# BMJ Open Pulmonary complications and mortality among COVID-19 patients undergoing a surgery: a multicentre cohort study

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#### **ABSTRACT**

Objectives Our primary objective was to assess the association between symptoms at the time of surgery and postoperative pulmonary complications and mortality in patients with COVID-19. Our secondary objective was to compare postoperative outcomes between patients who had recovered from COVID-19 and asymptomatic patients and explore the effect of the time elapsed between infection and surgery in the former. Our hypotheses were that symptomatic patients had a higher risk of pulmonary complications, whereas patients who had recovered from the infection would exhibit outcomes similar to those of asymptomatic patients.

**Background** Managing COVID-19-positive patients requiring surgery is complex due to perceived heightened perioperative risks. However, Canadian data in this context remains scarce.

**Design** To address this gap, we conducted a multicentre observational cohort study.

Setting Across seven hospitals in the province of Québec, the Canadian province was most affected during the initial waves of the pandemic.

Participants We included adult surgical patients with either active COVID-19 at the time of surgery or those who had recovered from the disease, from March 22, 2020 to April 30, 2021.

Outcomes We evaluated the association between symptoms or recovery time and postoperative pulmonary complications and hospital mortality using multivariable logistic regression and Cox models. The primary outcome was a composite of any postoperative pulmonary complication (atelectasis, pneumonia, acute respiratory distress syndrome and pneumothorax). Our secondary outcome was hospital mortality, assessed from the date of surgery up to hospital discharge.

Results We included 105 patients with an active infection (47 were symptomatic and 58 were asymptomatic) at the time of surgery and 206 who had recovered from COVID-19 prior to surgery in seven hospitals. Among patients with an active infection, those who were symptomatic had a higher risk of pulmonary complications (OR 3.19, 95% CI 1.12 to 9.68, p=0.03) and hospital mortality (HR 3.67, 95% CI 1.19 to 11.32, p=0.02). We did not observe any significant effect of the duration of recovery prior to surgery on patients who had recovered

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The study examines the effect of symptoms at the time of surgery on postoperative outcomes in the context of perioperatives a comprehensive dataset of patient characteristics, COVID-19 statuses and adjustments for confounders.

The variability in the severity of symptoms at the time of surgery may have affected our results, despite our adjustments for confounders.

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The variability in the severity of symptoms at the time of surgery may have affected our results, despite our adjustments and sensitivity analyses.

Focused primarily on patients from the province of Québec, Canada, the findings might not be applicable to other geographic regions or healthcare systems.

From their infection. Their postoperative outcomes were also similar to those observed in asymptomatic patients. Interpretation Symptomatic status should be considered in the decision to proceed with surgery in COVID-19-positive patients. Our results may help optimise surgical care in this patient population.

Study registration ClinicalTrials, gov Identifier:

NCT04458337 registration date: 7 July 2020.

BACKGROUND

The COVID-19 pandemic has ushered in unparalleled challenges for healthcare systems globally, not least in the realm of surgical care for patients afflicted with the virus. An urgent concern in this context was the heightened risk of perioperative complications and potential virus transmission to healthcare workers and other patients. 

During the earlier stages of the pandemic, the absence of comprehensive knowledge both in mainstream and scientific circles



further compounded these difficulties. Recently, there has been a gradual evolution in the scientific literature, focusing on the complex relationship between COVID-19 and postoperative complications.<sup>3</sup> Initial data from Europe and the Middle East hinted at alarming postoperative 30-day mortality rates of 19%-24% and more than half of the patients experiencing postoperative pulmonary complications. 4-7 Although COVID-19 has become less virulent with increased immunity in the population, the emergence of more virulent strains or other respiratory viruses highlights the need to learn from the early phase of the pandemic to better anticipate and manage surgical care in future public health crises.

A key aspect in this emerging field has been the distinction between symptomatic and asymptomatic carriers of the virus. Symptomatic patients, characterised by potential pulmonary involvement, significant systemic inflammation and higher viral loads, have been shown to incur a greater risk of perioperative complications. In contrast, the perceived lower risks associated with surgery in asymptomatic carriers contributed to the multifaceted challenges in perioperative management. 10 Emphasising the need for detailed investigation into these complexities, research efforts must focus on the comprehensive documentation of surgical needs and an array of procedures and their related outcomes among COVID-19-positive patients. Such studies have provided valuable insights into the effects of active infection on surgical outcomes and the varying risk factors among symptomatic and asymptomatic patients.<sup>2-4</sup> Despite burgeoning global research, Canadian data has remained conspicuously sparse.

