Perioperative management of patients with suspected or confirmed COVID-19. Recommendations based on a rapid review and retrospective cohort study of outcomes in Tongji Hospital, Wuhan.

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Perioperative management of patients with suspected or confirmed COVID-19.
Recommendations based on a rapid review and retrospective cohort study of outcomes in Tongji Hospital, Wuhan.

Short title: COVID-19 perioperative management

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Abstract

Background: Current guidelines for perioperative management of COVID-19 are mainly based on extrapolated evidence or expert opinion. We aimed to systematically investigate how COVID-19 affects perioperative management and clinical outcomes, to develop evidence-base guidelines.

Methods: First, we conducted a rapid literature review in Embase, Medline, PubMed, Scopus, and Web of Science (1st January to 1st July 2020), using a predefined protocol. Secondly, we performed a retrospective cohort analysis of 166 women undergoing Caesarean section at Tongji Hospital, Wuhan during the COVID-19 pandemic. Demographic, imaging, laboratory, and clinical data were obtained from electronic medical records.

Results: The review identified 26 studies, mainly case reports/series. One large cohort reported greater mortality in elective surgery patients diagnosed after, rather than before surgery. Higher 30-day mortality was associated with emergency surgery, major surgery, poorer preoperative condition and surgery for malignancy. Regional anaesthesia was favoured in most studies and personal protective equipment (PPE) was generally used by healthcare workers (HCW), but its use was poorly described for patients. In the retrospective cohort study, duration of surgery, oxygen therapy and hospital stay were longer in suspected or confirmed patients than negative patients, but there were no differences in neonatal outcomes. None of the 262 participating HCWs was infected with SARS-CoV-2 when using level 3 PPE perioperatively.

Conclusions: When COVID-19 is suspected, testing should be considered before non-urgent surgery. Until further evidence is available, HCWs should use level 3 PPE perioperatively for suspected or confirmed patients, but research is needed on its timing and specifications. Further research must examine longer-term outcomes.

Registration: The rapid review was registered in PROSPERO (ID: CRD42020182891).

Keywords: Coronavirus, COVID-19, SARS-CoV-2, perioperative, Caesarean section, rapid review
Introduction

Coronavirus disease 2019 (COVID-19), resulting from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, has become a global pandemic since it was first described in Wuhan, China in December 2019 \(^1\), and was declared a public health emergency. As of 10\(^{th}\) August 2020, over 19 million cases and over 728,000 deaths have been reported worldwide \(^2\). In the UK alone, 310,829 cases have been reported with 46,574 deaths, and in China there have been 89,270 cases and 4,693 deaths \(^2\). In response to this health crisis, guidelines have been published on the clinical management of patients undergoing surgery to prevent transmission to healthcare workers (HCW) and adverse outcomes in patients \(^3,4\). However these are mainly based on pre-existing practices rather than on data from patients with suspected or confirmed COVID-19, and little is known about how perioperative techniques affect transmission rates and outcomes in patients with COVID-19. Furthermore, a rapid review of clinical guidelines published early in the COVID-19 pandemic concluded that their overall quality was low and their focus should be on evidence-based recommendations, rather than consensus \(^5\). This study therefore had 2 objectives:

I. To conduct a rapid review of studies and case reports examining the management of patients with suspected or confirmed COVID-19 undergoing surgery, and subsequent morbidity, mortality, length of hospital stay, use of intensive care, respiratory and pain support, and COVID-19 transmission to HCWs.

II. To examine perioperative approaches and outcomes in a series of Caesarean section operations undertaken in Tongji Hospital, Wuhan, during the COVID-19 outbreak.
Methods

I. Rapid Review

The reporting of this review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Due to the fast-evolving nature of COVID-19 and the need to produce clinical evidence for making recommendations on patient care that are readily available to HCWs in a timely manner, we chose to adopt a rapid approach to the review. This involved a streamlined protocol whereby article identification, appraisal and data extraction were shared between two reviewers, with some overlap for quality control, instead of complete independent duplication. Details of the protocol were registered on PROSPERO: International prospective register of systematic reviews (ID: CRD42020182891) and can be accessed at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=182891.

Eligibility Criteria

Population: Any patient undergoing surgery who had confirmed or suspected COVID-19 at the time of surgery.

Intervention: Any form of surgery and perioperative management undertaken whilst the participant was suspected or confirmed as having COVID-19, except where the procedure was conducted to treat COVID-19. Any studies not reporting details of patient management at any time during the perioperative period (defined as 24 hours before and after surgery) were excluded from the review. Studies were also excluded if they included patients who did not undergo surgery, and where it was not possible to identify them separately from surgical patients.

Comparator: Where relevant, patients with suspected or confirmed COVID-19 who were not subject to perioperative interventions.

Outcomes: Patient, HCW and neonatal postoperative outcomes, where relevant.

Study type: Observational studies including cross-sectional, case-control and cohort designs as well as case-series or case-reports and randomized control trials (RCTs) could be included. As the database search, article screening and data extraction
processes were conducted by UK-based authors, only English language articles were considered, to avoid misinterpretation of the data. Unpublished studies, conference abstracts and research theses or dissertations were also excluded (Table 1).

We searched PubMed, MEDLINE, EMBASE, Scopus, and Web of Science for original articles, reported in English. Databases were searched from 1st January 2020, with initial search to 4th May 2020; the search was updated on 1st July 2020. As the purpose of this study is to provide both clinical evidence and recommendations for further research in a timely manner, it was decided to exclude studies with a sample size of less than 15 in the rerun of search terms (4th May-1st July 2020). Such studies are likely to be dominated by lower quality case reports, which would not contribute substantially to the overall evidence presented in this study. In addition the reference sections of included studies were also checked for relevant studies.

The search terms used for all 5 databases included words related to COVID-19 (the population), surgical interventions and perioperative management (the interventions). Comparator, outcomes and study type search terms were not used. Where available, the study year filter was set to 2020 (Supplementary Table S1).

After retrieving articles from the databases, non-English language and duplicates were removed. HLH and LAC then independently screened the titles and abstracts according to the inclusion and exclusion criteria to identify relevant studies. Remaining articles then went through full-text review (HLH and LAC), noting reasons for all exclusions. Any differences in opinion were settled by discussion between the reviewers and, where necessary, the wider research team.

Data Extraction

A pro forma spreadsheet was constructed and data extraction was conducted independently by HLH and AC, who reviewed an equal number of studies with a 6-study overlap for quality control. Any differences in data extraction for the overlapped studies were resolved between HLH and AC. Due to the rapid nature of the review, study authors were not contacted to resolve missing data or identify
further studies.

The following data items were extracted:

1. **Study details** – authors, journal of publication, date of publication, country/countries where the study took place, sample size and study design.

2. **Patient characteristics** – age, gender, body mass index (BMI)/weight, comorbidities and method of diagnosing or suspecting COVID-19.

3. **Surgical details** – type, schedule, indications, duration and other relevant details.

4. **Perioperative management** – HCW use and level of personal protective equipment (PPE), patient use of PPE, patient time between symptoms and surgery, type of anaesthesia (e.g. general/regional), analgesics used, pain assessment, vasopressors used, blood loss and any other relevant details.

5. **Postoperative outcomes** – HCW COVID-19 status, patient discharge status, length of hospital stay, use of intensive care unit (ICU) or high dependency unit (HDU), level of respiratory support, use of analgesia, mortality and, where relevant to the study, neonatal COVID-19 status, Apgar score, mortality, discharge status and any other relevant reported details.

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**Risk of Bias (Quality) Assessment**

The quality of reporting of all included studies was evaluated by HLH and AC according to the CAse REport (CARE) guidelines for case reports/series or the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional, case-control and cohort studies. A quality score was calculated for each article based on a checklist of 36 items for CARE (Supplementary Table S2) and 32-34 items for STROBE (Supplementary Table S3), depending on the type of observational study. The presence of an item scored one, absence scored zero and the total was calculated. A percentage of the maximum possible score was also calculated and “high quality” was defined as any study achieving a score of 80% or greater. “Low quality” was defined as any study with...
a score of less than 80%. Higher scores indicate studies with reporting of higher quality. Disagreements were resolved via discussion between the 2 reviewers.

