 30, with the day of surgery being day 0. All consecutive

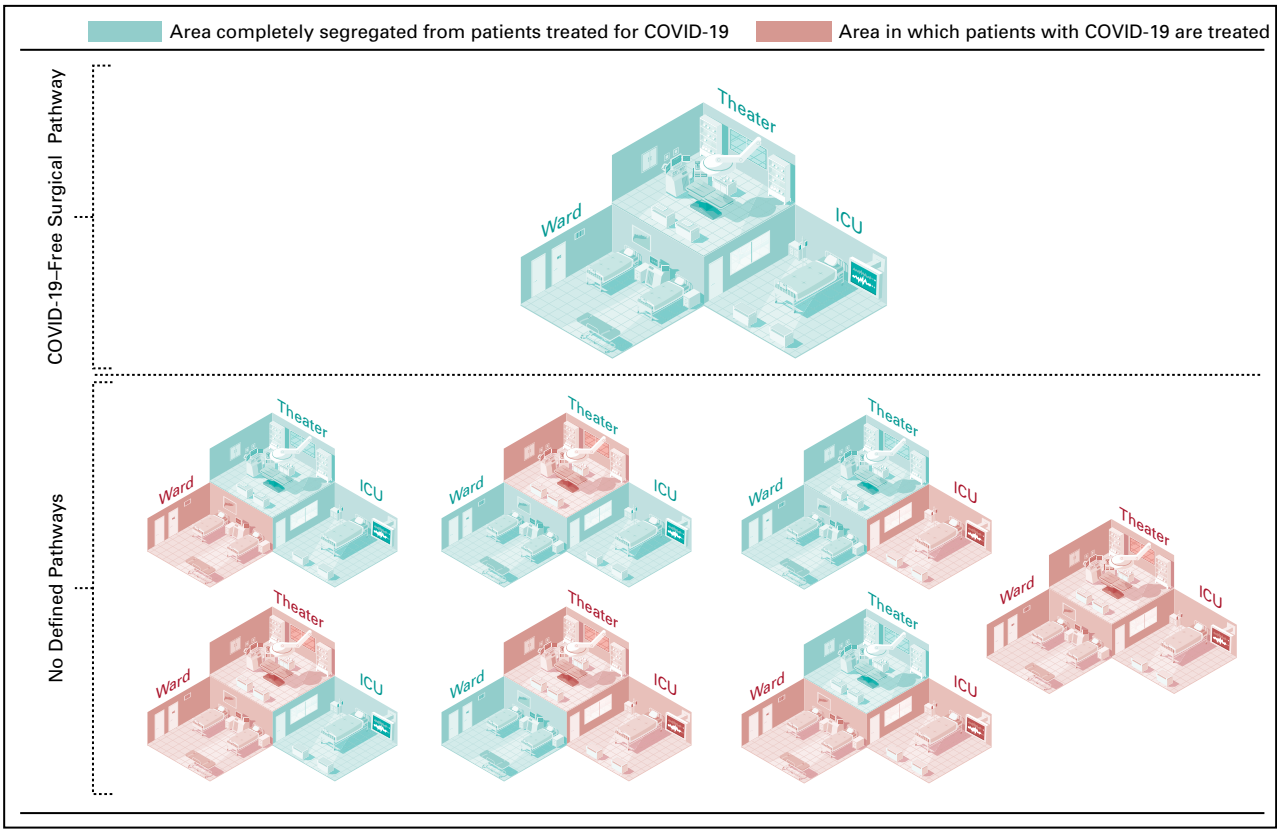


FIG 1. Differences between hospitals with a coronavirus disease 2019 (COVID-19)–free surgical pathway and hospitals with no defined pathway. COVID-19–free surgical pathways: complete segregation of operating room, critical care, and inpatient ward areas for elective cancer surgery away from patients being treated for COVID-19. No defined pathways: hospitals where there was mixing of patients who were undergoing treatment for COVID-19 and elective surgical patients in any operating room, critical care, or inpatient ward area. ICU, intensive care unit.

patients who underwent eligible surgery were included (Data Supplement, online only). Eligible cancers included colorectal, esophagogastric, head and neck (oral, oropharyngeal, laryngeal, hypopharyngeal, salivary, thyroid, paranasal sinus, skin), thoracic (lung, pleural, mediastinal, chest wall), hepatopancreatobiliary (liver, pancreatic), urologic (prostate, bladder, renal), gynecologic (uterine, ovarian, cervical, vulvar, vaginal), and breast as well as sarcoma (soft tissue, bony) and intracranial malignancies (Data Supplement). Participating centers could contribute data for either single or multiple cancers depending on local services and capacity.[16] Patients who had clinical symptoms consistent with COVID-19 or who were confirmed to have SARS-CoV-2 infection (by quantitative reverse transcription polymerase chain reaction and/or positive thoracic computed tomography [CT] imaging performed within 72 hours before surgery) at the time of surgery were excluded.

Data Variables

To account for different tumor grading and staging systems across solid cancers, disease status was classified as early stage (organ confined, non-nodal, nonmetastatic, fully resectable) or advanced stage (growth beyond organ, nodal, metastatic operated with curative intent). Full definitions are provided in the Data Supplement. Grade of surgery was categorized on the basis of the Clinical Coding & Schedule Development Group as either minor (minor/intermediate) or major (major/complex major).[17,18] Preoperative testing was defined as a swab test and/or thoracic CT imaging performed in the 72 hours before surgery to confirm SARS-CoV-2 status.