To contend with this, we launched an observational cohort study in Ouébec, one of the most severely affected Canadian provinces during the pandemic.11 12 Our primary objective was to investigate the association between the presence of COVID-19-related symptoms among patients with COVID-19 infection at the time of surgery and postoperative pulmonary complications and mortality. Our second objective was to describe the postoperative outcomes of patients who underwent a surgical procedure after recovering from COVID-19 based on the number of days elapsed between the first positive test and the surgery and to compare them with those of asymptomatic COVID-19 patients. Our hypotheses were that (1) the presence of symptoms would be associated with an increased risk of pulmonary complications and (2) asymptomatic patients would have similar outcomes to patients who had recovered from the infection.<sup>13</sup>

# **METHODS Design and setting**

We conducted a multicentre observational cohort study at seven university hospitals situated in the province of Québec from March 22, 2020 through April 30, 2021. During the study period, the prevalent strains of the virus were the initial strain, along with the Alpha, Beta

and Gamma variants. 14 Prompted by the urgency engendered early in the pandemic, we had previously published preliminary data focusing on postoperative mortality from this study. 15 The current study, however, boasts a larger sample size and shifts its focus to postoperative pulmonary complications. Our findings are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for transparent reporting of observational studies. Approval from the Research Ethics Board (REB) was obtained at all participating sites. REBs waived the need for written informed consent.

Patient and public involvement

This study was not carried out with patients, carers or members of the public.

Study participants

We included all adult patients undergoing surgery who tested positive for COVID-19 by PCR test, conducted transparent reporting of observational studies. <sup>16</sup> Approval

tested positive for COVID-19 by PCR test, conducted either before surgery or within 72 hours postoperatively (systematic testing was implemented for all patients starting June 8, 2020). PCR tests were performed using oronasopharyngeal swabs or endotracheal aspirates. Patients were identified through the electronic medical data system or the operating room database at each site. We excluded patients younger than 18 years old and those who were already enrolled in the study.

### **Exposure variables**

To address our first objective, our exposure was the presence of symptoms at the time of the surgery based on patient-reported COVID-19 symptoms such as fever or respiratory failure, among others, as assessed by the attending clinicians (see online supplemental table S2). For our secondary objective, our exposures were the time elapsed (in days) from the initial positive COVID-19 test to surgery in patients who had recovered at the time of surgery and the infection status, categorised as either 'recovered' or 'active and asymptomatic'.

We thus categorised patients into three groups to answer our different objectives.

- 1. Symptomatic active infection: patients with a positive COVID-19 PCR test and exhibiting symptoms at the time of surgery.
- time of surgery.

  2. Asymptomatic active infection: patients with a positive test but without symptoms at the time of surgery.

  3. Recovered infection: patients who had a positive test grade infection and infection are patients.
- at least 10 calendar days before surgery and met one & of the following criteria: (1) two consecutive negative PCR tests before surgery, (2) one negative test and a clinically significant symptom-free period between the last positive test and the negative one and (3) no negative test, but considered recovered based on complete symptom resolution. This definition of recovery is aligned with Quebec's hospital protocol, which became less restrictive in November 2020 (online supplemental table S1).



#### **Outcomes**

Our primary outcome was a composite of any postoperative pulmonary complication. We used a definition of postoperative pulmonary complications, informed by an established one we believed better adapted to our population.<sup>17</sup> Our primary outcome included atelectasis, pneumonia, acute respiratory distress syndrome (ARDS) and pneumothorax. We substituted, from the original definition, the incidence of pulmonary aspiration for pneumothorax since we believed there might not be any causal relationship between active COVID and pulmonary aspiration, while the reported incidence of pneumothorax was high in this population.<sup>18</sup> Our secondary outcome was hospital mortality, assessed from the date of surgery up to hospital discharge. Our exploratory outcomes were the incidence of postoperative non-pulmonary infectious complications, acute kidney injury (AKI), thromboembolic events such as myocardial infarction and stroke, surgical reinterventions, need for new postoperative intensive care unit (ICU) admission, length of hospital stay, any requirement for postoperative mechanical ventilation and the number of organ dysfunction-free days within 30 days. Non-pulmonary infectious complications were defined as infections requiring antibiotics for more than 72 hours. AKI was classified following the Kidney Disease: Improving Global Outcomes-AKI criteria. 19 Myocardial infarction and stroke were based on physician reporting. Mechanical ventilation included both noninvasive and invasive modalities. For all 30-day outcomes, we considered each day on which the outcome occurred. Additionally, our 30-day organ dysfunction-free days adhered to established definitions.<sup>20</sup>