Summary Measures
For case reports and series with sample size ≤5, numeric values are reported individually. Otherwise summary statistics are presented (e.g. median, mean, range, interquartile range [IQR] or standard deviation [SD]) as reported in original papers. Qualitative variables are reported as counts. A synthesis of the extracted data was constructed, structured around the type of surgery performed, surgical practices, population demographic and clinical characteristics, and type of outcome. Recommendations for the perioperative management of patients with COVID-19 were developed from the synthesised evidence, and tables were constructed to aid the presentation of the extracted data and quality assessment of each article.

II. Cohort Study
Study design and data sources and ethics
This single-centre, retrospective study was approved by the Institutional Review Board of Tongji hospital, Tongji Medical College, Huazhong University of Science and Technology (TJ-IRB20200421). The requirement for informed consent from participants was waived under the regulations of the Institutional Review Board. Data, including demographic, clinical, imaging, laboratory, perioperative management, and maternal and fetal outcomes, were extracted from the electronic database of medical records at Tongji Hospital, and anonymised for analyses. Data from all parturients who underwent Caesarean section (including emergency surgery) during the COVID-19 pandemic in Wuhan were included in this study. In order to ensure completeness of reported data, we included all patients who had undergone Caesarean section in the defined time period. Part of this data has been reported previously by other groups. COVID-19 case definitions were based on
the National Health Commission of China’s diagnostic criteria (seventh edition) (Box 1). A confirmed case of COVID-19 was defined as a suspected case with a positive result of real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assay of respiratory tract specimens or serum-specific antibodies to SARS-CoV-2. If the results of 2 RT-PCR tests taken at least 24-hour apart, and serum-specific antibodies to SARS-CoV-2 detected at least 7 days after the onset of the disease, were negative in a suspected case, the diagnosis of COVID-19 was excluded. All patients were tested with RT-PCR or antibodies or CT when possible. If COVID-19 was suspected or confirmed, follow-up tests were performed after surgery.

Perioperative management

Before entering the operating room, triage was performed by obstetricians and anaesthetists, including medical history review, brief physical examination, and reviewing blood test results, chest computed tomography (CT), test for nucleic acid of SARS-CoV-2 or SARS-CoV-2 antibodies. Because individuals might be infected with SARS-CoV-2 but be asymptomatic, all patients were placed in an isolation holding area and transferred to a dedicated negative pressure system operating room with an anteroom beside it (buffer area). The patients wore surgical or N95 masks throughout the process. After the patient entered the operating room, routine monitoring including continuous electrocardiograph, regular non-invasive blood pressure, and peripheral pulse oximetry were performed. Spinal anaesthesia or combined spinal epidural anaesthesia was the primary choice. General anaesthesia with tracheal intubation was an option under certain circumstances such as contraindications of spinal anaesthesia, maternal or fetal emergencies, or failed spinal anaesthesia. During the intubation, surgeons and nurses remained in the operating room, to ensure that surgery started as soon as possible after induction. The neonatal team was notified before delivery, in order to attend and make any necessary preparations. After delivery, the newborns were cleaned immediately to remove blood clots, meconium and amniotic fluid. The newborns were then placed
under a radiant warmer in a cordoned-off area in the operating room. The Apgar
scores of newborns were assessed at 1 and 5 minutes. For patients with suspected or
confirmed COVID-19, their newborns were transferred to a neonatology isolation
room shortly after delivery. SARS-CoV-2 nucleic acid tests were then carried out as
soon as possible in all newborns. Maternal contact was not allowed. One day after
surgery, full blood count and coagulation tests were performed in parturients. If
COVID-19 was suspected or confirmed, chest CT, nucleic acid of SARS-CoV-2 or
SARS-CoV-2 antibodies were tested again. Body temperatures or any other symptoms
associated with COVID-19 were recorded daily by nurses, throughout the hospital
stay. According to the parturients' clinical condition, supplemental oxygen was
delivered via nasal cannula or mask to maintain an SpO2 of 95% and above. Other
methods of non-invasive or invasive ventilation were considered if necessary.
Diclofenac and/or dezocine was given, as requested by the parturients, to relieve
postoperative pain.

Perioperative protection and postoperative evaluation of healthcare workers
Self-protection precautions were strictly followed by all participating HCWs. Level 3
PPE including N95 mask, fluid-resistant gown, goggle, face shield, disposable hair
cover, head covering, 2 layers of gloves, and fluid-resistant shoe covers, was used by
all HCWs involved. PPE was donned before entering the operating room and was
doffed after exiting operating room in buffer area. All HCWs involved had a 24-hour
duty shift every one to two weeks. They were required to report any COVID-19
related symptoms such as fever, cough or fatigue. At the beginning of April, 2020, all
HCWs were required to have a SARS-CoV-2 antibodies detection test, a test for
nucleic acid of SARS-CoV-2 on nasopharyngeal swabs and a chest CT scan.

Statistical analysis
Suspected or confirmed cases were categorised together and compared with
negative cases. Maternal outcomes including duration of operation, oxygen therapy
and hospital stay, and fetal outcomes such as Apgar scores at 1 minute and 5 minutes were compared between groups. Continuous variables are presented as median (IQR). These data failed the Shapiro-Wilk test for normality and significance was calculated using Mann-Whitney U tests. Categorical variables are expressed as number (%) and analysed using chi-square tests. SPSS 21.0 statistical software (SPSS, Inc. Chicago, IL, USA) was used for all statistical analyses. A 2-sided P-value <0.05 was considered to be statistically significant.
Results

I. Rapid Review

Study Selection

The workflow for identifying and screening articles is provided in figure 1. The initial literature searches yielded 3,227 papers. The re-run of the search yielded a further 107 articles. After removal of duplicates, non-English language papers and title and abstract screening, 64 articles remained for full-text review. Articles identified during the re-run of search terms (from 4th May to 1st July, 2020) that were excluded on the basis of having a sample size ≤15 are shown in Supplementary Table S4. A full list of the 38 articles excluded on full-text review, with reasons, is provided in Supplementary Table S5. We therefore identified 26 articles for inclusion in this review.

Study Characteristics

The characteristics of each included study are summarized in Table 2. There were no RCTs. Twenty-two of the papers were lower quality case reports or case series21, 17, 19, 21-32, 34-39, 41. The remaining 4 were observational studies, of which 2 were cohort studies20, 33, 1 was a small cross-sectional study (n=7)18 and 1 was a retrospective 4-centre clinical study (n=37)40. The cross-sectional study was published without peer-review18. Only one study met our definition of “high quality”33.

Sixteen of the studies were conducted in China, where the virus was first reported19, 21, 22, 25, 27, 29, 30, 32, 34-41. Three were conducted in Italy18, whilst 1 study was conducted in each of Iran18, Peru16, Portugal31, Republic of Korea28, Sweden26 and USA24. One paper was a multi-centre cohort study conducted in 24 different countries, led by a centre in the UK33.

Risk of Bias (Quality) Assessment

CARE Quality assessment scores ranged from 7 to 26 (out of 36) for the case reports
and case series STROBE scores ranged from 10 to 33 (out of 34) for the observational studies (Table 2). A full breakdown of scores for each study is provided in Supplementary Tables S6 and S7. Due to the limited sample sizes of the included studies, the heterogeneity in surgeries performed and approaches to perioperative management, and the inherent lack of comparative groups in the case reports, it was not possible to conduct a meta-analysis to estimate effect sizes and we could not quantitatively assess risk of bias across studies.

