

Rapid review of literature on a perioperative COVID-19 infection in cancer patients undergoing surgery

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1.0 Clinical question

In patients with cancer who are undergoing surgery does a perioperative COVID-19 infection affect mortality?

Population:	Patients with cancer undergoing surgery
Intervention:	COVID-19 infection
Comparison:	-
Outcome:	Mortality

2.0 Summary

The overall quality of the evidence to address this question is low but consistently suggests that perioperative COVID-19 infection increases risk of mortality in patients undergoing surgery.

Evidence from the beginning of the pandemic came in the form of case reports published in the comments or letter to the editor sections of journals. Most of the evidence cannot be generalised, each paper should be appraised to consider the stage of the pandemic it relates to and to take into account geographical differences and differences in the patient pathway used (e.g. triaging and testing of patients). There may also be publication bias as a small study was identified that found no association with a COVID-19 infection and mortality (1).

The best quality evidence comes from a recent prospective study from October 2020 which aimed to determine whether COVID-19-free surgical pathways were associated with lower postoperative pulmonary complication rates in cancer patients compared with hospitals with no defined pathway (2). The study found that of 2,481 cancer patients treated in a COVID-19-free surgical pathway 53 (2.1%) had a postoperative diagnosis of COVID-19. Of the 6,689 patients treated in a hospital with no defined pathway 238 patients (3.6%) had a postoperative diagnosis of COVID-19. In the COVID-19-free surgical pathway the mortality rate amongst the patients with a postoperative diagnosis of COVID-19 was 11.5% (6 of 52) compared to 0.5% (12 of 2,414) in patients who did not have a COVID-19 diagnosis. In the hospital with no defined pathway the mortality rate amongst the patients who had a postoperative diagnosis of COVID-19 was 22.7% (53 of 238) compared to 0.9% (63 of 6,411) in patients who did not have a COVID-19 diagnosis. The aim of this study was not to assess mortality but pulmonary complications, but the results suggest that mortality is higher in patients with a COVID-19 infection in both a hospital with a COVID-19-free surgical pathway and a hospital with no defined pathway. It also suggests that COVID-19-free surgical pathways reduce pulmonary complications, rates of COVID-19 infection and mortality in cancer surgical patients.

A review of international guidelines also found very limited information to answer this question. The most relevant of these were a position statement from SIGN (3) on “reducing the postoperative mortality due to COVID -19 in patients undergoing elective surgery,” and guidelines from the American College of Surgeons (ACS)(4) on “triage and management of elective cancer patients during the acute and recovery phases of Coronavirus Disease 2019 (COVID-19) pandemic”. Both of these draw on the primary literature to support their guidance with SIGN citing the COVIDSurg Collaborative (5) who reported an overall 30-day mortality of 23.8% in patients undergoing surgery who had SARS-CoV-2 infection confirmed within 7 days before or 30 days after surgery. ACS cite Liang (6) as emerging evidence of poorer outcomes amongst patients with cancer with COVID-19 infection. This paper showed that 39% of cancer patients who underwent chemotherapy or surgery required ICU care with ventilation or died, compared to 8% of patients without cancer. However, these results should be interpreted with caution as the number of COVID-19 patients in the study with a history of cancer was small (18 cases).

One of the most commonly cited papers to address this question is Lei et al. which found a 20% mortality rate in patients who underwent elective surgery (7). This was a low quality retrospective study that was not specific to cancer patients, and included a small number of patients (n=34) and was conducted across four hospitals in China at the very beginning of the outbreak (January 1 – February 5 2020) prior to the implementation of COVID-19 infection prevention and control measures.

A review of all relevant papers identified can be found below in the '3.0 Review of Primary literature' section broken down by cohort type – surgery, cancer surgery, gynaecological cancer, gastrointestinal cancer, thoracic cancer.

