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# Selection criteria and triage in extracorporeal membrane oxygenation during coronavirus disease 2019

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## Purpose of review

Coronavirus disease 2019 (COVID-19) pandemic changed the way we had to approach hospital- and intensive care unit (ICU)-related resource management, especially for demanding techniques required for advanced support, including extracorporeal membrane oxygenation (ECMO).

## Recent findings

Availability of ICU beds and ECMO machines widely varies around the world. In critical conditions, such a global pandemic, the establishment of contingency capacity tiers might help in defining to which conditions and subjects ECMO can be offered. A frequent reassessment of the resource saturation, possibly integrated within a regional healthcare coordination system, may be of help to triage the patients who most likely will benefit from advanced techniques, especially when capacities are limited.

## Summary

Indications to ECMO during the pandemic should be fluid and may be adjusted over time. Candidacy of patients should follow the same prepandemic rules, taking into account the acute disease, the burden of any eventual comorbidity and the chances of a good quality of life after recovery; but the current capacity of healthcare system should also be considered, and frequently reassessed, possibly within a wide hub-and-spoke healthcare system.

## Video Abstract

<http://links.lww.com/COCC/A43>.

## Keywords

ARDS, coronavirus disease 2019, extracorporeal support, resource availability, veno-venous extracorporeal membrane oxygenation

## INTRODUCTION

Over the last two and a half years, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected almost 500 million people worldwide, causing over 6 million fatalities and requiring a major effort by healthcare systems all over the world [1]. In fact, symptoms caused by coronavirus disease 2019 (COVID-19) required hospital admission of hundreds of thousands of people around the world, peaking over 350 admissions per million population per day in three different pandemic waves – at the beginning of 2020, 2021 and 2022 – in most Western countries [2]. SARS-CoV-2 infection causes multiple organ dysfunction, but mainly a pulmonary involvement ultimately leading to respiratory insufficiency and requiring intensive care unit (ICU) admission in a substantial proportion of patients [3].

## Limited availability of intensive care resources

During the COVID-19 outbreak, the availability of ICU beds and related management (like mechanical ventilators) has rapidly emerged as a critical

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## KEY POINTS

- Extracorporeal membrane oxygenation (ECMO) for the treatment of coronavirus disease 2019 patients has been shown to represent a promising and viable strategy, although very demanding in terms of healthcare resources.
- Identifying *a priori* those patients who are more likely to benefit from extracorporeal support is paramount during pandemics, as ECMO availability may be limited.
- The establishment of contingency capacity tiers may be of help to decide which kind of extracorporeal support may be offered at a given time.
- The establishment of regional coordination is of paramount importance to optimize resources allocation in time of constraints.

bottleneck in responding to the ongoing pandemic needs. The lack of critical care resources dramatically raises the mortality rate of COVID-19, requiring to institute emergency measure to increase their availability or, even, carefully selecting the patients for more advanced treatments in all countries worldwide [4].

A census of ICU beds in Europe was performed in 2012: a total of 73 585 critical care beds were identified, averaging 115 beds per million population. Important differences emerged among different nations: Germany reported 292 beds per million population, whereas Portugal had 42 beds per million population [5]. A similar study was performed in Asia: data from 2017 identified 141 034 critical care beds – averaging 36 per million population. Bangladesh reported 7 ICU beds per million population, Taiwan had 285 beds per million population [6]. Based on a 2009 survey of 5752 hospitals, Rubinson *et al.* [7] estimated that in the United States 62 188 full-featured ICU beds existed (205 per million population). Of note, base capacity for lower-income countries was approximately one ICU bed per million population in the same time frame [8].

In many Western countries, daily ICU admissions for COVID-19 alone during the pandemic peaked over 60 patients per million population, with France and Belgium hitting 100 ICU admissions per million population per day in both March and November 2020 [9]. At this rate, the existing ICU bed capacity was rapidly saturated in many countries following the COVID-19 outbreak, and physicians were forced to triage patients on the basis of available resources. In March 2020, the Italian Society of Anesthesia, Analgesia, Resuscitation and

Intensive Care (SIAARTI) published a document titled ‘Clinical Ethics Recommendations for the Allocation of Intensive Care Treatments in exceptional, resource-limited circumstances’ [10] stating that in a context of shortage of healthcare resources, intensive treatments must be allocated to those with ‘greatest life expectancy’. The same guideline states that extracorporeal membrane oxygenation (ECMO) – being one of the most resource-consuming treatments – should have been reserved for extremely selected patients, for which prompt weaning from extracorporeal support can be anticipated [11].

