6 Anesthetic Consideration for Patients with Corona Virus Disease

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6.1 Preoperative Evaluation

Suspension of elective surgical procedures was one of the first measures to mitigate hospital overload in anticipation of a surge in demand for critical care services during the COVID-19 pandemic [1–3]: many professional societies have released statements on delaying, restricting, and rescheduling non-urgent procedures, to preserve medical resources including healthcare providers, hospital capacities (mostly ICU resources), and personal protective equipment (PPE) [4, 5]. This is an additional effect on healthcare induced by the COVID-19 pandemic and risk/benefit ratio, including consequences related to canceling or postponing the procedure should be considered for each patient.

Patients affected by COVID-19 have higher perioperative morbidity and mortality, due to a high rate of ARDS, cardiac injury, kidney failure, and even deaths observed after surgical procedures [6, 7]. In COVID-19 patients, who underwent elective or emergency surgery, male gender, age > 70 years, presence of comorbidities [American Society of Anesthesiologists (ASA) grades 3–5], and cancer surgery were associated with an increase of pulmonary complications and 30-day mortality [8]. Furthermore, preexist comorbidities—hypertension, chronic obstructive pulmonary disease, diabetes, and cardiovascular disease—increase susceptibility in developing severe COVID-19 [9]. Higher risk to be infected by COVID-19 and poor outcomes were reported also in immunocompromised and oncologic patients caused by respiratory viral infections: indeed conventional coronaviruses are often associated with higher rates of oxygen requirement and
mortality. The fatality rate of cancer patients affected by COVID-19 is 5.6%; furthermore, these patients have a greater risk to develop perioperative complications than those without COVID-19 [7, 10].

To increase patients’ and healthcare workers’ safety, it is essential to include a multimodal screening work up in all patients scheduled for surgery and the procedure should be accomplished before the access to the operating room (OR) [3]. Considering that SARS-CoV-2 mucosal swab testing used to detect COVID-19 has a sensitivity that ranges between 70 and 90%, therefore, it is associated with a potential of non-detecting the virus in up to 30% of infected patients; the ASA suggests to separate patients positive or suspected for SARS-CoV-2 infection from those with a negative swab test. A flowchart given by ASA reports the correct conduct to evaluate patients for elective surgery, in countries where SARS-CoV-2 is present:

- All patients should be screened for signs and symptoms (fever, cough, shortness of breath, chills, muscle pain, headache, sore throat, and/or new loss of taste or smell within the prior 2 weeks) before admission to the hospital. All other patients should undergo nucleic acid amplification testing (including PCR tests) before non-emergent surgery.
- Because false-negative tests may occur, droplet precautions (surgical mask and eye covering) should be used by OR staff.
- For all patients with positive SARS-CoV-2 swab tests, elective surgical procedures should be delayed until the patient is no longer infectious and proven full recovery from COVID-19 infection.

Considering that signs and symptoms referable to COVID-19 infection can be minimal or the infection might be in the incubation phase, it is important to consider that the interval between the preanesthetic consultation and the intervention may evolve into a full disease [11]. It is therefore useful that patients scheduled for surgery complete a “home questionnaire” before the hospital consultation with the anesthesiologist. When the “home questionnaire” is completed, patients should be informed that new onset of signs or symptoms referable to COVID-19 infection should be communicated to the anesthesia team promptly before hospitalization. Temperature monitoring is a key element of pre-hospital evaluation. Although non-specific, fever is a very common symptom of SARS-CoV-2 infections (75–95%) [9]. The use of telemedicine could be an alternative to face-to-face consultation, as also approved by the World Health Organization. Of course, teleconsultation is carried out using tools that guarantee the security of patient data.

Because SARS-CoV-2 testing has moderate sensitivity, some authors suggested that CT imaging examinations could be a complementary exam to detect indirect signs of virus presence and to isolate patients with typical imaging findings, such as a ground-glass pattern that indicates interstitial rather than alveolar edema [12].

