



Perioperative Anaesthetic Management of Confirmed or Suspected COVID-19 Patients

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Abstract

The outbreak of coronavirus disease (COVID-19) that started in Wuhan, China, has spread to 210 countries, infecting 2,726,274 patients and causing 191,075 deaths by April 24, 2020, and has turned into a global threat. Although various measures have been taken to stop human-to-human transmission in many countries, health care workers are in the high-risk zone for transmission as they deliver patient care. It is evident that anaesthesiologists will keep encountering patients with confirmed or suspected COVID-19 infection who will undergo emergency surgeries. Anaesthesiologists carry a higher risk of being infected during aerosol-creating procedures, hence appropriate protective measures should be taken, both during preoperative evaluation and management anaesthesia. Anaesthesia management of patients with COVID-19 also is a challenge for anaesthesiologists as it is an infection that may affect not only the respiratory system but also other vital organs. The aims of this review are to provide prudent safety measures to protect anaesthesiologists and other health care workers in the operating theatre and recommendations or the safest anaesthesia management of patients with suspected or confirmed COVID-19 undergoing surgery.

Keywords: Anaesthesia management, COVID-19, safety

Introduction

The outbreak of coronavirus disease (COVID-19) became a global threat. Although not as deadly as other severe acute respiratory diseases (SARS) outbreaks like the SARS of 2003 and Middle East Respiratory Syndrome (MERS) of 2012, one person carrying the virus can infect up to 5.7 people whereas with MERS, the number of 'R₀' (reproductive number; a mathematical term used to define how contagious an infectious disease is) is 0.45 person only (1). The spread of COVID-19 may increase further as it has a longer asymptomatic period that can prolong up to 14 days in some cases (2). Anaesthesiologists carry a higher risk during aerosol-creating procedures, such as tracheal intubation, mask ventilation, extubation, tracheostomy, or bronchoscopy, as the transmission greatly increases with exposure to droplets as well as direct contact with secretions (3, 4).

Although elective surgeries in most centres were ceased and many surgeries postponed or cancelled, emergency and oncological surgeries are still performed in many centres as in our hospital. Hence, considering that elective surgeries will also eventually commence, safe medical practices and protocols to prevent transmission to anaesthesiologists must be established. Anaesthesia management of patients with COVID-19 is a challenge for anaesthesiologists as it is an infection that may affect not only the respiratory system but also other vital organs of the patient.

The aims of this review are to provide recommendations to protect anaesthesiologists and other health care workers in the operating theatre and for the safe anaesthesia management of patients with suspected or confirmed COVID-19 undergoing surgery.

Preoperative Evaluation and Preparation

Although the first symptom of COVID-19 infection is usually a fever and dry cough, other non-significant symptoms such as fatigue, diarrhoea, and mild myalgia are also recorded (5). In addition, the number of asymptomatic

cases who are still infectious is projected to be around 50%, complicating the perioperative period (6). Ten percent of the patients in the ICU are in dire need of mechanical ventilation owing to respiratory distress, sepsis, and multiple organ dysfunction. Severe hypoxaemia is observed usually following the 7th day of the start of the symptoms (7). The radiographic imaging is specific, especially for computerised tomography, usually with multiple small band film shadows and interstitial changes in the sub-pleural and peripheral areas that advance into ground-glass opacity and consolidations in both lungs; however, pleural effusion is rare (8).

As in most viral diseases, white blood cells decrease with an increase in neutrophils and a more evident decrease in lymphocytes in COVID-19 patients. There are studies showing mild increases in aspartate and alanine amino transferase (AST and ALT), total bilirubin, cardiac troponin levels, and a decrease in albumin (9).

Most patients with COVID-19 have high Factor VIII levels and prolonged activated partial thromboplastin time but normal prothrombin time. Increased D-dimer levels, prothrombin time, and thrombocytopenia are predictive of adverse outcome and a possible disseminated intravascular coagulation that can escalate the blood loss during surgery (10, 11).

Thromboembolic events are not rare in COVID-19 patients, including pulmonary embolism and cerebrovascular events probably because of both platelet activation and endothelial dysfunction (10, 12).

There are studies showing acute kidney disease is high in patients with COVID-19 (13) and conclude that this is probably

due to the direct cytopathic effect of the virus on kidneys. Elevated creatinine and blood urea nitrogen (BUN) levels are associated with higher mortality and morbidity (13). However, other studies showed only a mild increase in creatinine and BUN, which returned to normal levels without any therapy (14). Regardless, avoiding the use of nephrotoxic drugs and close follow-up of the creatinine levels are essential.