### **Covariables**

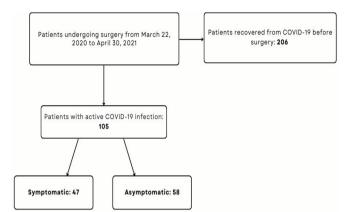
We collected characteristics related to the COVID-19 presentation, including factors such as demographic variables, pre-existing comorbidities, surgical and anaesthetic characteristics, the level of urgency for the surgery, baseline laboratory measurements, the preoperative Sequential Organ Failure Assessment, the requirement for oxygen supplementation or invasive mechanical ventilation prior to surgery and the administered treatments (eg, antiviral medications, steroids and antibiotics). Moreover, multiple intraoperative variables were documented. The characterisation of surgical disease was based on the surgeon's reporting and classified into distinct categories. Surgeries categorised as neurosurgical, cardiac, thoracic, major vascular or non-vascular abdominal were defined as major surgeries. Minimally invasive surgery was characterised as those that avoided anatomical cavity opening (laparoscopy, thoracoscopy and endoluminal procedures). The urgency of surgery was classified into two categories: emergent or urgent surgeries that necessitated completion within 24 hours and non-urgent surgeries that could be deferred beyond 24 hours.

### **Data sources and management**

Research staff collected data prospectively up to hospital discharge or retrospectively as reported in the electronic medical records. Data were prospectively collected to identify eligible patients and surgeries throughout the recruitment period (April 4, 2020-April 30, 2021). Some eligible patients were identified retrospectively in April 2020, including patients who had surgery prior to the start of the study (April 4, 2020), as authorised by our REB. Perioperative data, complications and outcomes at discharge were extracted from medical records during the hospitalisation or after discharge when electronic medical records were available. Each site entered the data into a centralised electronic database (Research Electronic Data Capture electronic data capture tools hosted at the Centre Hospitalier de l'Université de Montréal), adhering to a manual of standardised operating procedures following necessary training.<sup>21</sup> Data cleaning processes were implemented prior to analyses.

## Statistical analyses

We sampled all eligible patients over the recruitment period. We used descriptive statistics (means (SD), medians (IQR) or proportions, as appropriate) summarise baseline characteristics and the outcomes of COVID-19 patients, stratified based on the presence of symptoms, and for those who had recovered from COVID-19. For the primary objective, we fitted a multivariable mixed-effect logistic regression model to estimate the association between the presence of any symptom before the surgery and the incidence of postoperative pulmonary complications in COVID-19 patients who underwent surgery, adjusted for the following potential **a** confounders: preoperative hospitalisation, preoperative **3** requirement for oxygen support, urgency of surgery and categorisation of surgery as either 'major' or 'minor'. We selected these variables as potential confounders based on their potential association with both our exposures (symptoms, recovering status and recovering time) and postoperative pulmonary complications, while not being in the causal pathway between the two. In cases of multiple complications, only the first occurrence of any postoperative pulmonary complication was counted as an event for each patient. We also fitted a multivariable Cox proportional hazard model to estimate the association between the presence of symptoms and time to in-hospital mortality among COVID-19 patients adjusted for the same potential confounders but stratified for the preoperative requirement for oxygen. We used random effects & and shared frailty factors to account for the clustered nature of the data within the same site. However, since the logistic mixed-effect model showed singularity with a null variance of the random effect, we reported estimates from a model without random effects. We conducted post hoc sensitivity analyses for each outcome by estimating the same models, first by excluding patients who had a tracheostomy as their index surgery or had preoperative respiratory failure, and then by excluding only those who



**Figure 1** COVID-19 status of surgical patients (March 22, 2020–April 30, 2021). This flowchart illustrates the COVID-19 status of patients who underwent surgery during the specified period. Out of all patients, 206 had recovered from COVID-19 prior to surgery, while 105 had an active COVID-19 infection at the time of surgery. Among the active cases, 47 patients were symptomatic, and 58 were asymptomatic.

had a tracheostomy as their surgery. Finally, we reported an unadjusted Kaplan-Meier survival curve with 95% confidence bands.