Another possible approach to stratify the clinical conditions of patients with COVID-19 and to evaluate the associated perioperative risk is to use dedicated clinical tools [13]. One study reported a score to measure functional status over time of COVID-19, especially to follow patients after discharge and to evaluate
the respiratory consequences of this syndrome like related COVID-19 pulmonary fibrosis [14]. This scale has six steps ranging from 0 (no symptoms) to 5 (death) and covers the entire range of functional outcomes by focusing on limitations in usual duties/activities either at home or at work/study, as well as changes in lifestyle. Respiratory consequences of COVID patients could be very serious, and, in some patients, lung transplantation was performed as a therapeutic option [15].

Another relevant evaluation to screen patients with increased perioperative risk comes from blood exams of COVID-19 patients. One study found a relationship between blood biomarkers and mortality with an accuracy of 90%: lactic dehydrogenase (LDH), lymphocyte, and high-sensitivity C-reactive protein (hs-CRP). High levels of LDH reflect tissue breakdown occurring in various diseases such as pneumonia and seems to be an important sign to predict COVID-19 stage and prognosis [16].

Mechanisms of cardiac injury in COVID patients remain unknown: myocardial injury, myocarditis, acute coronary syndromes, heart failure, arrhythmias, and venous thromboembolism were reported as serious consequences [17]. Of though, ECG evaluation and cardiac markers before surgery are suggested to evaluate patients, especially for drugs used for COVID-19 like azithromycin and hydroxychloroquine and their rhythms alteration [11].

Preoperative evaluation should be performed by the physicians with self-protection (including medical gowns, medical gloves, eye protection shields, disposable surgical caps, and surgical masks or test-fit N95 or FFP2 masks or respirators), and patients should be received one by one to minimize close contact with the clinician and other individuals [3]. Hand hygiene must be accomplished before and after contact with each patient with 2–3% hydrogen peroxide solution or gel or by washing hands with soap and water.

Patients with suspicious or affected by COVID-19, in whom the surgical procedure cannot be delayed, need to be scheduled in a specific route that includes a dedicated OR and surgical/anesthesiology team [18] (see Chap. 3).

6.2 Operating Room Organization and Self-Protection

In the COVID-19 outbreak, surgery is limited to urgent and emergent procedures [1, 2]. Two separate routes are dedicated to COVID-19 or suspected patients and no-COVID-19 patients with different spaces and teams (Fig. 6.1). This approach reduces the risk of contamination of patients and physicians and improves hospital resources [1, 19]. Caregivers working in OR dedicated to patients affected by COVID-19 must be straightly necessary to reduce the risk of contamination [2, 20]. In OR dedicated for COVID-19 patients, there should be three different ambiances:

- Zone 1 clean: it is a zone necessary to wear the caregivers.
- Zone 2 filter: it is a zone necessary to separate the clean and the dirty zone.
- Zone 3 dirty: it is a zone inside the COVID-19 spaces (wait to bb).
The perioperative phase is critical for viral and bacterial transmission, especially during induction and emergence of anesthesia \[3, 4, 20\]. Viral pathogen survival on environmental surfaces extends for several days and SARS-CoV2 can survive for at least 3 days on a variety of materials commonly used in operating rooms. The multimodal strategy is crucial to remove residual environmental contamination and to reduce intraoperative risk of pathogen transmission events. These include:

**Fig. 6.1** Work up for operating room admission to patients presenting for emergent surgical procedures

- **Emergency Surgery Patient**
  - **PCR, Exams, Medical History, Body Temperature**
  - **Suspicious or Confirmed SARS-CoV-2** → **COVID Dedicated team and OR** → **COVID ICU**
  - **No suspicious SARS-CoV-2** → **Routine surgery and anesthesia**

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(a) Self-protection of patient and caregivers.
(b) Environmental cleaning.

Hand hygiene should be performed with 2–3% hydrogen peroxide solution or gel, or by washing hands with soap and water. Because hand hygiene is not sufficient alone for control of perioperative virus spreading, a double pair of gloves is recommended especially during high-risk maneuvers. Frequency and quality of environmental cleaning are crucial to reduce the overall contamination of the work area: it’s suggested to use a top-down approach, spray all surfaces, the anesthesia, and circulating nurse workspace with a quaternary ammonium compound and wait the required time per agent of cleaning. Evidence of the last decade reported that a combination of deep cleaning with surface disinfectants and ultraviolet light (UV-C) is useful to reduce bacterial and viral contamination across a variety of healthcare settings by addressing both surface and air column disinfection; UV-C has been shown to reduce the incidence of both bacterial and viral healthcare-associated infections [5]. Disposable covers should be used whenever possible to reduce equipment contamination.

