

Anesthesia Management in Patients with Covid-19

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The coronavirus disease 2019 (COVID-19) pandemic that started in China in 2019 has led to millions of infection cases worldwide. As the number of people with COVID-19 has increased, the number of patients with health problems that require surgery during the pandemic also increased, and at the same time, anesthesia is needed for these patients. In patients infected with acute respiratory syndrome coronavirus 2, some features related to the clinical course of the disease should be known and considerations for the protection of healthcare workers and other patients due to increased contagiousness must be adopted. This review of the literature presents approaches in cases of patients diagnosed with COVID-19 and issues to be considered during anesthesia management.

Keywords: COVID-19, anesthesia management, 2019-nCoV virus infection

The 2019 novel coronavirus (2019-nCoV) infection (COVID-19) was first described as a new pneumonia syndrome in patients clustered around the Huanan Seafood Bazaar in Wuhan, China, in December 2019. The World Health Organization (WHO) declared this situation as a pandemic on March 11, 2020, and on the same day, the first case was reported in Turkey. According to the WHO data of June 09, 2020, 7,039,918 cases were detected worldwide, 404,396 of which resulted in death (1-7).

The agent of the disease, which is defined as COVID-19 in the current literature, also called 2019-nCoV or acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is an enveloped RNA virus belonging to the Nidovirales subgroup of the Coronaviridae family, which includes Bat-SARS-like-(SL)-ZC45, Bat-SL ZXC21, SARS-CoV, and MERS-CoV.10 (1, 8, 9). 2019-nCoV with 9-12-nm long pointed protrusions varies in diameter from 60 to 140 nm. 2019-nCoV is inactivated by ultraviolet light, heat (56 min at 30°C), ethyl ether, 75% ethanol, chlorine used as a disinfectant, peracetic acid, and chloroform. It is not sensitive to chlorhexidine (1).

The virus is transmitted from infected individuals by respiratory droplets or by close/direct contact which is transmission vectors. Aerosol dispersion is also possible when exposed to high concentrations in a closed environment (1, 10). Although persons of all ages are sensitive to 2019-nCoV, the clinical course is usually symptom-free or mild in healthy individuals, and severe among elderly persons and in patients with comorbidities; It may even result in death (1-5, 11). In the literature, the incubation time of COVID-19 is reported to be between 1-14 days, most frequently 4 (2-7) days (1-5, 9, 12). In patients infected with COVID-19, fever, weakness, and dry cough are the most common symptoms. Tremors, muscle pain, headache, sore throat, loss of taste and smell senses (anosmia), and respiratory distress are also other common symptoms. Pneumonia is detected in approximately 15-20% of infected cases. In addition, respiratory failure, myalgia, diarrhea, widespread urticaria, erythematous rash, chickenpox-like vesicles, or embolism-related problems are reported. Rare symptoms such as sudden respiratory failure and circulatory disorders have also been reported. The severity of COVID-19 disease is classified as mild, moderate, severe, and serious based on clinical findings, laboratory tests, and imaging studies. In serious cases, dyspnea and/or hypoxemia may develop one week after the onset of the first symptom, and the patient may progress rapidly to acute respiratory distress syndrome, septic shock, refractory metabolic acidosis, coagulopathy, and multiorgan failure (1-5, 12-17).

The standard method of COVID-19 testing is reverse transcriptase-polymerase chain reaction (rRT-PCR, polymerase chain reaction). The test is performed by taking throat or nasal secretions with swabs. Nucleic Acid Amplification Test

(NAAT) is based on the determination of specific viral RNA sequences such as rRT-PCR and verification by nucleic acid sequence analysis method, which are used in the confirmation of COVID-19 cases. In cases in which the NAAT tests are negative and/or associated with COVID-19 infection, the study of serological tests such as ELISA or IgM/IgG rapid antibody tests in serum samples may be beneficial for the diagnosis (2, 6, 12, 16, 18).

Laboratory findings of COVID-19 are leucopenia, lymphopenia, thrombocytopenia, low albumin levels, and high C-reactive protein, erythrocyte sedimentation rate, neutrophil, and d-Dimer values. Levels of lactate dehydrogenase (LDH), creatinine, creatinine kinase, alanine aminotransferase (ALT) or aspartate aminotransferase (AST), IL-6, Ferritin, and IgG and M may also increase. Procalcitonin was normal in most cases. (3, 5, 13, 16). Thorax computed tomography (CT) and posteroanterior chest X-ray show mostly bilateral multifocal ground-glass appearance and focal consolidations with peripheral and posterior distribution, especially in the lower lobes, and a large number of small band shadows and apparent multiple interstitial changes in the extranodal lungs in the early period of the disease, while multiple ground-glass opacities are observed in both lung bases and infiltration in both lung areas in the following period. Severe cases may also cause pathology in the lung parenchyma, but pleural effusion is rare in COVID-19 (1, 16).