For our secondary objective, we estimated the association between the recovery duration in days (as an integer) from COVID-19 to the surgery and the incidence of postoperative pulmonary complications and hospital mortality. We also compared both outcomes between patients who recovered from COVID-19 to those with an active asymptomatic infection. We used mixed-effect logistic regression models and Cox proportional hazard models with shared frailty factors adjusted for the same confounders. The statistical significance level was set at 0.05. For all analyses, we reported OR and HR with 95% CI. We did not have any missing data in our regression analyses. All analyses were performed using R statistical software (R Foundation for Statistical Computing, Vienna, Austria, V.4.2.3).

### **RESULTS**

Between 22 March 2020 and 30 April 2021, we included 105 COVID-19 patients who underwent a surgical procedure and 206 patients who had recovered from COVID-19 at the time of surgery for our secondary objective (figure 1).

# Symptomatic versus asymptomatic COVID-19 patients

Among patients with confirmed COVID-19 at the time of surgery, 47 (45%) exhibited symptoms and 58 (55%) were asymptomatic carriers. The baseline characteristics of these patients are presented in table 1, online supplemental tables S2, S3. Online supplemental tables S2 specifically highlights the breakdown of symptoms among the symptomatic patients prior to surgery, as assessed by the attending clinicians. Both groups displayed similar baseline characteristics in terms of sex distribution, but

symptomatic patients were older, had a higher body mass index (BMI) and a greater prevalence of diabetes (table 1). The presence of pulmonary infiltrates, as determined by the radiologist's chest X-ray report, was more common among symptomatic patients, and these patients were more likely to receive steroids before surgery and require preoperative respiratory support (table 1). Both groups showed a balanced distribution in terms of major and minor surgeries, urgency and duration of surgery (table 1). Out of 47 patients who had symptoms at the time of surgery, 13 (28%) had a tracheostomy as their surgery, and 25 (53%) had either a tracheostomy as their surgery or preoperative respiratory failure (not in tables).

The postoperative outcomes of COVID-19 patients are summarised in table 2. 30 symptomatic patients (64%) experienced at least one postoperative complication compared with 19 asymptomatic patients (33%) (table 2). Among them, 16 symptomatic patients (34%) and 8 asymptomatic patients (14%) experienced at least one postoperative pulmonary complication (table 2). Symptomatic patients had a higher incidence of pneumonia, ARDS and pneumothorax and a higher requirement for postoperative ICU admission and postoperative mechanical ventilation (table 2). Mortality was higher among symptomatic patients, with 15 deaths (32%) during hospitalisation in the symptomatic group compared with 6 deaths (10%) in the asymptomatic group (table 2).

Patients with COVID-19 symptoms were found to have a higher risk of developing pulmonary complications compared with asymptomatic patients (OR 3.19, 95% CI 1.12 to 9.68, p=0.03) (table 3). These patients also faced significantly a higher hazard of in-hospital mortality significantly a higher hazard of in-hospital mortality compared with asymptomatic patients (HR 3.67, 95% as CI 1.19 to 11.32, p=0.02) (table 4). From our sensitivity  $\blacksquare$ analyses, after excluding 13 symptomatic patients who underwent a tracheostomy, we observed a weaker and non-significant effect between the presence of symptoms and the incidence of postoperative pulmonary complications (OR 2.89, 95% CI 0.94 to 9.31) (online supplemental table S4& online supplemental figure S1). A similar pattern was noted when excluding 25 symptomatic patients who either had a tracheostomy or preoperative respiratory failure (OR 2.45, 95% CI 0.67 to 8.89, see online supplemental table S4). The presence of symptoms on hospital mortality also showed a weaker, nonsignificant association in these analyses (HR 2.60, 95% CI 0.75 to 8.99 and HR 1.35, 95% CI 0.32 to 5.76, respectively, online supplemental table S6 and S7).

