Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Providing safe perioperative care in cardiac surgery during the COVID-19 pandemic

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The coronavirus disease 2019 (COVID-19) pandemic has potentiated the need for implementation of strict safety measures in the medical care of surgical patients – and especially in cardiac

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surgery patients, who are at a higher risk of COVID-19-associated morbidity and mortality. Such measures not only require minimization of patients' exposure to COVID-19 but also careful balancing of the risks of postponing nonemergent surgical procedures and providing appropriate and timely surgical care. We provide an overview of current evidence for preoperative strategies used in cardiac surgery patients, including risk stratification, telemedicine, logistical challenges during inpatient care, appropriate screening capacity, and decision-making on when to safely operate on COVID-19 patients. Further, we focus on perioperative measures such as safe operating room management and address the dilemma over when to perform cardiovascular surgical procedures in patients at risk.

Introduction

The pandemic caused by the coronavirus disease 2019 (COVID-19) has affected all areas of public and private life. Although the first wave of the pandemic was a "shock" for health care systems worldwide, it nonetheless potentiated the implementation of strict safety measures in the medical care of surgical patients. These guidelines have played a critical role in ensuring best medical care during surges of patients with COVID-19, in balancing the risks of postponing nonemergent surgical procedures, and minimizing potential exposure to COVID-19. This includes stratifying the patients in a phased approach based on the urgency of the medical condition. There is a thin line between increasing the medical capacity at the local and regional levels, overburdening entire health care systems, and ensuring the safety of both patients and medical personnel. The key to controlling the disease is to limit its spread. With rising numbers of COVID-19 infections, the current surge puts whole patient populations – such as patients with cardiovascular disease – at an increased risk. In this review, we focus on the existing evidence for perioperative protective measures and strategies to increase the safety of cardiac surgery during a (respiratory) viral pandemic.

Preoperative strategies for cardiac surgery patients

Risks of cardiovascular disease and the need for surgical interventions– when to postpone and for how long

COVID-19 patients with underlying cardiovascular disease are at higher risk of morbidity and prolonged hospitalization stays, with increased mortality ranging between 7.6% and 41.8% [1–6]. Cardiovascular diseases, especially arterial hypertension, and comorbidities including diabetes, obesity, age > 65 years, chronic pulmonary disease, and evidence of immunosuppression are most commonly associated with worse prognosis in hospitalized COVID-19 patients [3,4,7,8]. Myocardial injury is frequently reported in COVID-19 cases and is associated with increased risk of arrhythmia or death [9]. Although myocarditis, stress cardiomyopathy and type I myocardial infarction were reported as direct consequence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the most common etiology of myocardial injury or type II myocardial infarction remain non-cardiac conditions like respiratory failure with hypoxia and sepsis. The incidence of myocardial injury has been reported at >25% of critically ill COVID-19 patients [9–11]. Additional organ failures commonly observed in critically ill COVID-19 patients include pulmonary hypoxic failure and renal and cerebrovascular dysfunction [12]. A large meta-analysis including over 70.000 COVID-19 patients identified preexisting cardiovascular comorbidities as a significant predictor of cardiovascular complications, and patients with preexisting

cardiovascular comorbidities or developing COVID-19-related cardiovascular complications had an average fatality rate of 9.6% [5].

Performing surgery on patients with an active SARS-CoV-2 infection has been associated with significantly increased overall mortality averaging 20% [13]. Mounting evidence points toward severely impaired immunological functions in COVID-19 patients [14]. Although there is limited data on the case fatality rate in cardiac surgery patients with COVID-19, the current data suggest elevated mortality, ranging between 16% and 44% [15,16]. Patients undergoing cardiac surgery are becoming medically more complex and have increased cardiovascular risk profiles. Although current risk scores have a high predictive value for perioperative mortality risk in cardiac surgery [17], they fail to include the elevated risks of active or previous COVID-19.

During peak surges of the pandemic, all efforts should be focused on preventing health care systems from reaching the maximum capacity. As cardiac surgery is a resource-intensive discipline, expert societies and regional authorities have created guidance documents and strategies to minimize the caseload of cardiac surgeries, aiming for a balance between ensuring medical care for increasing numbers of COVID-19 patients and for those patients in need of essential cardiac surgical services. This includes postponing nonemergency cardiac surgeries, creating safe time-to-treatment delays, and developing strategies to minimize the risk of exposure to COVID-19 for patients and medical personnel alike [7,18–23].