Although there are no methods, vaccines, and medication whose effectiveness have been demonstrated in an evidence-based prospective randomized controlled trial in the prevention and treatment of infected patients, antivirals, hydroxychloroquine, serum from immune individuals, antibiotics, nucleoside analogs, protease inhibitors, recombinant soluble ACE2, Type I interferon, corticosteroids, intravenous immunoglobulins, drugs that block cytokines, and NSAIDs are used empirically (19-22).

Perioperative Management of Patients Infected with the Novel Coronavirus

With the declaration of a pandemic, the work patterns of both patients without COVID-19 and healthcare personnel have been changed by taking the protective measures, but due to the increase in the number of patients and the prolongation of the process, surgery and anesthesia applications have become inevitable for infected cases (23, 24).

The definitive diagnosis of COVID-19 is established at the right time by PCR from nasopharyngeal swabs and by IgM and IgG tests from the blood. However, reliable results will not be achieved if the test is not carried out according to the stage of the infection and the disease. Taking precautions against the possibility of COVID-19 in each patient will increase safety when contagiousness is common in the community.

When a surgical indication is needed for patients with COVID-19, the first thing to do is to arrive at an agreement with the surgical team regarding the importance, necessity, and urgency of the surgery. In COVID-19 cases, surgeries should be limited to life-threatening, rapidly progressing malignancies, and cases requiring urgent surgical intervention (25). It is an appropriate approach to postpone all non-urgent and non-emergent surgical and endoscopic procedures.

The patients diagnosed with COVID-19 should not walk around freely in the hospital, but should be moved along the specified route (1, 25). Stretchers and elevators should be disinfected with bleach, chlorine disinfectant tablets, or 70% alcohol after each patient.

For the anesthesiologists, balloon mask ventilation, non-invasive ventilation procedures (CPAP), endotracheal intubation, surgical airway access, bronchoscopy, extubation, disconnection of the anesthesia circuit, and cardiopulmonary resuscitation are the highest risk approaches because of the intense aerosol exposure (14). Therefore, anesthetists are likely to become infected (1). All the anesthetic approaches applied in the preoperative preparation, operating room, device preparation, and intraoperative-postoperative periods should be standardized in order to reduce this risk and increase the safety of patients.

Anesthesiologists and other healthcare professionals in the surgery room should wear personal protective equipment (PPE) such as protective gowns/clothes, N95/FFP2 masks, disposable surgical caps, goggles, face shields, gloves, and overshoes. In addition, some accessories such as ring, watch, key, wallet, and the phone should not be allowed to enter the surgery room (1, 26).

Preoperative Evaluation

In the preoperative evaluation, anesthesiologist should use PPE, and patients should wear a medical mask. The patients should be taken to the room alone to minimize close contact with infected cases, preoperatively. Before the evaluation of the case, body temperature should be measured with an electronic ear thermometer, and cases whose body temperature is higher than 37.3°C should be reported to the infection control team (1).

It should be questioned whether the cases have a close contact history with COVID-19 positive individuals, and detailed physical examination including fever measurement, lung examination, laboratory tests (Complete blood count, liver function tests, BUN, creatinine, CRP, Pro-calcitonin, Ferritin, CPK, LDH, D-Dimer, IL-6), Electrocardiography (ECG, especially QT distance), chest radiographs, and thorax CTs, if available (1, 10). Radiological findings are not expected to be seen in the first 48 hours of the infection; 98% of CT shows diagnostic features. Lung ultrasonography can be used in pregnant women whose CT evaluation cannot be done (27). Patients with comorbid diseases should be consulted with the relevant branches if necessary.

After the physical examination, hand hygiene should be provided by washing with a 2–3% hydrogen peroxide solution or with plenty of water and soap. Examination room equipment, floors, and surfaces should be disinfected with 2–3% hydrogen peroxide (1).

At the end of the preoperative evaluation, the patient or patient's relatives and the surgical team were informed about the possible risks and adverse side effects, and written consent was obtained from the patient/guardian and archived.

After evaluation, COVID-19 positive or strongly probable cases should be taken directly to the operating room. Surgery, if any, it should be performed in the COVID-19 operating room; otherwise, routine room cleaning and contact follow-up should be done when the surgery is finished (1).