Patients with COVID-19 use antipyretics, antivirals, and other drugs. These drugs may affect liver and pancreas functions and increase ALT, AST, and gamma-glutamyl transferase (GGT) (15). The pre-evaluation of increases in laboratory values is important in terms of selecting the drugs that will be used for anaesthesia.

Several drugs such as chloroquine, hydroxychloroquine, atazanavir, lopinavir/ritonavir, remdesivir, favipiravir, ribavirin, azithromycin, tocilizumab, and interferon beta are used for the experimental treatment of COVID-19 for their potential benefits. Some of these drugs can interact with anaesthetics such as propofol, sevoflurane, and tramadol. Co-administration of lopinavir/ritonavir, chloroquine, hydroxychloroquine, azithromycin, and dexmedetomidine with these anaesthetics can cause cardiac arrhythmias; hence, the patients should be monitored very closely (16). Atazanavir and lopinavir/ritonavir can potentiate the effects of bupivacaine, ketamine, rocuronium, fentanyl, metamizole, tramadol, and pethidine (16). Tocilizumab can decrease the effects of bupivacaine, ketamine, fentanyl, and oxycodone (16). Favipiravir can increase the effect of paracetamol (16). Cisatracurium, succinylcholine, desflurane, isoflurane, nitrous oxide, remifentanyl, ephedrine, diclofenac, ibuprofen, and naproxen can be used safely with no significant interactions with the COVID-19 therapies mentioned above (16).

Usually, surgeons or emergency physicians are the first clinicians to inspect and record the medical history and order radiological and laboratory tests. To decrease human traffic and decrease cross contamination, it is suggested that anaesthesiologists, surgeons, infectious disease, and emergency physicians should create a protocol for the preoperative evaluation (7). First responders should be informed by the anaesthesiologist of any additional test that might be needed in specific patients, such as arterial blood gas analysis, C-reactive protein, and procalcitonin levels.

All patients admitted to the operation room should be considered infected with COVID-19 as the rate of asymptomatic patients is high. Although all patients should be screened with PCR testing prior to surgery, this might not be possible in many hospitals, and the false negativity of the test may be as high as 30% (17). Chest C/T is shown to be more sensitive to diagnose COVID-19 infection and suggested as a primary

Main Points:

- During the pandemic all patients should be presumed Covid-19 positive and should be act accordingly as anaesthesiologists carry a higher risk.
- Use of personal protection equipment during the preoperative evaluation, intraoperative and postoperative period is essential for all anaesthesiologists.
- Regional anaesthesia should be preferred over general anaesthesia wherever possible in order to minimise aerosol-generating procedures such as intubation and extubation. Rapid sequence intubation is recommended in order to minimise the spread of aerosols for general anaesthesia. A senior anaesthesiologist should perform the intubation.
- Lung-protective ventilation strategies should be followed to decrease ventilator induced injury.
- Extubation must be swift and smooth to decrease aerosol spread by coughing and bucking. Lidocaine administration, deep extubation before the airway reflexes recover, or extubating under remifentanyl or dexmedetomidine infusions are possible techniques for a smooth extubation.

method to detect the disease in epidemic areas, but it is not feasible in all patients and the radiation risk should be taken into account (18).

As mentioned before, according to the protocol between surgeons and anaesthesiologists, the information about the history and test results of the patient is already known to the anaesthesiologists, which will enable them to spend minimum face-to-face time with the patient. Thorough airway evaluation is essential even though strict infection control measures can complicate a complete examination. The protective gowns, eye protection, and other personal protective equipment (PPE) for safety may further compromise intubation. Thus, every patient should be considered to have a difficult airway.

Hypoxaemia can be evident in some patients. If the surgery cannot be postponed until the patient can be stabilised, follow-up in the intensive care unit may be necessary. As thrombocytopenia is a symptom observed in severe patients, platelet levels should be checked before the operation and if needed, thrombocyte suspensions and other blood products must be prepared (11).

Even in patients with no cardiac history, COVID-19 can present itself with cardiac arrhythmias. Furthermore, azithromycin and hydroxychloroquine used in the COVID-19 treatment, as well as anaesthetics such as propofol, sevoflurane, and tramadol, may prolong the QT interval, leading to arrhythmias in the patient (16).

In addition to routine informed consent, patients must be informed of the particular additional risks of COVID-19 such as severe respiratory disease, kidney injury, and thromboembolic events. Patients with no symptoms or negative tests should also be informed about the possibility of an infection or cross contamination although they are operated upon in another non-COVID-19 operating theatre.