3.0 Review of Primary literature

3.1 Surgery

COVIDSurg Collaborative, 2020 (5)

Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study

An international prospective cohort study including 1,128 patients who had SARS-CoV-2 infection confirmed within 7 days before or 30 days after surgery between Jan-March across 24 countries. The study found that predictors of 30 day mortality included a surgical diagnosis of cancer (OR 1.55, 95% CI 1.01-2.39, $p=0.046$) and undergoing major surgery (major or complex major according to the Bupa schedule) (OR 1.52, 95% CI 1.01-2.31, $p=0.047$), neither of these were statistically significant. A postoperative SARS-CoV-2 diagnosis was also found not to be a predictor of 30 day mortality (OR 0.94, 95% CI 0.65-1.39, $p=0.753$).

Lei et al., 2020 (7)

Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection

A retrospective cohort study including 34 operative patients who underwent elective surgery between January and February 2020 in three Chinese hospitals found all patients developed COVID-19 pneumonia shortly after surgery and 15 (44.1%) patients needed ICU care, and the mortality rate was 20.5%.

3.2 Cancer surgery

Glasbey et al., 2020 (2)

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

An international multicentre cohort study, aimed to determine whether COVID-19-free surgical pathway for elective cancer surgery was associated with lower postoperative pulmonary complication rates compared with hospitals with no defined pathway.

Mortality was higher 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, 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).

Liang et al., 2020 (6)

Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China

A comment in the lancet oncology from March 2020 which presented results from a review of 2,007 cases from 575 hospitals in China found that patients who underwent chemotherapy or surgery in the past month had a numerically higher risk of clinically severe events (a composite endpoint defined as the percentage of patients being admitted to the intensive care unit requiring invasive ventilation, or death) than did those not receiving chemotherapy or surgery (seven [39%] of 18 patients vs 124 [8%] of 1,572 patients; Fisher's exact $p=0.0003$). These odds were further confirmed by logistic regression (odds ratio [OR] 5.34, 95% CI 1.80-16.18; $p=0.0026$) after adjusting for other risk factors, including age, smoking history, and other comorbidities.

3.3 Gynaecological cancer

Dursun et al., 2020 (1)

Performing gynecologic cancer surgery during the COVID-19 pandemic in Turkey: A multicenter retrospective observational study

Reported on perioperative outcomes in 200 gynaecological patients who underwent surgery in Turkey March-May 2020. Only two patients developed symptoms related to COVID-19 during the postoperative follow-up and neither was polymerase chain reaction (PCR)-positive in multiple samples.

3.4 Gastrointestinal cancer

Liu et al., 2020 (8)

Postoperative Onset and Detection of SARS-CoV-2 in Surgically Resected Specimens From Gastrointestinal Cancer Patients With Pre/Asymptomatic COVID-19

This retrospective study included 52 gastrointestinal cancer patients who underwent surgery between January 2 and January 21, 2020 at Renmin Hospital of Wuhan University in Wuhan, China. The median follow-up time were 101.5 (97.0–107.0) days. Six (11.5%) patients experienced symptom onset and were confirmed to be COVID-19 after surgery. One patient (Patient 4) required care in the intensive care unit, was ventilated for acute respiratory distress syndrome (ARDS) but passed away. The case fatality rate in patients with COVID-19 was 16.7% (1 out of 6 patients) and was 2.2% (1 out of 46 patients) in those without COVID-19

Note- patients in this study did not undergo preoperative nasopharyngeal swabs for COVID-19 testing to exclude infection.

3.5 Thoracic cancer

Cai et al (2020) (9)

Coronavirus Disease 2019 in the Perioperative Period of Lung Resection: A brief report from a single thoracic surgery department in Wuhan, People's Republic of China

April 2020

This paper reports on seven cases of patients with confirmed COVID-19 in the perioperative period of resection for a lung tumour from a thoracic surgery department in Wuhan, China. Six patients had NSCLC and one was diagnosed with sclerosing pneumo-cytoma. Median patient age was 60 and five were men. None of the patients had surgery-related postoperative complications. Three of the seven patients died of respiratory failure due to COVID-19 on postoperative days 5, 42, and 35 (5, 19, and 25 days after symptom onset, respectively). Two patients recovered and were discharged from hospital, while two remained in hospital but in a stable condition at the time the paper was submitted for publication.