The Preparation of the Operating Room and Devices

The operating room reserved for patients with COVID-19 should be away from other operating rooms and should be marked with routers so that employees can find it without searching. The operating room reserved for COVID-19 cases should be ventilated with <5Pa, 12 air. hour-1 negative pressure systems and negative pressure levels should be checked frequently. If there are no negative pressure systems, positive pressure systems and air conditioners should be closed. If it is determined that the negative pressure in the environment is not sufficient, additional portable high-impact particle air filters (≥ 25 cycles/hour) should be used (1, 14, 26, 28-30).

The surgery room should be organized into two areas; dirty and clean. Two anesthetists using PPE (above-mentioned), surgeons and their team, and nurses should be in the dirty area, while another anesthesia and surgical team should be in a clean area and everyone should protect their regions (14).

The door of the operating room should be kept closed during the surgery, the entrance and exit of the employees should be limited to essential situations, and only anesthesia personnel should remain in the room during the intubation and extubation stage (1, 30).

Medicines that are likely to be used in anesthesia should be brought into the room in a tray, syringes should be thrown away into medical waste after the procedure, the tray was sterilized (1, 28).

Anesthesia device of the operating room reserved for patients with COVID-19 should be fixed in the room. Devices used in the operating room such as anesthesia machines and defibrillators should be covered with full transparent nylon covers and discarded after each surgery. Breathing circuits should be disposable, and HME filters should be placed on the inspiratory and expiratory connections of the breathing circuits (1). The end-tidal carbon dioxide line should be placed close to the machine after the filters, and the end-tidal carbon dioxide and water trap should also be disposable (26). Waste management should be planned in advance (28, 31).

Cleaning staff should use masks, gowns, and gloves. The reusable equipment should be sterilized with glutaraldehyde and the operating room should be sterilized with UV. The suspended droplets in the air should be expected to precipitate in 30–60 minutes. Therefore, it is necessary to wait for 30–60 minutes between the two surgeries (32).

Management of Anesthesia

Patients with COVID-19 may be candidates for any surgery. Zhao et al. (33) retrospectively evaluated 37 cases who underwent an emergency surgery on 23–31 January 2020; Abdominal surgery (10), cardiovascular surgery (2), orthopedic surgery (6), obstetric and gynecological surgery (11), neurosurgery (2), and the others (6); 70% of the surgeries were performed with general anesthesia and 30% with spinal anesthesia. Zhong et al. (34) performed spinal anesthesia in 49 patients who were confirmed to be COVID-19 radiologically and underwent cesarean or lower extremity surgery. Rong et al. (35) also performed cesarean section by applying regional anesthesia with an epidural catheter to 14 of 17 cases with COVID-19 and general anesthesia with 3 endotracheal intubation.

General anesthesia and endotracheal intubation are recommended to reduce the risk of COVID-19 transmission in patients with COVID-19 diagnosed or suspected. Other methods can be selected depending on the patient's condition. For example, spinal anesthesia is preferred in cesarean procedures. If spontaneous breathing continues, patients should also wear an N95 or surgical mask during the surgery (1).

General Anesthesia

If it is not essential for general anesthesia, rapid serial induction should be applied without mask ventilation (1). During induction, neuromuscular blockers, intravenous general anesthetics, and opioids are recommended, respectively (10). There are also published articles suggesting that endotracheal intubation should be performed in a negative pressure room or ICU, from where the surgery is monitored preoperatively instead of the operating room (26).

The application of 5 min pre-oxygenation with 100% oxygen (26), covering the patient's nose and mouth with two layers of wet gauze or a nylon cover that covers the face and surrounding to avoid secretions of the patient during pre-oxygenation (1), reduction of ventilation by a mask during intubation, and no cricoid compression (1), [If the anesthetist is experienced, cricoid compression may be applied (26)] are recommended. For endotracheal intubation, oral intubation with a video laryngoscope or bronchoscope is recommended (1). Lyons (36) stated that using fiber optic laryngoscopy did not give extra speed and even high flow oxygen applied by nasal route during the procedure increased the risk of contamination. It is necessary to show the ultimate attention to prevent coughing in laryngoscopy (1). Aminnejad et al. (37) reported that administration of lidocaine at the beginning and the end of intubation and extubation in patients with COVID-19 reduced possible cough, and also reduced secondary aerosol spread. The adequate neuromuscular blockade should be provided to prevent cough (10), for this purpose, a high-dose rocuronium ($1\text{--}1.2\text{ mg.kg}^{-1}$) is recommended. Suxamethonium can be given at a dose of 1.5 mg.kg^{-1} , given the duration of the apnea and cough (38). Ketamine or etomidate may be used not to suppress the cardiac functions in hypotensive patients. However, etomidate can cause adrenal suppression (39).