# Patients who recovered from COVID-19

Online supplemental table S8–S13 provide the baseline characteristics and postoperative outcomes of patients (n=206) who had recovered from COVID-19 prior to surgery, categorised on the number of weeks elapsed since their initial positive COVID-19 test as well as according to the period of recruitment. The time elapsed since the initial positive COVID-19 test in these patients was not associated with a higher risk of pulmonary complications

	Symptomatic status at ti	me of surgery	
Variable	Asymptomatic (n=58)	Symptomatic (n=47)	
Baseline characteristics			
Age (years)	57.5 (36.5–74.8)	66.0 (52.5–72.5)	
Sex (female)	30 (52%)	25 (53%)	
BMI* (kg/m²)	27.4±7.4	30.8±6.0	
Diabetes	14 (24%)	15 (32%)	
Hypertension	11 (19%)	6 (13%)	
White blood cell count† (×10 <sup>9</sup> /L)	8.8 (6.9–13.0)	9.5 (6.6–12.5)	
Hemoglobin† (g/L)	117.0 (104.0–133.0)	101.0 (81.0–122.5)	
Creatinine‡ (µmol/L)	77.0 (56.3–96.0)	83.0 (56.0–131.5)	
COVID characteristics			
Days from first positive COVID test to surgery	4.0 (1.0–9.8)	10.0 (3.0–22.5)	
Pulmonary infiltrates	12 (21%)	28 (60%)	
Steroid	14 (24%)	20 (43%)	
Antibiotic	16 (28%)	33 (70%)	
Preoperative respiratory support			
No oxygen	45 (78%)	17 (36%)	
Oxygen only	4 (7%)	7 (15%)	
Non-invasive mechanical ventilation	0 (0%)	1 (2%)	
Invasive ventilation	9 (16%)	22 (47%)	
Surgical characteristics			
Preoperative location			
Home	15 (26%)	7 (15%)	
Emergency department	14 (24%)	7 (15%)	
Ward	23 (40%)	10 (21%)	
Intensive care unit	6 (10%)	23 (49%)	
Urgent surgery (≤24 hours)	24 (41%)	22 (47%)	
Major surgery	21 (36%)	17 (36%)	
Duration of surgery (minutes)	60.0 [40.3–97.3)	47.0 [27.5–98.5)	

Categorical variables are presented as frequency (proportion).

Continuous variables are presented as mean±SD or as median (first quartile-third quartile).

(OR 1.00, 95% CI 0.99 to 1.00, p=0.47, see table 5) or mortality (HR 1.00, 95% CI 0.99 to 1.01, p=0.70) (online supplemental table S14). Patients who had recovered from COVID-19 did not have a higher risk of postoperative pulmonary complications or hospital mortality when compared with asymptomatic carriers (online supplemental table S15,S16).

### DISCUSSION

In this study, we included 105 surgical patients with active COVID-19 at the time of surgery and 206 who had recovered from the virus prior to surgery. We observed an important difference between symptomatic and asymptomatic COVID-19 patients undergoing surgery regarding the risk of adverse postoperative outcomes. The presence of an active symptomatic disease was associated with an increased risk of developing postoperative pulmonary complications and increased mortality. Within this cohort, symptomatic patients who underwent a tracheostomy and those with preoperative respiratory failure encompassed half of the sample. When excluding these cases, point estimates suggested that the association between symptoms and postoperative pulmonary

<sup>\*</sup>Missing value for 28 and 17 patients, respectively.

<sup>†</sup>One missing value in the asymptomatic group.

<sup>‡</sup>Three missing values in the asymptomatic group.

