CovidSurg-3: Outcomes of surgery in COVID-19 infection

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Summary

- Any hospital worldwide that can participate in one or both components of CovidSurg-3:
  - Patient-level component: Collection of 30-day outcome data for all consecutive patients with peri-operative SARS-CoV-2 (positive PCR swab in the 7 days before or 30 days after surgery). **No** changes should be made to normal patient care/ follow-up pathways.
  - Hospital-level component: Collection of aggregated case-mix data.
- Collaborators will be PubMed-citable co-authors on publications their data contributes to.

1 Background

Data collected in 2020 found patients with perioperative SARS-CoV-2 infection to be at increased risk of postoperative mortality (up to 24% at 30-days), pulmonary complications (up to 51% at 30-days), and venous thromboembolism[1-5]. Perioperative SARS-CoV-2 infection has been associated with increased mortality, morbidity, longer length of stay, and increased health system burdens compared to SARS-CoV-2 negative patients[6-8].

During the first COVID-19 wave, over 28 million elective operations worldwide were either cancelled or delayed[9]. This enabled redistribution of staff and resources to meet COVID-19 demand, but resulted in substantial treatment delays, including for cancer patients[10-11]. COVID-19 lockdowns were associated with one in seven patients awaiting cancer surgery not being operated, and those patients who were operated experienced delays[10].

In 2020 CovidSurg captured outcomes on over 190,000 patients across >2,000 hospitals in 116 countries. This resulted in data-driven guidance for surgical systems during the pandemic, including:

- Guidance regarding the optimal delay prior to surgery following SARS-CoV-2 infection[4].
- The establishment of COVID-19-free surgical pathways to reduce nosocomial infection and complication[2].
- The non-effectiveness avoidance of preoperative isolation[12].
- Optimal preoperative SARS-CoV-2 screening protocols[13].
- Potential benefits of preoperative vaccination[14].

The Omicron SARS-CoV-2 variant of concern was first reported on 25 November 2021 and has spread globally rapidly[15]. There is a high-level of evidence indicating Omicron has increased transmissibility and potential to evade immunity[16-18]. However, there is little robust evidence regarding disease severity associated with Omicron in both vaccinated and unvaccinated patients (including in surgical patients), nor is there data to guide patient risk stratification during Omicron COVID-19 waves[18].

COVID-19 has significant detrimental impacts on surgical systems and patient outcomes. CovidSurg has provided the best available evidence to guide delivery of safe surgery during the pandemic. However, CovidSurg data were collected in 2020 when the wildtype SARS-CoV-2 virus was dominant, and therefore there is a need to for renewed rapid data to guide global practice during Omicron COVID-19 waves.

2 CovidSurg-3

CovidSurg-3 has two separate components:

- Patient-level component: Collection of outcome data for patients with peri-operative SARS-CoV-2.
- Hospital-level component: Collection of aggregated case-mix data. Hospitals in countries with low community SARS-CoV-2 infection rates **can** contribute towards this component.

Hospitals can choose to participate in:

- Patient-level component only, or
- Hospital-level component only, or
- Both components. *If possible, hospitals are encouraged to participate in both components*.

2.1 Primary objective

To determine 30-day mortality in patients with peri-operative SARS-CoV-2 infection. This will inform future risk stratification, decision making, and patient consent.

2.2 Secondary objectives

- To determine 30-day postoperative pulmonary complication and venous thromboembolism rates in patients with peri-operative SARS-CoV-2 infection.
- To evaluate implementation of SARS-CoV-2 mitigations and adaptations (vaccination, preoperative testing, COVID-free surgical pathways, patient selection).
- To determine the frequency of peri-operative SARS-CoV-2 infection.
- To determine the frequency of same-day elective surgery cancellations.

2.3 Hospital lead role

The hospital lead has responsibility for whichever study components (i.e. patient-level and/or hospital-level) that their hospital participates in. If participating in the patient-level component, the hospital lead should:

- Set up a patient-level data collection team (maximum 5 individuals, including the hospital lead).
- A REDCap login will only be issued to the hospital lead, so they are responsible for data upload.
- Submit authorship details (including ORCID IDs) for all their team members at the end of the study.

If participating in the hospital-level component, the hospital lead should recruit collaborators to collect case-mix data, ensuring there is no overlap in data collection between collaborators.

2.4 Authorship

All collaborators must have a publicly accessible ORCID account. This can be set up for free at https://orcid.org/register. Collaborators are responsible for ensuring they have correctly completed their name on their ORCID profile. No post-publication authorship changes will be permitted.

A corporate authorship model will be used. Collaborators will be recognised on resulting publications as PubMed-citable co-authors*. This means that collaborators are listed in both the article (PDF or supplement) and also on PubMed, which is the gold-standard index. Since services such as Scopus and ResearchGate are third-parties, we are unable to guarantee that publications will be correctly indexed by them.

The patient-level and hospital-level component data may be used for different analyses. Individuals will be included in the authorship for specific publications based on whether data they collected is used for that particular analysis.