## Limited availability of extracorporeal support equipment

A complete census of ECMO availability in different parts of the world is hard to fulfill. The German Interdisciplinary Association for Intensive Care and Emergency Medicine (DIVI) reports the availability of 779 ECMO machines in 214 centers in Germany [12]. The experience with veno-venous (V-V) ECMO in COVID-19 in Germany has been lately described in a nationwide cohort analysis: a total of 3875 V-V ECMO runs were reported between January 2020 and November 2021. Overall survival was 33%. A total of over 500 simultaneous runs were ongoing in April 2021 [13<sup>\*\*\*</sup>].

Extracorporeal Life Support Organization (ELSO) provides a list of affiliated ECMO centers and their activity [14]. ELSO report for 2020 includes a total of 7917 adult respiratory ECMO runs in 521 centers [15]. The registry reports an average run time of 466 h and an overall survival of 55%. These data are profoundly different from those of the previous year: in 2019, the ELSO Registry reports 4956 runs with an average run time on 292 h and an overall survival of 64%. An extended duration of ECMO runs during COVID-19 also emerged from EuroELSO reports [16]. Longer ECMO runs mean that more resources are needed to cure a single patient: predictors of long runs should therefore be considered when candidacy to extracorporeal support is assessed.

Gannon *et al.* [17<sup>\*\*\*</sup>] performed a so-called ‘natural experiment’ determining that among the 240 patients with COVID-19 referred for ECMO between January and August 2021, only less than 40 percentage actually received it due to limited available resources. Patients over the age of 60 were excluded *a priori* from extracorporeal support in the reported series, as this was considered an absolute contraindication to ECMO at Vanderbilt University Medical Center during COVID-19 pandemic [18<sup>\*\*\*</sup>].

## Rational use of extracorporeal membrane oxygenation in coronavirus disease 2019

In March 2020, ELSO provided its first Guidance Document about ECMO for COVID-19 patients. ELSO recommendation was against starting new ECMO centers during the pandemic, as 'ECMO is not a therapy to be rushed to the front lines.' [19] In the same document, the responsibility to decide about the use of ECMO for COVID-19 in experienced centers was deemed as a local responsibility, which should be assessed case-by-case on overall patient load, staffing, and other resource constraints. The Interim Guidelines that shortly followed [20], provided advice about ECMO provision based on system capacity. In a pandemic situation, descriptions for levels of diminishing ECMO capacity must be established. At each level, exclusion criteria become more stringent based on characteristics associated with limited ICU and personnel capacity, limited treatment facilities, as well as mortality and ECMO duration. The Guidelines advice that, while at conventional capacity extracorporeal support should be offered based on usual criteria, at contingency capacity tier 1, only younger patients with single-organ failure should find access to extracorporeal support, and extracorporeal cardio-pulmonary resuscitation (ECPR) should not be offered. Contingency capacity tier 2 requires application of restrictive criteria for V-V ECMO, while veno-arterial (V-A) ECMO and ECPR should not be offered. At crisis capacity, the Guidelines advice the suspension of all ECMO activities (Fig. 1) [20]. In an effort to optimize resource allocation in times of crisis, Minnesota ECMO consortium grouped indications for ECMO into three tiers based on expected outcome, further dividing into short or long expected duration of ECMO support, using a cutoff point of 5 days (Table 1) [21].