The paper describes the clinicopathological features of the disease.

Gonfiotti et al (2020) (10)

Clinical courses and outcomes of five patients with primary lung cancer surgically treated while affected by Severe acute respiratory syndrome coronavirus 2

May 2020

This is a retrospective study of the outcomes of five patients who underwent resection for primary lung cancer while infected with COVID-19. All patients were males, mean age 74 years (range 67 – 80). Four of the five men reported chronic comorbidities. Three of the 5 patients were treated with a minimally invasive approach. Mortality was 40% (2 of 5 patients).

[Peng et al \(2020\) \(11\)](#)

Clinical course of coronavirus disease 2019 in 11 patients after thoracic surgery and challenges in diagnosis

Month? 2020 [Patients underwent surgery between January 1 and January 24 2020]

Case series of 11 patients diagnosed with COVID-19 after thoracic surgery.

Of 121 patients who underwent surgery 11 subsequently were confirmed, by rt-PCR, as having COVID-19. Evidence of nosocomial transmission was apparent in the majority. At the last follow-up date of March 27 2020, 3 critical cases had died, and 4 severe and 4 mild cases were discharged upon recovery, giving a case fatality rate of 27.3%.

Resected lung volume (≥ 5 segments), persistent fever, and postoperative reduction of total protein and albumin were significantly associated with fatality ($p < 0.05$)

[Dai et al \(2020\) \(12\)](#)

Patients with Cancer Appear More Vulnerable to SARS-CoV-2: A Multicentre Study during the COVID-19 Outbreak

June 2020

[This paper was cited in Xu et al (2020) Clinical recommendations on lung cancer management during the COVID-19 pandemic, which has been excluded]

A multicentre study of 105 patients with cancer and 536 age-matched non-cancer patients confirmed with COVID-19.

Compared with COVID-19 patients without cancer, patients with cancer had higher observed death rates [OR 2.34 (95% CI 1.15 – 5.08), $p < 0.01$], higher rates of ICU admission [OR 2.84 (95% CI 1.59 – 5.08), $p < 0.01$], and higher rates of having at least one severe or critical symptom [OR 2.79 (95% CI (1.74–4.41), $p < 0.01$).

When data was analysed by cancer stage, it was found that patients with metastatic cancer had even higher risks of death [OR, 5.58; 95% CI (1.71–18.23); $P = 0.01$], ICU admission [OR, 6.59; 95% CI (2.32–18.72); $P < 0.01$], having severe conditions [OR, 5.97; 95% CI (2.24– 15.91); $P < 0.01$], whereas patients with non-metastatic cancer did not demonstrate statistically significant differences compared with patients without cancer, with all $p > 0.05$.

When data was analysed by treatment type, cancer patients who received surgery demonstrated higher rates of death (25%), higher changes of ICU admission (37.5%), higher changes of having severe or critical symptoms (62.5%) and higher use of invasive ventilation (25%) than other treatments, excluding immunotherapy. However, these data are based only on 8 patients underwent surgery.

4.0 Methodology

A literature review was conducted in Pubmed using the search strategy outlined below. 403 papers were identified in the search results. The 403 search results was sifted by one researcher and 67 full text papers were included for full text review, citations check of the included papers identified a further seven papers. In addition a search of relevant guidelines was conducted which identified two recent guidelines that address the clinical question.

