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# Temporary mechanical circulatory support: Devices, outcomes, and future directions

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Faced with a chronic donor shortage, clinicians and regulators both struggle to develop allocation systems which balance the challenges of waitlist mortality and donor availability. Most organ allocation systems across the globe have prioritized transplantation of patients supported on temporary mechanical circulatory support (tMCS) with regional variations. There are concerns that this approach might not produce optimal outcomes and is not without major drawbacks including lack of strict criteria for tMCS as bridge strategy, choice of optimal devices and wait time on tMCS.

The current manuscript outlines characteristics and limitations of current devices used for tMCS as a bridging strategy. The outcomes of transplantation following device support are evolving and are highlighted as well. Lastly, the allocation schema for heart transplantation in various countries are reviewed and compared.

Additionally, we propose key principles to guide changes in next iteration of donor allocation systems to balance waitlist mortality with optimal post-transplant outcomes. First, allocation should be on the basis of calculated scores which take into account a variety of pre-and post-transplant factors and cannot be easily manipulate by choice of support therapy. Next, time at high urgency statuses should be time-limited with strict criteria for renewal. Emphasis should be placed on the further refinement of durable mechanical support therapies. Patients on durable support need a pathway to qualify for transplantation in the absence of complications, and lastly, peer review of exceptions to organ allocation policy are critically important to ensure the appropriate allocation of donor organs.

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Nearly 70 years have passed since the development of cardiopulmonary bypass in 1953 and the beginnings of cardiac surgery.[1-3] Initially intended for temporary use during cardiac procedures, it was not long before there were patients who could not be successfully separated from bypass support, which was uniformly fatal in those years. This alongside lack of treatment options and poor survival from congestive heart failure and myocardial infarction led to a need for devices to assist or completely replace the heart. By the mid-1970s, there were reports of use of a "left heart assist device" which was an extracorporeal pump connecting cannulas from the left atrium to the ascending aorta for patients who failed to wean from bypass.[4] It was noted that shorter durations of support (<3 days) were associated

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with improved outcomes, a finding which remains valid today.

About this time, heart transplantation moved from the animal laboratory to the human operating room, with great fanfare and hope that this would be a solution for patients with critical heart disease.[5,6] Unfortunately, the understanding of allograft rejection was limited and with the paucity of drugs, the survival was poor by current standards with less than 50% surviving a year post-surgery.[7]

Mechanical circulatory support (MCS) evolved concurrently with transplantation. A surgical pump which allowed pulsatile blood flow from the left ventricular (LV) apical cannula to the aorta was developed and used for patients who failed to wean from cardiopulmonary bypass after valvular surgical procedures.[8] One of the first commercially approved temporary MCS (tMCS) devices was the Abiomed BVS 5000 which was a pneumatically driven paracorporeal ventricular assist system. This system facilitated uni-or bi-ventricular support via surgically placed cannulas and an external pump and was used as a bridge to transplantation for critically ill patients.[9]

Coming along 30 years, the MCS field has evolved, especially in the domain of durable implantable, dischargeable LV assist devices. As well, there has been great progress in the development of tMCS, particularly for patients where transplantation is the ultimate goal.

More recently, modification of the organ allocation system in 2018 in the United States has led to a significant rise in the use of tMCS as a BTT strategy to facilitate rapid transplantation for critically ill patients and reduce waitlist mortality.[10,11] The clinical impact of this prioritization of donor hearts to the highest acuity patients with high waitlist mortality is still evolving.[10-18] In this context, the purpose of this manuscript is to describe the current state of tMCS, in particular with reference to bridging to transplantation, and the outcomes following transplantation. Given the transplant focus, the issue of bridging strategy and its impact on transplant organ allocation policy will be discussed as well.

## MCS strategy and specific devices

Broadly, MCS strategy can be classified based on duration of support into short term, non−dischargeable tMCS, and durable (dischargeable from the hospital) MCS; among the tMCS devices, some are percutaneous, and others are surgically placed, but none of these patients can leave the hospital. The most used percutaneous systems are the intra-aortic balloon pump (IABP), the Impella (AbioMed, Danvers, MA), the TandemHeart (LivaNova, London, England, UK), and veno-arterial extracorporeal life support (VA-ECLS) (*Table 1*). Short-term devices can be used in various configurations, alone or in combination with each other. Durable MCS devices are outside the scope of this manuscript.