The 2021-update of ELSO Guidelines [22] reaffirm that, while indications for extracorporeal support in COVID-19 should remain unchanged and refer to established literature, patient selection must be judicious and equitable and should become more stringent as capacity diminishes. Common indication to extracorporeal support for respiratory failure according to EOLIA Trial [23] criteria is reported in Table 2. Although in time of pandemics it may be tempting to stretch the use of conventional therapy to avoid placing patients on ECMO due to resource constraints, the role of early ECMO should be stressed and recommended. Deferral of ECMO initiation until further decompensation is not recommended but might be preferable to not initiating ECMO at all when criteria are met. [24]

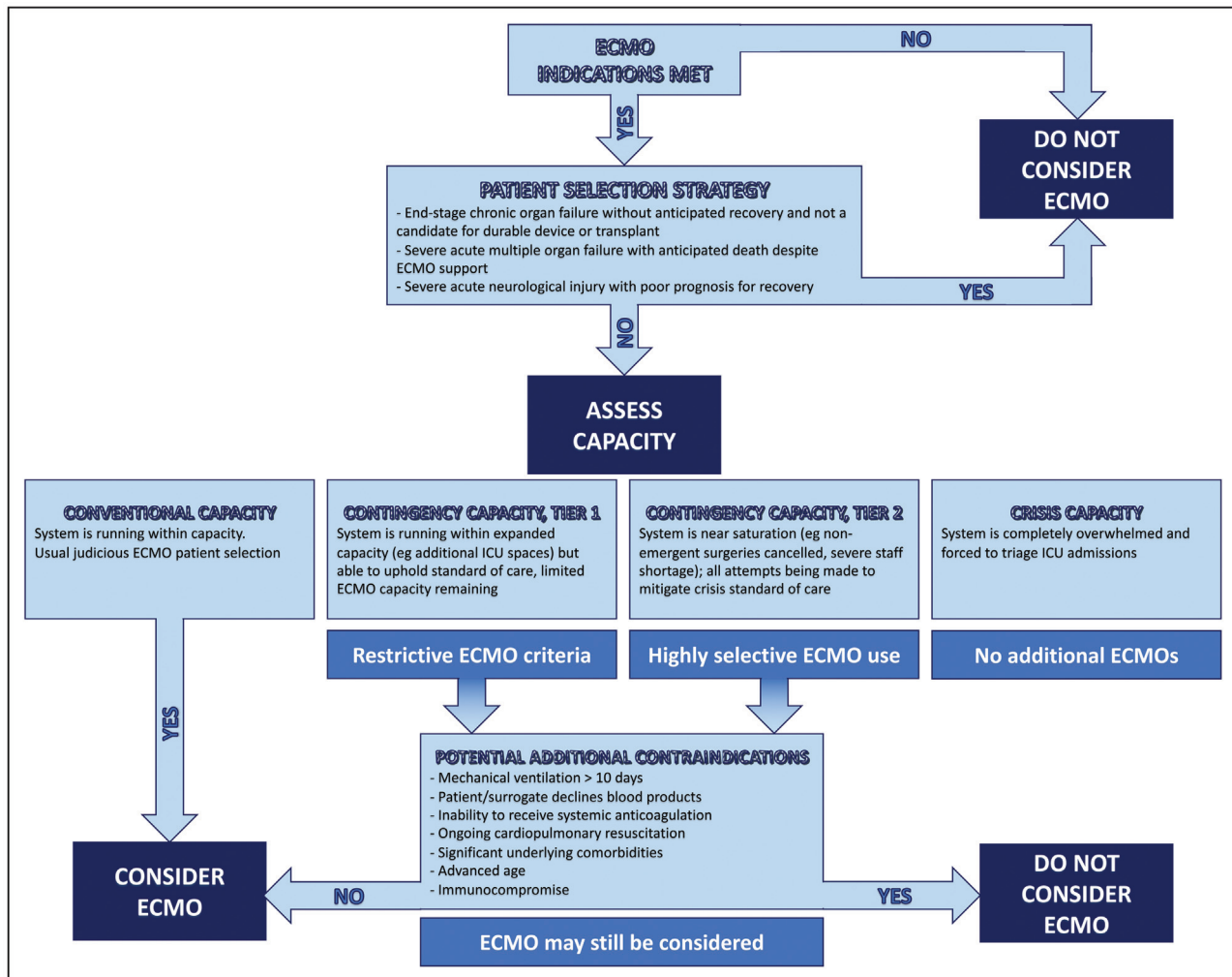
During the COVID-19 pandemic, indications to extracorporeal support remain unchanged, as they account for the severity of the acute disease; on the

other side, contraindications must be flexible to reflect the burden on the healthcare system, to optimize benefit-to-resource utilization ratio at any time. In situations in which healthcare capacity is diminished, patient selection should take into account characteristics associated with increased mortality. Nevertheless, the use of 'innovative' V-V ECMO configurations, including its use as Oxy-RVAD with right atrium-pulmonary artery (RA-PA) cannulae, has been reported by several groups around the world with promising results [25,26] and may require further consideration [27].