Table 2 Postoperative outcomes of COVID-19 confirmed patients

	Symptomatic status at time of surgery	
Variable	Asymptomatic (n=58)	Symptomatic (n=47)
Postoperative complications		
Any complication	19 (33%)	30 (64%)
Any pulmonary complication	8 (14%)	16 (34%)
Atelectasis	1 (2%)	4 (9%)
Pneumonia	6 (10%)	11 (23%)
Acute respiratory distress syndrome	2 (3%)	4 (9%)
Pneumothorax	1 (2%)	3 (6%)
Acute kidney injury	6 (10%)	9 (19%)
New postoperative renal replacement therapy	0 (0%)	1 (2%)
Myocardial infarction	0 (0%)	2 (4%)
Stroke	0 (0%)	1 (2%)
Non-pulmonary infection	6 (10%)	6 (13%)
Surgical reintervention	4 (7%)	10 (21%)
Resource utilisation and mortality		
Need for a new postoperative ICU admission	10 (17%)	20 (43%)
Hospital length of stay (days)	8.0 (3.0-31)	13.0 (7.5–31.5)
One or more days on postoperative mechanical ventilation	17 (29%)	26 (55%)
30-day organ dysfunction free days	27.7±6.8	19.9±11.9
Hospital mortality	6 (10%)	15 (32%)
Status at hospital discharge among living patients		
Discharged at home	40 (69%)	25 (53%)
Transferred to another acute care setting	7 (12%)	3 (6%)
Transferred to another long-term care setting	5 (9%)	4 (9%)

Categorical variables are presented as frequency (proportion).

Continuous variables are presented as mean±SD or as median (first quartile-third quartile).

Any pulmonary complication refers the first occurrence of a pulmonary complication in each patient. Patients with multiple complications were only counted once.

complications weakened and became non-significant, but its direction and strength remained similar. Asymptomatic carriers at the time of surgery exhibited a similar risk of adverse postoperative outcomes compared with

**Table 3** Association between the presence of symptoms and the incidence of postoperative pulmonary complications in patients with COVID-19 at the time of surgery

Variable	OR (95% CI)	P value
Presence of symptoms	3.19 (1.12 to 9.68)	0.03
Preoperative hospitalisation	0.91 (0.26 to 3.72)	0.89
Preoperative oxygen requirement	1.30 (0.45 to 3.72)	0.62
Urgent surgery	0.45 (0.15 to 1.21)	0.12
Major surgery	2.45 (0.91 to 6.77)	0.08
Reported estimates come from a multivariable model that		

Reported estimates come from a multivariable model that included all reported variables.

No random effect.

the 206 patients who had recovered from the infection prior to surgery. The length of the recovery period prior to surgery did not appear to influence the incidence of postoperative pulmonary complications and mortality in those who had recovered from the infection.

**Table 4** Association between the presence of symptoms and hospital mortality in patients with COVID-19 at the time of surgery

Variable	HR (95% CI)	P value
Presence of symptoms	3.67 (1.19 to 11.32)	0.02
Preoperative hospitalisation	1.46 (0.33 to 6.48)	0.62
Urgent surgery	0.92 (0.34 to 2.52)	0.88
Major surgery	3.42 (1.25 to 9.34)	0.02

Reported estimates come from a multivariable model that included all reported variables.

This model is stratified for preoperative oxygen requirement and has centreas a frailty effect. Number of events=21 (N=105).

**Table 5** Association between the elapsed time between first positive test and surgery and postoperative pulmonary complications in patients who had recovered from COVID-19 at time of surgery

Variable	Odds ratio (95% CI)	P value
Time from first positive COVID test	1.00 (0.99 to 1.00)	0.47
Preoperative hospitalisation	3.87 (1.08 to 13.82)	0.04
Preoperative oxygen need	2.69 (0.84 to 8.61)	0.09
Urgent surgery	0.42 (0.14 to1.24)	0.12
Major surgery	2.51 (0.95 to 6.65)	0.06

Reported estimates come from a multivariable model that included all reported variables.

This logistic regression model has centre as a random effect. Intracluster correlation=0.076.

The current study enhances our understanding of surgical care in the COVID-19 era, with a particular focus on assessing the risk of postoperative pulmonary complications and in-hospital mortality associated with COVID-19 symptoms prior to surgery. It builds upon prior research conducted by our group, which was spurred by the urgency of the pandemic and, as a result, reported preliminary data that focused primarily on postoperative mortality. 15 Other studies, including the one published by the COVIDSurg collaboration, have suggested that preoperative COVID-19 is associated with an increased risk of postoperative pulmonary or cardiovascular complications and mortality. 22-25 Interestingly, a more recent study has not observed the same association.<sup>26</sup> While the primary focus of these studies was not specifically on this aspect, it appears that the presence of symptoms at the time of surgery may account for the observed effect of preoperative COVID-19 on postoperative outcomes. Our findings are consistent with these results. Symptomatic patients are possibly more likely to exhibit severe pulmonary involvement, systemic inflammation and higher viral loads. These factors collectively contribute to an escalated risk of perioperative complications.<sup>22</sup> <sup>23</sup> Moreover, the markedly higher hazard of in-hospital mortality among symptomatic patients emphasises the significant impact that active disease can have on postoperative patient survival. 5 15 22 27-30 Our results underscore the necessity of considering the symptomatic status of patients when assessing their suitability for surgery and evaluating the risk of postoperative complications.

