Ansökan om etikprövning
Ansökan om ändring

1.1. Ange diarienummer på den tidigare godkända grundansökan.
2020-01-365

1.2. Ange ansvarig forskare för den tidigare godkända grundansökan.
Malin Sund

1.3. Ange forskningshuvudman för den tidigare godkända grundansökan.
Kirurgcentrum Norrlands Universitetssjukhus, Region Västerbotten

1.4. Ange titel på den tidigare godkända grundansökan.
Kirurgi under pandemin COVID-19: en internationell studie (CovidSurg)

1.5. Beskriv kortfattat den ändring av tidigare godkänd ansökan som planeras.
Målet med tillägget är att bestämma risken för perioperativ morbiditet och mortalitet bland patienter som genomgått Covid-19-infektion. Under en sjudagarsperiod kommer över 1000 sjukhus världen över att inkludera samtliga operationer och följa upp dessa en månad. Subgrupper omfattar patienter som haft Covid-19, de som inom 30 dagar drabbas av Covid-19, och de som aldrig haft eller drabbas av Covid-19 (kontrollgrupp). Det primära utfallsmåttet är samma som i huvudstudien det vill säga 30-dagarsmortalitet, medan sekundära utfallsmått är venös trombembolism och lungkomplikationer. Alla patienter kommer att samlas in på liknande sätt som i huvudstudien CovidSurg och registreras på samma sätt. Inga patienter kommer att kunna identifieras.

1.6. Ange de skäl som ligger till grund för den planerade ändringen.
Grundansökan syftade till att värdera risken för perioperativ mortalitet bland patienter sjuka i Covid-19. Med ändringsansökan finns det dels möjlighet att skapa en kontrollgrupp aldrig sjuka patienter, dels möjlighet att undersöka risken för perioperativ mortalitet bland tidigare sjuka patienter. Detta kan vara av stor betydelse för hur sjukvården ska kunna ta ställning till operativ risk under olika faser av pandemin.

1.7. Gör en värdering av hur förhållandet mellan riskerna och nyttan av projektet förändras med anledning av den planerade ändringen.
Det finns inga ytterligare risker med denna studie jämfört med huvudstudien.

1.8. Beskriv i förekommande fall hur informationen till forskningspersonerna förändras med anledning av den planerade ändringen.
Inte aktuellt

1.9. Beskriv i förekommande fall hur annan information/bilagor förändras med anledning av den planerade ändringen.
Inte aktuellt

1.10. Ange i förekommande fall vilka bilagor som bifogas ansökan.
Bifogar den brittiska projektplanen. Studien bedrivs precis som huvudstudien, över hela världen med säte i Birmingham.

I och med att ansökan undertecknas intygar du som är ansvarig forskare följande:

Att den information som lämnas i ansökan om etikprövning och samtliga medföljande bilagor [illegible] fullständig.

Att verksamhetsansvariga i samtliga medverkande verksamheter är informerade om forskningsprojektets innehåll och utförande och att de har samtyckt till att delta i studien.

Att du säkerställt att det i samtliga medverkande verksamheter finns resurser som garanterar forskningspersonernas säkerhet och integritet vid genomförandet av den forskning som [illegible]

Att du tagit del av Etikprövningsmyndighetens information om hantering av personuppgifter på myndighetens webbplats.

Underskrift ansvarig forskare (eller behörig företrädare för forskningshuvudman)
Malin Sund, professor/överläkare
2020-08-18

GlobalSurg-CovidSurg Week: Determining the optimal timing for surgery following SARS-CoV-2 infection

Contact information:
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Summary

- Prospective, observational international cohort study.
- Any hospital worldwide can participate (including hospitals that have not admitted SARS-CoV-2 infected patients).
- All patients undergoing a surgical procedure in an operating theatre will be included. All consecutive eligible patients should be included.
- 7-day data collection period, with follow-up at 30 days after surgery for each patient. However, **no** changes should be made to normal patient care/ follow-up pathways
- Primary outcome is 30-day mortality.
- All collaborators will be included as PubMed-citable co-authors on resulting publications.