Patients with suspected or confirmed COVID-19 that are going to be operated upon should be operated in a COVID-positive operation room with negative pressure. Clear and visible marking of the contaminated areas is crucial. It is essential that patients should be transferred via the shortest and the least crowded pre-designated route to decrease the number of workers coming in contact with the patient. Staff segregation and limiting the operation theatre staff are also important in terms of cross contamination (19). The patient should also wear a facemask during transport and in the operating theatre.

During the preoperative evaluation, protective measures should be taken carefully with personal protection equipment (PPE) used as needed. If the patient is a suspected or

a confirmed case, N95 respirators, eye protection, a disposable surgical cap, gowns, and double gloves should be worn. If no aerosol-producing examination is planned, non-sterile, disposable isolation gowns would be sufficient; however, surgical gowns known as the Association of the Advancement of Medical Instrumentation (AAMI) Level III gowns should be worn when an aerosol- or blood-producing intervention is probable (20).

Intraoperative Period

Although for many emergency or oncological surgeries, general anaesthesia is recommended, regional anaesthesia should be preferred over general anaesthesia wherever possible in order to minimise aerosol-generating procedures such as intubation and extubation (21). Both neuraxial anaesthesia and peripheral nerve blocks are not considered aerosol-generating procedures. Regional anaesthesia also reduces postoperative pulmonary complications, which can complicate the respiratory failure in a COVID-19 infection further. Necessary care must be taken to perform the surgery completely under regional anaesthesia and prevent transition to general anaesthesia. To prevent this transition, location, duration of surgery, and local anaesthetic dose to be used should be taken into consideration, and open communication with the surgeon is essential. It would be preferable to start with a planned general anaesthesia rather than converting to general anaesthesia during surgery when regional anaesthesia is not sufficient as risk of transmission increases with emergency or unplanned interventions. Regional anaesthesia interventions should be performed in a negative pressure operating theatre by the most experienced anaesthesiologist.

Currently, routine indications and contraindications for regional anaesthesia also apply for Covid-19-positive patients. The contraindications such as bleeding disorders must be taken into account as it is a common finding mainly in severe COVID-19 patients (22). Platelet count should be monitored before neuraxial block administration (23).

Standard monitoring suggested by the European Society of Anaesthesiology (ESA) should be used for all patients. Disposable plastic sheets can be used to wrap the screens of the monitors and most sections of the anaesthesia machines to decrease the risk of contamination by touching (20).

Deep sedation should be avoided in order to reduce the need for airway manipulations (23).

During regional anaesthesia, patients should wear surgical mask at all times even when they are receiving supplementary oxygen therapy. Self-protection of the anaesthesiologist is immensely important, and he or she must be wearing N95 respirators during the regional anaesthesia intervention.

Zhong et al. (21) showed that N95 masks are safer both for the anaesthesiologists and the patients compared to surgical masks while performing spinal anaesthesia on patients with COVID-19.

Routine aseptic techniques should be complied within neuraxial anaesthesia and peripheral block applications. Since Covid-19 virus remains viable on plastic material for a longer period of time, paper drapes should be preferred instead of plastic (24). Since virus is isolated from the cerebrospinal fluid (CSF) of patients with Covid-19 encephalitis, free flow of CSF should not be allowed during lumbar puncture (25).

Peripheral nerve blocks may be favoured over neuraxial blocks as they are safer in terms of thrombocytopenia and hypotension. For upper extremity surgeries, peripheral nerve blocks that affect the diaphragm and additional respiratory muscles should not be preferred so as to prevent respiratory depression (23), i.e., infraclavicular block or axillary block should be selected instead of supraclavicular or interscalene blocks, which can lead to phrenic nerve paralysis. At present, no suggestions are made to adjust the local anaesthetic dose in spinal anaesthesia in any patient group; however, adjuvant opioid use is not advocated (23).

Normally, execution of peripheral nerve blocks and the onset of action can be relatively time consuming. This can be considered a disadvantage compared to other anaesthesia techniques. Nevertheless, when performed by a skilled anaesthesiologist and ultrasound-guided techniques, the time needed for block performing will decrease.

Neuraxial anaesthesia is shown to be safe for Caesarean delivery in COVID-19 patients and is still the first choice of anaesthesia (26).

