A Risk Model of Admitting Patients With Silent SARS-CoV-2 Infection to Surgery and Development of Severe Postoperative Outcomes and Death

Projections Over 24 Months for 5 Geographical Regions

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Objective: To model the risk of admitting silent COVID-19-infected patients to surgery with subsequent risk of severe pulmonary complications and mortality.

Summary Background Data: With millions of operations cancelled during the COVID-19 pandemic, pressure is mounting to reopen and increase surgical activity. The risk of admitting patients who have silent SARS-CoV-2 infection to surgery is not well investigated, but surgery on patients with COVID-19 is associated with poor outcomes. We aimed to model the risk of operating on nonsymptomatic infected individuals and associated risk of perioperative adverse outcomes and death.

Methods: We developed 2 sets of models to evaluate the risk of admitting silent COVID-19-infected patients to surgery. A static model let the underlying infection rate (R rate) and the gross population-rate of surgery vary. In a stochastic model, the dynamics of the COVID-19 prevalence and a fixed population-rate of surgery was considered. We generated uncertainty intervals (UIs) for our estimates by running low and high scenarios using the lower and upper 90% uncertainty limits. The modelling was applied for high-income regions (eg, United Kingdom [UK], USA [US] and European Union without UK [EU27]), and for the World (WORLD) based on the WHO standard population.

Results: Both models provided concerning rates of perioperative risk over a 24-months period. For the US, the modelled rates were 92,000 (UI 68,000–124,000) pulmonary complications and almost 30,000 deaths (UI 22,000–40,000), respectively; for Europe, some 131,000 patients (UI 97,000–178,000) with pulmonary complications and close to 47,000 deaths (UI 34,000–61,000) were modelled. For the UK, the model suggested a median daily number of operations on silently infected ranging between 25 and 90, accumulating about 18,700 (UI 13,700–25,300) perioperative pulmonary complications and 6400 (UI 4600–8600) deaths. In high-income regions combined, we estimated around 259,000 (UI 191,000–351,000) pulmonary complications and 89,000 deaths (UI 65,000–120,000). For the WORLD, even low surgery rates estimated a global number of 1.2 million pulmonary complications and 350,000 deaths.

Conclusions: The model highlights a considerable risk of admitting patients with silent COVID-19 to surgery with an associated risk for adverse perioperative outcomes and deaths. Strategies to avoid excessive complications and deaths after surgery during the pandemic are needed.

Keywords: COVID-19, mortality, perioperative death, presymptomatic, pulmonary complications, risk, SARS-CoV-2, silent disease, surgery

In the ongoing pandemic, an unprecedented number of nonessential elective surgery have been postponed or cancelled resulting in a huge back-log of operations, estimated at 28 million cancelled operations globally over a peak period.1 Real pressures now exist to reopen surgical elective activity, but with concerns of risk of second waves of pandemic outbursts and potentially introducing spread by reopening activities.

As the worst peak of hospital admissions fade and the effects of societal lock-down set in, there is a mounting pressure to restart surgical activity, catch up with the mounting back-log of surgical operations and restore economy. Of note, the primary focus of the pandemic has been on critical and emergency response with need for prioritizing essential surgical services,2 but with very little focus on the postpandemic phase.3 As society reopens, the control of “silent” COVID-19, for example, those without symptoms (asymptomatic or presymptomatic) will be a challenge.4–6 Current tests have a low specificity for individuals without symptoms which makes screening unreliable, as the false negative rate is too high.7,8

From recent models, the SARS-CoV-2 virus is likely to circulate in the population for a considerable time.9 Furthermore, even the highest endemic regions are nowhere close to herd immunity.10 Available serological tests may not yet be universally available or reliable.11 The rate and re-emergence of peaks and further pandemic outbreaks depend on several factors. However, expected variation from modelled studies suggest a duration of at least another 2 years with ongoing viral concerns.12

Better understanding of the incidence and implications of perioperative COVID-19 infections is needed to plan the delivery of surgical services. Providing time-sensitive surgical care and catching up on the back-log of operations ought to be balanced against system and patient-level risks of perioperative COVID-19. Admitting patients with no symptoms who have silent COVID-19 to surgery is a real concern as pressure increases to restore surgical activities.

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recent study found deaths occurred in 1 in 4 of all who underwent surgery, and pulmonary complications to occur in half of all who had or contracted SARS-CoV-2 in the perioperative period. However, this study did not include the denominator of patients undergoing surgery during the same time period; the risk of perioperative COVID-19, either community or nosocomial acquired remains unknown.

