Mechanical Circulatory Support - Challenges, Strategies and Preparations

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Abstract

Background COVID-19 is usually mild, but patients can present with pneumonia, acute respiratory distress syndrome (ARDS) and circulatory shock. Although the symptoms of the disease are predominantly respiratory, involvement of the cardiovascular system is common. Patients with heart failure (HF) are particularly vulnerable when suffering from COVID-19. Aim of the Review To examine the challenges faced by healthcare organisations, and mechanical circulatory support management strategies available to patients with heart failure, during the COVID-19 pandemic. Results Extracorporeal membrane oxygenation (ECMO) can be lifesaving in patients with severe forms of ARDS, or refractory cardio-circulatory compromise. The Impella RP can provide right ventricular circulatory support for patients who develop right side ventricular failure or decompensation caused by COVID-19 complications, including pulmonary embolus. HT are reserved for only those patients with a high short-term mortality. LVAD as a bridge to transplant may be a viable strategy to get at-risk patients home quickly. Elective LVAD implantations have been reduced and only patients classified as INTERMACS profile 1 and 2 are being considered for LVAD implantation. Delayed recognition of LVAD-related complications, misdiagnosis of COVID-19, and impaired social and psychological well-being for patients and families may ensue. Remote patient care with virtual or telephone contacts is becoming the norm. Conclusions HF incidence, prevalence, and undertreatment will grow as a result of new COVID-19-related heart disease. ECMO should be reserved for highly selected cases of COVID-19 with a reasonable probability of recovery. Special considerations are needed for patients with advanced HF, including those supported by durable LVADs.

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Conclusions

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COVID-19

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease is usually mild, although occasionally severe with patients presenting with pneumonia, acute respiratory distress syndrome (ARDS), and circulatory shock (CS).[1] In a recent report, 26.1% of 138 COVID-19 patients needed to be admitted to the intensive care unit (ICU), of which 61.1% were suffering from ARDS. The heterogeneity of responses between individual patients is marked indicating host characteristics promote progression of the disease with a range of different presentations from mild symptoms to multiorgan failure.

Although the clinical symptoms of the disease are predominantly respiratory, direct and indirect involvement of other organs is common, with the cardiovascular (CV) system being particularly affected. Moreover,

pre-existing conditions, largely linked to CV disease (CVD), increase the risk of severe outcomes of the infection. A large Chinese study analysing data of 44,672 confirmed COVID-19 cases revealed 12.8% had hypertension, 5.3% diabetes, and 4.2% CVD.[2] A further study of 5,700 patients from the USA reported a similar message that hypertension (56.6%), obesity (41.7%), diabetes (33.8%), CAD (11.1%) and congestive heart failure (6.9%) were common comorbidities in patients with COVID-19.[3] Older patients are more likely to experience ICU admission, mechanical ventilation, or death compared with younger patients, and males seem to be more susceptible to COVID-19-related complications.

COVID-19 has resulted in substantial policy change and strain on existing healthcare infrastructure. Many healthcare providers have had to scale down outpatient services and defer elective cardiac procedures and operations with re-deployment of the workforce to help manage the pandemic. The long-term clinical impact of scaling down outpatient activity, reduced access to investigations, and cancellation of routine procedures will have consequences beyond the pandemic. In addition, the perceived risk of being exposed to COVID-19 has led to a delay in presentation of acute cardiac emergencies with a likelihood of increasing cardiac mortality and morbidity. Until now, no specific treatment has been recommended for COVID-19, although extracorporeal membrane oxygenation (ECMO), providing effective respiratory or cardiac support, can be regarded as a rescue therapy for severe ARDS.

COVID-19 and Cardiovascular Disease

Patients with cardiovascular risk factors and established cardiovascular disease, including heart failure (HF), are particularly vulnerable when suffering from COVID-19[4][5] and patients with cardiac injury in the context of COVID-19 have an increased risk of morbidity and mortality.[6]

Guzik et al.[7] report a mortality rate 0.9% for patients with no comorbidities and much higher for patients with comorbidities (10.5% for patients with CV disease, 7.3% for those with diabetes, 6% for those with hypertension and 6.3% for those with chronic respiratory disease.[8]

SARS-CoV-2 anchors on transmembrane ACE2 to enter the host cells including type 2 pneumocytes, macrophages, endothelial cells, pericytes, and cardiac myocytes,[9] leading to inflammation, severe microvascular[10] and macrovascular dysfunction and multiorgan failure.