If general anaesthesia is indicated, rapid sequence intubation (RSI) is recommended in order to minimise the spread of aerosols. A senior anaesthesiologist should perform the intubation. The logic behind this recommendation is to shorten the duration and avoid multiple attempts of intubation. With PPE and other barriers that will be discussed later, such as plastic sheets or aerosol box, even the easiest ventilation and intubation can be hard to achieve as those measures create a reasonable ineptness in controlling the laryngoscope and endobronchial tube. Video laryngoscopes are advocated as it will both decrease the duration of the procedure and increase the distance of the anaesthesiologist from the airway. Capnography may be preferred over auscultation to confirm a successful intubation; however, auscultation should be performed to ensure bilateral equal ventilation (4). Tracheal tube cuff should be inflated immediately after intubation to seal the airway, and then ventilation may be started (4). Cuffs should be inflated until the pressure is 5 cmH₂O over plateau pressure

to disable any leaks. The second generation supraglottic airway devices may be used for unanticipated difficult airway (4). Patients with predicted difficult airway should be evaluated individually. Usually, awake fibroptic intubation is not recommended because of the high risk of aerosol generation but can be used if that is the best choice for the patient.

Preoxygenation is important before RSI. Using a well-fitting face mask, that does not allow any leaks, prevents the aerosols from scattering and hence is safer. Preoxygenation should be done with 100% oxygen at least for 5 minutes. Another method for preoxygenation that the patients may benefit from is the use of high flow nasal oxygen (HFNO) therapy to avoid desaturation during RSI (27). Contrary to popular belief, it has been shown that both oxygenation with masks and HFNO therapy share a similar risk in terms of aerosol generation (28). Novel methods are developed to protect the staff from the aerosolisation of the laryngoscopy. A see-through polycarbonate cube covering the patient's head and upper torso with two holes opened to allow the anaesthesiologist to reach through and perform the intubation by a video laryngoscope has been reported and used by many anaesthesiologists (Figure 1). The plans for the 'aerosol box' have been released by Hsien Yung Lai (29). Another method described is using see-



Figure 1. Intubation with aerosol box

through plastic covers and performing ventilation and intubation under it (Figure 2). These techniques are successful in containing aerosols; however, further complicates the performance of ventilation and intubation. However, if the patients are already hypoxaemic and cannot tolerate apnoea during RSI, they should be ventilated by the mask using either aerosol box or plastic covers to contain the aerosol generation.

'Heat and moisture exchanger filters' (HMEF) and 'high-efficiency particulate absorbing (HEPA) filters' must be used between the circuit and the mask during ventilation. Using one of those filters attached to the intubation tube's proximal end will stop aerosols from creating turbulence through the intubation tube and scatter around. Using filters on both inspiration and expiration port of the respiratory circuit may protect the anaesthesia machine from viral contamination (30).

Using a closed anaesthesia circuit and a closed airway suction system is recommended (7). If it is not possible to minimise the number of essential suction, the ventilator must be always paused before any airway disconnections (7).

In addition to using routine drugs (2 mg kg⁻¹ propofol, 1 mg kg⁻¹ rocuronium) in RSI, it is suggested that administration of intra-

venous lidocaine (1.5 mg kg⁻¹) before intubation and extubation can effectively reduce coughing (31). To suppress coughing related to opioids such as fentanyl, it is suggested that they should be given following induction but before intubation. Ensuring that the patient has full muscle relaxation is also essential as bucking due to incomplete relaxation can cause aerosolisation.

Following intubation, gloves should be taken off and a new pair should be worn. Each time contact with a secretion occurs, gloves must be changed before they contaminate the environment and hands disinfected.

The electrocautery must be in the lowest possible setting to reduce the surgical smoke, which may be a source of aerosolisation and infection as shown in studies for other viral infections (20, 32).

As viral RNA is traced in the plasma of 15% of the patients, transmission via transfusion is a possibility (30). This might be a problem in non-COVID or suspected patients undergoing surgery. Studies are needed to show the safety of transfusion, but precautions must be taken, especially by screening the blood donors' history of symptoms, such as fever, cough, and suspicious contact with infected patients (33). Transfusion must be retained if possible, using other blood salvaging methods.

An unanticipated finding of COVID-19 pneumonia is severe hypoxaemia accompanying normal or mildly decreased compliance (34). Although mild cases of COVID-19 do not show any sign of hypoxemia, severe cases fulfil the Berlin Criteria for acute respiratory distress syndrome (ARDS). As in all ARDS cases, lung-protective ventilation strategies should be followed to decrease ventilator induced injury (35). The use of low tidal volume (4-6 mL kg⁻¹ of predicted body weight) and limiting plateau pressure under 30 cmH₂O with the lowest possible PEEP settings is recommended (36). In mild cases, inhalation anaesthetics can be used to manage anaesthesia. However, in severe cases, as severe hypoxemia in compliant lungs is explained with the loss of hypoxic vasoconstriction, the use of total intravenous anaesthesia may be preferred (34).