COVID-19 status

Diagnosis of COVID-19, and timing of diagnosis (relative to surgical procedure) were variably reported, applying a range of diagnostic criteria. Suspected COVID-19 was usually based on relevant symptoms. All of the studies used RT-PCR for SARS-CoV-2 RNA or chest CT scans for diagnosis (though 1 study did not report diagnostic criteria). Four studies used RT-PCR only, 2 studies used CT scans only, and 19 studies used a combination of both. In some places RT-PCR was not available. Specimens used for RT-PCR included nasopharyngeal, oropharyngeal, sputum, tracheal tube tip and bronchoalveolar lavage. Although not fully reported in all studies, RT-PCR tests were negative in some cases despite CT findings (and in some cases, symptoms) being indicative of COVID-19.

Perioperative management

The total number of surgical procedures reported in the included studies was 1,370, including gastrointestinal/abdominal (n=393), orthopaedic (n=352), obstetric/gynaecological (n=166), cardiothoracic/vascular (n=146), hepatobiliary (n=62), neurosurgical (n=47), head and neck (n=40), urological (n=37), other surgeries (n=63) and missing details (n=64). The schedule of the surgeries, where reported, were classed as elective (n=316), and urgent, or emergency (n=949). At least 153/166 of
the obstetric/gynaecological surgeries were Caesarean sections. Most of the other surgeries were for cancer or trauma (Supplementary Table S8).

Most studies reported surgical procedures performed under neuraxial anaesthesia (Table 3). Ten reported procedures (53 Caesarean sections, 17 orthopaedic) using neuraxial anaesthesia only \(^{17, 22, 26, 28, 30, 31, 34, 36, 37, 41}\) and 3 reported procedures (5 aortic dissections and 1 Caesarean section) using general anaesthesia only \(^{16, 24, 27}\), whilst 6 reported a mix of surgeries performed using either general or neuraxial anaesthesia \(^{19, 20, 32, 33, 35, 40}\). When reported, spinal, epidural or a combination of the 2 methods were used. Exact details of which anaesthetics and analgesics were used were only reported in 5 of the 26 studies \(^{19, 28, 34, 37, 41}\). It is not clear whether there were any changes from standard anaesthetic/analgesic practice because of COVID-19.

Use of Personal Protective Equipment (PPE) and infection reduction strategies

Patient use of PPE was poorly reported, with only 9 studies stating that patients wore any protection \(^{19, 21-23, 28, 29, 35, 38, 39}\). Six of these reported the use of surgical masks only \(^{19, 21, 22, 28, 35, 38}\), with N95 masks being more specifically mentioned in 3 studies \(^{21, 22, 28}\). HCW use of PPE was more comprehensively reported, with 16 studies describing its perioperative use \(^{19, 22-31, 35-38, 41}\). The reported type of PPE used by HCWs was wide-ranging with N95 mask, disposable surgical cap, medical goggles or positive-pressure headgear, and disposable protective clothing, gloves and shoes/shoe covers described. However, details on duration of PPE use, and at what points during the perioperative period (e.g. only during intubation/aerosol generating procedures) were lacking.

Nine of the studies in our review reported using operating rooms with negative pressure \(^{19, 21, 22, 24, 28, 29, 35, 36, 38}\). Only 1 of these studies also described the postoperative care of a patient in a negative pressure ICU \(^{24}\), although 2 studies described sending neonates to negative-pressure wards immediately after birth \(^{29, 31}\).
However details on other elements of ventilation such as air changes per hour, direction and filtration were lacking.

Twelve of the studies describing Caesarean sections reported immediate separation of the neonates from their mothers following delivery, aiming to reduce risks of postpartum infection. Eight of these were conducted in China\textsuperscript{19, 21, 30, 34-36, 38, 39}, while the other 4 were conducted in Italy\textsuperscript{23}, Portugal\textsuperscript{31}, Peru\textsuperscript{16}, and the Republic of Korea\textsuperscript{28}.

Three studies reported on the decontamination of the anaesthesia machine following surgery\textsuperscript{19, 24, 40}, with two of the studies reporting no HCW infection with COVID-19\textsuperscript{19, 24} (the third study did not report HCW COVID-19 status\textsuperscript{40}). A further study reported the discarding of disposable anaesthetic devices after single use\textsuperscript{27}.

Patient outcomes

Patient outcomes reported included length of hospital stay, requirement for critical care, level of respiratory support and respiratory complications, discharge status, and mortality (Supplementary Table S9). None of the included studies reported on all these outcomes. Reporting on discharge status was very limited. Twelve studies reported length of stay in hospital, which ranged from 5 to 52 days\textsuperscript{18-20, 22, 25, 26, 28-31, 33, 35}.

In the largest cohort study (n=1,128), the median length of stay in hospital (IQR) was 10 days (3-27) for minor surgery and 17 days (8-29) for major surgery, reported in a total of 1,083 patients\textsuperscript{33}. This study reported an overall 30-day mortality of 23.8%, with a higher rate of mortality in patients undergoing elective surgery where the presence of SARS-CoV-2 virus had been confirmed postoperatively rather than preoperatively (20.4% vs 9.1%). A number of patient factors were found to be associated with higher 30-day mortality including male sex (odds ratio [OR] = 1.75, 95% confidence interval [CI] = 1.28-1.40), emergency surgery (OR = 1.67, 95% CI = 1.06-2.63), major surgery (OR = 1.52, 95% CI = 1.01-2.31), older age (>70 years) (OR = 2.30, 95% CI = 1.65-3.22), poorer preoperative condition as assessed by American Society of Anesthesiologists’ physical status classification (OR = 2.35, 95% CI =
1.57-3.53) and undergoing surgery for malignancy (OR = 1.55, 95% CI = 1.01-2.39).

Pulmonary complications, defined as pneumonia, acute respiratory distress syndrome or unexpected postoperative ventilation, occurred in 51.2% of patients with COVID-19, and was associated with increased mortality compared to those who did not develop complications (38.0% vs 8.7%).

Postoperative use of ICU was poorly reported and where it was reported (9 studies)\textsuperscript{18, 20, 22-25, 27, 32, 33}, it was not always clear whether the patients had been transferred there due to COVID-19, or whether they would have been transferred there anyway because of the indication for surgery\textsuperscript{27}. Postoperative respiratory support was described in 10 studies\textsuperscript{17, 18, 20, 23, 24, 26, 27, 31, 33, 37}, but as with ICU use it was not clear in some papers whether this would have occurred anyway. Postoperative use of analgesia was only reported in 3 studies\textsuperscript{17, 28, 37}, with only 1 reporting any formal pain assessment\textsuperscript{19}.

Reporting of outcomes in neonates was more consistent, with 16 studies (out of 19 studies involving obstetric surgeries) reporting COVID-19 status\textsuperscript{16, 19, 21-23, 26, 28-31, 34-39} and 12 of those studies reporting only negative test results, mainly for RT-PCR\textsuperscript{19, 21, 22, 26, 28-31, 34-38}. Of the other 4 studies, 2 reported only positive tests\textsuperscript{23, 39} and 2 reported a mix of positive and negative results\textsuperscript{16, 35}. Apgar scores were reported in 14 studies (of the 19 involving obstetric surgeries), and these were generally very good or excellent\textsuperscript{16, 19, 21-23, 26, 28, 30, 31, 34-38}. No neonatal mortalities were reported in any of the studies.