## Characteristics associated with increased mortality

Identification of significant predictors of death before implant of extracorporeal support has been a major study topic over the last two decades. In an attempt to improve resource allocation, the Italian ECMONet developed the ECMONet score to predict mortality risk in patients undergoing V-V ECMO for acute respiratory distress syndrome (ARDS) due to influenza A (H1N1) pneumonia. Over 60 patients receiving ECMO in 2009 with a 68% survival rate, hospital length of stay before ECMO institution, bilirubin, creatinine, hematocrit values and mean arterial pressure were identified as significant predictors of death before implantation [28]. A larger effort carried out by ELSO led to the publication of the Respiratory ECMO Survival Prediction (RESP) score in 2014, based on 2355 runs with a 57% survival rate [29]. Many different factors were associated with mortality, including a partial pressure of carbon dioxide above 75 mmHg, a peak inspiratory pressure over 42 cmH<sub>2</sub>O, age over 60 and length of mechanical ventilation over 1 week. Based on the abovementioned scores, restrictive criteria suggested by ELSO Guidelines include age  $\geq 65$  years, obesity and immunocompromised status as relative contraindications, while advanced age, Clinical Frailty Scale category  $\geq 3$ , mechanical ventilation  $>10$  days, significant underlying comorbidities, contraindications to anticoagulation, inability to accept blood products and ongoing CPR are listed among absolute contraindications [22].

Age deserves some further considerations: the German cohort analysis conducted between January 2020 and November 2021 included 924 COVID-19 patients over 65 years of age, close to one fourth of the total [13<sup>\*\*\*</sup>]. The series reported a low overall survival rate of 34%, with less than one fifth of elderly patients surviving decannulation. Japanese researchers reported a smaller – yet different – experience: only 35 ECMO runs were reported among 4695 in-hospital elderly patients, but



**FIGURE 1.** Algorithm for ECMO use during a pandemic based on system capacity. COVID-19, coronavirus disease 2019; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; PaCO<sub>2</sub>, partial pressure of carbon dioxide in arterial blood; PaO<sub>2</sub>:FiO<sub>2</sub>, ratio of partial pressure of oxygen in arterial blood to the fractional concentration of oxygen in inspired air; PEEP, positive end-expiratory pressure; V-A, veno-arterial; V-V, veno-venous. Previously published in Badulak J, Antonini MV, Stead CM, *et al.* Extracorporeal membrane oxygenation for COVID-19: Updated 2021 guidelines from the extracorporeal life support organization. *ASAIO J.* 2021;67:485–95.

survival was over 50% [30]. These contrasting data call for a particular attention to age in relation to initiation of extracorporeal support: in modern era, age cannot be considered an absolute contraindication for extracorporeal life support, but comorbidities and chances of recovery must be carefully weighted prior to initiation of support in times of limited available resources, as the inaccessibility of elderly population to transplantation programs leaves physicians with no plan B in case of lack of pulmonary recovery.

Using length of mechanical ventilation as a contraindication to ECMO initiation has also been recently questioned. Olivier *et al.* reported a 69% survival rate in patients under 60 years of age

cannulated after more than 7 days of mechanical ventilation [31]. However, most of the ECMO centers around the world seem to have strongly limited their indications of late cannulation in times of pandemic: a recent meta-analysis reports a mean mechanical ventilation of 4.25 [3.32–5.18] days prior to ECMO initiation in 1747 patients in 26 studies [32]. Similar data are reported in the ELSO registry [33].