Some authors especially for aerosol-generating procedures—as recommended by the WHO guidance on COVID-19—reported the role of the negative pressure rooms inside the OR and the anteroom because it has proven to be an effective measure to avoid cross-contamination during the SARS epidemic [6, 7, 21]. Negative pressure rooms are an engineering control created and maintained by a ventilation system that allows extra air to enter the isolated room by differential pressure and be exhausted directly to the outside or be filtered through a high-efficiency particulate air (HEPA) filter directly before recirculation; it aims to prevent the spread of contagious airborne pathogens from room to room and to avoid the accidental release of pathogens into a larger space and open facility, thereby protecting healthcare workers and patients in a hospital setting [21]. If negative pressure rooms are not available—as occurred in a pandemic setting—is suggested to work with engineering to turn off the positive pressure system [4].

Intubation and extubation are the most critical situations with a high risk of aerosolizing of oral droplets: moreover, many barriers were developed to protect personal during these maneuvers (boxes, transparent plastic sheet) (see Airways Management). Before performing an aerosol-generating procedure, healthcare providers within the room should wear fitted respirator masks (N95 respirators, FFP2, or equivalent), as opposed to surgical/medical masks, in addition to other personal protective equipment (gloves, gown, and eye protection). The N95 mask that conforms to United States Federal Drug Agency standards and the FFP2 that conforms to European standards—European Committee for Standards—can block 95–99% of aerosol particles. Before using it is necessary that caregivers test them and verify their integrity. Surgical/medical masks can block large particles, droplets, and
sprays, but are less effective in blocking small particle aerosols (<5 μm) [21, 22]. During the hospitalization, patients should use surgical/medical mask (like caregivers and other personal staff), even when they come to OR.

Eyes protections must be used for every contact with a patient suspected or infected by COVID-19, especially during aerosolizing maneuvers: protect every possible door for this virus is crucial. The gown is recommended to protect caregivers and to reduce the contamination especially during contact with biological fluids [8].

### 6.3 Airway Management

General anesthesia represents a serious problem in patients affected by COVID-19. Indeed, it is hard to decide to undergo a patient to surgery for imposing biological risk and for higher complication risk.

General anesthesia in COVID-19 patients requires adequate attention on two main issues:

- Airway management.
- Anesthesia management.

Airway management in COVID-19 patients is a complex and debated topic that requires adequate knowledge of guidelines and a defined order of work. Airway manipulation in patients with COVID-19 pneumonia is a serious risk for healthcare providers [18]. Therefore, it is necessary to maximize the use of PPE during aerosol-generating procedures, such as endotracheal intubation, non-invasive ventilation, and high-flow nasal oxygen. The use of N95/FFP2 masks, eye protections, and adopting the double glove technique is recommended [22]. It is strongly recommended to perform rapid sequence intubation with full dose of neuromuscular blockade (aminosteroid neuromuscular blockers such as rocuronium are preferred) to minimize the risk of coughing. The use of video-laryngoscopy, possibly with a separate screen, should be considered and a preloaded bougie or stylet should be routinely adjunct to maximize first-pass success [22, 23]. Any maneuver, which increase aerosolization—including mask ventilation—should be avoided. Unfortunately, hypoxemia is a hallmark of COVID-19 patients requiring tracheal intubation, and apnea should be minimized. Preoxygenation might be partially ineffective and for patients receiving noninvasive ventilation it is important to turn off the ventilator and to depressurize the circuit before proceeding to tracheal intubation [22–24]. However, for ventilation-dependent patients, respiratory assistance should be provided using Mapleson C circuit with a double filter setting [22, 23]. Despite the time-critical nature of airway management in COVID-19 patients, it is recommended to assess airway difficulty and to appropriately plan the most effective approach to avoid unexpected deterioration [24, 25]. It is necessary to assign the most experienced anesthesiologist to perform intubation. Awake fiberoptic
intubation and the use of atomized local anesthetic should be discouraged unless specifically indicated because of the increased risk for virus spreading [26].