Outcome Measures

The primary outcome measure was the rate of postoperative pulmonary complications within 30 days after surgery. This included pneumonia, acute respiratory distress syndrome, and/or unexpected postoperative ventilation (Data Supplement[19]). The secondary outcomes were postoperative SARS-CoV-2 infection and mortality within 30 days after surgery. Postoperative SARS-CoV-2 infection was defined as a positive swab, positive thoracic CT imaging, or a clinical diagnosis of symptomatic COVID-19 in patients for whom these tests were unavailable.

Community SARS-CoV-2 Incidence

The community SARS-CoV-2 incidence within each participating hospital's local community was extracted from WHO,[20] European Centre for Disease Prevention and Control,[21] or US Centers for Disease Control and Prevention[22] statistics. SARS-CoV-2 incidence was calculated for 2-week windows in March and April 2020 on the basis of the number of confirmed SARS-CoV-2 cases at the smallest available administrative level (city, region, or country).[23] Hospitals were classified as being in communities with either low (< 25 cases per 100,000 population) or high (≥ 25 cases per 100,000 population) SARS-CoV-2 incidence (Data Supplement).

Data Integrity

Previous international outcomes studies have achieved > 95% case ascertainment and > 98% data accuracy during external validation.[24] We identified low-volume centers (predefined as five or fewer patients per participating specialty) and asked local principal investigators to confirm case ascertainment against MDT records. If a specialty within a hospital was found to have incomplete case ascertainment, any data entered from this specialty were excluded from analysis.

Statistical Analysis

The study was conducted according to Strengthening the Reporting of Observational Studies in Epidemiology[25] and reported according to Statistical Analyses and Methods in the Published Literature.[26] Nonparametric data were summarized with medians and interquartile ranges, and differences between groups were tested using the Mann-Whitney *U* test. The χ^2 test was used for categorical data. Missing data were included in flowcharts and summary tables, which allowed denominators to remain consistent in calculations.

Bayesian univariable and multivariable mixed-effects logistic regression was used to calculate odds ratios (ORs) and 95% CIs. Clinically plausible patient-, disease-, operation-, and location-specific factors were selected a priori for inclusion in adjusted analyses to identify independent predictors of postoperative pulmonary complications (primary outcome). Country was included as a random effect in both the unadjusted and the adjusted models. An exploratory analysis was conducted of the association between components of the COVID-19–free surgical pathway and the primary outcome measure. Analyses were carried out using R version 3.1.1 packages finalfit, tidyverse, and BRMS[27] (R Foundation for Statistical Computing, Vienna, Austria; Data Supplement).

Sensitivity Analyses

We anticipated a selection bias, with lower-risk patients being more likely to be treated within COVID-19–free surgical pathways. To account for this risk of bias, we explored differences in the postoperative pulmonary complications stratified by three common risk factors (age, sex, and American Society of Anesthesiologists [ASA] grade); performed a sensitivity analysis for pulmonary complications, including low-risk (ASA grade 1 or 2) patients only; and performed propensity score matching using a nearest neighbor method, including patients within COVID-19–free surgical pathways in a 1:1 ratio with those with no defined pathway (Data Supplement). To exclude a potential confounding effect of presymptomatic carriage of SARS-CoV-2 in the association between hospital type and the primary outcome, we performed a further sensitivity analysis that included only patients with a negative preoperative SARS-CoV-2 swab test.

RESULTS

Patients and Procedures

At the time of this analysis (June 15, 2020), a total 9,171 patients from 445 hospitals were included. These patients were from the United Kingdom (29.2%; 2,679 patients), Italy (17.3%; 1,583 patients), Spain (8.3%; 764 patients), United States (6.3%; 574 patients), and 50 other countries. Overall, 39.2% of patients (3,698) were male, 17.9% (1,644) were age < 50 years, and 8.3% (761) were age ≥ 80 years. Complete baseline patient, disease, and operative characteristics are listed in Table 1.

A total of 2,481 patients (27.1%) underwent surgery within COVID-19–free surgical pathways, and 6,689 (72.9%) underwent surgery within no defined pathway. Patients in COVID-19–free surgical pathways were younger, had fewer comorbidities, and had better performance scores. Major surgery accounted for 75.6% (1,866 of 2,481) of operations in COVID-19–free surgical pathways and 77.7% (5,179 of 6,689) where there was no defined pathway; a full list of operations performed is provided in the Data Supplement. The missing data rates were low (Data Supplement). Changes in local SARS-CoV-2 incidence over the study period are listed in the Data Supplement.

Preoperative Testing

Overall, 27.0% (2,473 of 9,409) of patients underwent preoperative SARS-CoV-2 testing; 75.9% (1,878 of 2,473) of these were performed using a swab test. The preoperative testing rate was higher in COVID-19–free surgical pathways versus no defined pathway (39.1% [970] *v* 22.5% [1,503]; $P < .0001$).