The timing of cardiac surgery should be assessed in relation to the severity and progression of the primary disease and the urgency of a surgical procedure. Many strategies have been proposed [7,19,24–26]. George et al. suggest a more adaptive response, with allocation of resources depending on the stage of the pandemic, thus differentiating between early and steady-state stages with plentiful resources and no interruption of medical services, and the peak phases, where COVID-19 cases reach the maximum level and cause maximum stress for the health care services [22]. The majority of recommendations suggest stratification of cases according to disease urgency, distinguishing between emergency cases in need of surgical treatment immediately or urgently within 72 h post admission – such as critical coronary artery disease, the need for vasoactive support, a valvular pathology resulting in cardiogenic shock, pulmonary embolism, acute type A aortic dissection, and acute heart failure [7,19,22].

It seems imperative to differentiate between cases where the underlying cardiovascular condition may allow a treatment delay. The delay should be as long as deemed safe for the individual patient, and may be categorized in different urgency groups – e.g., a delay of >4 weeks, <3 months, and >3 months – to help facilitate logistical planning [21]. The prognosis of each pathology is highly relevant. As an example, patients with severe symptomatic aortic stenosis have a poor overall survival without treatment with mortality of 50.7% at one year, as showed by the PARTNER 1 trial [27]. Furthermore, the risk of mortality is pronounced during the first 6 months while waiting for surgical aortic valve replacement (3.7% at 30 days treatment delay, and 11.6% at 6 months treatment delay) [28]. Conversely, the ISCHEMIA study showed that the survival rate in patients with chronic coronary syndrome without left main stenosis but including 3-vessel disease is favorable throughout 3 years [29].

The assessment should be performed by a multidisciplinary team consisting of a cardiac surgeon, an anesthesiologist, a cardiologist, and an intensive care unit (ICU) physician and should be reevaluated at regular intervals, under constant consideration of current ICU capacities. This allows to establish treatment schedules for affected individual patients. Such cases include, but are not limited to, chronic coronary syndromes, stable severe valvular pathologies, or the presence of a large aortic aneurysm (>6 cm diameter), although some discrepancies exist. If the timing of cardiac surgery cannot be delayed or if the epidemiological situation deteriorates further, an increase in the resource allocation may be necessary. This includes reducing the operating capacities to an absolute minimum by postponing all nonemergent cases and (re-)evaluating interventional/percutaneous or conservative treatment options in cases where such an option is applicable, even if these are considered inferior or less durable [7,19,21,22]. Fig. 1 presents a suggested decision-making algorithm for planning and screening of cardiac surgery patients in COVID-19 pandemic.

Navigating through the pandemic using a staged approach allows for stepwise adaptation to the ongoing regional epidemiological situation and the current inpatient COVID-19 load [20]. It also requires daily coordination at regional levels. The European Society of Cardiology (ESC) guidance document on COVID-19 even suggests performing cardiac surgeries in “COVID-19-free” hospitals [7], although this may be politically and logistically difficult. As the dynamic situation continues to evolve,