There is no direct data concerning fluid therapy for COVID-19 patients. Restricted fluid strategy is recommended based on studies concerning sepsis and ARDS by Surviving Sepsis Campaign Guideline (36). Balanced crystalloids should be chosen over colloids (36). Norepinephrine and vasopressin can be used as vasoactive agents in shock (36). Serum lactate, skin temperature, and urine output should be monitored for adequate fluid administration for every patient individually.

Inadvertent perioperative hypothermia should be prevented. Body temperature of the patient should be monitored. The safest method to measure body temperature is using dispos-



Figure 2. Ventilation with plastic covers

able ear thermometers during surgery. Hypothermia, when combined with acidosis and coagulopathy, which can already be observed in COVID-19 patients, may worsen the patient's condition. However, forced air-warming systems should not be used as they may increase aerosol generation. Instead, warming intravenous and irrigation fluids must be preferred to achieve normothermia.

Extubation and postoperative period

Much like intubation, extubation must be swift and smooth to decrease aerosol spread by coughing and bucking. Lidocaine administration as described before, deep extubation before the airway reflexes recover, or extubating under remifentanyl or dexmedetomidine infusions are possible techniques for a smooth extubation. Aerosol box, wet gauzes covering the mouth and the nose of the patient, or clear plastic covers should be used to decrease contact with patient secretions (7).

Patients who are extubated successfully and do not need ICU should be followed in a negative pressured post-anaesthesia recovery room until they are eligible for release to the ward. During the postoperative follow-up period, both nurses and the doctors in the recovery unit should wear N95 masks, AMII level III gowns, eye protection, and head caps.

However, most patients with COVID-19 may require oxygen or ventilator support in ICU even if they are extubated. Patients with preoperative hypoxemia or respiratory distress should be taken to an isolated ICU room with negative pressure. During the transport, it is important for the patient to wear a surgical mask. Throughout the transport of intubated patients, a HMEF must be inserted between the intubation tube and a self-inflating bag.

Post-anaesthesia Infection Control Measures

The operating theatres reserved for COVID-19-positive patients must include as minimum equipment and supplies as possible. If any supply other than the anticipated ones are needed, it can be transported to the theatre by auxiliary personnel. Using disposable equipment whenever possible is suggested, including anaesthesia masks, filters, circuits, water traps, and carbon dioxide sampling tubes (7). After the end of the operation, they should be regarded as waste and disposed of as infective material. Non-disposable equipment should be disinfected with 3% hydrogen peroxide, 75% alcohol, or 5 g L⁻¹ chlorine according to manufacturers' recommendations (7). Chlorohexidine is known to be ineffective on prior SARS-CoV agent and therefore should not be preferred (37).

HMEF or HEPA filters are enough to eliminate the risk of contaminating the anaesthesia machine internally. If such filters are used in both the inspiratory and expiratory ports, special cleaning procedures are not needed. If internal ster-

ilisation is necessary, the manufacturers' recommendations should be followed. The surface decontamination of the anaesthesia machine and cart should also be done with 3% hydrogen peroxide, 75% alcohol, or 5 g L⁻¹ chlorine. If plastic covers were used, they should be disposed of. The operation room should be disinfected for the next patient according to the measures taken by the infection committee. At least an hour is needed between each operation.

Following the end of the surgery, doffing of the PPE should be done carefully. After the removal of the gloves, hands should be disinfected, and goggles and face shields should be removed. Gowns should be removed following the re-disinfection of the hands. After securing hand-hygiene again, N95 respirator should be removed and put in a paper bag if reuse is planned. Cap should be removed after re-disinfection of the hand. Finally, hands must be disinfected first with disinfectants and then with soap. If possible, a full body shower is also suggested.

Conclusion

Being a University Hospital with a high number of admitted Covid-19 patients, we strongly suggest that any patient who will undergo surgery during the pandemic should be considered as 'Covid-19 positive' and be treated accordingly. The pandemic of COVID-19 has altered most of our daily life routines from personal relationships to interactions with patients. Both our safety and the safety of fellow health care personnel is essential in all interactions with suspected or confirmed patients. Even non-COVID-19 patients should be regarded as positive, and personal protection must be prioritised. Strict accord to the guidelines for personal and environmental asepsis will reduce the risk. However, anaesthesia management of the patients should be specific to the type of surgery and the general condition of the patient.

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