Postoperative Pulmonary Complications

The overall 30-day pulmonary complication rate was 4.2% (385 of 9,171), which was lower for patients within a COVID-19–free surgical pathway than within no defined pathway (2.2% [55 of 2,481] *v* 4.9% [329 of 6,689]; unadjusted OR, 0.49; 95% CI, 0.36 to 0.66). After adjustment, surgery in a COVID-19–free surgical pathway remained associated with a lower postoperative pulmonary

TABLE 1. Characteristics of Patients Treated Within COVID-19–Free Surgical Pathways and With No Defined Pathway

Characteristic	COVID-19–Free Surgical Pathway, No. (%)	No Defined Pathway, No. (%)	*P*
No. of patients	2,481	6,689	
Age, years			
< 50	558 (22.5)	1,086 (16.2)	< .001
50-59	576 (23.2)	1,404 (21.0)	
60-69	633 (25.5)	1,911 (28.6)	
70-79	552 (22.2)	1,689 (25.3)	
≥ 80	162 (6.5)	599 (9.0)	
Sex			
Female	1,743 (70.3)	3,832 (57.3)	< .001
Male	737 (29.7)	2,856 (42.7)	
Missing	1	1	
BMI			
Normal	996 (40.1)	2,542 (38.0)	.050
Overweight	796 (32.1)	2,091 (31.3)	
Obese	469 (18.9)	1,443 (21.6)	
Underweight	53 (2.1)	164 (2.5)	
Missing	167 (6.7)	449 (6.7)	
ASA grade			
1-2	1,959 (79.2)	4,640 (69.7)	< .001
3-5	515 (20.8)	2,016 (30.3)	
Missing	7	33	
RCRI			
0	949 (38.3)	1,942 (29.0)	< .001
1	1,181 (47.6)	3,453 (51.6)	
2	306 (12.3)	1,023 (15.3)	
≥ 3	45 (1.8)	271 (4.1)	
Respiratory comorbidity			
No	2,249 (90.6)	5,929 (88.6)	.007
Yes	232 (9.4)	760 (11.4)	
ECOG PS			
0	1,657 (67.1)	4,087 (62.2)	< .001
1-2	775 (31.4)	2,367 (36.0)	
3-4	36 (1.5)	115 (1.8)	
Missing	13	120	
Cancer type			
Colorectal	437 (17.6)	1,873 (28.0)	< .001
Breast	827 (33.3)	1,313 (19.6)	
Gynecologic	330 (13.3)	772 (11.5)	
Head or neck	253 (10.2)	884 (13.2)	
Hepatopancreatobiliary	161 (6.5)	515 (7.7)	
Intracranial	34 (1.4)	130 (1.9)	
Thoracic	172 (6.9)	385 (5.8)	
Esophagogastric	75 (3.0)	312 (4.7)	
Sarcoma	118 (4.8)	143 (2.1)	
Urologic	74 (3.0)	362 (5.4)	

(continued on following page)

TABLE 1. Characteristics of Patients Treated Within COVID-19–Free Surgical Pathways and With No Defined Pathway (continued)

Characteristic	COVID-19–Free Surgical Pathway, No. (%)	No Defined Pathway, No. (%)	*P*
Disease stage			
Early	1,822 (73.5)	4,707 (70.4)	.004
Advanced	657 (26.5)	1,978 (29.6)	
Missing	0.08	0.06	
Booking type			
Day case	206 (8.4)	524 (7.9)	.493
Inpatient	2,259 (91.6)	6,117 (92.1)	
Missing	0.6	0.08	
Anesthetic			
Regional/local	99 (4.0)	388 (5.8)	.001
General	2,382 (96.0)	6,301 (94.2)	
Operation grade			
Minor	601 (24.4)	1,488 (22.3)	.042
Major	1,866 (75.6)	5,179 (77.7)	
Missing	0.6	0.3	
Preoperative testing			
Not screened	1,511 (60.9)	5,186 (77.5)	< .001
Screened	970 (39.1)	1,503 (22.5)	
Community SARS-CoV-2 risk			
Low	1,948 (78.5)	6,079 (90.9)	< .001
High	533 (21.5)	610 (9.1)	

NOTE. See the Data Supplement for full definitions. Percentages calculated as a proportion of column total. *P* values calculated using χ^2 test.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; COVID-19, coronavirus disease 2019; ECOG PS, Eastern Cooperative Oncology Group performance status; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

complication rate (adjusted OR [aOR], 0.62; 95% CI, 0.44 to 0.86). Older age, male sex, ASA grades 3-5, poorer performance status, higher cardiac risk, preexisting respiratory disease, advanced disease stage, major surgery, esophagogastric surgery, and surgery in high SARS-CoV-2 incidence areas were also associated with a greater odds of pulmonary complications (Fig 2; Table 2; Data Supplement).

Sensitivity Analyses

Postoperative pulmonary complication rates stratified by age, sex, and ASA grade in hospitals with and without COVID-19–free surgical pathways are shown in the Data Supplement. In a sensitivity analysis including only low-risk patients (n = 6,489), COVID-19–free surgical pathways remained associated with a reduced odds of pulmonary complications (aOR, 0.58; 95% CI, 0.36 to 0.93; Data Supplement).