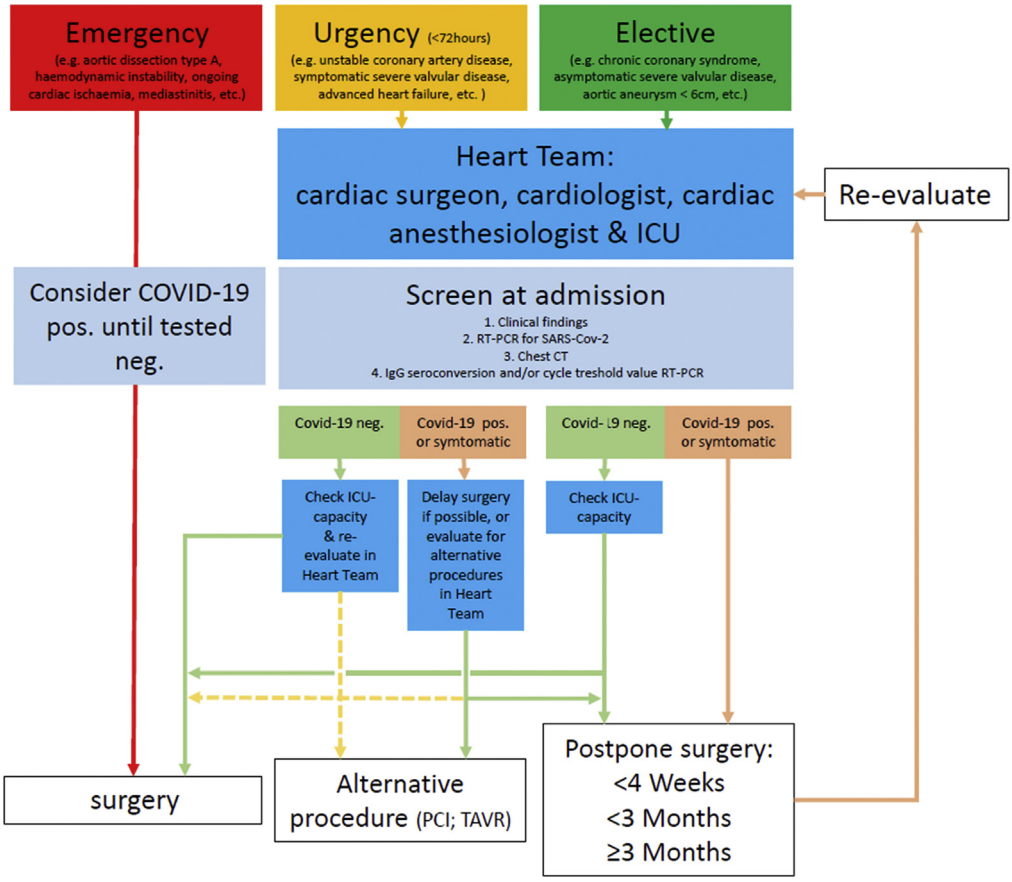

Fig. 1. Algorithm for planning and screening of patients for cardiac surgery during COVID-19 pandemic.

the implemented strategies need to be adapted accordingly. Specifically in cardiac surgery, the proposed strategies should be aimed at structural and organizational changes that allow for the continued delivery of cardiac surgical care with comparable outcomes as those reported before the pandemic [30]. This includes continuous and daily reevaluation of the anticipated need for resources and the actuarial resources available for intra- and postoperative care, and should again include close coordination between intensivists, anesthesiologists, cardiologists, cardiac surgeons, and perfusionists [23,25,31]. This can be challenging, as considerable case diversity may exist, resulting in challenges regarding which conditions to postpone, for how long, and when to reevaluate [32].

Special attention should be given to patients with chronic heart failure, left ventricular assist devices (LVAD), heart or lung transplantation and other forms of immunocompromise, as these are at increased risk of infection, and are considered to have a significantly elevated two-fold risk of mortality in COVID-19 infections compared to that in the general population [33–35]. As LVAD patients with active COVID-19 infection may be prone to thromboembolic events associated with COVID-19 coagulopathy and respiratory distress, they may be particularly difficult to manage, and it may be reasonable to delay LVAD implantation surgeries in these patients. In peak surges of the pandemic, it may be reasonable to postpone LVAD candidates in Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) stage $\geq$ 4 [22,36–38].

It may be reasonable to perform minimally invasive cardiac procedures in selected and COVID-19-negative patients, as minimally invasive surgery has been associated with earlier postoperative

recovery, shorter hospital and ICU stay. However, minimally invasive surgery should only be performed by surgeons already experienced in minimally invasive techniques. In patients positive for SARS-CoV-2, minimally invasive cardiac procedures should be avoided to reduce the exposition to the virus and the risk of aerosolization [39,40].

Telemedicine for preoperative assessment and risk stratification

When operational routines and normal patient flows are interrupted or deviated, resistance arises. Therefore, intensified communications are needed between referring hospital and tertiary treatment center regarding treatment urgency and referral urgency. Therefore, the use of telemedicine in patients undergoing cardiac surgery has been widely implemented during the COVID-19 crisis. Especially during peak surges of a pandemic, telemedicine can help assess primary disease progression and treatment urgency of cardiac surgery patients, thus dampening the burden of hospitalizations. Telemedicine helps to provide relevant medical information as part of preoperative assessment and subsequent follow-ups by omitting physical contact and thus limiting the spread of the disease. As a further precaution, prior to hospital admission patients should receive a brief telemedicine evaluation for suspected COVID-19 symptoms or risk factors or to clarify a suspicious chest X-ray or CT scan [7,22,41–44].