## Intra-aortic balloon pump (IABP)

The IABP was developed by Kantrowitz[19,20] in the late 1960s and owing to its simplicity and relatively low cost, it is the most widely available and commonly deployed tMCS device and modern catheters require a 2.5 to 2.7 mm femoral arteriotomy (7.5-8 French).

Given the increase in coronary perfusion, the IABP was extensively studied in the setting of acute myocardial infarction (AMI), however with disappointing results. Use of the IABP in post-AMI patients with cardiogenic shock was not shown to reduce mortality.[21,22] There is debate about the degree to which the device augments cardiac output, ranging from 0.5 liters per minute to 1.5 liters per minute.[23,24] A recent review highlights the data on the use of IABP in detail.[25] In addition, there is increasing recognition that the pathophysiology of acutely decompensated chronic heart failure is distinct from cardiogenic shock due to an acute ischemic insult.[26] Unfortunately there are no large, randomized trials of IABP in the acutely decompensated chronic heart failure setting.

## IABP placement strategies

The IABP is typically placed via the femoral artery, though it can be inserted via a surgical graft into the axillary artery and utilized for prolonged support.[27-29] Percutaneous access to the axillary artery has become more routine especially given the relatively modest size of the IABP catheter. For patients waiting for transplant, avoiding further physical deconditioning is extremely important, so combining tMCS with the ability to ambulate and exercise is essential. Recent reports detail axillary IABP use and the associated complication profile.[30,31] The largest experience is from a single center with 195 patients who underwent axillary IABP placement (before the change in transplant allocation in October 2018). 120 of 195 (61.5%) were bridged to transplant, and an additional 13 patients were bridged to durable MCS. The incidence of device exchange was 37%, with some patients requiring multiple exchanges. The most common adverse events include need for exchange or repositioning (37%), hematoma (5%), infection (9.2%), and bleeding requiring transfusion (2.6%).[31] The axillary arterial approach is becoming more common though as centers become familiar with this access route for other procedures. Interestingly, one center has reported the safety and feasibility of ambulation with femoral IABP as well.[32] Lastly, there is a novel surgically implantable IABP device which has reported encouraging pilot data, but this is not available outside of a clinical trial at this time (NuPulse, Raleigh, North Carolina).[33]

## Impella

The Impella (Abiomed, Danvers Massachusetts) is a microaxial transvalvular pump which transfers blood from the LV cavity to the aorta above the aortic valve. It directly unloads the LV and decreases wall tension and myocardial oxygen consumption along with improvement in mean arterial pressure, peripheral perfusion, and reduction in wedge pressure.[34] Compared to IABP, the Impella devices provide greater increases in cardiac output.

**Table 1** Characteristics of Contemporary Temporary MCS Devices.

| | Catheter /CannulaSupport timevessel size | Benefits | Contraindications | Complications | Considerations |
|---|---|---|---|---|---|
| IABP | 7 to 8 Fr<br>0.3 to 1.0 L/min<br>Weeks<br>Femoral / Axillary artery size 2.5 to 3 mm | Small size, wide availability in most hospitals. Vascular complications lower than other larger devices<br>Can be placed via axillary artery | Severe Peripheral Vascular Disease<br>Severe Aortic Regurgitation | Vascular Injury/Bleeding<br>Aortic Dissection<br>Limb Ischemia<br>Air or Plaque Embolism | With uncontrollable tachycardia, consider other devices, consider axillary approach in patients with severe peripheral arterial disease |
| Impella Family of devices | 13 to 23 Fr<br>1.0 to 5.0 L/min<br>7 to 14 days<br>Femoral artery $\geq$ 4.3 to 4.7 mm | Familiar device to interventional cardiologists. Higher flow than IABP | Severe Aortic Stenosis<br>Severe Aortic regurgitation<br>Mechanical Aortic valve<br>LV thrombus | Pump migration<br>Ventricular Arrhythmia<br>Hemolysis<br>Vascular Injury/bleeding<br>Limb Ischemia | Impella CP helpful for LV venting with percutaneous VA-ECLS, run at low (P-3) support setting |
| TandemHeart Left Atrium- Femoral Pump | 15 to 19 Fr arterial<br>21 Fr venous<br>2.5 to 5.0 L/min<br>14 days<br>Femoral artery $\geq$ 5 to 6 mm | Useful with inability to cross aortic valve or with LV thrombus/ small chamber | Severe Aortic regurgitation | Cannula migration<br>Pericardial Tamponade<br>Thromboembolism<br>Inter-atrial shunt | Uses standard 3/8 inch tubing. Can add oxygenator unit in series for ECLS<br>Requires trans-septal puncture expertise |
| Peripheral VA-ECLS | 15 to 19 Fr arterial<br>22 to 28 Fr venous<br>6 to 8 Fr antegrade superficial femoral arterial perfusion cannula<br>3.0 to 7.0 L/min<br>Weeks<br>Femoral artery $\geq$ 5 to 6 mm | Bedside implantation possible<br>Full cardiopulmonary support<br>Can be done in variety of care settings | Severe aortic regurgitation | Thromboembolism<br>Differential upper body/brain hypoxia<br>LV distention /pulmonary Edema<br>Limb Ischemia<br>Vascular Injury/Bleeding | LV venting with Impella when significantly reduced LV function<br>Conversion to VAV or Central cannulation for persistent upper body hypoxia despite optimal ventilator support<br>Proactive antegrade cannulation to minimize distal ischemia<br>Altered Drug pharmacokinetics |
| CentriMag | Surgical cannulas (30 French or higher)<br>Flow 4 to 8 L /min<br>Weeks<br>Can be placed to central vessels directly or via graft | Single ventricle or biventricular support possible<br>Oxygenator can be added in series if needed | Inability to anticoagulate | Thromboembolism<br>Pericardial Tamponade<br>Surgical trauma | LV apical cannulation preferable to LA cannulation |