Healthcare worker outcomes

Most of the studies reported outcomes within a few days to 2 weeks after surgery. HCW COVID-19 outcomes were only reported in 10 studies\textsuperscript{19, 22-24, 28, 30, 32, 35, 37, 41}. One of these, a case series of 49 patients including outcomes from 44 anaesthetists, reported 5 anaesthetists testing positive for SARS-CoV-2 on RT-PCR testing, following delivery of spinal anaesthesia during Caesarean section or orthopaedic surgery\textsuperscript{41}. One of the 5 anaesthetists testing positive for SARS-CoV-2 had worn level 3 PPE (2.7%
of all who wore level 3 PPE), while 4 of them had worn level 1 PPE (57.1% of all who wore level 1 PPE), suggesting better HCW protection with level 3 PPE. This also appears to be supported by 8 of the other 9 studies where no HCW SARS-CoV-2 infections were reported when using PPE. Three of these studies reported level 3 PPE, 1 reported biosafety level 3, and 4 studies described PPE in detail including N95 mask, eye goggles, face shield and surgical gown. However we can only make tentative recommendations on the use of PPE as it was not clearly reported how long the PPE was worn before, during and/or after the surgery and whether any changes were made to the level of PPE worn at any stage (for example following intubation/extubation of the patient). Furthermore, we cannot be sure that HCW infection occurred as a result of caring for patients with COVID-19 rather than other sources such as infected colleagues or in the wider community.

II. Cohort Study

Patient characteristics

Between 23rd January 2020 and 31st March 2020, 166 parturients underwent Caesarean section and were included in this study. Before surgery, 2 patients were confirmed to be infected with SARS-CoV-2 and 36 patients were considered as suspected cases based on the above criteria (Box 1). After surgery, 5 suspected cases were confirmed and 11 suspected cases were ruled out. Finally, 7 confirmed cases and 20 suspected cases of COVID-19 were identified. One case report and 5 patients (patient 1, 4, 5, 6 and 7) from a case series were reported previously by others. The other 2 patients (patient 2 and 3) in the case series undergoing caesarean section between 1st January, 2020 and 23rd January, 2020 were not included in the current study. All 20 suspected cases had imaging features of COVID-19. They were tested with RT-PCR only before discharge and the results were negative. For analysis, we combined these suspected cases and confirmed cases as 1 group (n=27) and patients not (suspected to be) infected with COVID-19 as a second
‘negative’ group (n=139). As shown in Supplementary Table 10, the BMI of suspected
or confirmed patients was higher than that of negative patients (P = 0.034). Symptoms associated with COVID-19 occurred only in suspected or confirmed
patients; fever was the commonest with an incidence of 44.4%, followed by cough
(14.8%) and diarrhoea (3.7%).

Laboratory findings of patients before and after Caesarean section are summarised in
Supplementary Table 11. Compared with baseline pre-procedural values, increased
leukocyte and neutrophil counts were observed after surgery in all patients. Compared with negative patients, suspected or confirmed patients had lower
leukocyte (P = 0.003 before surgery; P = 0.047 after surgery) and lymphocyte (P =
0.030 before surgery; P = 0.041 after surgery) counts during the perioperative period.
Baseline preprocedural C-reactive protein levels in confirmed or suspected patients
were higher than negative patients (P = 0.014), but were not difference from
postsurgical levels. In negative patients, there were significantly elevated levels of
CRP (P = 0.006) and D-dimer (P = 0.011) after surgery compared with baseline
preprocedural values.

Characteristics of anaesthesia and surgery
An overview of parturients’ intraoperative characteristics is shown in Supplementary
Table 10. Regional anaesthesia was the commonest type of anaesthesia and was
performed in 142 (85.5%). Duration of operation in suspected or confirmed patients
was longer than that in negative patients (P = 0.003). However, there were no
significant differences in blood loss, fluid management, or use of vasoactive drugs
and flurbiprofen.

Maternal and fetal outcomes
As listed in Supplementary Table 10, 48.8% of patients received diclofenac and/or
dezocine for postoperative pain. There was no significant difference between
suspected or confirmed patients and negative patients. Both the duration of oxygen
therapy (P < 0.001) and length of hospital stay (P < 0.001) were significantly longer in suspected or confirmed patients than negative patients. No suspected or confirmed patients developed severe pneumonia or received non-invasive or invasive mechanical ventilation. However, a negative patient with liver cancer was intubated and died due to pulmonary embolism after surgery.

The medians of Apgar scores were 8 at 1 minute and 9 at 5 minutes. There were no apparent differences in the neonates when comparing the suspected or confirmed group with the negative group. In the negative group, a neonate delivered at 25 weeks' gestation died 10 min after birth. In the confirmed group, a neonatal COVID-19 infection with positive results of RT-PCR assay on pharyngeal swabs was reported 36 hours after birth, and this had been reported in a previous study. However, the results of nucleic acid tests for SARS-CoV-2 on placenta specimens, cord blood and mother's breast milk in this mother–neonate dyad were all negative.

Postoperative evaluation of healthcare workers

A total of 262 HCWs including 71 anaesthetists, 60 obstetricians and 131 nurses (circulating nurses, instrument nurses and neonatal nurses) were involved in these Caesarean sections. Level 3 PPE was used by all the HCWs during the operation. None of them reported COVID-19 related symptoms during the COVID-19 pandemic.

As of 15th April, 2020, none of them has been infected with the SARS-CoV-2 according to the CT scan findings, RT-PCR testing and/or SARS-CoV-2 antibodies testing.
Discussion

Our rapid literature review identified 26 studies reporting perioperative management of patients with suspected or confirmed COVID-19. To our knowledge this is the most comprehensive such review to date. Most studies were low quality case reports/series with low sample size, and even amongst the observational studies, perioperative management was not necessarily the main focus of any quantitative analysis conducted\textsuperscript{20,33} and was poorly reported\textsuperscript{18}. Thus, a cohort study of Caesarean sections, especially focusing on perioperative management and patients and HCW outcomes, was performed to augment the included evidence base.

All studies included in the review used either RT-PCR or CT scans to diagnose SARS-CoV-2/COVID-19. This approach appears to be supported by the fact that RT-PCR testing did not always produce positive results, despite the presence of relevant clinical symptoms and the elimination of other viruses or comorbidities that could potentially explain those symptoms. In our cohort study, only 5 out of 27 participants with suspected or confirmed COVID-19 were positive for SARS-CoV-2 by RT-PCR. The wider literature has also reported uncertainty in diagnostic performance of RT-PCR\textsuperscript{42} and when compared to CT scans their sensitivity ranges from 50-81\%\textsuperscript{43-45}.

The use of CT scans does need to be balanced against the extra risk of exposing patients to radiation, particularly for women undergoing Caesarean section whose fetus will also be exposed\textsuperscript{46}. This is an area that requires further investigation, but consideration should be given to using both approaches in diagnosing COVID-19.

The timing of COVID-19 testing also needs to be considered since higher mortality was reported in patients undergoing elective surgery where the presence of SARS-CoV-2 virus has been confirmed postoperatively rather than preoperatively (20.4\% vs 9.1\%)\textsuperscript{33}. Performing tests preoperatively will enable informed decisions about the postponement of surgeries to be made for patients who test positive and are thus at increased risk of postoperative complications. There may also be requirements to ensure appropriate levels of care, such as facilities or staffing, are...
available for the postoperative period should complications arise. COVID-19 testing may also influence ICU admissions and transmission to HCWs\textsuperscript{47-49}. This further suggests that testing for possible SARS-CoV-2 infection should take place before surgery, as supported by The American Society of Anesthesiologists and Anesthesia Patient Safety Foundation joint guidelines\textsuperscript{50}. However this might be difficult for emergency surgery, therefore a standardised diagnosis and treatment protocol for emergency patients should be developed. This is already happening in some places and whilst pre-operative screening will potentially increase the time between admission and surgery, initial evidence suggests that this risk can be minimised to the point that it can be balanced against the potential risk of performing surgical procedures in COVID-19 patients\textsuperscript{51}. Further research is needed to establish whether the testing pathway is of more clinical benefit than not having it. In patients with suspected or confirmed COVID-19, the COVID-19 status of newborns should also be taken into account where relevant, and testing should be performed as soon as possible after delivery to help prevent transmission to HCWs and to ensure risk to the newborn is minimised, with early recognition and management of symptoms.