Search term	Number of results
("Surgical Procedures, Operative"[Mesh] OR "General Surgery"[Mesh]) AND ("SARS-CoV-2"[Mesh] OR "COVID-19"[Mesh])) AND ("Neoplasms"[Mesh]) AND ("Neoplasms"[Mesh] OR (cancer OR tumour OR neoplasm))	403
("Neoplasms"[Mesh] OR (cancer OR tumour OR neoplasm) ""Neoplasms""[MeSH Terms] OR ""cancer s""[All Fields] OR ""cancerated""[All Fields] OR ""canceration""[All Fields] OR ""cancerization""[All Fields] OR ""cancerized""[All Fields] OR ""cancerous""[All Fields] OR ""Neoplasms""[MeSH Terms] OR ""Neoplasms""[All Fields] OR ""cancer""[All Fields] OR ""cancers""[All Fields] OR ""cysts""[MeSH Terms] OR ""cysts""[All Fields] OR ""cyst""[All Fields] OR ""neurofibroma""[MeSH Terms] OR ""neurofibroma""[All Fields] OR ""neurofibromas""[All Fields] OR ""tumor s""[All Fields] OR ""tumoral""[All Fields] OR ""tumorous""[All Fields] OR ""tumour""[All Fields] OR ""Neoplasms""[MeSH Terms] OR ""Neoplasms""[All Fields] OR ""tumor""[All Fields] OR ""tumour s""[All Fields] OR ""tumoural""[All Fields] OR ""tumourous""[All Fields] OR ""tumours""[All Fields] OR ""tumors""[All Fields] OR ""neoplasm s""[All Fields] OR ""Neoplasms""[MeSH Terms] OR ""Neoplasms""[All Fields] OR ""neoplasm""[All Fields])"	810,548
""cancer OR tumour OR neoplasm ""cancer s""[All Fields] OR ""cancerated""[All Fields] OR ""canceration""[All Fields] OR ""cancerization""[All Fields] OR ""cancerized""[All Fields] OR ""cancerous""[All Fields] OR ""neoplasms""[MeSH Terms] OR ""neoplasms""[All Fields] OR ""cancer""[All Fields] OR ""cancers""[All Fields] OR ""cysts""[MeSH Terms] OR ""cysts""[All Fields] OR ""cyst""[All Fields] OR ""neurofibroma""[MeSH Terms] OR ""neurofibroma""[All Fields] OR ""neurofibromas""[All Fields] OR ""tumor s""[All Fields] OR ""tumoral""[All Fields] OR ""tumorous""[All Fields] OR ""tumour""[All Fields] OR ""neoplasms""[MeSH Terms] OR ""neoplasms""[All Fields] OR ""tumor""[All Fields] OR ""tumour s""[All Fields] OR ""tumoural""[All Fields] OR ""tumourous""[All Fields] OR ""tumours""[All Fields] OR ""tumors""[All Fields] OR ""neoplasm s""[All Fields] OR ""neoplasms""[MeSH Terms] OR ""neoplasms""[All Fields] OR ""neoplasm""[All Fields])"	810,548
("Surgical Procedures operative""[MeSH Terms] OR ""General Surgery""[MeSH Terms]) AND ("SARS-CoV-2""[MeSH Terms] OR ""COVID-19""[MeSH Terms]) AND ""Neoplasms""[MeSH Terms]"	40,309
""Neoplasms""[Mesh]" Most Recent ""Neoplasms""[MeSH Terms]	410,402
("SARS-CoV-2""[Mesh] OR "COVID-19""[Mesh]) ""SARS-CoV-2""[MeSH Terms] OR ""COVID-19""[MeSH Terms]	54,109
("Surgical Procedures Operative""[Mesh] OR ""General Surgery""[Mesh]" Most Recent ""surgical procedure""[MeSH Terms]" Most Recent ""COVID-19""[MeSH Terms]	235,803
""SARS-CoV-2""[Mesh]" Most Recent ""SARS-CoV-2""[MeSH]	53,637
""SARS-CoV-2""[Mesh]" Most Recent ""SARS-CoV-2""[MeSH]	42,950

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