Healthcare professional protection is a priority and PPE be available for all providers to ensure droplet/contact isolation. Patients with confirmed or suspected COVID-19 infection should be kept in the OR, transferred to a dedicated ICU or a negative pressure room. In order to ensure high standard of patient-generated aerosolization (removal of 99.97% of 0.3 microns airborne particles) during the transport, it is necessary to place an high-quality heat- and moisture-exchanging filter between the ETT and reservoir bag [22–25]. In extreme conditions, when intubation failed, it is suggested to proceed with early cricothyrotomy independently on saturation values [24, 27]. Finally, a capnography trace or ultrasounds for tube position confirmation should be integrated to the visual and auscultatory confirmation in order to overcome difficulties due to PPE. A dedicated “intubation spots” with disposable flexible video-endoscopic system, monitors, defibrillator, and high-efficiency closed system suction unit and anesthetic medications should be kept available in isolated/negative pressure areas [23, 24, 27].

6.4 General Anesthesia

General anesthesia in COVID-19 patients should ensure adequate depth along with appropriate airway and respiratory management intended to provide necessary ventilation but also to prevent droplets viral spreading. Other types of anesthesia (locoregional, spinal, etc.) can also be considered for specific types of surgery and according patient’s individual needs [28–30].

In these patients, anesthesia induction is an especially delicate phase and involves the use of the selection and titration of the most suitable hypnotic drug. In COVID patients, rapid sequence induction is the recommended approach, and this should be accomplished using aminosteroid neuromuscular blocking (rocuronium 1.2 mg/kg). First-choice hypnotic is propofol but associated use a second drug (benzodiazepines, ketamine, etc.) should be evaluated by the attending anesthesiologist in order to minimize the hemodynamic changes [31, 32]. Midazolam has been shown to have important interactions with ritonavir/lopinavir therefore induction with this benzodiazepine may be associated with an increase in its adverse effects [33, 34].

Induction and maintenance of anesthesia also require opioids, and the various pharmacological available drugs (fentanyl, sufentanil, remifentanil) can be used according the individual anesthesiologist experience [33, 35]. The use of fentanyl (at a dose of 3–5 μg/kg) in patients receiving ritonavir/lopinavir may lead to an increase in the adverse effects of the opioid; therefore, in this case remifentanil could be a valid pharmacological alternative [36, 37]. There are no contraindications to the use of halogenates in COVID patients, but special attention should be paid to titrate delivered concentration in hypovolemic, hypotensive, or hemodynamically compromised patients [38, 39]. Often in the first phase of COVID-19, patients have good compliance, poor oxygenation, and without dyspnea. Many authors reported two different
patterns of respiratory disease connected with COVID-19: one with high compliance and a low response to PEEP values and one with low compliance and a high response to PEEP values. Either it should consider widespread micro- and macro-thromboses in the lung (and in other organs) that could compromise oxygenation. So patients who present good compliance could be ventilated with tidal volumes of 7–8 mL/kg (ideal body weight), although, in an advanced stage of the disease, in patients who present low compliance, it is advisable to apply lung-protective strategy with higher PEEP ($\leq$15 cm H$_2$O) and lower tidal volume (6 mL/kg) [40–42].

6.5 Regional Anesthesia

As previously described, regional anesthesia is not the first choice in COVID patients. However obstetric surgery necessarily requires the execution of a neuraxial procedure as general anesthesia is associated with an unsatisfactory fetal APGAR [43, 44]. Moreover, the general anesthesia drugs (except the curaries) pass the placental filter, reach the fetus and promote a state of fetal distress at birth [43, 45]. COVID-19 patients with hypoxia and concomitant physiologically decreased functional residual capacity from pregnancy will be likely to become more hypoxic, develop further atelectasis with intubation and mechanical ventilation, and possibly require postoperative critical care admission [46, 47].

However, anesthesiologists should take into account the risk of meningitis or encephalitis associated with neuraxial procedures in the context of untreated viremia.

Recent data in the literature do not report cases of post-neuraxial complications in COVID patients after childbirth [48].