Our study's analyses of patients who had fully recovered from COVID-19 prior to surgery offer additional insights into the dynamic relationship between infection and surgical outcomes. Contrary to previous research on COVID-19-positive patients, we did not observe any effect of the time elapsed from COVID-19 diagnosis to surgery on postoperative outcomes in patients who had recovered from COVID-19.<sup>24 31 32</sup> Notably, in a recent study, an increased mortality risk was observed in patients who had recovered from COVID-19 undergoing surgery within

2 weeks of a positive test compared with longer recovery time. 33 Beyond this period, the mortality risk aligns closely between patients with and without prior COVID-19. Our research diverges as it does not explore the timing between COVID-19 diagnosis and surgery in a categorised fashion, nor does it compare our cohort to non-COVID patients. Furthermore, these studies often overlook the distinction between patients who had fully recovered at the time of surgery and those with persistent symptoms. Our results support the fact that patients who have fully recovered and those with an active asymptomatic disease tend to have similar postoperative outcomes. 'Post-COVID syndrome' is an entity that describes patients who, despite no longer having an active viral infection, continue to experience residual effects of the illness such as deconditioning, inflammation, fatigue, headaches, memory disturbances, difficulty with concentration and depression. <sup>34</sup> Given the potential complications associated with post-COVID syndrome, the importance of thoroughly assessing a patient's suitability for surgery, especially in the context of ongoing recovery from COVID, cannot be overstated. Recovery timelines remain uncertain, and parallels from current literature emphasise the need for complete clinical recovery from major medical events before proceeding with non-emergent surgery.

The clinical context has changed significantly since the early stages of the pandemic, particularly with the widespread adoption of vaccination, the emergence of new variants, and the development of population-level immunity from prior infections. As such, the specific findings from the first wave may not be fully generalisable to every contemporary patient undergoing surgery with active COVID-19. Nonetheless, unvaccinated patients infected **5** with current SARS-CoV-2 variants may still exhibit similar **∃** clinical behaviours. Mostly, the value of this study lies in the lessons learnt from the early pandemic, which can inform preparedness and response strategies for future pandemics of respiratory viruses. This includes a better understanding of how symptomatic status and disease severity influence perioperative risks and how surgical protocols should be adapted in the face of emerging infectious threats. Our findings should therefore be viewed in the broader context of improving healthcare system resilience and patient management strategies during public health crises. Finally, it may also inform clinicians on how to manage patients presenting for surgery with viral upper respiratory infections.

# **Strengths and limitations**

While our study sheds valuable light on the association between COVID-19 status and postoperative outcomes, there are several limitations that should be acknowledged. First and foremost, patient data were sourced from electronic medical records and operating room databases, which may lead to incomplete or inconsistent information. The reliance on these sources could result in missing or inaccurately recorded data, potentially impacting the validity of our findings. Furthermore, the