If there is a suspicion of a difficult airway, difficult intubation guidelines should be taken into consideration. Spraying local anesthetics into the respiratory tract during awake fiberoptic intubation should not be applied unless indicated, as this may cause the virus to spread as aerosol (28). ETT placement following the supraglottic airway is another recommended method in cases that cannot be intubated (26, 38). Intubation should be done with a tube distally clamped without bending the patient's face. If difficult intubation is predicted, a guidewire should be inserted into the tube, the endotracheal tube should be reached to the ideal depth at one time (often the rim is 22 cm), the cuff should be inflated (to the extent that the leak is not allowed), then the clamp of the tube should be removed, and its location verified. The continuity of the breathing circuit should be checked during the surgery. If the line needs to be separated; the tube must be clamped first and the separation must be made from the farthest distance to the HME filter. If possible, it is recommended to use the closed airway aspirator systems to

reduce viral aerosol production. If not possible, suction applications should be minimized (1).

In the maintenance of anesthesia, to reduce lung damage due to the ventilator, a lung-protective ventilation strategy at low tidal volume should be applied. Tidal volume 4–8 mL/kg, inspiratory plateau pressure <30 cmH₂O, PEEP <8 cmH₂O and recruitment maneuver every 30 minutes, blood gas analysis during surgery, and close monitoring of ventilation with EtCO₂ are recommended (10).

Inhalation anesthesia or total intravenous anesthesia depending on the clinical condition of the patient can be preferred for the maintenance of anesthesia. The primary aim of both methods is to provide fast recovery without a cough. It is emphasized that this can be achieved by avoiding the use of preoperative midazolam, with the lowest possible dose, and the shortest effective drugs (avoiding deep anesthesia and deep muscle relaxation and minimizing the opioid dose, etc.) (40).

The use of other drugs that will contribute to QT prolongation, metabolic, and electrolyte disorders should be avoided because hydroxychloroquine used in COVID-19 treatment causes QT prolongation on ECG (41).

Regional Anesthesia

Proper planning should be done so that the surgery can be performed entirely with regional anesthesia, without the need to return to intraoperative general anesthesia, which can be achieved with the harmony of the anesthesia and surgical team.

Although spinal anesthesia is recommended in patients with COVID-19 for lower extremity surgery or cesarean section, it should be proven that there is no thrombocytopenia (14, 34). In cases with COVID-19 encephalitis, the free drop of cerebrospinal fluid (CSF) should be prevented after lumbar puncture, since the virus is isolated from CSF (42). Although some articles are indicating that epidural and general anesthesia can also be applied in a cesarean procedure (35), febrile patients with COVID-19 may have a lumbar puncture during epidural catheter insertion, and neuraxial anesthesia can cause meningitis and encephalitis, even at a very low rate (43).

If it is decided to perform the peripheral nerve block, the block that will least affect the respiratory functions should be selected and carried out under the guidance of ultrasound to reduce the local anesthetic systemic toxicity (44).

N95 or surgical masks should be used for patients undergoing regional anesthesia during the surgery, if oxygen support is needed, the nasal cannula should be inserted, or oxygen should be given through the mask (1, 34).

Monitorization

All vital functions should be monitored as reported in the ASA standard (45). Since the medicines used in the treatment of COVID-19 can cause toxic myopathy and myocarditis, close ECG monitoring should be performed, and whether there is a QT prolongation on the ECG should be checked (41, 46). In patients with COVID-19, EtCO₂ should be measured as a standard, if sedation is also performed during regional anesthesia (40). EtCO₂

is also critical in confirming the endotracheal intubation. Aerosol spread may be reduced by monitoring the cuff pressure. Non-invasive monitoring of vital parameters is needed in patients with COVID-19. However, considering the clinical condition of the patient, intraoperative blood gas analysis, and close EtCO₂ monitoring can be performed depending on the severity of lung involvement. Acute kidney injury (47) may be seen in patients with COVID-19. The urinary catheter will also provide monitoring for fluid management. Echocardiography (ECO), USG (Vena Cava Inferior diameter measurement) can be used to evaluate tissue perfusion. Pulmonary pressure and blood lactate levels may be measured. Central venous pressure monitoring (CVP), and the effect of respiration on vena cava sizes can be evaluated by USG (Mmod) (48-50). Since the aim is a rapid recovery among patients with COVID-19, the use of high-dose neuromuscular blockers can be prevented by neuromuscular monitoring during the surgery.