The aim of this study was to project a temporal risk model of operating SARS-CoV-2 infected patients with no symptoms of COVID-19 and the estimated risk of perioperative adverse outcomes.

METHODS

The assumptions used are derived from available studies and models reported to the COVID-19 pandemic. The prevalence of silent COVID-19 disease is reported as those with no symptoms, either as asymptomatic (ie, those who never develop symptoms) and those that are presymptomatic (ie, have the disease but in incubation phase or before developing symptoms). For ease of use due to overlap in definitions, we use silent, asymptomatic and presymptomatic COVID-19 to mean all individuals with no symptoms at time of presentation (eg, at admission to surgery). The “silent” or “presymptomatic” rate (or, asymptomatic or incubation phase) was assumed to be between 45% and 55% of all with COVID-19 disease.

This study includes 2 sets of models to evaluate the risk of surgery on silent COVID-19 infected patients, with a large degree of overlapping assumptions and use of available data for modelling. The former set of models involve static situations where we let the underlying infection rate and the gross amount of surgeries vary. The second set of models have fixed gross amount of operations, but we assume a stochastic model similar to that of Kissler et al for the dynamics of the infection situation.

Static Model

The static model attempts to count the yearly number of operations performed on presymptomatic COVID-19-infected, divided into groups by age and sex, for a given population. Subsequently this information may be used in conjunction with data from the COVIDSurg Collaborative study to infer the expected numbers of 30-day mortality and pulmonary complications.

The static models, for all outcomes of interest, take the form of

$$S \cdot r \cdot \beta$$

where $S$ is the overall number of surgeries per 100,000 person-years, $r$ is the instantaneous proportion of infected in the population and $\beta$ represents the numbers “at risk” for the outcome of interest (measured in the unit 100,000 person-years). The coefficients $\beta$ for different outcomes of interest are calculated, for a given population, based on:

- The relative rates of surgery for the different group, adapted from Omling et al, which are scaled to absolute rates for the population when multiplied by $S$ in Eq. (1) (Supplement, Appendix A, http://links.lww.com/SLA/C695).
- The demographics of the population in question, using 5-year age groups (Supplement, Appendix B, http://links.lww.com/SLA/C695).
- An infection loading function which, when multiplied by $r$ in (1), results in higher than $r$ proportions of infected in the middle age groups, while ensuring that the overall proportion of infected is still $r$.
- The proportion of asymptomatic infected, set equal to 0.5 here, is based on Gudbjartsson et al. Note that the asymptomatic rate scales each $\beta$ linearly.

Further, the $\beta$s for pulmonary complications and 30-day mortality are obtained by appropriately scaling the age-group-wise expected numbers of operations on presymptomatic infected, using the probabilities from COVIDSurg Collaborative study data.

The model was applied for Australia (AUS), Canada (CAN), United Kingdom (UK), European Union without UK (EU27), USA (US), and the World (WORLD), based on the WHO standard population scaled to 7594 million persons. Details of the calculations, including the demographic data and per-group surgery rates are provided in Supplementary Appendix A-C, http://links.lww.com/SLA/C695. The values of $\beta$ for these populations and the different quantities of interest may be found in Table S3, http://links.lww.com/SLA/C695.

Stochastic Dynamic Model

Building on the static model, also a stochastic dynamic model is considered with the aim of accounting for uncertainty related both to daily variation in surgery demand, and more importantly, uncertainty in COVID-19 infection scenarios (Supplementary, Appendix D and E, http://links.lww.com/SLA/C695). The model is considered only for a selection of high-income countries/regions (AUS, CAN, EU27, UK, and US) as it relies on common infection dynamics for the whole population.

Conditionally on some infection trajectory $r(t)$ (in proportion of population) at day $t$, the surgery demand model is constructed so that the day $t$ daily outcomes of interest are in expectation

$$S \cdot r(t) \cdot \beta(t)$$

Under this model the daily number of infected scheduled for surgery per group, the daily number of scheduled silent SARS-CoV-2 infected per group, the daily number of 30-day mortalities and the daily pulmonary complications are given nested stochastic models consistent with (2) in expectation. The exact specification of this stochastic model is given in Supplementary Appendix E, http://links.lww.com/SLA/C695.