Furthermore, COVID-19 infection leads to systemic inflammation and immune cell overactivation, and a 'cytokine storm', with resultant release of in an elevated level of cytokines such as IL-6, IL-7, IL-22, and CXCL10. Subsequently, activated T cells and macrophages may infiltrate infected myocardium, resulting in the development of fulminant myocarditis and severe cardiac damage and impairment of left ventricular function.[11]

Thus, the mechanisms by which COVID-19 affects the cardiovascular system possibly include direct myocardial injury, indirect injury through sepsis, hypoxia, cytokine release, a prothrombotic state causing microvascular thrombosis, and exacerbation of underlying cardiovascular disease, for example, plaque rupture in susceptible patients.[12][13][14] Supply/demand mismatch (Type 2 myocardial infarction (MI)) or microvascular thrombosis can lead to left ventricular dysfunction and ventricular arrhythmias. Fulminant myocarditis can lead to rapidly progressive cardiogenic shock from decompensation in patients with known or subclinical cardiomyopathy. Among hospitalized patients, the presence of cardiac injury has been independently associated with a 4-fold increased risk of mortality in patients infected with COVID-19.[15]

In patients with COVID-19 infection, hypoxemic respiratory failure and ARDS can exacerbate pulmonary vasoconstriction and interstitial oedema, worsening pulmonary hypertension even in patients without pre-existing lung disease.[16] In patients with pre-existing biventricular failure, further elevation in pulmonary pressures secondary to ARDS can worsen right ventricular function.

In a large cohort study of 138 patients, 8.7% of patients presented with shock, 7.2% with acute cardiac injury and 16.7% with arrhythmias.[17] Various other reports show new-onset heart failure/cardiomyopathy in up to one-third of critically ill patients admitted with COVID-19 infection.[18][19]

A special population at risk for COVID-19 includes patients supported with left ventricular assist devices (LVADs). These patients are chronically affected by long-standing cardiovascular diseases and are subjected to variations of the normal cardiovascular physiology due to a non-pulsatile blood flow, exposure of the blood to artificial surfaces, and risk of haemorrhagic and thrombotic events. Patients with advanced HF, including those with durable LVAD support, have severely reduced functional capacity[20][21], as measured by peak VO_2, and impaired ability to augment cardiac output in response to physiological stressors. These factors collectively decrease their cardiopulmonary reserve.

Patients with COVID-19 infection are at higher risk for thrombosis in the arterial and venous circulations due to endothelial dysfunction, inflammation, oxidative stress, and platelet activation[22]; both may trigger decompensation of pre-existing HF or development of de novo acute HF. Right ventricular failure can also develop secondary to elevated pulmonary pressures in the setting of ARDS and/or pulmonary embolism.[23]

HF incidence, prevalence, and undertreatment will likely grow as a result of new COVID-19-related heart disease, delays in the recognition and treatment of ischemic heart disease, rising unemployment, and loss of income and health benefits for large segments of the population. Special considerations are needed for patients with advanced HF, including those supported by durable LVADs and heart transplantation (HT) recipients.

ECMO

Treatment options for COVID-19 myocarditis are still evolving. However, mechanical circulatory support devices and life support therapies such as veno-venous ECMO (VV-ECMO) and VA-ECMO may be beneficial in select cases.

The mortality in COVID-19 patients who require mechanical ventilation is high. Extracorporeal membrane oxygenation can be lifesaving in patients with severe forms of ARDS, or refractory cardio-circulatory compromise. While accepting that resource scarcity may be the overwhelming concern for healthcare systems during this pandemic, VA-ECMO can be considered in highly selected cases of refractory CS and biventricular failure. The decision to initiate this therapy should take into consideration the availability of resources, perceived benefit, and risks of transmitting disease to patients and staff.