Impella is available in different sizes, including percutaneous implantation (13 French Impella 2.5 and 14 French CP) for partial support as well as full support (>5 liters per minute flow) with 21 to 23 French (7-8 mm) pumps which are implanted via surgically placed grafts, typically to the right axillary artery (Impella 5.0 and 5.5).[35]

## Impella CP

The Impella CP is approved for femoral arterial placement and has been reported to be used via the axillary artery on an off-label basis. Ambulation is possible only if the patient has axillary insertion of the device which is feasible but uncommon.[36] The device has a pigtail which is designed to keep it away from the mitral apparatus and the cardiac apex, but routine echocardiographic imaging is essential to ensure the device is neither too deeply inserted nor too shallow in the LV outflow tract.

## Surgical Impella devices—5.0 / 5.5

The surgically placed Impella pumps may be used as a short-term bridge to transplant in the setting of isolated LV failure. The pumps flow 5 or more liters per minute approximately, and catheter migration is less common than with smaller percutaneous devices. Sometimes a separate extracorporeal membrane oxygenation circuit is added to manage biventricular failure or concomitant poor oxygenation. In these cases, the Impella functions as a LV venting device to prevent LV distension. Creative approaches have been developed to allow placement of the Impella in combination with an ECLS circuit via a composite graft to the axillary artery (so-called ECMELLA—see below).[37]

## Tandem heart

Tandem Heart refers to the name of a temporary extracorporeal, centrifugal, continuous flow pump, as well as a special catheter for transseptal placement into the left atrium, as well as the company name (since acquired by LivaNova Inc., London, UK). The pump is central to all of the support systems sold by the company, and it is provided with integral standard 3/8-inch blood tubing. Depending on which access cannulas are inserted, the system can be used for uni- or bi-ventricular support. The original TandemHeart pump was FDA approved in 2003 and a newer version ("LifeSparc") is now available with higher flow rates. If needed, an oxygenator can be placed in series in the blood circuit to achieve blood oxygenation and removal of carbon dioxide.

When used to support the left ventricle (LV), a cannula is placed via the femoral vein, and lodged in the left atrium following transseptal puncture and dilation. The blood return is to the femoral artery (typical 15-17 French cannula). In this configuration, Tandem Heart indirectly reduces LV preload, stroke volume, and myocardial oxygen demand. Placement of TandemHeart left atrium to femoral artery circuit has been associated with improvement in cardiac index, blood pressure, renal function, urine output, lactic acidosis and pulmonary capillary wedge pressure in patients with severe refractory cardiogenic shock.[38,39] The pump is FDA approved for 6 hours of use and CE-marked for up to 30 days of use.

When right ventricular support is needed, the cannulation strategy consists of a large cannula (typically 23-25 French) draining the superior and inferior vena cavae and a separate cannula placed in the main pulmonary artery via the contralateral femoral vein or via the right internal jugular vein. A newer alternative is the dual lumen Protek Duo cannula (LivaNova) which is a 29 or 31 French cannula placed via the right internal jugular vein.[40,41] This multilumen cannula has drainage in the right atrium with return directly to the pulmonary artery. If needed, an oxygenator can be placed in series in the blood circuit to achieve extracorporeal membrane oxygenation.