Minimizing the exposure & logistical challenges during inpatient care

At any stage, the risk of the untreated cardiovascular disease should be weighed against the risk of nosocomial infection during hospitalization as well as the predicted allocation of available resources. Patients are required to wear a surgical mask during any transfer between wards, diagnostics, and operating theatres, and all nonventilated patients should wear a surgical mask. Whenever feasible, diagnostics should be performed in the patient's room to reduce the risk of transmission, and all medical personnel should use personal protective equipment (PPE) at all times. Invasive diagnostic tests – especially aerosol-generating procedures such as transesophageal echocardiography (TEE) or bronchoscopy – should be reduced whenever possible, with alternative diagnostic tools applied. Stringent cleaning measures should be performed at regular intervals in all diagnostic rooms [7,45–48]. Some suggest nasal swab screening of asymptomatic medical personnel at regular intervals to minimize the risk of a possible nosocomial transmission of COVID-19 by asymptomatic hospital personnel [41].

Increasing screening capacities for COVID-19

To protect patients and health care personnel alike, widespread screening for SARS-CoV-2 using reverse-transcription polymerase chain reaction (RT-PCR) via a nasopharyngeal or oropharyngeal swab should be performed in transfers from other hospitals as well as in symptomatic patients or those with a high clinical suspicion for disease [30]. Depending on the local situation, the phase of the epidemic, demography, healthcare capacity, and regulations adopted by the local government, screening with a nasal swab may be expanded to include all inpatient admissions. Some expert societies recommend that patients self-isolate for 14 days prior to surgery as well as provide a negative nasal swab test 72 h prior to cardiac surgery [24]. To ensure the highest level of protection, these patients should be regarded as possibly infected by SARS-CoV-2, and level II and III protection measures should be used until a negative test has been confirmed, as recommended by the guidance document of the ESC. This includes isolating respective patients in a dedicated area of the ward with private rooms and bathrooms until the test results are available, and using appropriate level II or III PPE (disposable surgical cap, medical protection mask of N95 or FFP2 level, work uniform, gown, disposable surgical gloves, and goggles) [7]. Repeat testing using a nasal swab, endotracheal aspirate, or a computed tomography (CT) scan of the chest should be performed in patients with newly developed symptoms of fever, chest pain, increasing oxygen requirement, or other suspicious clinical symptoms of COVID-19, appreciating the limited sensitivity of swab tests. In inconclusive cases, a chest CT scan has shown good correlation with pulmonary involvement of the disease [42,49]. In emergency cases, rapid PCR testing should be performed, and a COVID-19 screening CT scan of the chest may be performed, although the latter may be false negative in the early stages of the disease [24,50].

When to operate on COVID-19 patients? – weighing risks and benefits

As the mortality risk in cardiac surgery is significantly higher in patients with an active COVID-19 infection, conservative management or a delay in surgery until recovery from COVID-19 should be the aim, as endorsed by multiple expert societies. All efforts should be made to postpone the surgery during an active COVID-19 infection, for as long as is tolerated by the patient [7,19,22,24,48,51,52]. When to operate should be a decision shared by the surgeon, the cardiologist, the intensivist and the anesthesiologist, and the treatment of COVID-19 patients should be interdisciplinary [53]. While it remains unclear why COVID-19 patients undergoing cardiac surgery have significantly elevated mortality, one explanation could be the additive effect of cytokine release during surgery and cardiopulmonary bypass, possibly resulting in an overwhelming cytokine storm as well as the pulmonary involvement with resulting acute hypoxemic respiratory failure [53,54]. Although the latter may be treated with veno-venous extracorporeal membrane oxygenation support (ECMO), the overall mortality at 90 days after ECMO support in COVID-19 remains high at 39% [8,55]. Specifically in patients who present with acute heart failure or cardiogenic shock and in whom a concomitant COVID-19 infection is suspected, the use of ECMO should be weighed against the increased risk for coagulopathy disorders, as well as the need for specific treatment of acute respiratory failure, such as prone positioning. Specifically in COVID-19 patients who develop acute heart failure, significantly elevated mortality of 52% has been observed compared to 12% in COVID-19 patients without acute heart failure [56].

If the cardiac surgery cannot be delayed, however, conservative and percutaneous treatment options should be evaluated. The decision to operate should be weighed between the elevated risk of the surgical procedure, the expected need for ICU treatment and hospitalization, and the inherent risk of delayed treatment of the underlying cardiac condition [47]. It may be reasonable to avoid minimally invasive cardiac procedures in COVID-19 patients, due to its transthoracic and trans-pleural access, and the use of electrocautery and CO_2-insufflation, as these may increase the aerolization of viral particles and increase the exposure risk to SARS-CoV-2 [39,40].