### Cardiocirculatory support and coronavirus disease 2019

Myocardial injury in COVID-19 is not an infrequent issue: various degrees of myocardial involvement

**Table 1.** ECMO tiers based on survival and anticipated ECMO duration – adapted from Prekker ME *et al.* [21]

| Tier                     | Short anticipated ECMO duration                                           | Long anticipated ECMO duration                                                                     |
|--------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| Tier 1 (survival > 60%)  | Status asthmaticus causing hypercarbic respiratory failure                | Viral infection causing acute respiratory failure with single organ failure                        |
|                          | Severe accidental hypothermia causing cardiac arrest or cardiogenic shock | Trauma causing acute respiratory failure with single organ failure                                 |
|                          | Pediatric cardiogenic shock (pre or post cardiotomy)                      | Pediatric myocarditis                                                                              |
|                          | Neonatal meconium aspiration syndrome                                     | Neonatal sepsis, congenital diaphragmatic hernia, persistent pulmonary hypertension of the newborn |
| Tier 2 (survival 30–60%) | Poisoning-induced cardiogenic shock                                       | Acute respiratory failure (any cause) with multiorgan failure                                      |
|                          | Massive pulmonary embolism                                                | Pediatric/neonatal cardiac arrest from cardiac etiology                                            |
| Tier 3 (survival < 30%)  | Adult postcardiotomy cardiogenic shock                                    | Bridge to LTx for irreversible respiratory failure                                                 |
|                          | Extracorporeal CPR in OHCA with favorable prognostic features             | Acute respiratory failure and severe immunocompromise                                              |
|                          | Extracorporeal CPR in IHCA with unfavorable prognostic features           | Refractory shock with multiorgan failure of any cause                                              |

CPR, cardio-pulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; IHCA, In-hospital Cardiac Arrest.

have been reported in up to 2.3% of cases of SARS-CoV-2 infection [34]. Few cases of COVID-19-related acute myocarditis, presenting with severe reduction in the left or biventricular function have been described [35]. If severe cardiogenic shock occurs, mechanical circulatory support may be required. As fulminant myocarditis has been previously associated with high rates of myocardial recovery [36], immediate V-A ECMO should be offered even in limited resources environments. In few selected cases without pulmonary involvement, the use of Impella (Abiomed, Danvers, MA) pumps (for isolated LV support or for biventricular support – the ‘BiPella’ approach) may be effective and associated with higher rate of myocardial recovery [37]. As mentioned, however, several experiences with immediate right ventricular support associated with V-V ECMO using the RA-PA ECMO configuration, lead to impressive clinical outcome (survival rate higher than 80%) indicating that prophylactic cardiac support, particularly of the right ventricle, might have avoided or largely reduced, myocardial compromise often observed in the most severe forms of COVID-related ARDS [25,26].

### Extracorporeal cardio-pulmonary resuscitation during coronavirus disease 2019 pandemic

Even before COVID-19, ECPR was considered a resource-intensive intervention, with very few patients meeting eligibility criteria, and even fewer successfully receiving the therapy within acceptable timeframes. The pandemic poses additional challenges in terms of safety and appropriateness of this demanding technique [35]. Four main concerns about ECPR during the pandemic were identified:

- (1) Staff protection: the necessity of personal protection equipment increases the difficulties of emergent cannulation for ECPR.
- (2) Emergency system overload: out-of-hospital cardiac arrest patients may receive less prompt assistance due to emergency system overload during the pandemic: in fact, ECPR relies on refined processes that may be significantly impacted by pandemic conditions.
- (3) SARS-CoV-2 patients: in a patient who is known, or suspected, to have COVID-19, cardiac arrest may be related to the effects of the virus or

**Table 2.** Indications to V-V ECMO

|                                                                                                                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PaO <sub>2</sub> /FiO <sub>2</sub> <80 mmHg for >6 h                                                                                                                                  |
| PaO <sub>2</sub> /FiO <sub>2</sub> <50mmHg for >3 h                                                                                                                                   |
| pH <7.25 with PaCO <sub>2</sub> >60 mmHg for >6 h with respiratory rate >35 breaths/min and ventilatory settings adjusted to keep a plateau airway pressure of <32 cmH <sub>2</sub> O |

ECMO, extracorporeal membrane oxygenation; FiO<sub>2</sub>, fractional concentration of oxygen in inspired air; PaCO<sub>2</sub>, partial pressure of carbon dioxide in arterial blood.

the virus may simply be a bystander. In all circumstances, SARS-CoV-2 positivity will increase the burden of care once admitted to the hospital for ECPR.