The TandemHeart left atrium to femoral artery system was first used as a bridge to transplant in 2005 (a patient who required six days of support until successful heart transplantation).[42] Later reports on a handful of patients replicated these results.[38,43] The Tandem Heart remains unique with left atrial drainage, but its use has been supplanted by devices such as Impella which are a single catheter design, without the need for a transseptal puncture. However, in cases where there is clot in the LV, or a metallic prosthetic aortic valve, or severe hypertrophic cardiomyopathy, the TandemHeart may be the only feasible support device.

## Veno-arterial extracorporeal life support

Veno-Arterial extracorporeal life support (VA-ECLS) consists of a blood pump combined with a "membrane lung" and owing to its versatility, low equipment cost, and relative ease of implantation, it has become a common tool in the management of patients with severe cardiogenic shock.[44] When initially used for post-cardiotomy cardiogenic shock, survival was low (25%).[45] However, with experience and improved circuits, survival has increased, though these patients still have a significant risk of mortality (40%).[46]

VA-ECLS involves blood being drawn into the circuit via a venous inflow cannula (typically 24-27 French), propelled by a centrifugal, continuous flow pump, oxygenated and returned to the patient via the arterial outflow cannula (15-19 French). Importantly, VA-ECLS is useful in uni- or bi-ventricular failure, with or without deficits in oxygenation or elevated pulmonary vascular resistance. Additionally, apart from supporting the failing heart and failing lungs, it has been used for severe sepsis and refractory vasoplegia where "hyperperfusion" is needed temporarily— and all this can be provided minimally-invasively by peripheral access.[47] Unlike TandemHeart and Impella, VA-ECLS can be quickly implanted at bedside in urgent situations.

The main weakness of VA-ECLS support is the risk of bleeding or clotting due to the membrane and extracorporeal circuit. In addition, VA-ECLS increases LV afterload and myocardial oxygen demand which may result in LV distention, pulmonary edema and hypoxia in patients with

severely reduced LV function.[48] Subclinical LV distention defined as radiographic evidence of pulmonary edema and pulmonary artery diastolic pressure >25 mm Hg can be seen in 20% of patients, while clinical LV distention requiring immediate decompression can occur in 10% of patients.[49] This condition can be minimized or avoided by inotrope use, or LV venting/unloading with an IABP or an Impella, or an interatrial balloon septostomy.

In clinical practice, the axillary and femoral artery are most often used for ECLS cannulation. If no other pathology is present, the femoral artery is often the quickest to cannulate, which makes it the ideal access vessel for time-critical situations like refractory shock or CPR. Downsides of this technique include the risk for regional perfusion syndromes and the inability to mobilize the patient rigorously. Cannulating the axillary artery offers almost central access to the circulation. Surgical preparation is more time-consuming and less amenable to percutaneous technique and is very demanding during mechanical CPR. Once arterial cannulation is complete, either directly or via an 8 to 10 mm graft, antegrade flow and secure perfusion of the supra-aortic vessels are established. The patient is reasonably safe from regional perfusion syndromes and − especially if venous drainage is established using the internal jugular vein− may be fully mobilized.[50] Continuous monitoring of arm perfusion by blood pressure measurement or near-infrared spectroscopy (NIRS) is advisable. A significant downside of this technique is the higher probability of right hemispherical strokes. A decisive survival benefit has not been shown when comparing access via femoral and axillary artery.[51]

An important modification of approaching the axillary artery is cannulation of the innominate artery, which requires an upper hemi-sternotomy and is accomplished using an 8 to 10 mm vascular graft, which is sutured to the artery and then cannulated. This approach has proven useful in patients at risk for regional perfusion syndromes, requiring prolonged ECLS, while having peripheral arteries, which are too small for direct cannulation.[52]

## Combination of ECLS and Impella

In cases of left ventricular distension on ECLS for left ventricular failure, a percutaneously placed Impella CP provides enough support to lower left ventricular load and simultaneously prevent damage to the lungs as well as promote ventricular recovery. This approach has proven to be beneficial as compared to ECLS alone and is often referred to as "ECMELLA."[53,54]