Despite being included in perioperative anaesthesiology guidelines for HCWs in both America and China\textsuperscript{3, 50}, PPE use was poorly reported by studies in patients (9 studies)\textsuperscript{19, 21-23, 28, 29, 35, 38, 39}. Current guidance in the UK is that anyone with suspected or confirmed COVID-19 should wear a surgical face mask in clinical areas, communal waiting areas and during transportation as long as this does not compromise their clinical care\textsuperscript{52}. In tuberculosis patients, the use of surgical facemasks has been shown to confer a 56% decreased risk of transmission compared to those not wearing a mask\textsuperscript{53}. Furthermore, a literature review of studies analysing the effectiveness of respiratory protection for healthcare workers against infectious diseases found that guidelines were consistent in recommending at least an N95 respirator for care of patients with tuberculosis\textsuperscript{54}. Despite this, there is currently no evidence that patient use of face masks reduces risk of COVID-19 transmission to HCWs, despite these studies not reporting any HCW infections\textsuperscript{19, 21-23, 28, 29, 35, 38, 39}. Better reporting was
observed relating to HCWs themselves. A recent study has demonstrated the
effectiveness of HCWs wearing PPE in preventing COVID-19 infection and advocated
its continued use in the absence of a vaccine\textsuperscript{55}. In our cohort study, none of the 262
HCWs developed COVID-19, suggesting that both regional and general anaesthesia
can be delivered safely to patients with COVID-19, when surgical or N95 masks are
applied in patients and level 3 PPE is used by HCWs during the perioperative period.
The use of aprons, sterile fluid resistant disposable gown, sterile gloves, fluid
resistant surgical masks and eye protection is recommended in the UK for Caesarean
sections\textsuperscript{56}. However, high level PPE is difficult to work in. For this reason it is
important that future studies report on the duration of PPE use, whether they were
used at particular points in the surgical process as some procedures are considered
particularly high risk of airborne transmission and what levels constitute safe use\textsuperscript{57}. It
is also important to establish when PPE use is not necessary, to prevent wastage.
Until these questions are addressed, HCWs should continue to use level 3 PPE during
the perioperative period for all untested, suspected or confirmed cases of COVID-19
during times of pandemic and local outbreak\textsuperscript{55}.

Although this was not analysed directly with respect to postoperative outcomes, we
found that 9 of the studies reported conducting surgical procedures in negative
pressure operating rooms\textsuperscript{19, 21, 22, 24, 28, 29, 35, 36, 38}. Negative pressure rooms are
commonly used in infection control and ensure that air continually flows into the
room, rather than the surrounding area. However, most hospitals only have a limited
number of negative pressure operating rooms and therefore have to adapt additional
rooms for this purpose. As current recommendations on minimum environmental
ventilation requirements are based on previous non-COVID-19 work, further analysis
and reporting on ventilation characteristics is required\textsuperscript{3}.

We identified 12 studies reporting the separation of neonates from mothers
following Caesarean section\textsuperscript{16, 19, 21, 23, 28, 30, 31, 34-36, 38, 39}. In our cohort study, newborns
of mothers with suspected or confirmed COVID-19 were also transferred to an
isolated observation ward after birth. At least in China, where 9 of those studies were
conducted, this represents a significant change from standard practice where
normally mother and child skin-to-skin contact is encouraged, with recognised
neurobiological benefits for mother and neonate. Although a newborn whose
mother was confirmed with COVID-19 tested positive 36 hours after birth in our
cohort study, whether the case was a contact transmission or a vertical transmission
remains to be confirmed. Since the remaining studies did not accurately report level
of mother and child contact, it is not possible to determine whether separation
decreases the risk of SARS-CoV-2 infection. Emerging data suggest that allowing
neonates to room in with their mothers and breastfeed confers low risk of perinatal
and vertical transmission when a face mask is worn and proper hygiene is observed.58
Because of these clinical implications and the potential impact on maternal-neonate
interaction, this area requires urgent investigation.

A large cohort study identified patient and surgical factors associated with 30-day
mortality. This multi-centre study is easily the largest study of postoperative
outcomes in patients with COVID-19 and because of the size and quality of the
analysis, it is the only study from which we can make strong conclusions. Consequently, future studies should consider longer-term reporting of health
outcomes.

Previous studies found low mortality rates (1%) and requirement for respiratory
support (10%) amongst pregnant women with COVID-19, as well as low neonatal
transmission (5%), which our study supported. However, the duration of
operation, oxygen therapy and length of hospital stay were significantly longer in
suspected or confirmed patients than negative patients. An optimal approach to
perioperative management in COVID-19 patients including appropriate use of
anaesthetics and analgesics needs to be determined in future studies.

**Strengths and Limitations**

A major strength of the rapid review approach is the ability to quickly synthesise
relevant original articles and identify current perioperative practices that are
associated with favourable postoperative outcomes. This has already enabled us to
make early clinical recommendations (Box 2) on the perioperative management of
COVID-19 to the Scottish Government, via the Scottish Intercollegiate Guidelines
Network (SIGN), which can be disseminated to policymakers and HCWs and inform
future perioperative practice (Roberta James, SIGN Programme Lead, personal
communication, 2020). Because COVID-19 is a new and developing disease, hospital
departments are having to adapt quickly to ensure optimum care and they rely on
quick and accurate clinical guidance on how to provide this. However, many hospitals
are not set up to conduct rapid research involving data collection, particularly during
a global pandemic, and consequently there are gaps in reporting that this review has
identified. A possible solution to this is to implement electronic health (eHealth)
recording of patient data to ensure automated availability of relevant items of
interest.

Converse to the rapid synthesis of the current literature, the short period of time that
COVID-19 has been in existence, relative to other infectious diseases, means that
there has not been enough time for many large and comprehensive cohort studies to
be published and therefore the majority of studies included in this review are case
reports and series. This means that the clinical implications of these studies should
be treated with caution until further robust studies are published, preferably in the
form of RCTs such as the Randomised Evaluation Of COVID-19 Therapy (RECOVERY)
Trial (https://www.recoverytrial.net/). The rapid nature of this review means that more recently published articles may have
been missed, though we mitigated this risk by conducting a further (targeted)
literature search prior to submission. Excluding those not in English is pertinent given
the global status of the COVID-19 pandemic. We also had to exclude 2 studies from
Tongji Hospital in Wuhan as some of the participants were also included in the cohort
study for this paper.
Conclusions

From this rapid literature review and cohort study, we can make early clinical and research recommendations around the perioperative management of patients with suspected or confirmed COVID-19. These are presented in Box 2 and include timing of COVID-19 testing prior to surgery, more detailed reporting of patients’ and HCWs’ use of PPE, more detailed reporting of the perioperative use of anaesthesia and analgesia, and research into the longer term consequences of COVID-19. Together it is anticipated that these recommendations will contribute to improved postoperative outcomes for both patients with COVID-19 and HCWs treating those patients.
1. **Details of Author Contributions**

2. Study conception and design: HZ, WM, BHS, JH and LAC

3. Data acquisition: HZ, JY, ZZ, XZ, AL, LW, WZ, HLH and AC

4. Data analysis and interpretation: all authors

5. Drafting the article and revising for important intellectual content: all authors

6. Final approval of the published version: all authors.

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9. **Declaration of Interests**

10. The authors declare that they have no conflict of interest.

11. **Funding**

12. This work was partly supported by the University of Dundee Global Challenges Research Fund.
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12 Zamboni K, Baker U, Tyagi M, Schellenberg J, Hill Z, Hanson C. How and under what circumstances do quality improvement collaboratives lead to better outcomes?