LVAD implantation should be avoided in COVID-19 patients, until the infection has resolved. Some reports observed rapid clinical deterioration and prolonged critical illness in SARS-CoV-2 infection, which may be potentiated by the functionally immunocompromised state in LVAD recipients. If the hemodynamic and respiratory situation deteriorates, veno-venous or veno-arterial EMCO support may be installed as a temporary solution. LVAD patients with active COVID-19 infection and consecutive pulmonary failure may require additional veno-venous ECMO support. However, the significantly elevated risk for coagulopathy and bleeding disorders should be appreciated in these patients [35–38,57].

Heart and lung transplantation should be avoided in COVID-19 patients. COVID-19-positive heart or lung transplant candidates should be made inactive on the waiting list. The International Society for Heart and Lung Transplant (ISHLT) recommends relisting for an active waitlist when at least 14 days have passed since the initial diagnosis of COVID-19, and two consecutive PCR-based test at least 48 h apart have been obtained. SARS-CoV-2 infection must be ruled out through a negative RT-PCR test in both donor and recipient, and in inconclusive cases, a diagnostic chest CT scan not older than 72 h prior to organ procurement may provide further diagnostic value. The risk of community exposure to SARS-CoV-2 should be weighed against the increased risk of mortality if not transplanted, under consideration of the available resources and ICU capacity. A minimum number of personnel should perform the organ procurement, and a local explantation team should procure the organ whenever possible. Further consideration should be made to logistical and regulatory restrictions on interregional and international travel for procurement teams, and a prior negative SARS-CoV-2 test might be required for all team members. Depending on the epidemiological situation, the transplantation services may be paused in peak surges of the pandemic, if the local health care services are overwhelmed by the pandemic [35,38,58,59].

How long after a confirmed COVID-19 diagnosis is it safe to operate?

Nonurgent surgical procedures should be postponed until the patient is determined to be noninfectious or not infected. Patients who test positive for COVID-19 or who experience symptoms of COVID-19 should be regarded as infectious and isolated in a designated ward accordingly. Repeat nasal

swabs should be performed, usually within 10–14 days after the initial diagnosis of COVID-19, and at least 24 h after being free of symptoms [41].

Currently, the evidence in cardiac surgery patients is still scarce, but the general belief is that patients should not have a significantly elevated risk for cardiac surgery after being symptom-free from COVID-19 for a minimum of 2–5 days, and if they have tested negative on two consecutive nasal swabs. However, it should be noted that some patients continue to test positive with PCR weeks after full recovery from COVID-19. In such patients, a serological antibody test for seroconversion of IgG for SARS-CoV-2 may be performed [60].

In inconclusive cases, the cycle threshold (Ct) value of a RT-PCR test may be used as a surrogate marker for detecting early stages of the disease, as it was shown inversely proportional to the viral load of SARS-CoV-2 in the nasopharynx. Furthermore, lower Ct values (<20) have been shown to correlate with increased shedding of viral particles in early stages of the disease, and have been associated with more severe clinical outcome of the disease [61–63]. While further research in this field is needed, operating on COVID-19 patients may be reasonable in those who remain free of symptoms and show high Ct values (>39).

Perioperative management

Operating room management

Performing cardiac surgery on patients positive for COVID-19 should be avoided. If the surgery cannot be postponed, strategies have been proposed to minimize the spread of the disease. These include designating a specific operating room entirely for COVID-19 patients, and equipping it with negative pressure ventilation [31]. Alternatively, the positive pressure ventilation should be switched off for the duration of surgery [24,64]. A high frequency of airflow exchange ($\geq$25 exchanges per hour) is recommended to significantly reduce the airborne viral load [65]. Whenever possible a dedicated operating room should be used for COVID-19 cases [66]. There are contradictory opinions concerning the best location for such rooms inside the operating facilities. Coccolini et al. recommended a room close to the entrance, whereas others favor a remote room inside the complex [67,68]. It is recommended that these dedicated rooms have an anteroom [68].

Reduce the exposure to the virus

There is no clear evidence that surgical smoke can transport COVID-19 viral particles; however, precautions should be taken to limit the production of smoke by reducing the cautery level to its surgically most acceptable minimum. Caution should also be given to the use of CO_2-insufflation in the operative field, as this may increase the aerolization of viral particles [40,69,70].