A modification of this technique is described as "ECMELLA 2.0." For this configuration a single, branched graft is sutured onto the right axillary artery. One branch of the graft is the used to accommodate a 17Fr. arterial ECLS cannula, the other for an Impella 5.5 pump. Venous drainage may be from the femoral or jugular vein.[37,55]

By this approach vascular manipulation is limited to the minimum, and powerful support is possible even in deep shock, without risking left ventricular distension. Additionally, the system offers the option of tailored down-tapering of support as individually needed. For example, once shock has resolved and provided gas exchange and right ventricular function are sufficient, ECLS may easily be removed at the bedside, leaving only the Impella in place. As the axillary artery was the only vessel used for arterial access, mobilization and ambulation are possible at all times.[37,55]

## Surgically implanted non−dischargeable tMCS

Surgical extracorporeal tMCS devices are implanted via a sternotomy or a lateral thoracotomy with an external pumping chamber and a drive console. One of the most utilized devices is the CentriMag pump (Abbott) which is a third-generation magnetically levitated, extracorporeal, centrifugal-flow pump designed for short-term support. It may be used for both uni- and biventricular support and can also be used as the pump for a VA-ECLS circuit.

Such pumps can be utilized (in off-label fashion) for several weeks, thereby supporting patients who cannot be weaned from cardiopulmonary bypass as well as semi-elective placement for patients who are failing on other support.[56-58] The aortic return can be placed via a small upper hemi-sternotomy. Ambulation is encouraged as long as cannulas are secured with this possibility in mind.

If the transplant waiting time is anticipated to be prolonged, it is possible to use the CentriMag device, but connect it to the heart with Berlin Heart Excor cannulae in European centers. This way the more cost-effective CentriMag device can be used in the beginning. Later on, if no suitable donor organ is found, it is possible to change to a Berlin Heart Excor pump, support the patient long term, and even discharge home.[59] This device is available for children but not adults in the United States, however. Additionally, the recently described minimally invasive apico-axillary CentriMag ventricular assist device (VAD) combined with ECLS (Ec-VAD) is an attractive approach.[18] However, the use of surgical devices like the CentriMag is waning with increasing experience with the Impella 5.5 platform which doesn't require sternotomy.

## Outcomes post-heart transplant after tMCS as bridging therapy

### IABP

In a retrospective study by Duran et al. of 1,945 patients listed with IABP, 1-year survival following transplantation was 84.3%.[60] Not surprisingly, a lower survival noted in patients bridged with IABP in some reports could be driven by subgroup of patients who required transition from IABP to other forms of MCS due to progressive hemodynamic impairment while awaiting HT. Indeed, a multi-institutional registry from Spain reported a significantly lower 1-year post-transplant survival (43%) in this subgroup.[61] *Table 2* provides a summary of reports regarding tMCS as a bridge to transplantation including waiting time and waitlist mortality.