EClinicalMedicine 2020; 21: 100331


56 ICM Anaesthesia COVID-19. Updated advice regarding PPE to be worn when managing pregnant women with known or suspected COVID-19. 2020. Available from https://static1.squarespace.com/static/5e6613a1dc75b87df82b78e1/t/5e96d79ef01cf06d99c34920/1586943905918/OAA-PPE-infographic_11.04.20.pdf (accessed 14 July 2020)


60 Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ* 2020; **369**: m2107

Figure 1 - PRISMA flow diagram for the identification and screening of articles for inclusion in the review
<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Patients with confirmed or suspected COVID-19 who have undergone surgery or</td>
<td>1. Unpublished studies, conference abstracts and research theses or dissertations</td>
</tr>
<tr>
<td>healthcare workers who have treated surgical patients with confirmed or suspected</td>
<td></td>
</tr>
<tr>
<td>COVID-19</td>
<td></td>
</tr>
<tr>
<td>2. Observational studies including case reports, case series, case-control,</td>
<td>2. Studies that do not provide any perioperative management details (defined as</td>
</tr>
<tr>
<td>cross-sectional, cohort and randomised control trials.</td>
<td>the time from when the decision to operate was made to 24 hours after surgery).</td>
</tr>
<tr>
<td>3. Written in English</td>
<td></td>
</tr>
<tr>
<td>3. Studies where the patients are not suspected of or confirmed as having COVID-19</td>
<td></td>
</tr>
<tr>
<td>4. Studies that do not report patients that have undergone surgery separately</td>
<td></td>
</tr>
<tr>
<td>from those that have not undergone surgery.</td>
<td></td>
</tr>
<tr>
<td>5. Studies reporting surgery only conducted to treat COVID-19</td>
<td></td>
</tr>
<tr>
<td>6. Studies\textsuperscript{13,14} that included participants that have also been</td>
<td></td>
</tr>
<tr>
<td>included in the cohort study of this paper.</td>
<td></td>
</tr>
</tbody>
</table>

COVID-19, Coronavirus disease 2019
<table>
<thead>
<tr>
<th>Authors</th>
<th>Date of Publication</th>
<th>Country</th>
<th>Study Design</th>
<th>Surgery</th>
<th>Method of Suspecting/Diagnosing COVID-19 in Patient(s)</th>
<th>Sample Size</th>
<th>STROBE/CARE core (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzamora et al.</td>
<td>18/04/2020</td>
<td>Peru</td>
<td>Case report</td>
<td>Caesarean section</td>
<td>Nasopharyngeal RT-PCR, CT scan</td>
<td>1</td>
<td>22 (61%)</td>
</tr>
<tr>
<td>Catellani et al.</td>
<td>30/04/2020</td>
<td>Italy</td>
<td>Case series</td>
<td>Orthopaedic</td>
<td>Oropharyngeal RT-PCR, thoracic CT scan</td>
<td>16 (13 underwent surgery)</td>
<td>21 (58%)</td>
</tr>
<tr>
<td>Chehrassan et al.</td>
<td>14/04/2020</td>
<td>Iran</td>
<td>Cross-sectional</td>
<td>5 Orthopaedic, 1 abdominal</td>
<td>High resolution CT scan</td>
<td>7 (6 underwent surgery)</td>
<td>12 (37%)</td>
</tr>
<tr>
<td>Chen et al.</td>
<td>16/03/2020</td>
<td>China</td>
<td>Case series</td>
<td>Caesarean section</td>
<td>Nasal RT-PCR, chest CT Scan</td>
<td>17</td>
<td>22 (61%)</td>
</tr>
<tr>
<td>Doglietto et al.</td>
<td>12/06/2020</td>
<td>Italy</td>
<td>Cohort</td>
<td>22 Orthopaedic, 7 vascular, 6 neurological, 5 general, 1 thoracic</td>
<td>Nasopharyngeal RT-PCR, chest CT scan, chest radiography</td>
<td>41</td>
<td>26 (76%)</td>
</tr>
<tr>
<td>Dong et al.</td>
<td>26/03/2020</td>
<td>China</td>
<td>Case report</td>
<td>Caesarean section</td>
<td>Nasopharyngeal RT-PCR, chest CT scan</td>
<td>1</td>
<td>18 (50%)</td>
</tr>
<tr>
<td>Du et al.</td>
<td>19/05/2020</td>
<td>China</td>
<td>Case report</td>
<td>Caesarean section</td>
<td>Pharyngeal RT-PCR, CT scan</td>
<td>1</td>
<td>18 (50%)</td>
</tr>
<tr>
<td>Ferrazzi et</td>
<td>27/04/2020</td>
<td>Italy</td>
<td>Case series</td>
<td>Caesarean section</td>
<td>Throat swab RT-PCR</td>
<td>42 (18)</td>
<td>19 (52%)</td>
</tr>
<tr>
<td>Name</td>
<td>Date</td>
<td>Country</td>
<td>Study Type</td>
<td>Procedure</td>
<td>Test(s) Description</td>
<td>Cases</td>
<td>Positive Cases</td>
</tr>
<tr>
<td>------</td>
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<td>------------</td>
<td>-----------</td>
<td>---------------------</td>
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</tr>
<tr>
<td>Firstenberg et al.</td>
<td>19/04/2020</td>
<td>USA</td>
<td>Case report</td>
<td>Cardiothoracic CT scan</td>
<td>CT scan (preoperatively), RT-PCT (postoperatively, not explicitly stated)</td>
<td>1</td>
<td>25 (69%)</td>
</tr>
<tr>
<td>Gao et al.</td>
<td>18/04/2020</td>
<td>China</td>
<td>Case series</td>
<td>Abdominal Chest CT scan and radiography</td>
<td>Chest CT scan and radiography (preoperatively), oropharyngeal RT-PCR (postoperatively)</td>
<td>4</td>
<td>17 (47%)</td>
</tr>
<tr>
<td>Gidlöf et al.</td>
<td>06/04/2020</td>
<td>Sweden</td>
<td>Case report</td>
<td>Caesarean section Nasopharyngeal RNA test</td>
<td>Nasopharyngeal RNA test</td>
<td>1</td>
<td>15 (41%)</td>
</tr>
<tr>
<td>He et al.</td>
<td>21/03/2020</td>
<td>China</td>
<td>Case series</td>
<td>Cardiothoracic CT scan and clinical symptoms</td>
<td>CT scan and clinical symptoms</td>
<td>4</td>
<td>13 (36%)</td>
</tr>
<tr>
<td>Lee et al.</td>
<td>31/03/2020</td>
<td>Republic of Korea</td>
<td>Case report</td>
<td>Caesarean section Sputum and nasopharyngeal RT-PCR, chest CT-Scan and chest radiography</td>
<td>Sputum and nasopharyngeal RT-PCR, chest CT-Scan and chest radiography</td>
<td>1</td>
<td>21 (58%)</td>
</tr>
<tr>
<td>Li et al.</td>
<td>2020, exact data unclear</td>
<td>China</td>
<td>Case report</td>
<td>Caesarean section RT-PCR (not explicitly stated) of sputum sample</td>
<td>RT-PCR (not explicitly stated) of sputum sample</td>
<td>1</td>
<td>20 (55%)</td>
</tr>
<tr>
<td>Lu et al.</td>
<td>24/04/2020</td>
<td>China</td>
<td>Case report</td>
<td>Caesarean section Throat swab RT-PCR, chest CT-scan</td>
<td>Throat swab RT-PCR, chest CT-scan</td>
<td>1</td>
<td>24 (66%)</td>
</tr>
<tr>
<td>Lyra et al.</td>
<td>20/04/2020</td>
<td>Portugal</td>
<td>Case report</td>
<td>Caesarean section Nasopharyngeal and oropharyngeal RT-PCR</td>
<td>Nasopharyngeal and oropharyngeal RT-PCR</td>
<td>1</td>
<td>18 (50%)</td>
</tr>
<tr>
<td>Mi et al.</td>
<td>09/06/2020</td>
<td>China</td>
<td>Case series</td>
<td>Not reported</td>
<td>Not reported</td>
<td>28</td>
<td>7 (19%)</td>
</tr>
<tr>
<td>Reference</td>
<td>Date</td>
<td>Country</td>
<td>Study Design</td>
<td>Procedure</td>
<td>Results</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
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<td>---------</td>
<td>--------------</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Nepogodiev et al.</td>
<td>29/05/2020</td>
<td>24 countries (led by UK)</td>
<td>Cohort</td>
<td>373 gastrointestinal and general, 302 orthopaedic, 86 cardiothoracic, 62 hepatobiliary, 51 obstetric, 45 vascular, 40 head and neck, 39 neurosurgery, 37 urological, 57 other and 36 missing</td>
<td>Nasal swab or bronchoalveolar lavage RT-PCR, relevant clinical symptoms (including cough, fever or myalgia), or radiological findings (thorax CT)</td>
<td>1128</td>
<td>33 (97%)</td>
</tr>
<tr>
<td>Song et al.</td>
<td>26/02/2020</td>
<td>China</td>
<td>Case report</td>
<td>Caesarean section</td>
<td>Throat and faecal RT-PCR, chest CT scan</td>
<td>1</td>
<td>22 (61%)</td>
</tr>
<tr>
<td>Sun et al.</td>
<td>28/04/2020</td>
<td>China</td>
<td>Case series</td>
<td>Caesarean section</td>
<td>Pharyngeal, laryngeal, throat and tracheal tube tip RT-PCR</td>
<td>3</td>
<td>18 (50%)</td>
</tr>
<tr>
<td>Wang et al.</td>
<td>28/02/2020</td>
<td>China</td>
<td>Case report</td>
<td>Caesarean section</td>
<td>Throat swab RT-PCR, chest CT scan</td>
<td>1</td>
<td>21 (58%)</td>
</tr>
<tr>
<td>Xia et al.</td>
<td>17/03/2020</td>
<td>China</td>
<td>Case report</td>
<td>Caesarean section</td>
<td>Oropharyngeal RT-PCR, chest CT-scan</td>
<td>1</td>
<td>14 (38%)</td>
</tr>
<tr>
<td>Zeng et al.</td>
<td>26/03/2020</td>
<td>China</td>
<td>Case series</td>
<td>Caesarean section</td>
<td>Symptoms, chest CT scan and RT-PCR</td>
<td>6</td>
<td>9 (25%)</td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>08/04/2020</td>
<td>China</td>
<td>Case series</td>
<td>Caesarean section</td>
<td>Suspected: Abnormal CT scan (ground-glass opacity and</td>
<td>4</td>
<td>17 (47%)</td>
</tr>
</tbody>
</table>
bilateral patchy shadowing),
coupled with typical clinical
symptoms (fever, cough,
headache, sore throat,
shortness of breath), sputum.
Confirmed: Nasopharyngeal
RT-PCR