*For an example, see PubMed entry for previous CovidSurg paper in The Lancet: pubmed.ncbi.nlm.nih.gov/32479829/ (click “expand” under ‘COVIDSurg Collaborative’ to see a full list of PubMed-citable co-authors).

3 Patient-level component

3.1 Inclusion criteria

Patients should be included if:

- They underwent surgery performed by a surgeon in an operating theatre, **AND**
- They had a positive SARS-CoV-2 PCR swab or rapid antigen test (if PCR swab is not available) within 7 days before or 30 days after surgery. Patients can be included regardless of whether a specific variant is suspected or unknown.

Patients should be excluded if:

- They underwent minor procedures listed in the Appendix.
- Their SARS-CoV-2 infection was diagnosed more than 7 days before surgery (regardless of their symptomatic status at the time of surgery) or beyond 30 days after surgery.

All consecutive patients fulfilling inclusion criteria across all specialties should be captured.

Individual participating centres can apply an age cut-off to the inclusion criteria (e.g. to include children only, adults only, or both children and adults).

All surgical specialties are included. Patients can be included regardless of surgical indication (benign surgery, cancer surgery, trauma, obstetric), anaesthetic type (local, regional, general), surgical approach (minimally invasive surgery, open surgery), or whether it is day-case or inpatient surgery.

3.2 Study period & patient enrolment

The overall patient inclusion period is 13 December 2021 to 28 February 2022. Patients can be included if they were operated between these dates (inclusive).

Whenever possible, patients should be identified prospectively:

- At the time of surgery (positive SARS-CoV-2 PCR swab before surgery).
- At the time of positive SARS-CoV-2 PCR swab (patients in whom SARS-CoV-2 is diagnosed within the 30 days following surgery).

This extension to CovidSurg was initiated in response to the emergence of the Omicron variant. It may take participating hospitals several weeks to secure study approvals. Therefore, the following approaches can be taken with respect to defining the patient inclusion period:

- Hospitals can choose to only prospectively enrol patients from the date of study approval to 28 February 2022. However, each team must enroll consecutive patients for ***at least*** 4 weeks. Therefore, if taking this approach, data collection must start on 1 February 2022 or earlier.
- Some hospitals will have treated many SARS-CoV-2 patients during their local 'Omicron wave' before study approvals are granted. It is important to capture their experience, so **retrospective patient identification and data entry is permitted**. E.g. if study approval is granted on 7 February 2022, they could retrospectively enrol patients operated on 13 December 2021 to 6 February 2022, and then prospectively enrol patients operated on 7 February 2022 to 28 February 2022.
- If permitted, prior to formal local study approval, collaborators prospectively collect data on hard copy case report forms. However, no data should be uploaded to the REDCap database before study approval is confirmed.

3.3 Outcomes

The primary outcome is 30-day mortality. Secondary outcomes (definitions provided in the Appendix) are:

- 30-day COVID-19 pulmonary complications, a composite of pneumonia, acute respiratory distress syndrome (ARDS), and /or unexpected postoperative ventilation.
- 30-day venous thromboembolism, a composite of deep vein thrombosis and pulmonary embolism

3.4 Follow-up

30-day postoperative outcomes should be collected for all patients. In this is an observational study **NO** changes should be made to normal patient pathways. Therefore, no additional patient follow-up should be completed for this study beyond what is normal practice at the hospital. Follow-up data can be collected at 30-days based on written patient notes, computer records, or telephone or in-person follow-up (if patients are normally followed-up at 30-days at the hospital).

3.5 Data collection

Data will be collected and stored online through a secure server running the Research Electronic Data Capture (REDCap) web application. REDCap allows collaborators to enter and store data in a secure system. Hospital Leads will be provided with REDCap project server login details, allowing them to securely submit data on to the REDCap system. REDCap has been successfully used for previous CovidSurg studies. The REDCap server is managed by the University of Birmingham, UK.

Only anonymised data will be uploaded to the database. **No patient identifiable data will be collected.** Data collected will be on comorbidities, SARS-CoV-2 status, surgery, and outcome (see Appendix).

3.6 Analysis

The analysis will describe the primary and secondary outcomes in the cohort. Outcomes will be reported stratified by age, sex, ASA grade, urgency of surgery, grade of surgery, and country income.

Non-parametric data will be summarised with medians and interquartile ranges and differences between groups tested using the Mann-Whitney U test. The $\chi 2$ test was used for categorical data. Missing data will be included in flowcharts and summary tables, allowing denominators to remain consistent in calculations. Hierarchical multivariable, mixed-effects logistic regression will be used to identify risk predictors of 30-day mortality, 30-day postoperative pulmonary complications, and 30-day venous thromboembolism, summarised as odds ratios and 95% confidence intervals. Clinically plausible patient, disease, operation and location specific factors have been selected *a priori* for inclusion in these adjusted analyses. Sensitivity analyses will be performed including only those patients who had a positive SARS-CoV-2 PCR swab.