**Table 2** Studies of patients with temporary MCS and Heart Transplant.

| Device | Author,region | Study period | Patients transplanted on TMCS | *Median support/ waitlistduration (days)* | Waitlist mortality | Post HT survival |
|---|---|---|---|---|---|---|
| IABP | Castleberry US (1) | 2004 to 2011 | 571/1095 | 22 | 27% | 1 year: 90% |
| | Umakanthan US (2) | 2007 to 2010 | 13/18 | 19 | 27.8% | NR |
| | Estep US (3) | 2007 to 2012 | 42/50 | 18 | 8% | 90 day: 90% |
| | Tanaka US (4) | 2011 to 2014 | 58/61 | 21 | 5% | NR |
| | Barge- Caballero Spain (5) | 2010 to 2015 | 194/281 | 10.9 | 7.1% | 30 day: 88.1%<br>1 year: 76%<br>5 year: 67.8% |
| Impella | Trivedi US (UNOS registry) (6) | 2015 to 2019 | 266 (255 directly to HT+11 as LVAD to HT)/378 | New: 12<br>Old: 45 | 17% | - |
| Impella 5.0 | Chung US (7) | 2014 to 2018 | 37/47 | 13.2 | 21.3% | 100% survival to discharge |
| | Seese US (8) | 2010 to 2018 | 57/236 | 13 | 20% | 30 day: 96.5%<br>90 day: 93.8%<br>1 year: 90.3% |
| | Lima US (9) | 2009 to 2015 | 15(13 as Impella to HT+2 as Impella to LVAD to HT)/20 | 7 | 25% | 30 day: 93% |
| | Monteagudo-Vela UK (10) | 2014 to 2019 | 8 | 16 | | 30 day: 87.5%<br>6 month: 87.5% |
| | Kearns US (11) | | 47(33 old and 14 new allocations)/129 | Old: 14.6<br>New: 7.1 | 19% | Old allocation<br>3 & 6 month- 100%<br>New Allocation<br>3 & 6 month: 88.9% |
| Impella 5.5 | Ramzy US (12) | 2019 to 2020 | 5 | 35.1 | 16.3% | |
| | Kennel US (13) | 2020 | 4/14 | 12 | 28.5% | - |
| ECMO | Jasseron France (14) | 2010 to 2011 | 46/866 | 9 | **22.5%** | 30 day: 77.8%<br>1 year: 70.4% |
| | Mishra Norway (15) | 2005 to 2012 | 15/259 | 9.1 | **13.3%** | 30 day: 86.7%<br>1 year: 70%<br>5 year: 70% |
| | Karamlou US (16) | 2000 to 2010 | 316/13250 | - | - | 1 year: 62%<br>**5 year: 54%** |
| | Zalawadiya US (17) | 2000 to 2015 | 157 | - | - | 30 day: 71.9%<br>1 year: 57.8%<br>3 year: 50s<br>5 year: 50s |
| | Yin ISHLT (18) | 2005 to 2016 | 134/6528 | - | - | 1 year: 71.2% |
| | Lechinacole Italy (19) | 2005 to 2017 | 32/300 | 10 | **18.7%** | 30 day: 81.3%<br>APACHE<47 (>47): 1 year: 89.7% (26.6%), 5 year: 81.5% (26.6%) |
| | Fukuhara US (20) | 2003 to 2016 | 40/25168 | Most <10 | - | 90 day: 74.8%<br>3 year: 69.3% |
| | Barge-Caballero Spain (21) | 2010 to 2015 | 129/169 | 9.6 | 19.5% | Pre-discharge: 66.7%<br>1 year: 54.4% |
| | Coutance France (22) | 2012 to 2016 | 118/415 | 9 | **15.7%** | 1 year: 85.5%<br>3 year: 80.3% |
| | Poptspov Russia (23) | 2013 to 2017 | 166/786 | 5.8 | **8.8%** | Pre-dayischarge: 86.1%<br>1 year: 83.3%<br>3 year: 74.2%<br>5 year: 72.3% |
| | Moonsamy US (24) | 2005 to 2017 | 177/24,905 | 89 | 19% | 30 day: 79%<br>1 year: 61%<br>5 year: 52% |
| | Khush ISHLT (25) | 2009 to 2016/17 | 189/30824 | - | - | 1 year: 67.8% |
| | Carter US (26) | 1999 to 2018 | 146/26918 | 26 | - | 30 day: 89.3%<br>4 year: 70.3%<br>12 year: 50.9% |
| | Giordanino Argentina (27) | 2006 to 2018 | 14/333 | **6.5** | **0%** | 30 day: 85.7%<br>**No further deaths: 44 months** |
| | Lui US (28) | 1996 to 2018 | 118/29644 | 24 | - | 30 day: 79%<br>360 day: 68% |
| | Jaiswal US (29) | 2000 to 2018 | 202/627 | 9 | 26% | 30 day: 85.6%<br>1 year:78.7%<br>3 year: 74.7%<br>5 year: 74.3% |
| | Gonzales US (30) | 2015 to 2019 | 59/191 (old allocation)+62/105 | Old: 7<br>New: 3 | 63 (32.9% in old) & 15 (14.3% in new) died | Before 2018<br>180 day: 74.6%<br>After 2018<br>180 day:91.2% |

United Network for Organ Sharing (UNOS) and National Inpatient Sample data showed that candidates bridged to transplant with an IABP had similar perioperative mortality, length of hospital stay, incidence of renal failure requiring dialysis and early acute rejection as compared to patients bridged to transplant with a durable VAD.[62-64] It is important to note however that IABP was typically utilized in patients where a more durable option was not felt to be feasible or advisable, as opposed to a preferred modality of support.