Further, the uncertainty in COVID-19 infection scenarios $r(t)$ is generated using a stochastic version of the SEIR-type (Susceptible, Exposed, Infectious, and Recovered individuals) dynamic model, as considered in Kissler et al (see Figs. 6 and S9 in Kissler et al). Specifically, we let several of the parameters of the infection scenario model — for example, the effect of social distancing measures, and on-off triggers for social distancing measures — vary stochastically. The ranges of variation are consistent with Flaxman et al with respect to the effect of social distancing, and otherwise with the parameter values used by Kissler. Further, the silent/presymptomatic rate (or, asymptomatic or incubation phase) varies in the range of 45% to 55%, as reported previously. More details regarding the stochastic infection scenario model are given in Supplementary Materials, Appendix D, http://links.lww.com/SLA/C695. Further, details on integration with the surgery demand model and Monte-Carlo simulations are given in Appendix E.

RESULTS

Static Model

Graphical representations of the output of the static model for the different populations is shown in Figure 1AB. For all populations scenarios up to 20,000 operations per 100,000 person years and infection rates up to 0.015 are considered, except for WORLD where rates are <5000 operations per 100,000 person years (see Supplementary info, http://links.lww.com/SLA/C695).
FIGURE 1. AB: Graphical representations (Contour plots) of the static model of risk. (A) for AUS, CAN, EU27 and (B) for UK, US and WORLD. Left column: the expected yearly number of operations on silent COVID-19 infected persons ≥70 years. Middle column: expected number of pulmonary complications due to operations performed on silent COVID-19 infected persons. Right column: expected yearly number of 30-day mortalities due to operations performed on silent COVID-19 infected persons. The plots give expectations for different combinations of overall surgery rates $S$ (in number of operations per 100,000 person-years) and the proportion on the population with Covid-19 infection at any given time $r$. AUS: Australia (total population in 2016: 23.4 million). CAN: Canada (total population in 2016: 35.2 million). EU: EU27 (total population 445 million). UK: United Kingdom (total population in 2011: 63.2 million), US: United States (total population in 2010: 309 million), WORLD: World standard population with total population 7594 million. Notice the lower values of $S$ considered in the World scenario, as the total number of operations per 100,000 person years has been estimated to be around 3400.
Stochastic Dynamic Model

Selected output from the stochastic dynamic model is applied to the US in Figure 2. The figure gives indications on magnitudes and ranges of variation over time.

The estimated number of adverse events is presented in Table 1, with uncertainty interval (UI) for “best case scenario” (5% quantile) and “worst case scenario” (95% quantile) for each region and for the 5 high-income regions combined. Figure 2A shows daily quantiles of the infection trajectories $r(t)$ from the stochastic SEIR model, in median consistent with on the order of 0.25% to 0.5% of the population is potentially silent carriers at any given time. Panel 2B shows the daily cases of operations on silently infected COVID-19, which in mean are scaled with infection trajectories $r(t)$ and thus resembles the pattern of Figure 2A.

At the population size of the US, and the assumed $S$ the model implies median daily numbers of operations on silent SARS-CoV-2 carriers ranging somewhere between 150 and up to 500 cases (Fig. 2B). Figure 2C and D give the corresponding daily, and cumulative cases of pulmonary complications due to operations on silent cases, respectively. The model-implied median of daily new cases ranges between approximately 12 and 45 per day. Figure 2E and F are similar to C and D but for 30-day mortality.
FIGURE 2. A–F: The stochastic dynamic risk model applied to the US population. Selected output of the stochastic dynamic model applied to the US population assuming $S = 15,000$ operations per 100,000 person years. Throughout black lines are the daily median and the red lines are the corresponding 5% and 95% quantiles. A: Proportion of population being infected and potentially silent carriers of COVID-19. B: Daily number of operations on silent COVID-19 infected patients. C: Daily 30-day mortalities following surgery on presymptomatic infected. D: Cumulative 30-day mortalities following surgery on presymptomatic infected since July 1, 2020. E: Daily cases of pulmonary complications following operations on silent COVID-19 infected patients. F: Cumulative cases of pulmonary complications following surgery on presymptomatic infected patients.
and, show 12-months accumulated numbers of such cases roughly ranges between 2000 and 4500.

The US projections in Figure 2 for the other regions (data not shown) is similar up to a scaling factor equal to the population size of the remaining countries relative to that of the US (modulus minor corrections due to different age and sex compositions relative to US).

Also choosing different surgery rates $S$ scales the results linearly, as can be seen from the equation in (2).

Figure 3 shows cumulative cases of pulmonary complications (left, Fig. 3A) and 30-day mortalities (right, Fig. 3B) for all of the high-income regions considered (similar to Fig. 2D and 2F). Again $S = 15,000 \text{ operations per 100,000 person-years}$ is assumed.