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relatively modest sample size of our cohort, particularly in specific subgroups, such as patients who were symptomatic prior to surgery, limited the power of our analyses. However, this shows that few patients had surgery while being actively symptomatic in our centres. Mostly, 24% of the sample of COVID-19 patients were symptomatic patients who either had a tracheostomy during their surgery or respiratory failure prior to surgery. In this subgroup of patients, it is more likely that a higher incidence of complications may have been secondary to the severity of the primary respiratory insult and its progression rather than to the surgery itself. Although the direction and strength of the estimates were similar in our sensitivity analyses excluding these patients, the power of these analyses was limited by the smaller sample size after exclusions. 35 Our results became non-significant in such sensitivity analyses, potentially suggesting that the effect of COVID-19 symptoms on postoperative outcomes may warrant further exploration in less severe cases. Although this composition of the symptomatic study population may limit the inference of our results in relation to a more general surgical population without preoperative respiratory failure, such a broad approach to inclusion increases the generalisability of the results to every level of preoperative COVID-19 severity. Also, the cohort's composition primarily consists of patients from the province of Québec, which could potentially limit the external validity of our results to other geographic regions or healthcare systems, despite acknowledging that this province was among the ones most impacted by the pandemic. Also, our study was conducted during a period of the pandemic featuring different variants than the more contemporary ones. Moreover, the assessment of symptoms and COVID-19 recovery was reliant on the accuracy of medical documentation and clinical judgement. Variability in symptom reporting, diagnostic methods, and the interpretation of recovery criteria could introduce bias and imprecision in patient categorisation. The comprehensive definition of recovery we employed aims to account for the diverse presentations of COVID-19 patients, but it is inherently subjective and could lead to misclassification. Also, this definition changed over the study period (after November 2020, approximately halfway through the study period). However, the clinical characteristics of the included patients were similar before and after the criteria change. Finally, the potential influence of vaccination status on postoperative outcomes would have merited consideration, though it was not specifically analysed in our study since most of it was conducted prior to the availability of vaccines.<sup>23</sup>

Our study possesses several strengths that contribute to a comprehensive understanding of the relationship between COVID-19 status, surgical outcomes and recovery and inform clinical practice and decisionmaking. One of the primary strengths of our study is its multicentre design. Conducted across seven academic hospitals within the province of Québec, the study benefits from a diverse patient population

and surgical practices, enhancing the generalisability of our results. This diversity in healthcare settings reduces the potential for single-centre biases and increases the likelihood of capturing a broader spectrum of COVID-19 patients undergoing surgery. We documented various aspects of patient characteristics, COVID-19 status, surgical procedures and postoperative outcomes. This detailed information allows for more robust analyses, including adjustments for potential confounding variables, contributing to the reliability of our results. We also conducted sensitivity analyses, which provided a more nuanced understanding of how preoperative respiratory failure can potentially affect postoperative results. The study's inclusion of both symptomatic and asymptomatic COVID-19 patients, as well as those who had recovered from the infection, further adds to its strength. By comparing these distinct patient groups, we were able to identify specific trends and associations that might otherwise have been overlooked. In addition, our study benefitted from a relatively long observation period, spanning from March 2020 to April 2021, thus capturing various phases of the pandemic. Lastly, our study fills a crucial gap in the literature by providing 8 data on Canadian surgical patients either infected

with COVID-19 or having recently recovered.

The COVID-19 pandemic has profoundly transformed surgical care, introducing complex challenges in managing patients with COVID-19 or those who recovered from the infection. As one of the few studies conducted within a Canadian perioperative context, our findings contribute to a comprehensive understanding of the complex interplay between COVID-19 status and postoperative outcomes in this patient population. These insights hold vital implications for patient management and care decisions, as they **\geq** provide crucial guidance to healthcare professionals in optimising postoperative care and mitigating risks for patients with COVID-19 undergoing surgery. Our results highlight important trends, suggesting the need for further investigation with larger sample sizes to draw more conclusive insights regarding the impact of these factors on in-hospital mortality, especially in patients without preoperative respiratory failure.

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Competing interests None declared.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants. This study was centrally approved by the 'Research Ethics Board (REB) of the Centre Hospitalier de l'Université de Montréal' (#19.386) that waived the need for informed consent. The study was subsequently approved by all local REB from each institution ('REB of the Centre universitaire de santé McGill', 'REB of the CHU-de-Québec-Université Laval', 'REB of the Centre intégré universitaire de santé et de services sociaux (CIUSSS) de l'Est-de-l'Île-de-Montréal', 'REB of the CIUSSS de l'Estrie-CHUS', 'REB of the CIUSSS du Nord-de-l'Île-de-Montréal' and the 'REB of the Institut universitaire de cardiologie et de pneumologie de Québec'). All methods were carried out in accordance with relevant guidelines and regulations, exempted this study.

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Data availability statement Data are available upon reasonable request. Due to national regulations in the province of Quebec (Canada), health medical data cannot be made available publicly. However, access to the research dataset is possible for research purposes after appropriate privacy agreements between research parties have been completed. Data access requests may be sent to the corresponding author (francois.martin.carrier@umontreal.ca) or directly to the CHUM REB (ethique. recherche.chum@ssss.gouv.qc.ca). The R code will be available upon request to the corresponding author.

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