Cerebral events, microvascular encephalopathy, septic encephalopathy, and cerebral autoregulation disorder may be seen in critical patients with COVID-19 (42). Therefore, the balance between cerebral oxygen delivery and consumption should be monitored by non-invasive methods, as well as blood pressure measurement in the evaluation of cerebral perfusion (51).

Fluid Replacement

It is recommended to apply fluid to meet the needs of patients provided that hypovolemia is avoided, since patients with COVID-19 may experience restrictive lung diseases, kidney failure, and thrombosis (52). The purpose of fluid treatment is to balance the amount of fluid that the patient takes and extracts and avoid excessive fluid overload. Therefore, close monitoring is recommended.

In fluid management, crystalloids should be preferred over colloids. Anaphylactoid reaction with crystalloids is not seen in volume replacement, but if there is endothelial damage, it may lead to extravasation and related problems. Colloids, although it is a good option for maintaining oncotic pressure, synthetic colloids also have negative effects on the coagulation and less frequent risks of allergic reactions (53).

In fluid management, passive leg raise test, mini-fluid loading test, and the ratio of pulsatile flow to non-pulsatile flow (PVI) in the capillary bed should be evaluated conservatively (54).

Extubation Period

If the patient meets the extubation criteria, the patient should be extubated in the operating room using the closed aspiration system. Soft extubation should be applied to prevent aerosol scattering by cough, and IV lidocaine should be applied if there are no contraindications (37). McGrath et al. (55) reported that coronaviruses caused laryngitis without causing sore throat, resulting in airway edema and that dysphagia and dysphonia might be observed after extubation. During extubation, two layers of wet gauze can be used to cover the patient's nose and mouth or the mask is placed under a transparent nylon cover to reduce aerosol exposure. Extubation can be performed under the transparent cover via a hole allowing only the connector portion under the transparent cover. While one of the HME filters is removed with ETT, the second is immediately attached to the face mask. When sufficient spontaneous ventilation is pro-

vided, the patient can be transferred from the operating room with a face mask and O₂ if necessary (1, 14).

Patients should not stay in the recovery room or postoperative care unit. However, they should be transferred to a room where they are monitored under negative pressure or to the intensive care unit (26). If the patient is to be transferred without extubation, a filter should be added to the endotracheal tube and ventilation should be continued with a disposable manual ventilator. If the patient is to be transferred with the transport ventilator, the filter should be attached to the endotracheal tube and connected to the breathing circuit; the breathing circuit should be discarded after the transfer (1).

Postoperative Period

When the patient with COVID-19 is transferred to the room monitored under negative pressure or to the ICU depending on its clinical condition, a consultation with the infectious diseases team should be made (1, 31).

In the postanesthetic care unit, patients should be periodically evaluated for respiratory, cardiovascular, neuromuscular functions, mental state, temperature, pain, nausea, vomiting, fluid therapy, urine output, drainage, and bleeding. An appropriate monitoring standard should be maintained until full recovery. If the patient will remain intubated or the airway will be provided with a supraglottic or similar tool, pulse-oximetry, non-invasive blood pressure monitoring, ECG, and airway continuity should be closely monitored. Difficult airway equipment, a nerve stimulator, a thermometer, and patient warming tools should be available to assess the neuromuscular blockade (56). Due to the fact that patients with COVID-19 may have renal failure, limited fluid treatment should be applied, and the amount of urine and possible bleeding should be closely monitored. In cases where thrombosis is expected, thromboprophylaxis can be applied with low molecular weight heparin.

Since pulmonary, myocardial, and renal damage may occur in critically ill patients with COVID-19 in postanesthetic care, lung compliance, airway pressure, oxygen index, arterial blood pressure, CVP, myocardial enzymes, and intracranial pressure can be monitored.

Postoperative nausea and vomiting should be treated aggressively using 2 to 3 antiemetics to prevent transmission. Although all known analgesics and methods can be used in the treatment of pain, liver, kidney, and bleeding coagulation system functions and side effects of selected analgesics should be considered. In pain management, the option should be individualized for the patient. High-dose opioids may cause undesirable effects such as respiratory depression and airway obstruction requiring airway manipulation. Local anesthetics should be preferred if appropriate (40).

As a result, the anesthetic management of patients with COVID-19 has distinctive features in terms of both protecting the healthcare workers and other patients and coping with the reasons resulting from the patient's clinic. Appropriate precautions and proper anesthesia management can prevent employees and anesthesiologists from injuries related to COVID-19.

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