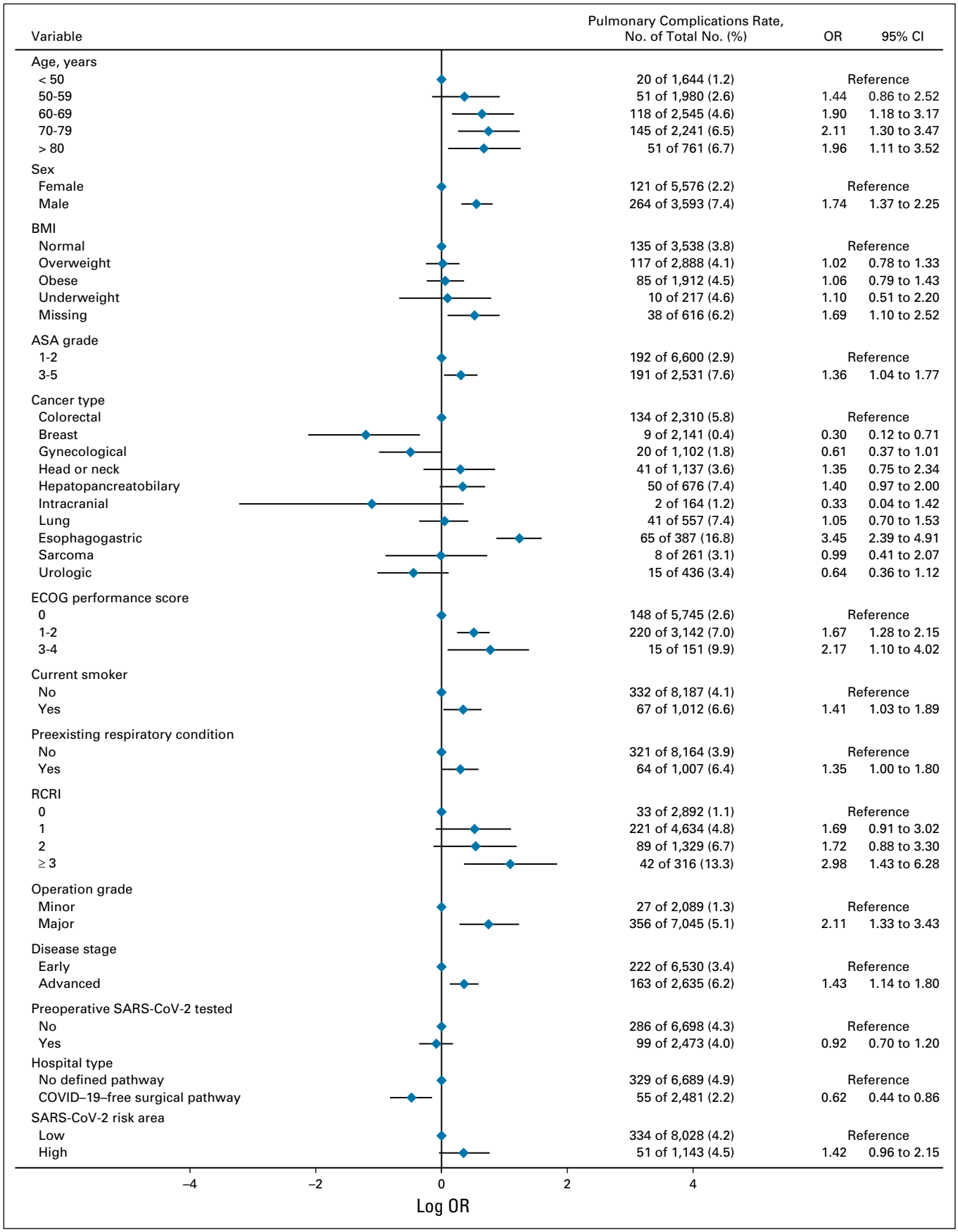
Propensity score matching created well-balanced groups (Data Supplement), with 2,449 patients within COVID-19–free surgical pathways matched to 2,449 with no defined pathway. After adjustment, surgery within a COVID-19–free surgical pathway was associated with a lower odds of pulmonary complications (aOR, 0.65; 95% CI, 0.44 to 0.96; Data Supplement). In a sensitivity analysis including only patients with a negative preoperative SARS-CoV-2 test (n = 2,447), again a COVID-19–free surgical pathway was associated with lower pulmonary complication rates (aOR, 0.52; 95% CI, 0.29 to 0.91; Data Supplement).

Surgical Pathway Components

Consecutive data were available for 4,505 patients. Of these, 45.6% (2,053) were classified as having a COVID-19–free surgical pathway. Of 2,451 patients with no defined pathway, 86.5% (2,120) had an operating room, 21.5% (526) a critical care area, and 59.8% (1,466) had a ward space shared with patients with COVID-19. Treatment in both a COVID-19–free ward and a critical care area (aOR, 0.43; 95% CI, 0.24 to 0.77) or a complete COVID-19–free surgical pathway (aOR, 0.30; 95% CI, 0.17 to 0.54) was significantly associated with a lower odds of pulmonary complications versus treatment in shared operating room, critical care, and ward areas (Data Supplement).