**TABLE 1.** Estimated Number of Pulmonary Complications and 30-day Mortality Modelled Over a 12- and 24-Months Period

| Periods          | 12-months period | 24-months period |
|------------------|------------------|------------------|
|                  | 5%   | 50%  | 95%  | 5%   | 50%  | 95%  |
| Pulmonary complications |      |      |      |      |      |      |
| AUS              | 556  | 608  | 5052 | 5055 | 6941 | 9474 |
| CAN              | 864  | 473  | 7654 | 7645 | 10499| 14244|
| EU27             | 565  | 742  | 9517 | 9657 | 131505| 178482|
| UK               | 670  | 737  | 13627| 13685| 18718 | 25282 |
| US               | 375  | 9762 | 66898| 67538| 91795 | 124276|
| **Combined**     | 9789 | 13535| 188979| 190683| 259248| 351552|
| 30-day mortality |      |      |      |      |      |      |
| AUS              | 850  | 1210 | 1704 | 1693 | 2323 | 3164 |
| CAN              | 1322 | 1899 | 2635 | 2634 | 3614 | 4928 |
| EU27             | 17197| 24421| 33986| 34337| 46761 | 63262|
| UK               | 2342 | 3312 | 4621 | 4630 | 6357 | 8612 |
| US               | 10936| 15438| 21582| 21817| 29601 | 40192|
| **Combined**     | 32587| 46265| 64724| 65022| 88583 | 120677|

*Legend:* from the stochastic dynamic model with $S = 15,000 \text{ surgeries per 100,000 person-years}$.

*UI*: uncertainty interval for estimates by running low and high scenarios using the lower and upper 90% confidence limits.

**Figure 3.** AB: Cumulative cases of (A) pulmonary complications and (B) 30-day mortality. Cumulative cases of pulmonary complications (left) and 30-day mortalities (right) since July 1, 2020 for the different high-income countries/regions considered, assuming $S = 15,000 \text{ operations per 100,000 person-years}$. Solid lines correspond to median, and the shaded regions give 90% model implied confidence intervals (5% and 95% quantiles) for best-case and worst-case estimates. Plots have same interpretation as panels D and F of Figure 2, but show further countries/regions.
DISCUSSION

This study models a temporal and regional risk for perioperative pulmonary complications and deaths from performing surgery on silent SARS-CoV-2 carriers over a 2-year period. The high numbers are of concern as they are based on conservative estimates, and real numbers may even exceed these figures. The data suggest an added burden for critical care resources and an excessive number of deaths due to perioperative COVID-19 complications. Even modeling for low surgical rates – simulating constrained surgical activity in high-income countries or the existing situation in low- and middle-income countries – the accumulated number of pulmonary complications and deaths is high and should be considered a public health concern when planning for reopening surgical services. Further, the models anticipate an ongoing pandemic situation up to 24 months, which may be prolonged depending on several unknown factors – ranging from political, scientific and medical standpoint. Also, we have anticipated surgical activity depending on COVID-19 prevalence up to a given threshold of intensive care bed capacity, beyond which most surgical services would be deferred or even cancelled. Hence, we believe the model to project conservative numbers that in a worst-case setting may be exceeded. The data should be considered by stakeholders, policy makers, health care managers, and surgical societies when considering the type, structure, and extent of surgical activities to reopen or increase in the upcoming period. Maintaining surgical services during the pandemic is essential for patients. Economic pressures on health care systems and managers should carefully be balanced against the potential risk of unchecked admissions of silent SARS-CoV-2 carriers to surgical care.

Surgery is an essential part of health care service with about 330 million operations done globally each year. Most of these procedures are done in high-income countries, as essential surgery is lacking in several low and middle-income countries. Opting out of surgery may not be an alternative in several situations, such as oncological surgery or emergency conditions. Although lower surgery rates or, even cancellations of surgery, in the population will mitigate some of the postoperative adverse events modelled in this study, unsubstantiated delays or cancellations may deprive patients of time-essential procedures that may be life-saving or life-prolonging. Also, the accumulated back-log of procedures in the COVID-19 pandemic has forced several health care systems to look into strategies to build capacity above regular levels. Hence, the surgical rates in some regions may potentially become higher for some time period, further increasing the risk of SARS-CoV-2 exposure and adverse perioperative events. The population-based surgery rates are difficult to estimate across systems due to varying definitions and coding, but far exceeds >10,000 procedures per 100,000 inhabitants per year for most high-income regions, with data from Sweden suggesting even an excess of 25,000 procedures per 100,000 inhabitants per year for high-income regions. The high-income regions also bear the highest demographic burden of elderly with comorbidity and, hence, a higher risk of adverse events from COVID-19 in general. Further, this further substantiates the risk of surgery on silent SARS-CoV-2 carriers.