- (4) Resource allocation: the institution of crisis standards, and limitations on staffing and equipment are forcing the critical care community to confront the ethical boundaries between individual patient benefit, distributive justice, and resource allocation.

ELSO Guidelines discourage centers without established ECPR programs from initiating ECPR for out-of-hospital cardiac arrest during surge situations. Guidelines also recommend against conversion to V-A ECMO in the setting of a cardiac arrest in a patient receiving V-V ECMO or during cannulation due to the poor outcomes anticipated. However, conversion to V-A ECMO may still be considered in the setting of refractory shock (both cardiogenic and septic shock), although with restrictive indications arising from resource allocation.

The current pandemic situation triggered a status in which critical care demand outstrips capacity. Even conventional CPR may be impaired by delayed response times, time to allow personal protection equipment donning, and system pressures diverting the resuscitation team. In this scenario, indications to ECPR are limited to very selected cases, eventually excluding completely out-of-hospital cardiac arrests. Patients experiencing cardiac arrest during coronary angiography may still withhold candidacy to ECPR, as rapid cannulation is possible, etiology of cardiac arrest is known and treatable, and the environment is favorable to safe deployment of ECPR.

Surge-specific protocols are required to offer ECPR in time of pandemic. ECPR candidacy and feasibility should take into account both patient-specific and healthcare system-specific factors; therefore, local tools with the prompt involvement of senior decision-makers are required in order to promote acceptable outcomes.

### Regional planning for extracorporeal membrane oxygenation allocation

In several countries, ECMO networks have been established since 2009 influenza A (H1N1) pandemic to face the increase in ECMO demand, stimulated by favorable outcomes and improvements in safety and transportability [38]. However, in most regions, ECMO availability is often inconsistent, and regional coordination is still lacking [39]. These challenges only amplify the vulnerability of ECMO to resource saturation during a pandemic.

In Minnesota, a network has been recently established among five ECMO centers capable of providing extracorporeal support for 55 patients at peak capacity over a 5.5 million population [40]. The ECMO consortium of Minnesota developed an online surveillance tool which displays center-specific and aggregate census data for actual ICU, ventilator, and ECMO capacity at all involved centers. A surge in demand may trigger resource conservation measures, such as the discontinuation of ECPR for out-of-hospital cardiac arrest, deferring elective procedures likely to require post-operative ECMO, and an earlier weaning from V-V ECMO for patients already on survival tiers reported in Table 1 – and on health system load, allowing for an optimal management of local resources.

A major effort to optimize resources allocation in time of constraints was performed in the Greater Paris area, in which all ECMO proposals were centralized at Pitié-Salpêtrière Hospital [41] and evaluated in a staff meeting, including at least two intensivists. Once the indication was approved, the mobile ECMO retrieval team was sent to perform bedside cannulation and then transfer the patient to one of the Paris-Sorbonne University Hospital Network ICUs. This organization provided uniformity in the indications for ECMO cannulation during the pandemic, and allowed for equal opportunities to be provided for all patients experiencing respiratory failure in the early phases of the pandemic.

### CONCLUSION

In time of crisis, the candidacy of patients to extracorporeal support should rely on a multifaced process, which should take into account the acute disease, the burden of any eventual comorbidity, the chances of a good quality of life after recovery, and weight the benefit to resource allocation ratio depending on current health system status. As such, indications to ECMO during the pandemic should be fluid and may be adjusted over time. In order to give the best chances to all patients, ECMO should be considered a trial of support rather than an indefinite resource assignment. Patients and family members should be aware that extracorporeal therapy may be withdrawn depending on response to therapy.

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## Conflicts of interest

Roberto Lorusso is consultant for Medtronic, LivaNova, Getinge, and Abiomed. He is also part of the Medical Advisory Board of Eurosets and Xenios.

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