Background

- The CovidSurg and CovidSurg-Cancer cohort studies have captured outcomes on 36,000 patients across 1,005 hospitals in 86 countries.
- The CovidSurg cohort study captured the outcomes of surgery in patients with perioperative SARS-CoV-2 infection. The first CovidSurg paper in The Lancet* reported that 51% of these patients experienced a postoperative pulmonary complication and 24% died within 30 days of surgery. However, analyses were limited by the lack of contemporary comparators. The next CovidSurg analysis is exploring risk stratification in SARS-CoV-2 infected patients.
- The CovidSurg-Cancer captured data on patients who were diagnosed with operable cancer during the COVID-19 pandemic. The first CovidSurg-Cancer analysis will evaluate the impact of establishing COVID-free patient pathways (cold surgical units).
- Early signals based on data from around 150 patients from the CovidSurg-Cancer show that preoperative SARS-CoV-2 diagnosis is associated with poor outcomes, even if surgery is several weeks after initial diagnosis. However, more granular data are needed to explore the optimal timing of surgery after SARS-CoV-2 infection, including determination of what factors predict which of these patients are at increased risk.
- Unlike the completed CovidSurg study, GlobalSurg-CovidSurg Week will collect data about all patients (elective/emergency) having surgery, including comparator data from patients who are not diagnosed with SARS-CoV-2.

*COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. Lancet. 2020;396(10243):27-38.

Primary aim
To determine the optimal timing for surgery following SARS-CoV-2 infection.

Primary analysis
Mortality rates will be compared between patients preoperatively infected with SARS-CoV-2 and those presumed to be unexposed at the time of surgery.

The main exposure are patients with a diagnosis of SARS-CoV-2 at any time before surgery (preoperative SARS-CoV-2 group).

- This includes patients diagnosed at any time before surgery (diagnosis could be days to months before surgery).
- This includes patients who (1) were never symptomatic, (2) symptomatic at the time of diagnosis, but whose symptoms have now resolved (patient is not symptomatic on the day of surgery), (3) have ongoing symptoms of SARS-CoV-2 infection.
- This group will be stratified by time since diagnosis (if known), severity of initial SARS-CoV-2 infection, and whether they are symptomatic at the time of surgery.

There will be two comparator groups, (1) patients with postoperative SARS-CoV-2 diagnosis, and (2) patients who have not had a SARS-CoV-2 diagnosis. The groups are defined below.

- Non-SARS-CoV-2 group: patients who have not had a diagnosis of SARS-CoV-2 before surgery or within 30 days after surgery.
- Postoperative SARS-CoV-2 group: Patients who were diagnosed with SARS-CoV-2 postoperatively within 30 days after surgery (this includes both patients who do and do not have symptoms).

For this study, SARS-CoV-2 can be diagnosed with any one or more of the following:

- Positive RT-PCR swab.
- Positive antibody test.
- Positive CT thorax.
- Clinical diagnosis of SARS-CoV-2 (no negative swab results). The diagnosis should be made contemporaneously (i.e. at the time that the patient has the symptoms) by a healthcare provider. A chest x-ray may be used as part of a clinical diagnosis.
- Sensitivity analyses will be performed including only those patients who had a positive swab.

Secondary outputs relating to SARS-CoV-2

- Monitor incidence of SARS-CoV-2 in surgical patients, and explore risk prediction of which patients develop SARS-CoV-2 (patient, disease, hospital, community factors).
- Monitor uptake and impact of COVID-19 free surgical pathways (cold / COVID-light units) and screening across the world.

Secondary aims
To model key country-level surgical indicators, including:

- Surgical volume and case-mix, based on hospital-level survey data. This will allow the unmet need for surgery to be estimated, in order to inform post-pandemic planning for increasing access to surgery.
- Specialty-specific postoperative mortality rates, based on patient-level data. At present only nine countries routinely measure country-level postoperative mortality rates. Adverse outcomes associated with surgery are poorly understood at both global and country levels, so data from GlobalSurg-CovidSurg Week will fill these knowledge gaps and provide country-level benchmarking to support planning.
- Combining the surgical volume, case-mix, and postoperative mortality rate data will allow the global burden of postoperative death to be modelled.

Data will only be released at regional and country-level. As these analyses will be based on statistical modelling, it will not be possible to determine individual hospitals' outcomes from country-level results, even if only one hospital participates in a particular country or region. No hospital-level outcomes data will be published.

Methodology

- Prospective observational cohort study.
- All hospitals eligible to participate, including those that do not currently have COVID-19 outbreaks; these hospitals will enter data for the Non-SARS-CoV-2 comparator group.
- Collaborators will collect data on all consecutive eligible cases within their scope of practice (i.e. their surgical specialty / surgical team). Multiple specialties can contribute from each hospital, but it is not mandatory for all specialties to participate.
- A mini-team of up to three collaborators will collect data over 7 consecutive days:
    - The first day of data collection must be between 1-31 October 2020 (inclusive).
    - Multiple mini-teams may participate at the same hospital, either collecting data in different specialties, or in the same specialty during distinct 7-day blocks. A mini-team can also choose to collect data over multiple 7-day blocks.
    - We suggest that at least one mini-team participating within your specialty should include a senior (consultant/ attending) surgeon.