Although many low- and middle-income countries are struggling to deliver basic surgical care and have a low surgical rate to start with (eg, <5,000 operations per 100,000 person years), a different demographic composition of populations, for example, in African countries (eg, a lower rate of elderly and comorbid populations) may also result in a somewhat lower rate of population at risk. Nonetheless, the consequences of surgical risks should not be downplayed or minimized for these regions, as depicted in the WORLD estimates in the current study even for low surgical rates and result in a low surgical rate up to a given threshold of intensive care bed use and with little or few mitigation strategies in place.

Current mitigation of the risk may come from down-scaling or even cancelling of surgical activity across several regions. However, this is not sustainable in the long-run and will only increase a back-log of operations needed to be rescheduled for the future. Testing of all comers have been suggested and even takes place in several regions already. However, the existing problems with testing includes the huge variation in available tests and the variation in test accuracy, with sensitivity reported as low as 30% in the early phase of disease (hence, lower test accuracy for silent COVID-19). Added to this is the low-test sensitivity in those without symptoms – typically those who would be admitted for planned surgery if no symptoms to trigger testing. Further, even very low variance in specificity for a given test will cause large numbers of false negative test when applied to large populations. Even if the US has the highest per capita testing in the world (and higher than that in Canada) the case-fatality rate is lower in Canada, suggesting that testing or capacity for testing is not related to prevention of spread or the only mitigation strategy needed to avoid deaths.

Transmission patterns and spread is unpredictable, and several regions are now seeing a resurgence of cases after a period of low prevalence. So-called “second waves” after a period of lock down
society point to the risk of new widespread transmission when precautions and measures are not adhered to by the public. Super-spreaders may rapidly cause new outbreaks. Data suggest that infection rates are underestimated in the US and concerns about lasting immunity from other coronaviruses may suggest that infection may persist in society for a considerable period still. Thus, the 24 months model of the current study may even become longer, given a number of assumptions ahead.

Of note, the mortality risk and risk for pulmonary complications used in the current model stems from one study. Even though this is the largest data set available to date, the risk of bias and overestimation of risk is present and, must be considered for the presented prediction model. As further data are gathered, this may allow for adjustment of the current model for better prediction of risk.

Surgery is not without risk per se, and the European Surgical Outcome Study estimated 4% mortality before discharge from hospital and 8% admission to critical care services after noncardiac general surgery. Notably, postoperative mortality is highly variable within and between regions, and, related to a number of factors, including patients’ age and sex, comorbidity, type and severity of underlying disease, and type of surgery. Almost three-quarter of adverse events in the COVIDSurg study was related to emergency surgery, but this may also reflect a high degree of cancelled elective surgery during the period. Nonetheless, the available data from patients undergoing surgery with COVID-19 suggest an excessive risk of mortality. Whether surgery contributes to, or even triggers, an exaggerated inflammatory response is currently not known. However, an exaggerated cytokine storm and dysregulation of the complement system is described in severe COVID-19. This warrants further investigation related to the causes to the increased perioperative risk.

Of concern is the high estimated rate of pulmonary complications which, when added to an already considerable strain on intensive care resources may further put pressure on hospital systems in a pandemic setting. Also, pulmonary complications contributed to about 80% of all postoperative deaths from COVID-19 in a multicenter study. Particular SCCG groups and comorbidities are at higher risk for adverse outcomes, and this needs to be taken into account when scheduling surgery. The risk of disease deterioration, loss of life or loss of function from delaying or cancelling surgery needs to be balanced against the risk of perioperative adverse events. Planing of surgical and health services should consider the estimated impact of complications during rebuiling of surgical activity but also as we face subsequent waves of the pandemic. We provide population-level estimates of the complications of perioperative COVID-19 that should be used to inform such planning across various jurisdictions.

Uncertainty is inherent in any modelling, but the most recent datasets available are used for modelling estimates in the current study. SARS-CoV-2 viral spread and containment may be unpredictable and population prevalence influenced by serval factors (mitigation strategies, development of vaccines, medications, travel restrictions etc). Also, the estimated surgical risk can be particularly associated with certain demographic and disease groups and certain procedure types and hence not apply universally to surgery as such. Still, the risk is not negligible for “minor” surgery and elective surgery, based on the COVIDSurg Collaborative data. As further data are accrued, the risk modelling may become more precise and may potentially define areas of concern, where mitigation strategies and planning for surgery needs to be built into the pandemic setting by governments and health care systems. Further investigation into surgical areas of particular risk is warranted.

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