Postoperative SARS-CoV-2 Infection

The overall rate of postoperative SARS-CoV-2 infection was 3.2% (291 of 9,171). A majority was confirmed with a swab



test (85.6%; 249 of 291). The SARS-CoV-2 infection rate was lower in COVID-19–free surgical pathways (2.1%; 53 of 2,481) than with no defined pathway (3.6%; 238 of 6,820; aOR, 0.53; 95% CI, 0.36 to 0.76). This was consistent in a sensitivity analysis with swab testing only (aOR, 0.44; 95% CI, 0.28 to 0.68; Data Supplement) and was consistent across hospitals in high (3.9% *v* 8.2%) and low SARS-CoV-2 incidence areas (1.6% *v* 3.1%; Table 3). SARS-CoV-2 infection was associated with increased pulmonary complication rates compared with patients without infection (33.8% [130 of 385] *v* 1.8% [161 of 8,786]; OR, 29.78; 95% CI, 22.4 to 39.6).

Postoperative Mortality

The overall postoperative mortality rate was 1.5% (134 of 9,115). Mortality was higher in patients with pulmonary complications (OR, 25.64; 95% CI, 17.63 to 36.67) and in patients with SARS-CoV-2 infection (OR, 29.34; 95% CI, 20.13 to 43.04). It was lower in patients operated on in COVID-19–free surgical pathways (OR, 0.45; 95% CI, 0.25 to 0.78). Of the 30-day deaths, 49.3% (66 of 134) were associated with pulmonary complications, and 44.0% (59 of 134) were associated with SARS-CoV-2 infection (Fig 3). Mortality was higher after pulmonary complications in patients with SARS-CoV-2 (30.8%; 40 of 130) than in patients without infection with pulmonary complications (10.7%; 26 of 244).

DISCUSSION

This study identified that postoperative pulmonary complication rates were lower for patients in COVID-19–free surgical pathways during the SARS-CoV-2 pandemic. Despite a tendency for lower-risk surgeries to be performed in these pathways, effects persisted after risk adjustment, sensitivity analyses, and propensity score matching. The advantage of COVID-19–free pathways was also seen in patients with a negative SARS-CoV-2 test preoperatively. Older patients, males, and patients with cardiorespiratory comorbidities were consistently at greater risk of adverse outcomes. Mortality was primarily driven by pulmonary complications, which was low in COVID-19–free surgical pathways and high with postoperative SARS-CoV-2 infection. Overall, these data support major international redesign of surgical services, based on local available resources, to provide elective cancer surgery in COVID-19–free surgical pathways. While the greatest effect size was seen in areas of high SARS-CoV-2 incidence, there was also a significant difference in outcomes in low-incidence areas. Setup of COVID-19–free pathways is therefore likely to be justified during the end phases of current lockdowns in preparation for future wave.

It is likely that differences in SARS-CoV-2 transmission rates are responsible for differences in pulmonary complications between hospitals with COVID-19–free surgical pathways and those with no defined pathway. First, the rate of postoperative SARS-CoV-2 infection was consistently lower in COVID-19–free surgical pathways. Second, SARS-CoV-2 infection was associated with a very high rate of pulmonary complications. Third, the benefit of COVID-19–free pathways was greatest in high SARS-CoV-2 incidence areas. Finally, the effect size increased in proportion with the number of COVID-19–free components of the surgical pathway. The overall preoperative testing rate was low (27.0%), and testing was not associated with lower pulmonary complication rates in the main model. Furthermore, in a sensitivity analysis for patients with a negative preoperative swab test, the benefit of COVID-19–free pathways persisted.

Although we defined COVID-19–free pathways in the protocol, the exact nature varied across this pragmatic study. For example, we did not include elective and emergency admission areas or the perioperative recovery room in the definition of center status. Patients with comorbidities and who are elderly will still need to undergo surgery in major acute hospitals because of resource availability (eg, critical care, interventional radiology, multispecialty operations), and these hospitals are likely to continue to admit patients with COVID-19. COVID-19–free pathways must be robustly quality assured within these settings. Detailed evaluations of additional in-hospital measures to reduce SARS-CoV-2 exposure, including serial preoperative testing, personal protective equipment, drug prophylaxis, staff testing, and perioperative isolation, are still required.

The overall mortality rate with pulmonary complications (17.2%) is higher than would be expected compared with prepandemic rates.[22-27,28] Data from elective and emergency surgical patients have shown high mortality associated with perioperative SARS-CoV-2 infection, which is consistent with our series.[5] This information should be used routinely as part of informed consent for elective surgery.

There were limitations to this study. First, the risk of selection bias in COVID-19–free surgical pathways was accounted for through risk adjustment and planned sensitivity analyses. Despite this, COVID-19–free pathways may have been better resourced, and there may have been residual bias. However, establishing COVID-19–free areas did not seem to be determined by resource availability alone; patients were operated on in these pathways in 27 of 37 countries in which five

FIG 2. Factors associated with postoperative pulmonary complications after elective cancer surgery, including data from 8,971 patients with complete data. See Data Supplement for the full model, details around missing data, and full definitions. ASA, American Society of Anesthesiologists; BMI, body mass index; COVID-19, coronavirus disease 2019; ECOG, Eastern Cooperative Oncology Group; OR, odds ratio; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

TABLE 2. Comparison of Patients With and Without Postoperative Pulmonary Complications