Inclusion criteria

- Any operation (elective or emergency) done in an operating theatre by a surgeon, excluding minor procedures previously defined by Abbott TEF, Fowler AJ, Dobbs TD, Harrison EM, Gillies MA, Pearse RM. Frequency of surgical treatment and related hospital procedures in the UK: a national ecological study using hospital episode statistics. Br J Anaesth. 2017;119(2):249-257.
- All surgical specialties including: acute care surgery, breast surgery, cardiac surgery, colorectal surgery, general surgery, gynaecology, hepatobiliary surgery, neurosurgery, obstetrics, oesophagogastric surgery, ophthalmology, oral and maxillofacial surgery,

orthopaedics, otolaryngology, paediatric surgery, plastic surgery, thoracic surgery, transplant surgery, trauma surgery, urology, vascular surgery.
- Day case surgery and inpatient surgery included.
- Any SARS-CoV-2 status (positive at any time, negative, not tested).
- All ages including children and adults.

Outcomes
- Primary: 30-day mortality
- Secondary:
    - In-patient mortality
    - 30-day postoperative pulmonary complications (pneumonia [CDC definition], ARDS, unexpected ventilation)
    - 30-day venous thromboembolism (deep vein thrombosis/ pulmonary embolism)
    - 30-day Clavien-Dindo grade

Follow-up
This is an observational study and **no** changes should be made to normal patient pathways, and no additional patient follow-up is required. Patients should have clinical follow-up as per normal practice at their hospital. Follow-up data should be entered at 30-days following surgery based on written patient notes, computer records, or telephone/in-person follow-up (if patients are normally followed-up at 30-days at the hospital).

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. A designated collaborator at each participating site will be provided with REDCap project server login details, allowing them to securely submit data on to the REDCap system. REDCap has previously been successfully used for the CovidSurg/ CovidSurg-Cancer 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. The study will be carried out in accordance with national and international guidelines, as well as the basic principles of the protection of the rights and dignity of Human Beings, as set out in the Helsinki Declaration (64th Assembly Fortaleza, Brazil, in October 2013), and according to locally applicable legislation.

Hospital-level survey
In addition to collecting patient-level data, participating centres will complete a survey to submit hospital-level data. This will include:
- Total number of COVID-19 admissions over the week.
- Total number of hospital beds.
- Total number of operating theatres.
- Total number of surgical, obstetric, and anaesthetic staff.
- Total operations performed by each specialty over the 7-day data collection block.
- Total operations performed by each specialty in 2019.

Local approvals

Principal investigators at each participating site is responsible for obtaining necessary local approvals in line with their hospital's 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.

If you have already participated in CovidSurg or CovidSurg-Cancer, please approach your ethics committee/IRB to ask whether it is possible to approve GlobalSurg-CovidSurg Week as an amendment to the existing approval (some committees have allowed this).

Principal investigators should discuss with their head of department whether it is possible to expedite the approvals process in view of the urgency of global pandemic. Whatever approvals pathway is followed, it should be highlighted that this is an investigator-led, non-commercial, observational (no changes to normal patient care) study which is extremely low risk, as only routinely available non-identifiable data will be collected.

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.
- Clinical audit (this should be the default approval process in the UK). The following audit standards will be assessed in this study:
    - **"Emergency Admissions: all patients should be tested on admission."** Audit standard 100%. Based on NHS England guidance: Operating framework for urgent and planned services in hospital settings during COVID-19*.
    - **"Elective Admissions: patients should isolate for 14 days prior to admission. This should be supplemented with a pre-admission test [if feasible]."** Audit standard for patient isolation, 100%. Based on NHS England guidance, as above.
    - **"There should be a physical separation of COVID-19 positive and COVID-19 negative patients".** Audit standard 100%. Based on Royal College of Surgeons of England guidance: Recovery of surgical services during and after COVID-19†.

* https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/05/Operating-framework-for-urgent-and-planned-services-within-hospitals.pdf
† https://www.rcseng.ac.uk/-/media/files/rcs/coronavirus/rcs-guidance--recovery-of-surgical-services--updated-26-may-2020.pdf).

Authorship

Up to three collaborators may participate in each mini-team that collects data from a surgical specialty over a 7-day period. Multiple mini-teams may participate at the same hospital, either collecting data in different specialties, or in the same specialty during distinct 7-day blocks. If a very large volume of patients is anticipated, collaborators may seek permission from the central coordinating team to increase the number of collaborators in their mini-team.

Collaborators from each site who contribute patients will be recognised on any resulting publications as PubMed-citable co-authors. A corporate authorship model will be used, please see the PubMed entry for the previous CovidSurg paper in the Lancet here: https://pubmed.ncbi.nlm.nih.gov/32479829/ (click "expand" under 'COVIDSurg Collaborative' to see a full list of PubMed-citable co-authors).