The study will be conducted according to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) and SAMPL guidelines (Statistical Analyses and Methods in the Published Literature).

We anticipate recruitment from approximately 400 hospitals around the world with a mean of 5 patients per hospital, providing a sample size estimate of 2,000 patients. Hospital-level data will not be released. Country-level analyses will only be conducted with permission of National Leads. Local investigators can access their local data at any time directly from REDCap.

5.1 Local approvals for the patient-level component

The study will in accordance with national and international guidelines and legislation, as well as the basic principles of the protection of the rights and dignity of Human Beings, as set out in the Helsinki Declaration.

This is an **investigator-led, non-commercial, observational** (no changes to normal patient care) study which is extremely low risk; only routinely available non-identifiable data will be collected.

Principal investigators at each participating site are responsible for obtaining necessary local approvals in line with hospital / country regulations. Collaborators will be required to confirm that a local approval is in place at the time of uploading each patient record to the study database.

This study is an extension of previous CovidSurg projects. If your hospital participated in CovidSurg-1 or CovidSurg Week, please approach your ethics committee/IRB to explore whether this extension can be processed as an amendment to the previous approval.

If a new approval is needed, please explore with your ethics committee/IRB whether it is possible to expedite the process in view of the urgency of the pandemic/ Omicron wave.

Details of how this extension is related to CovidSurg-1 & CovidSurg Week is in the Appendix.

Possible pathways to register this study include:

- Research (e.g. research ethics committee or institutional review board approvals). Written patient consent should only be taken if required by your local ethics committee.
- Service evaluation or clinical audit (this should be the default approval process in the UK). Specific audit standards are defined in the Appendix based on benchmarking against UK and international data and guidelines[1,19,20].

4 Hospital-level component

One collaborator can participate per 7-day data collection block (listed below). They should complete the proforma below capturing all patients undergoing surgery for one or more body regions listed below. Up to 8 collaborators can participate per body region, collecting data over consecutive 7-day blocks. Collaborators should agree participation with their Hospital Lead, to ensure there is no overlap in data collection.

Data collection **MUST** be mapped to one or more body regions defined below; this is to ensure that consistent data is collected across all participating hospitals which can be pooled. **ALL** elective and emergency surgical activity relating to the selected body region(s) should be captured, even if it is split between different surgical units in the hospital.

In small hospitals a single collaborator may choose to capture data for all patients undergoing surgery.

Surgery is defined as an operation performed by a surgeon in an operating theatre, with the exception of minor procedures listed in the Appendix. Emergency surgery is defined as surgery on an unplanned admission. Elective surgery is defined as surgery on a planned admission.

4.1 Data collection blocks

Collaborators should collect data during one or more of the following 7-day blocks (if appropriate, by agreement with the Hospital Lead, start dates for data collection blocks can be amended, maintaining data collection over 7 consecutive days):

- 3 January 2022 – 9 January 2022
- 10 January 2022 – 16 January 2022
- 17 January 2022 – 23 January 2022
- 24 January 2022 – 30 January 2022
- 31 January 2022 – 6 February 2022
- 7 February 2022 – 13 February 2022
- 14 February 2022 – 20 February 2022
- 21 February 2022 – 27 February 2022

Collaborators can choose to collect data for multiple 7-day blocks or multiple specialties, if appropriate.

4.2 List of body regions

A breakdown of key procedures mapped to body regions is provided in the Appendix.

Specialty	Note
Blood vessels (vascular)	Includes aorta, arteries, veins
Brain	Includes skull
Colon, rectum and small bowel	
Eyes (ophthalmology)	
Female reproductive system	Includes fallopian tubes, ovaries, uterus, vagina
General surgery	Includes breast, endocrine, hernia and miscellaneous emergency surgery (see Appendix)
Head & neck	Includes ear, oral, nose, throat, and maxillofacial surgery
Heart	Includes mediastinum and pericardium
Hepatobiliary system	Includes bile ducts, gallbladder, liver, pancreas, spleen
Lung	Includes pleura and chest wall
Musculoskeletal	Includes bones, joints, muscles, tendons, and spinal surgery
Obstetric	
Oesophagus and stomach	
Skin (plastic surgery)	Includes burns surgery and flaps
Urinary and male reproductive systems	Includes kidney, bladder, ureter, prostate, testicles, renal transplant

4.3 Proforma

	Elective	Emergency
For selected body region:		
Total patients operated during the week		
Elective cases cancelled on the planned day of surgery		N/A
Patients who tested positive for SARS-CoV-2 in peri-operative period		
Across the whole hospital:		
Total patients operated during the week		

5.2 Local approvals for the patient-level component

Principal investigators at each participating site are responsible for obtaining necessary local approvals. If the hospital is participating in the patient-level component, we suggest that the hospital-level component is included within an overall submission including both the patient-level and hospital-level components.

If the hospital is not participating in the patient-level component, we suggest to explore with your ethics committee/IRB/ equivalent whether the need for formal study approval can be waived, as **only anonymised, aggregated (administrative) data will be collected**.

6 References

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