As viral particles may survive on surfaces for 72 h and up to seven days, there is the potential for transmission of virus particles in hospital wards and in the operating rooms, and environmental cleaning in operating rooms is of utmost importance [71–74].

An attempt was made to perform nasal decolonization of COVID-19 positive patients by administering a nasal solution of povidone-iodine twice within 1 h of incision as well as a single shot of chlorhexidine mouth rinse [75]. This led to debate, however, as these measures were potentially causing more harm by increasing the risk of coughing or sneezing following administration and subsequent shedding of viral particles [76].

Surgical management

The Centers for Disease Control and Prevention published recommendations for the minimum personal protective equipment a health professional should wear when caring for a patient with confirmed or suspected COVID-19. It comprises the use of an N-95 respirator, eye protection, gown and gloves. Forrester et al. described a decisional algorithm based on the degree of surgical urgency and the potential viral burden at the surgical site to protect the operating room team members [77].

Viremia is uncommon in COVID-19 infection, and exposure to blood should not elevate the risk of viral transmission, although one study identified SARS-CoV-2 RNA in the blood [78,79]. Even though the transmission risk is considered extremely low during cardiopulmonary bypass, the membrane oxygenator exhaust should be scavenged through a high efficiency particulate absorbing (HEPA) filter, and the oxygenator should be disposed of with the same precautions used for anesthetic ventilators [79,80]. To reduce the risk of aerosol transmission of viral particles on cardiopulmonary bypass, higher sweep rates and FiO_2 levels have been proposed, together with other modifications of cardiopulmonary bypass such as a higher heparinization loading dose, higher active coagulation time, and more frequent cardioplegia administration, although the current evidence in this field remains scarce [80,81]. Furthermore, a cytokine filtration device such as CytoSorb® 300 mL is used in some centers to reduce the inflammatory response syndrome caused by an active COVID-19 infection during cardiac surgery, and a large clinical trial in Germany is currently testing the efficiency of such filter in this fragile population [82].

Contact with other body fluids such as saliva or other mucus membranes should be avoided, and the use of PPE by all team members is recommended for the duration of the surgical procedure [24]. Intraoperatively, special care should be taken to avoid pleural entry or lung injury [22]. Furthermore, special care should be given to chest-tube management in suspected and confirmed COVID-19 cases, and a viral filter may be applied to the exhaust vent of the reservoir to minimize the aerosolization of viral particles in case of a leak. These filters should be changed daily [48]. In the ICU, strict hygiene measures should be continued and respective critically ill patients should be carefully investigated for complications such as hypoxic respiratory failure and thrombembolic complications.

Conclusion

The practice of cardiac surgery during the COVID-19 pandemic is inevitable. Cardiac surgery depends on an interdisciplinary structure with many interfaces such as ICU, anesthesia, and cardiology. Therefore, strict adhering to organizational agreements is mandatory. Meetings on a regular basis are necessary, and ensure continuous communication and provide overview of the situation. Thus, the needs and safety of both patients and staff must be well balanced, and the risks and benefits weighed for all parties. It is the job of the multidisciplinary team (a cardiac surgeon, an anesthesiologist, an intensivist, and a cardiologist) to carefully consider which treatments should be performed immediately and which could be postponed. Care must be given to navigate between delaying nonemergent cardiac surgeries without subjecting these patients to added harm. There must be consistent reevaluation of the primary disease progression and severity as well as the epidemiological situation and burden on the local and regional medical facilities.

Practice points

- Because of its nature and the high share of urgent or emergency surgeries, the practice of cardiac surgery during a pandemic is inevitable.
- Each new hospital admission should be considered as SARS-CoV-2 positive until at least one negative nasal swab or alternative form of testing has been confirmed.
- Cardiac surgery patients are at an elevated risk of developing COVID-19, and surgery should be postponed in all nonemergency patients with confirmed or suspected COVID-19 infection.
- Minimize exposure of hospital personnel and of the patients through stringent use of PPE.
- Establish a standardized institutional protocol for determining when nonemergent cardiac surgeries can be delayed without harm to the patients. Consistently reevaluate the primary disease progression and severity as well as the epidemiological situation and the burden on the local and regional medical facilities.

Research agenda

- While long-term damage to the respiratory system is obvious in severely affected patients, future research will reveal COVID-19's impact on the cardiovascular system.
- The adaptation of telemedicine for use during the COVID-19 pandemic provides a tremendous opportunity to expand on established settings. Future research will be needed to prove its long-term value and feasibility.

Contributions

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