Factor	No Pulmonary Complications, No. (%)	Pulmonary Complications, No. (%)	*P*
No. of patients	8,786	385	
Age, years			
< 50	1,624 (18.5)	20 (5.2)	< .001
50-59	1,929 (22.0)	51 (13.2)	
60-69	2,427 (27.6)	118 (30.6)	
70-79	2,096 (23.9)	145 (37.7)	
≥ 80	710 (8.1)	51 (13.2)	
Sex			
Female	5,455 (62.1)	121 (31.4)	< .001
Male	3,329 (37.9)	264 (68.6)	
Missing	2	0	
BMI			
Normal	3,403 (38.7)	135 (35.1)	.100
Overweight	2,771 (31.5)	117 (30.4)	
Obese	1,827 (20.8)	85 (22.1)	
Underweight	207 (2.4)	10 (2.6)	
Missing	578 (6.6)	38 (9.9)	
ASA grade			
1-2	6,408 (73.3)	192 (50.1)	< .001
3-5	2,340 (26.7)	191 (49.9)	
Missing	38	2	
Current smoker			
No	7,843 (89.3)	321 (83.4)	< .001
Yes	943 (10.7)	64 (16.6)	
Preexisting respiratory condition			
No	7,873 (89.6)	306 (79.5)	< .001
Yes	913 (10.4)	79 (20.5)	
RCRI			
0	2,859 (32.5)	33 (8.6)	< .001
1	4,413 (50.2)	221 (57.4)	
2	1,240 (14.1)	89 (23.1)	
≥ 3	274 (3.1)	42 (10.9)	
ECOG PS			
0	5,597 (64.7)	148 (38.6)	< .001
1-2	2,922 (33.8)	220 (57.4)	
3-4	136 (1.6)	15 (3.9)	
Missing	131	2	

(continued on following page)

TABLE 2. Comparison of Patients With and Without Postoperative Pulmonary Complications (continued)

Factor	No Pulmonary Complications, No. (%)	Pulmonary Complications, No. (%)	*P*
Cancer type			
Colorectal	2,176 (24.8)	134 (34.8)	< .001
Breast	2,132 (24.3)	9 (2.3)	
Gynecologic	1,082 (12.3)	20 (5.2)	
Head or neck	1,096 (12.5)	41 (10.6)	
Hepatopancreatobiliary	626 (7.1)	50 (13.0)	
Intracranial	162 (1.8)	2 (0.5)	
Thoracic	516 (5.9)	41 (10.6)	
Esophagogastric	322 (3.7)	65 (16.9)	
Sarcoma	253 (2.9)	8 (2.1)	
Urologic	421 (4.8)	15 (3.9)	
Disease stage			
Early	6,308 (71.8)	222 (57.7)	< .001
Advanced	2,472 (28.2)	163 (42.3)	
Missing	6	0	
Booking type			
Day case	729 (8.4)	1 (0.3)	< .001
Inpatient	7,994 (91.6)	383 (99.7)	
Missing	63	1	
Anesthetic			
Regional/local	458 (5.2)	29 (7.5)	.061
General	8,328 (94.8)	356 (92.5)	
Operation grade			
Minor	2,062 (23.6)	27 (7.0)	< .001
Major	6,689 (76.4)	356 (93.0)	
Missing	35	2	
Preoperative testing			
Not screened	6,412 (73.0)	286 (74.3)	.612
Screened	2,374 (27.0)	99 (25.7)	
Hospital type			
COVID-19–free surgical pathway	2,426 (27.6)	55 (14.3)	< .001
No defined pathway	6,360 (72.4)	329 (85.7)	
Missing	0	1	
Community SARS-CoV-2 risk			
Low	7,694 (87.6)	334 (86.8)	.692
High	1,092 (12.4)	51 (13.2)	

NOTE. See the Data Supplement for full definitions. Percentages calculated as a proportion of column total. *P* values calculated using χ^2 test.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; COVID-19, coronavirus disease 2019; ECOG PS, Eastern Cooperative Oncology Group performance status; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

or more centers participated. Second, we included swab, CT, and clinical diagnoses of COVID-19 in the definition of postoperative SARS-CoV-2 infection to reflect variable access to testing during early phases of the pandemic.[29,30] However, only 14.4% of patients infected had a CT or clinical diagnosis, which minimizes the risk of incorrect diagnosis. Third, borderline operable cancers and high-risk patients may not have been offered

TABLE 3. Clinical Outcomes for Patients Who Underwent Surgery in a COVID-19–Free Surgical Pathway Versus No Defined Pathway Split by Low Versus High Community SARS-CoV-2 Incidence

	COVID-19–Free Surgical Pathway (n = 2,481)		No Defined Pathway (n = 6,689)	
Community SARS-CoV-2 Incidence Area	**% (95% CI)**	**No. of Total No.**	**% (95% CI)**	**No. of Total No.**
Low				
Pulmonary complications	2.2 (1.6 to 3.0)	43 of 1,948	4.8 (4.2 to 5.3)	290 of 6,079
SARS-CoV-2 infection	1.6 (1.1 to 2.3)	32 of 1,948	3.1 (2.7 to 3.6)	188 of 6,079
30-day mortality	0.7 (0.4 to 1.2)	14 of 1,939	1.7 (1.4 to 2.1)	103 of 6,041
30-day mortality and SARS-CoV-2 infection	0.01 (0.001 to 0.04)	2 of 1,939	0.7 (0.5 to 1.0)	44 of 6,041
High				
Pulmonary complications	2.3 (1.2 to 3.9)	12 of 533	6.4 (4.6 to 8.6)	39 of 610
SARS-CoV-2 infection	3.9 (2.5 to 6.0)	21 of 533	8.2 (6.1 to 10.7)	50 of 610
30-day mortality	0.9 (0.3 to 2.2)	5 of 527	2.1 (1.1 to 3.6)	13 of 608
30-day mortality and SARS-CoV-2 infection	0.8 (0.2 to 1.9)	4 of 527	1.4 (0.7 to 2.8)	9 of 608