The Extracorporeal Life Support Organization (ELSO) recommends consideration of VA-ECMO in refractory CS that persists despite adequate fluid resuscitation, inotropes, and vasopressor support.[24] Contraindications to VA-ECMO include advanced age, life- threatening noncompliance, and significant medical comorbidities.[24]

The Society of Critical Care Medicine guidelines for the management of COVID-19 patients recommends the use of ECMO when conventional management fails.[25] Due to the intensive hospital resource utilization, substantial staff training, and multidisciplinary needs associated with starting an ECMO program, ELSO recommends against starting new ECMO centres for the sole purpose of treating patients with COVID-19. During the COVID-19 surge, it is reasonable to concentrate those patients with the greatest chance of benefit from receiving ECMO in a hospital where an experienced ECMO team is available.

Patient selection for VA-ECMO in the setting of COVID-19 infection is a challenging task. However, a multidisciplinary CS team that includes representation of cardiac surgery, cardiology, intensive care, anaesthesia, and advanced heart failure/transplant physicians may facilitate decision-making.

Although patients with COVID-19 infection are in a proinflammatory and prothrombotic state, coagulopathy occurs in up to one-fifth of cases.[26] Thus, vigilant monitoring for both thrombotic complications (intracardiac thrombi, aortic root/aortic valve thrombi, cannula thrombi, thrombosis of oxygenator) is necessary. Severe cases of COVID-19 tend to present with multi-organ failure. The use of VA-ECMO in such patients may be considered a futile resource-intensive endeavour. Use of validated prognostic scores such as the Sequential Organ Failure Assessment and Survival after Veno-arterial ECMO scores together with clinical judgment may identify those who are more likely to recover.[27]

The provision of ECMO, also is dependent on local institution and regional policies. ECMO requires specialized equipment, training (of physicians, nursing staff, and perfusionists), and delivery of care in specialized critical care units. MacLaren et al.[28] suggest, resources may well be better concentrated to ensure that enough ICU beds, ventilators, and personal protective equipment are available to deal with the influx of patients encountered during the pandemic. Providing this level of care should be considered dynamically on a case-by-case basis as the local situation and resource availability changes (ie, critical care beds, healthcare personnel, equipment).

Many factors could affect the outcomes of ECMO treatment, including the duration of mechanical ventilation, the severity of underlying disease, the experience of trained medical staff, and ECMO equipment. Use of ECMO in patients with a combination of advanced age, multiple co-morbidities, or multiple organ failure should be avoided.

Not all patients will improve with ECMO support. As is standard with usual ECMO care, clinicians should be continuously evaluating when ECMO no longer provides a positive benefit:risk ratio and should at that point return to conventional management. As prognosis is worse with time on invasive mechanical ventilation, patients on mechanical ventilation greater than 7 days can probably be excluded and observing no lung or cardiac recovery after approximately 21 days on ECMO can be considered futile.

In the present time of global uncertainty with limited evidence to guide care, we must be mindful of balancing resource scarcity. We anticipate that Extracorporeal Membrane Oxygenation for 2019 Novel Coronavirus Acute Respiratory Disease (ECMO-CARD), an ongoing multicentre prospective observational study of ECMO use in COVID-19, will inform practice for both VV-ECMO and VA-ECMO use when published.[29] For now, it seems reasonable to reserve VA-ECMO for highly selected cases of COVID-19 where there is a perceived reasonable probability of recovery.

Heart Transplantation and Ventricular Assist Devices

Heart transplantation and VAD patients face unprecedented challenges during the coronavirus disease 2019 (COVID-19) pandemic. These populations are at increased risk for acquiring COVID-19 infection. For heart transplant (HT) clinicians, the global pandemic has unique implications for patients, including those on the waiting list and transplant recipients.

Many centres have inactivated most of their HT waiting list, reserving active transplant status for only those patients with a presumed waiting list mortality of 1 to 2 weeks, thus limiting transplant to patients in tiers 1 or 2 of the new heart allocation policy. For listed patients who are hospitalized without a strict contraindication to durable left ventricular assist device implantation, LVAD as a bridge to transplant may be a viable strategy to get at-risk patients home and out of the hospital, minimizing their exposure to COVID-19. Left ventricular assist device implants should not be performed in elective cases because of resource constraints and potential for nosocomial infection.