<table>
<thead>
<tr>
<th>Study</th>
<th>Date</th>
<th>Country</th>
<th>Study Type</th>
<th>Inclusion Criteria</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhao et al. 40</td>
<td>18/03/2020</td>
<td>China</td>
<td>Clinical study</td>
<td>10 abdominal, 2 cardiovascular, 6 orthopaedic, 11 gynaecology and obstetrics, 2 neurosurgery and 6 other</td>
<td>Laboratory, imaging (CT-scan) and clinical findings (body temperature) 37 10 (29%)</td>
</tr>
<tr>
<td>Zhong et al. 41</td>
<td>28/03/2020</td>
<td>China</td>
<td>Case series</td>
<td>45 Caesarean section, 4 orthopaedic</td>
<td>Radiology for inclusion in study, confirmation through throat swab RT-PCR 49 26 (72%)</td>
</tr>
</tbody>
</table>

CARE, CAse REport; CT, computed tomography; RNA, ribonucleic acid; RT-PCR, reverse transcriptase-polymerase chain reaction; STROBE, Strengthening The Reporting of Observational Studies in Epidemiology; UK, United Kingdom; USA, United States of America.

*Details of the STROBE and CARE scores are provided in the methods section.
Table 3 – Perioperative management details of patients in the rapid review

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Surgery</th>
<th>HCW Use of PPE</th>
<th>HCW Level of PPE</th>
<th>Patient Use of PPE</th>
<th>Patient Level of PPE</th>
<th>Type of anaesthesia</th>
<th>Pain assessment</th>
<th>Analgesics used</th>
<th>Vasopressors used</th>
<th>Blood loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzamora et al. 16</td>
<td>1 Caesarean section</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>1 General</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Catellani et al. 17</td>
<td>13 Orthopaedic</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>13 spinal anaesthesia with nerve block</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Chehrassan et al. 18</td>
<td>5 Orthopaedic, 1 abdominal</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Chen et al. 19</td>
<td>17 Caesarean sections</td>
<td>Yes</td>
<td>BSL-3 (N95 masks, goggles, protective suits,</td>
<td>Yes</td>
<td>17 epidural</td>
<td>VAS</td>
<td>Epidural anaesthesia - 2% lidocaine,</td>
<td>Not reported</td>
<td>Epidural anaesthesia -</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
For Peer Review

disposable medical caps, and medical rubber gloves

0.75% ropivacaine

General anaesthesia - 8%

sevoflurane, 2% lidocaine, remifentanil, succinylcholine, zsufentanil, propofol

Doglietto et al.20 Orthopaedic, 7 vascular, 6 neurological, 5 general, 1

Not reported 21 local and 20 general anaesthesia

Mean: 300ml (SD: 100)

Doglietto et al.22 Orthopaedic, 7 vascular, 6 neurological, 5 general, 1

Not reported
<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Caesarean sections</th>
<th>PPE Level</th>
<th>N95 Mask</th>
<th>Combined Spinal and Epidural Anaesthesia</th>
<th>PPE Reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dong et al.²¹</td>
<td>Thoracic</td>
<td>1</td>
<td>Not reported</td>
<td>Yes</td>
<td>N95 mask</td>
<td>Not reported</td>
</tr>
<tr>
<td>Du et al.²²</td>
<td>Thoracic</td>
<td>Yes</td>
<td>Level 3</td>
<td>Yes</td>
<td>N95 mask</td>
<td>Combined spinal and epidural anaesthesia</td>
</tr>
<tr>
<td>Ferrazzi et al.²³</td>
<td>Thoracic</td>
<td>18</td>
<td>Yes</td>
<td>More strict PPE than just surgical masks</td>
<td>18 More strict PPE than just surgical masks</td>
<td>Not reported</td>
</tr>
<tr>
<td>Firstenberg et al.²⁴</td>
<td>Cardiothoracic</td>
<td>1</td>
<td>Yes</td>
<td>N95 masks with face shield or goggles (in addition to</td>
<td>N95 masks with face shield or goggles (in addition to</td>
<td>General anaesthesia implied from endotracheal</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Study</th>
<th>Procedure</th>
<th>Full PPE</th>
<th>Surgical Gown</th>
<th>Surgical Cap</th>
<th>Double Gown</th>
<th>Shoe Covers</th>
<th>PAP</th>
<th>Anaesthesia</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gao et al.25</td>
<td>Abdominal</td>
<td>Yes</td>
<td>Full PPE (Level 3)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Gidlöf et al.26</td>
<td>Caesarean section</td>
<td>Yes</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Spinal</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>He et al.27</td>
<td>Cardiothoracic</td>
<td>Yes</td>
<td>Level 3</td>
<td>Not reported</td>
<td>General</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Lee et al.28</td>
<td>Caesarean section</td>
<td>Yes</td>
<td>N95 mask, surgical cap, double gown, double gloves, shoe covers, powered air-purifying</td>
<td>Yes</td>
<td>N95 mask</td>
<td>Spinal anaesthesia</td>
<td>Not reported</td>
<td>0.5% marcaine, phenylephrine 400 cc</td>
<td>(injected intrathecally)</td>
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<tr>
<td>Reference</td>
<td>Procedure Type</td>
<td>Mask Protection</td>
<td>Rash Protection</td>
<td>Gloves Protection</td>
<td>Anaesthesia Type</td>
<td>Blood Loss</td>
<td>Mortality</td>
<td>Notes</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
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<td>-----------------</td>
<td>-----------------</td>
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<td>------------</td>
<td>-----------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>Li et al.</td>
<td>Caesarean</td>
<td>Yes</td>
<td>Yes</td>
<td>Not reported</td>
<td>Not</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Lu et al.</td>
<td>Caesarean</td>
<td>Yes</td>
<td>Level 3 (gown, N95 mask, eye protection and three-layer latex gloves)</td>
<td>Not reported</td>
<td>Combined spinal and epidural anaesthesia</td>
<td>Not reported</td>
<td>Not reported</td>
<td>~200ml</td>
<td></td>
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<tr>
<td>Lyra et al.</td>
<td>Caesarean</td>
<td>Yes</td>
<td>Level 2</td>
<td>Not reported</td>
<td>Regional anaesthesia</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Mi et al.</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>21 Spinal, 3 local and 4 general anaesthesia</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Nepogodiev</td>
<td>gastrointestinal</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>30-day mortality</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
</tbody>
</table>