Before performing a neuraxial procedure in these patients, it would be advisable to evaluate platelet count given that a third of patients with COVID-19 infection have been reported to have thrombocytopenia compared with 7–12% of patients during pregnancy alone [47, 48]. In pregnant women, a platelet count of 70,000 $\times$ 106/L has a low risk for spinal epidural hematoma, and lower levels should be considered in cases such as these with a high risk for respiratory compromise with general anesthesia [47, 48].

It’s recommended early epidural placement for parturients with suspected or confirmed COVID-19 to avoid exacerbation of the patient’s respiratory symptoms and avoiding the aerosol generation associated with general anesthesia. However, a potential unintended consequence of this recommendation is an increased incidence and severity of intrapartum pyrexia [46–48]. An increased incidence of intrapartum pyrexia during the COVID-19 pandemic, it may increase the risk of adverse neonatal neurological outcome (neonatal encephalopathy, cerebral palsy, and epidural hyperthermia) [49, 50]. The optimal time to site an epidural in a parturient with suspected or confirmed COVID-19 is not therefore as simple as “the earlier the better” [51]. It is imperative that decision be made on a case-by-case basis and must take into account the parturient’s respiratory status, the likelihood of progression to emergency cesarean delivery, and the likelihood of prolonged labor.
6.6 Fluid Management and Associated Therapy

In some patients affected by COVID-19, especially recovered in ICU, diarrhea (16.3%) and vomit (8.3%) were the main symptoms; of though fluid management is important for patient scheduled for surgical procedure. The volume depletion that occurred in the first phase of the disease must be replaced to maintain blood pressure and cardiac output especially during intubation and positive pressure ventilation: isotonic fluids must be preferred [53]. In the same way, fluid overload should be avoided for the risk to develop ARDS [21]. Monitoring of the fluid challenge should be performed during surgery to maintain a conservative strategy of fluid therapy.

Despite it is known that albumin could increase endothelial glycocalyx limiting permeability and disruption of this protein [54], its role remain controversial. Even there is no direct evidence on patients with COVID 19 and the use of albumin, some authors suggest against its routine use especially for the initial resuscitation of patients with COVID 19 and shock based on indirect evidence from critically ill patients in general [21]. Evidence reported that patients recovered in ICU with COVID-19 had less value of albumin with a bad prognosis [52]. Some studies in progress suggest that serum albumin carries antiviral drugs against virus and recommended its use a therapeutic material, stabilizer and deliverer of the drugs [55]. We should consider its cost and limited availability, mostly during a pandemic outbreak, and should be used for a particular situation.

In the COVID-19 outbreak, the number of blood donations has significantly decreased with a consequence limitation of resources. Many societies in the world have elaborated guidelines for blood management and to be safe blood donations; although the transmission of COVID-19 infection through transfusion of blood components is still debated. For these reasons the prevention of anemia especially in COVID-19 is a cornerstone of blood management, obtained with three approaches: optimizing the patient’s red cell mass, reducing perioperative blood loss, and enhancing anemia tolerance. In critically ill patients affected by COVID-19, it must be cared with two aspects in the blood management: the higher risk of thrombosis associated with erythropoiesis-stimulating agents and the use of anticoagulant agents with a therapeutic dosage that could increase risk of perioperative blood loss [56, 57]. To guide physicians to correct blood management, some studies reported an individualized goal-directed coagulation and transfusion algorithm in the case of blood loss or bleeding using rotational thromboelastometry.

Some studies reported high rates of thrombotic complications in patients affected by COVID-19, including stroke, acute limb ischemia, and acute coronary syndromes (25–30%), especially in mechanically ventilated patients. The use of prophylactic anticoagulation was supposed not only for antithrombotic effects but also for other mechanisms of action, including anti-inflammatory or antiviral effects. For these reasons all inpatients with COVID-19, in the absence of contraindications, should receive prophylactic antithrombotic and should be undergone to risk stratification for venous thromboembolism (VTE) [58]. The optimal intensity of anticoagulation in patients with COVID-19 remains unknown: prophylactic dosing is the most
widely used but higher intensity of anticoagulation (including intermediate-dose and full-therapeutic anticoagulation) is reported by many authors. It is important to screen the correct risk for thromboembolism (VTE): bilateral lower extremity ultrasound or computed tomography pulmonary angiography should be performed in the pre or postoperative period. Extended pharmacological prophylaxis (up to 45 days) should be considered for patients at high risk of VTE who do not have a high risk of bleeding. Additional studies are required to identify the optimal regimen in various patient groups with COVID-19 risk stratification for VTE should be done for hospitalized patients at the time of discharge.