The COVID-19 pandemic has had far-reaching implications for donor selection, organ procurement, waiting-list candidates, and transplant programmes.[30] Given the limitations of current testing and risks for asymptomatic transmission and infection, the HT community must be careful to select uninfected donors. As the pandemic continues to evolve, a centre's transplant volume may require staged reduction to meet ITU bed, staffing, and medical equipment needs of the majority nontransplant population.

Important decisions have already appeared about actively listed patients. At any given time, a significant portion of patients are waiting in-hospital for HT. These patients are at higher risk for contracting the virus compared with others waiting at home. If they subsequently contract COVID-19, they are at risk for more severe infection because of their underlying health conditions, and risk delisting. For listed patients, transplant centres should highlight the waiting list mortality risk–benefit ratio and provide institutional updates.

Left ventricular assist device patients are affected by long-standing cardiovascular diseases and subjected to variations of the normal cardiovascular physiology, thus requiring an even closer monitoring during the

COVID-19 outbreak. Potential deleterious effects of such a situation can be a delayed recognition of LVAD-related complications, misdiagnosis of COVID-19, and impaired social and psychological well-being for patients and families.

LVAD patients are at increased risk of COVID-19 infection for several reasons including most LVAD patients share the same risk factors for COVID-19 infection and represent a very vulnerable population. These patients may manifest impaired immunity with increased risk for opportunistic infections[1] and activation or enhanced release of the inflammatory cytokines in COVID-19 may augment the pre-existing myocardial injury.[31]This "functionally immunocompromised state" increases susceptibility to complications from opportunistic infections.

Due to the general reorganization of healthcare resources in many hospitals, elective LVAD implantations have been reduced to allow for a higher availability of intensive care beds. Consequently, only patients classified as INTERMACS profile 1 and 2 are being considered for LVAD implantation.

With suspension of elective surgeries there is a potential morbidity and mortality increase in LVAD candidates waiting for implantation. Furthermore, there is a risk that the close connection between LVAD patients and their treating centres becomes looser with increased LVAD-related complications and impaired well-being. Patients undergoing HT/LVAD evaluation experiencing delays in listing and/or surgery can develop worsening nutritional, functional, or hemodynamic status. LVAD supported patients with the indication of bridge to transplantation might decline an offer to undergo heart transportation because of the fear of being infected from the donor or because they fear they will not get the optimal care from the overstressed healthcare system. Although delay of these procedures may not immediately affect clinical outcomes, there are important long-term and indirect implications for patients with HF.

While it is important to prevent COVID-19, the routine care should not be discontinued to avoid severe complications both on clinical and psychological sides. Therefore, specific LVAD management algorithms should be implemented by every implanting and referring LVAD centre to aim for early diagnosis and treatment of COVID-19 or LVAD complications.

COVID-19 can create a prothrombotic environment in some patients resulting in acute pulmonary embolism which may lead to acute right ventricular failure. Early recognition of right ventricular dysfunction and early intervention in patients who are hypotensive can be lifesaving. The Impella RP is a temporary heart pump that provides right ventricular circulatory support for patients who develop right side ventricular failure or decompensation caused by COVID-19 complications, including pulmonary embolus. For critically ill patients the Impella RP can be rapidly deployed in a matter of minutes using a minimally invasive technique in the cardiac catheterization laboratory or operating room.

In LVAD patients with COVID-19 developing right ventricular (RV) failure, medical management is the mainstay of therapy. Management should be focused on volume management and optimization of RV preload, reduction in RV afterload, improvement in the contractile state of the right ventricle and optimization of cardiac rhythm.[32] Regulation of the LVAD parameters is equally as important. Device speeds are chosen to obtain satisfactory haemodynamic goals without inappropriate left ventricular unloading, maintaining a rightward or neutral position of the interventricular septum and limiting cardiac output while maintaining an adequate mean arterial pressure. Vasodilatation or low systemic perfusion pressures may result in inappropriate unloading of the left ventricle and can contribute to leftward septal shift and suction events which impair LVAD output and RV function and may additionally trigger ventricular arrhythmias.