and general, 15 local, 32 regional, 217 general anaesthesia;
302
orthopaedic, 86
cardiothoracic, 62
hepatobiliary, 51 obstetric, 45 vascular, 40
head and neck, 39
neurosurgery, 37 urological, 57 other and
36 missing

<p>| Song et | 1 Caesarean | Unclear | Unclear | Not | Not | Combined | Not | Tramadol | Yes | 300ml |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Caesarean section(s)</th>
<th>Anaesthesia Type</th>
<th>Level of Protection</th>
<th>Pain Management</th>
<th>Volume</th>
<th>Other Notes</th>
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<tbody>
<tr>
<td>Sun et al. 35</td>
<td>3 sections</td>
<td>Yes</td>
<td>Yes</td>
<td>1 Not reported</td>
<td>1 General and 2 spinal anaesthesia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Full (N95 mask, eye goggles, face shield, top-to-bottom tight-fitting gown)</td>
<td></td>
<td>2 face masks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang et al. 36</td>
<td>1 section</td>
<td>Yes</td>
<td>Level 3</td>
<td>Not reported</td>
<td>Not reported and combined spinal and epidural anaesthesia</td>
<td></td>
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<tr>
<td>Xia et al. 37</td>
<td>1 section</td>
<td>Yes</td>
<td>Third-level measure - N95 mask (fit tested)</td>
<td>Not reported</td>
<td>Not reported and combined spinal and epidural anaesthesia</td>
<td>1% ropivacaine Intravenous methoxamine</td>
</tr>
</tbody>
</table>
disposable surgical cap, medical goggles or positive-pressure headgear, disposable protective clothing, disposable gloves, disposable shoe covers

<table>
<thead>
<tr>
<th>Zeng et al.</th>
<th>6 Caesarean sections</th>
<th>Yes</th>
<th>Protective suits and double masks</th>
<th>Yes</th>
<th>6 masks</th>
<th>Not reported</th>
<th>Not reported</th>
<th>Not reported</th>
<th>Not reported</th>
<th>Not reported</th>
<th>Not reported</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Operations Description</td>
<td>Protection Details</td>
<td>Protection Reported</td>
<td>Level 2,3 Protection</td>
<td>Level 2,3 Protection Details</td>
<td>Level 2,3 Protection Reported</td>
<td>Level 2,3 Protection Details</td>
<td>Level 2,3 Protection Reported</td>
<td>Level 2,3 Protection Details</td>
<td>Level 2,3 Protection Reported</td>
<td>Level 2,3 Protection Details</td>
<td>Level 2,3 Protection Reported</td>
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<td>-------------------------------</td>
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<td>-------------------------------</td>
</tr>
<tr>
<td>Zhang et al.(^{39})</td>
<td>4 Caesarean sections</td>
<td>Not reported</td>
<td>Yes</td>
<td>1 Level 2, 3 level 3</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Zhao et al.(^{40})</td>
<td>10 abdominal, 2 cardiovascular, 6 orthopaedic, 11 gynaecology and obstetrics, 2 neurosurgery and 6 other</td>
<td>Unclear (the study states a protocol including level 3 protective measures for operating room staff but not)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>26 General anaesthesia and 11 spinal anaesthesia</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
specified for which cases PPE was used

| Zhong et al. | 45 Caesarean sections, 4 orthopaedic | Yes | 37 Level 3 and 7 Level 1 | Not reported | Not reported | Spinal anaesthesia | Not reported | 2% Lidocaine (2ml) and 0.75% isobaric ropivacaine |

BSL, biosafety level; cc, cubic centimeter; HCW, health care worker; ml, millilitre; PPE, personal protective equipment; SD, standard deviation;

A case that has any one condition of epidemiological history and any 2 clinical manifestations is considered as a suspected case. If there is no clear epidemiological history, then suspected cases need all 3 clinical manifestations.

A. Epidemiological history

1. History of residence or travel in Wuhan and its surrounding areas, or in other communities with cases reported within 2 weeks prior to the onset of the disease;
2. History of contact with SARS-CoV-2 infected patients (positive results of nucleic acid test) within 2 weeks prior to the onset of the disease;
3. History of contact with patients with fever and/or respiratory symptoms who are from Wuhan and its surrounding areas, or from other communities with cases reported within 2 weeks prior to the onset of the disease;
4. Cluster of infections: 2 or more cases with fever and/or respiratory symptoms occurred in a small area such as home, office, and school class within 2 weeks prior to the onset of the disease.

B. Clinical manifestations

1. Fever and/or respiratory symptoms;
2. Imaging features of COVID-19: multiple patchy shadows and interstitial changes in the early phase, and then multiple ground-glass opacities, infiltration shadows or even consolidation in advanced-phase;
3. Normal or decreased leucocyte and lymphocyte count in the early stage of disease.
Box 2 – Clinical recommendations for the perioperative management of people with suspected or confirmed COVID-19 and suggestions for further research

A. Clinical Recommendations
During the perioperative period, when COVID-19 is suspected or confirmed:

1. Testing for COVID-19 should be conducted preoperatively. During a pandemic or local outbreak, all patients should be tested.
2. RT-PCR and chest CT scans (along with relevant clinical signs) should be conducted together to confirm COVID-19 diagnosis and reducing waiting times.
3. Surgeries should be conducted in negative pressure operating rooms where possible, with HCWs using Level 3 PPE and patients wearing face masks, if practical, until further evidence is available. During a pandemic or local outbreak all HCWs should use Level 3 PPE for surgeries involving untested patients.
4. Clinicians should consider relevant risk factors of increased mortality in COVID-19 patients including male gender, age >70 years, poor preoperative condition, malignancy and the urgency and extent of surgery before deciding whether to conduct surgery.
5. Strategies should be implemented to reduce the risk of postoperative respiratory complications and associated mortality (e.g. use of regional anaesthesia over general anaesthesia and postponing surgery for patients with correctable pathophysiology).
6. Clinical management should take account of the potential need for prolonged hospital stay, particularly in high risk groups.
7. Clinicians should consider the isolation of neonates immediately after birth if the mother is suspected or confirmed as having COVID-19.

B. Research recommendations
1. Optimal approach to perioperative diagnosing of COVID-19 needs to be determined, taking into account false-negative rate of RT-PCR tests.
2. There should be routine recording and reporting of specific perioperative management approaches, when COVID-19 is suspected or confirmed, including anaesthetics/analgesics used, to allow understanding of their relationships with postoperative outcomes.
3. Individual studies should provide more detailed reporting on the duration of PPE use during the perioperative period, by HCWs and patients, when COVID-19 is suspected or confirmed, and whether any changes should be made for specific procedures (e.g. intubation/extubation).
5. The length of time following COVID-19 resolution before a patient can undergo surgery, without increased risk, needs to be established.
Figure 1. PRISMA flow diagram for the identification and screening of articles for inclusion in the review

221x214mm (120 x 120 DPI)