During the evaluation of patients affected by COVID-19, it must pay attention to any drugs interaction: at this moment even there are no efficacious treatments for COVID-19, many drugs were purposed as rescue therapy. Of these, lopinavir/ritonavir was used in the first phase for SARS experience: its inhibition of cytochrome P450 (CYP) 3A enzymes which are responsible for metabolism in the liver and intestines of various anesthetic drugs like midazolam could decrease themes metabolism increasing serum levels with a high risk of extreme sedation and respiratory depression. Recent studies reported conflicting results for the use of lopinavir/ritonavir but antiretroviral agents could be prospective therapy: it must be cared with the coadministration with these drugs [59–62]. The use of hydroxychloroquine for patients affected by COVID-19 is still debated [63] and its use exposed to many cardiovascular complications, especially older patients. Of though, some authors, based on high risk of interaction with common drugs like anti-diabetic medications, antipsychotics, and antiarrhythmics, such as digoxin and amiodarone, suggested simplifying therapy of older patients to reduce adverse events like QTc prolongation, torsade de pointes, and sudden death [64].

NSAIDs may be associated with worsening of symptoms during respiratory viruses: despite recent alerts, there is no scientific evidence to date linking NSAID use to the aggravation of SARS-CoV-2 infection. In a patient with an established or strongly suspected SARS-CoV-2 infection, the prescription of NSAIDs could be limited, although, in asymptomatic patients, there appears to be no contraindication to their use if their benefit is established.

It is not recommended to discontinue using corticosteroids in patients on long-term therapy. The single intraoperative injection of dexamethasone, at the usual recommended doses, does not appear to present an over-risk in the asymptomatic patient.

6.7 Postoperative Management

Patients who underwent surgery and affected by COVID-19 had a high risk to develop postoperative complications and should be transferred to ICU for monitoring the trend of the disease, in particular cardiologic, renal, and respiratory functions (Fig.6.1). As exposed in Chap. 3, ICU must be dedicated to COVID patients, in a separate route.
Extubation has high risk of aerosolizing of oral droplets and it must be used the airway management recommendations (see section 6.3). Before extubation, it suggested that two layers of wet gauze can be used to cover the patient’s nose and mouth to minimize exposure to the patient’s secretions. Caregivers must be the straightly necessary during this procedure. After surgery many authors suggested that patients with COVID-19 should be sent to an isolation room in the ICU, bypassing the postanesthesia care unit, or, if is stable after surgery and does not meet the criteria for admission to the ICU, he should be transferred directly back to the negative-pressure ward or isolation ward after extubation in the operating room [3].

SARS-CoV-2 has cytopathic effects on podocytes and proximal straight tubule cells that may cause acute kidney injury (AKI) in patients with COVID-19. Therefore, it is important to pay more attention to the early monitoring of renal function and cautiously handle the urine of COVID-19 patients during surgery and in the postoperative period [65].

At the end of the outbreak, the pandemic is crucial to resume surgical activity gradually for the categories of patients excluded in this phase. It is important to develop a program that ensures the safety and protection of patients and caregivers.

In conclusion, COVID-19 pandemic resulted in extensive changes in the organization of the healthcare system that included reframing perioperative setting. Several measures and dedicated consideration should be implemented to minimize the risk of infection spreading through patients—this includes a formal screening and separated track for those that result to be positive at mucosal swab—and to the healthcare professionals. Furthermore the shortage of blood derivatives induced a profound reconsideration of principles for transfusion. To deliver anesthesia to COVID-19 patients encompasses unique measures that encompass appropriate airway management and specific consideration of the possible pharmacological interactions. Dedicated training and structures play a paramount role in providing optimal clinical care.

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