Case Report Form

Baseline	
Age	<52 weeks, 1-4 years, 5-9 years, 10-17 years, 18-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, 80-89 years, ≥90 years
Sex	>Female >Male >Ambiguous
ASA	>Grade I >Grade II >Grade III >Grade IV >Grade V
Revised Cardiac Risk Index	>History of ischemic heart disease >History of congestive heart failure >History of cerebrovascular disease >Pre-operative treatment with insulin >Pre-operative creatinine >2 mg/dL / 176.8 μmol/L
Respiratory comorbidities	>Current smoker or smoked in last 6 weeks >Ex-smoker (stopped ≥6 weeks ago) >Asthma >COPD >Other respiratory comorbidity
SARS-CoV-2 status	
Hot/cold unit	Operating theatre >Cold: dedicated theatre for non-SARS-CoV-2 elective surgery patients, segregated from COVID-19 patients >Hot: area shared by elective surgery patients and COVID-19 patients Intensive care unit >Cold: dedicated ICU for non-SARS-CoV-2 elective surgery patients, segregated from COVID-19 patients >Hot: area shared by elective surgery patients and COVID-19 patients >Not applicable Postoperative ward >Cold: dedicated ward for non-SARS-CoV-2 elective surgery patients, segregated from COVID-19 patients >Hot: area shared by elective surgery patients and COVID-19 patients

Was the patient asked to self-isolate	>No >Before hospital admission only >After discharge from hospital only >Both before hospital admission and after discharge from hospital *If yes, duration of preoperative and postoperative isolation in days*
Were any of the following used to screen the patient for SARS-CoV-2 in the 7 days before surgery *(tick all that apply)*	>CT thorax scan >Chest x-ray >Swab >> how many negative swabs / positive swabs & timing of the last swab >Antibody test >Clinical screening (history, examination)
SARS-CoV-2 diagnosis	>None >Preoperative (at any time) >Postoperative (within 30 days after surgery)
If SARS-CoV-2 +ve How was the diagnosis made *(tick all that apply)*	>Positive swab >CT thorax >IgG antibody positive >IgM antibody positive >Clinical diagnosis
If preoperative infection How long before surgery was the diagnosis	>Day of surgery >1-7 days before surgery >8-14 days before surgery >15-28 days before surgery >5-6 weeks before surgery >7-8 weeks before surgery >3-4 months before surgery >5-6 months before surgery >6+ months before surgery
If preoperative infection Was the SARS-CoV-2 infection symptomatic*	>Yes- but all symptoms had resolved before the day of surgery >Yes- and some symptoms were ongoing on the day of surgery >No- the patient did not have symptoms *this includes both respiratory and non-respiratory symptoms
If symptomatic infection What symptoms did the patient have *(tick all that apply)*	>Respiratory symptoms (e.g. cough, shortness of breath) >Non-respiratory symptoms (e.g. fever, diarrhoea, fatigue)
If symptomatic infection Did the patient require hospital treatment for SARS-CoV-2	>No >Yes- did not require non-invasive or mechanical ventilation >Yes- required non-invasive or mechanical ventilation

If postoperative infection Was dexamethasone administered in the 10 days following infection	>No >Yes >> enter dose, duration
Intraoperative	
Urgency	>Elective >Emergency
Day-case surgery	>Performed as day-case (no overnight admission) >Performed with overnight admission
Procedure	Dropdown menu of procedures
Anaesthesia *Tick all that apply*	>Local >Nerve block >Spinal >Epidural >General
Indication	>Benign >Malignancy >> curative or palliative procedure >Trauma >Obstetric >Complication of COVID-19 >> free text field to describe
If abdominal surgery Operative approach	>Planned and performed as open >Planned and performed as laparoscopic (includes laparoscopic assisted cases) >Planned and performed as robotic >Laparoscopic converted to open >Robotic converted to open >Hybrid (e.g. laparoscopic abdomen, open chest)
How was the majority of the cost of surgery supported?	> Public insurance (funded by government) > Private insurance (insurance paid for by the patient) > Corporate insurance (funded by patient's employer) > External funds or grants awarded by charities/NGOs > Out of pocket payments (patient paid the hospital directly) > Other (free text)
Outcomes	
Mortality	>Alive at 30 days >Died in-hospital, within 30 days of surgery >Died after discharge, within 30 days of surgery

Complications	>None >Pneumonia >Acute respiratory distress syndrome >Unexpected ventilation >Pulmonary embolism >Deep vein thrombosis
Clavien-Dindo	>Grade I >Grade II >Grade IIIa/b >Grade IVa/b >Grade V