NOTE. Pulmonary complications were defined as pneumonia, acute respiratory distress syndrome, and/or unexpected postoperative ventilation. Areas defined as high (30-day cumulative notification rate of ≥ 25 cases per 100,000 population) or low (14-day cumulative notification rate of < 25 cases per 100,000 population) according to European Centre for Disease Control and Prevention reporting criteria during 2-week periods in March and April 2020. Proportions are presented as mean averages with 95% CIs calculated using the Pearson-Klopper exact method (R package binom.confint).

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

surgery during the pandemic, so the potential benefits of COVID-19–free surgical pathways may be even greater for this group.[31,32] Fourth, there is a possibility of incomplete case ascertainment, although we implemented a number of strategies to minimize this.

COVID-19–free surgical pathways and entirely separate elective surgery hospitals may lead to unintended consequences that include reduction in capacity for other health conditions. These consequences will need to be monitored at a whole-system level.

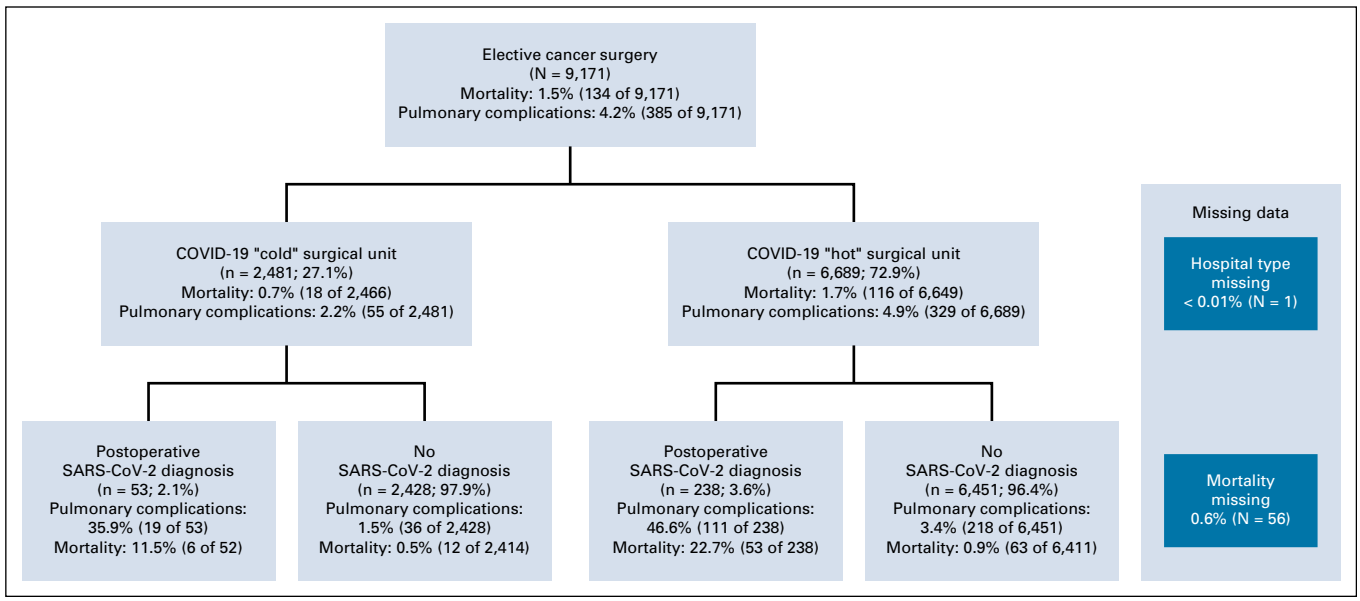


FIG 3. Rates of pulmonary complications, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and death in hospitals with coronavirus disease 2019 (COVID-19)–free surgical pathways *v* those with no defined pathway. Pulmonary complications were defined as pneumonia, acute respiratory distress syndrome, and/or unexpected postoperative ventilation.