Serum lactate dehydrogenase (LDH) is a recognized biomarker for early recognition of lung injury and assessment of severity in COVID-19.[18] In addition, a change in biomarker levels may be useful in grading COVID-19 severity in LVAD patients. Increase in LDH in LVAD patients may raise specific concerns of haemolysis or LVAD thrombosis and concomitant stroke. Infection, itself, acts as a trigger for inflammatory response predisposing to pump thrombosis, ischaemic or haemorrhagic stroke in LVAD patients.[33]

In patients with acute hypoxaemic respiratory failure due to COVID-19, prone ventilation may be effective

in COVID-19-related severe ARDS (improving lung mechanics and gas exchange). However, it may be problematic in HF patients on LVAD support as prone positioning could result in complications such as compression of outflow graft and driveline, impaired venous return from increased thoracic pressure, hardware malpositioning, and worsening right ventricular (RV) haemodynamics. However, the probability of impaired functioning of the LVAD by rotation or mechanical compression seems to be very low.

Virtual Follow-up

With the COVID-19 pandemic, LVAD supported patients, their close caregivers and the healthcare professionals face some completely unprecedented and unexpected challenges that may affect their ability to maintain optimal self-care. Accesses to the hospital should be discouraged to reduce the risk of hospital-acquired infection. Thus, monitoring of regular function of the device, laboratory tests, and clinical evaluation may be postponed or made less frequent.

Most LVAD centres have adapted their face to face contacts by organizing remote patient care with virtual or telephone contacts. Each LVAD recipient can be considered for a telemonitoring algorithm after an initial check of his/her status through a phone call to check the home-care situation, recent or current hospital admissions, and open clinical problems requiring regular access to the referring clinic such as in case of severe driveline infections undergoing specific treatments. Patients entering this monitoring programme should have been judged as adequately educated through extensive talks and training sessions with the VAD coordinator focused on driveline dressing techniques, battery and controller exchange, blood pressure, fluids, and anticoagulation self-management.

Through virtual visits, HF clinicians can maintain face-to-face interactions with their patients, gain familiarity with patients' domestic circumstances, obtain vital sign measurement through home blood pressure cuffs and pulse oximeters, perform limited physical examinations for jugular venous distention, peripheral oedema and driveline site integrity, functional capacity, resolve medication issues and interact with caregivers. Patients can send a picture of the driveline site through email or smartphone.

Assessment provided with a virtual visit can also include evaluation of LVAD controller parameters and screening for adverse events, in addition to counselling.[34] Since prevention is currently the best strategy for COVID-19, home management requires that healthcare professionals innovate ways to follow LVAD patients virtually and advise them with instructions to self-quarantine, take hygiene actions and social distancing measures for prevention of disease and transmission. Healthcare professionals should limit all elective medical visits and testing, arrange for in-home blood-testing and home international normalized ratio monitoring as well as emphasize the importance of nutrition, sleep and exercise. Patients' families and caregivers must also be protected and practice self-care measures for safety. Delivering optimal support to LVAD implanted patients during the COVID-19 pandemic include creating local support networks to deliver educational materials, extra pro-active phone calls from the VAD coordinator.

Those with limited access to the internet and/or "smart" devices may not derive benefit from the expansion of these innovations. Older adults may have educational, visual, auditory, and cognitive impairments that hinder their participation in remote care. The option for in-person clinic visits should remain available for patients without access to telemedicine services, high-risk patients or those for whom physical examination is critical for clinical decision making.

Additionally, time should be spent for psychological support and reassurance. Optimal self-care includes behaviour to maintain and increase psychological wellbeing to optimally cope with an LVAD. During the COVID-19 pandemic, patients have an increased level of anguish than the general population. [35] Patients worry about being infected and they worry about the wellbeing of their caregiver. They also worry about changes in their relationship with their close homebound caregiver on whom they become even more dependent. Psychological distress can be accelerated by the lack of physical activity, social deprivation, isolation and loneliness. The use of established behavioural and social science approaches need to identify the active components of "psychological support" that are most applicable to each individual patient with a VAD.

Disclaimer: ECMO has, and will certainly continue, to play a role in the management of COVID-19 patients. It should be emphasized that this initial guidance is based on the current best evidence for ECMO use during this pandemic. Guidance documents addressing additional portions of ECMO care are currently being assembled for rapid publication and distribution to ECMO centers worldwide.

Keywords: extracorporeal membrane oxygenation, acute respiratory distress syndrome, COVID-19, pandemic

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