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CLINICAL TRIAL INFORMATION

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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REFERENCES

1. COVIDSurg Collaborative: Elective surgery cancellations due to the COVID-19 pandemic: Global predictive modelling to inform surgical recovery plans. Br J Surg 10.1002/bjs.11746 [epub ahead of print on May 12, 2020]
2. Dai M, Liu D, Liu M, et al: Patients with cancer appear more vulnerable to SARS-COV-2: A multi-center study during the COVID-19 outbreak. Cancer Discov 10:783-791, 2020
3. Liang W, Guan W, Chen R, et al: Cancer patients in SARS-CoV-2 infection: A nationwide analysis in China. Lancet Oncol 21:335-337, 2020
4. Mehta V, Goel S, Kabarriti R, et al: Case fatality rate of cancer patients with COVID-19 in a New York hospital system. Cancer Discov 10:935-941, 2020
5. COVIDSurg Collaborative: Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: An international cohort study, in print. Lancet 396:27-38, 2020
6. Royal College of Surgeons of England: Guidance for surgeons working during the COVID-19 pandemic, 2020. https://www.rcseng.ac.uk/coronavirus/joint-guidance-for-surgeons-v1
7. COVIDSurg Collaborative: Global guidance for surgical care during the COVID-19 pandemic. Br J Surg 10.1002/bjs.11646 [epub ahead of print on April 15, 2020]
8. Saini KS, de Las Heras B, de Castro J, et al: Effect of the COVID-19 pandemic on cancer treatment and research. Lancet Haematol 7:e432-e435, 2020
9. NHS England and NHS Improvement: Advice to trusts on maintaining cancer treatment during the COVID-19 response, 2020 https://www.england.nhs.uk/coronavirus/publication/advice-to-trusts-on-maintaining-cancer-treatment-during-the-covid-19-response
10. Sud A, Jones M, Broggio J, et al: Quantifying and mitigating the impact of the COVID-19 pandemic on outcomes in colorectal cancer, 2020. https://www.medrxiv.org/content/10.1101/2020.04.28.20083170v1
11. British Association for Cancer Surgery: BASO guidance - strategy for cancer surgery sustainability and recovery in the COVID 19 pandemic, 2020. https://baso.org.uk/media/99217/baso_guidance_for_cancer_surgery_9th_april_2020_v7.pdf
12. Sullivan R, Alatise OI, Anderson BO, et al: Global cancer surgery: Delivering safe, affordable, and timely cancer surgery. Lancet Oncol 16:1193-1224, 2015
13. Woo YL, Kyrgiou M, Bryant A, et al: Centralisation of services for gynaecological cancers - a Cochrane systematic review. Gynecol Oncol 126:286-290, 2012
14. Faluyi OO, Connor JL, Chatterjee M, et al: Advanced pancreatic adenocarcinoma outcomes with transition from devolved to centralised care in a regional cancer centre. Br J Cancer 116:424-431, 2017
15. Harris PA, Taylor R, Thielke R, et al: Research Electronic Data Capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 42:377-381, 2009
16. National Confidential Enquiry into Patient Outcome and Death: The NCEPOD Classification of Intervention, 2004. https://www.ncepod.org.uk/classification.html
17. Bupa: Schedule of procedures, 2020. https://codes.bupa.co.uk/home
18. CCSD Schedule: The Clinical Coding & Schedule Development Group, 2020. https://www.ccsd.org.uk/ccsdschedule
19. Pearse RM, Abbott TE, Haslop R, et al: The Prevention of Respiratory Insufficiency after Surgical Management (PRISM) trial. Report of the protocol for a pragmatic randomized controlled trial of CPAP to prevent respiratory complications and improve survival following major abdominal surgery. Minerva Anestesiol 83:175-182, 2017
20. WHO: WHO Coronavirus Disease (COVID-19) Dashboard, 2020. https://covid19.who.int
21. European Centre for Disease Prevention and Control: Daily situation update worldwide, 2020. https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases
22. Centers for Disease Control and Prevention: CDC COVID Data Tracker, 2020. https://www.cdc.gov/covid-data-tracker/index.html
23. European Centre for Disease Prevention and Control: Coronavirus disease 2019 (COVID-19) pandemic: Increased transmission in the EU/EEA and the UK – seventh update, 2020. https://www.ecdc.europa.eu/sites/default/files/documents/RRA-seventh-update-Outbreak-of-coronavirus-disease-COVID-19.pdf

24. GlobalSurg Collaborative: Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: A prospective, international, multicentre cohort study. Lancet Infect Dis 18:516-525, 2018
25. Gharaibeh A, Koppikar S, Bonilla-Escobar FJ: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) in the International Journal of Medical Students. Int J Med Stud 2:36-37, 2014
26. Lang TA, Altman DG: Basic statistical reporting for articles published in biomedical journals: The "Statistical Analyses and Methods in the Published Literature" or the SAMPL Guidelines. Int J Nurs Stud 52:5-9, 2015
27. Wickham H: The split-apply-combine strategy for data analysis. J Stat Softw 40:1-29, 2011
28. Biccard BM, Madiba TE, Kluyts HL, et al: Perioperative patient outcomes in the African Surgical Outcomes Study: A 7-day prospective observational cohort study. Lancet 391:1589-1598, 2018
29. Kavanagh MM, Erondu NA, Tomori O, et al: Access to lifesaving medical resources for African countries: COVID-19 testing and response, ethics, and politics. Lancet 395:1735-1738, 2020
30. Fernandez-Bustamante A, Frendl G, Sprung J, et al: Postoperative pulmonary complications, early mortality, and hospital stay following noncardiothoracic surgery: A multicenter study by the Perioperative Research Network Investigators. JAMA Surg 152:157-166, 2017

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Elective Cancer Surgery in COVID-19–Free Surgical Pathways During the SARS-CoV-2 Pandemic: An International, Multicenter, Comparative Cohort Study

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