## TandemHeart and Impella

Based on the International Society for Heart and Lung Transplantation registry, bridging with either an Impella or TandemHeart ($N = 75$) was independently associated with greater risk of post-transplant mortality (hazard ratio, 1.83) with 80% survival at 1 year.[65] One of the largest experiences was by Seese et al. regarding Impella 5.0 use as bridge to transplant. About a quarter of the 236 patients were bridged directly to transplant, 37% received a durable ventricular assist device next, and 20% died on the Impella. The survival for the selected few who were directly transplanted was excellent, however. Post-transplant complications were infrequent, the most common was renal failure requiring dialysis (8.8%).[66]

The latest addition to the Impella family is the Impella 5.5 which has been modified to make it less susceptible to dislocation and improve hemocompatibility. The implantation is performed under fluoroscopy and echocardiography via a 10mm vascular graft sewn to the axillary artery. In this configuration, intense physiotherapy and even ambulation are possible on a regular basis. In the initial CE mark trial, no aortic valve damage was reported, and only 1 patient out of 46 suffered a stroke. However, every third patient suffered from bleeding requiring blood transfusion which may lead to formation of allo-antibodies that may prevent successful transplantation in the future. Up to 20% of the pumps needed to be exchanged over time for technical reasons.[67] This trial included, however, first version of the Impella 5.5 and learning curves from several centers. The current version of the Impella 5.5 catheter is longer and less prone for dislocation.

## VA ECLS

Several studies from the United States and Europe reported significantly lower survival during ECLS support and post transplantation compared to other forms of percutaneous tMCS and durable MCS (*Table 2*). Interestingly, for patients who survived the first 30-day post HT, survival was much improved and was almost comparable with other tMCS. As per the UNOS data, a 6-month patient survival ~88% to 89% for those registered as Status 1 including 160 patients with VA-ECLS use at the time of transplant is reported. Jaiswal et al. analyzed the Scientific Registry for Transplant Research database and reported that ECLS patients fared comparable to surgical BiVAD as BTT strategy under the prior heart allocation strategy.[68]

Multiorgan failure and primary graft dysfunction are the most frequent causes of death in BTT patients supported with ECLS. Although the pathophysiologic link between MCS as BTT and PGD is unclear, likely contributors include ischemic-reperfusion injury and dysregulated inflammatory pathways.

## Organ allocation policy and the effect on support choices

### United States

*Table 3* provides details on the US allocation system (past and present) as well as others across the world. As well *Figure 1* shows several of the major allocation schema graphically. Before October 18, 2018, the allocation schema in the United States as set by the United Network for Organ Sharing (UNOS) provided 3 categories for priority. Status 1A included patients in the hospital, with hemodynamic monitoring, or with tMCS such as IABP, Impella or VA-ECLS. Status 1B patients were those with chronic inotropic support or stable durable MCS patients after the first 30 days of support. Allocation was also based on geographic donor service areas which allowed organs to be distributed locally in preference to distant sharing. Waiting times for status 1A were long, measured in months at times, and the waitlist mortality was not uniform among the various types of support. Since there was no "advantage" to any support device, patients received the least invasive device which was required to stabilize them over a prolonged waiting time in the hospital.

It was noted that the highest mortality on the waitlist was for patients requiring VA-ECLS, and secondly, for patients on IABP support, though the numbers were quite small. In those years, tMCS was placed out of necessity, and patients were transitioned to durable MCS in most cases if this was an option. Therefore, patients who could not receive durable MCS and had a prolonged waiting time with tMCS (not designed for long periods of support) had a predictably high mortality rate.

The culmination of several years of debate was a new 6 tier allocation schema in the United States that began October 18, 2018.[69] The former 1A category was broken into 3 strata, with 1B being represented by 2 strata (Table 3 and Figure 1, bottom left). The new status 1 includes patients on VA-ECLS and non−dischargeable biventricular tMCS. Status 2 includes IABP, as well as Impella and other tMCS devices. Status 3 includes durable MCS devices with specific complications. The new system facilitated very short waiting time for eligible patients, but the ease of placing tMCS has resulted in a dramatic increase in such patients (rather than being the rarity with the highest mortality rate in the prior allocation scheme).

Consequently, this change may have incentivized transplant centers to preferentially use tMCS devices as a bridge to transplant. Unsurprisingly, in an analysis from the UNOS

**Table 3** Allocation Schema Across the World

| United StatesPre oct 2018 (3 tier) | United States 6 tier allocation system | Canada | Eurotransplant | France | Italy | Spain | United Kingdom |
|---|---|---|---|---|---|---|---|
| Status 1A<br>- ECLS<br>- IABP<br>- TAH<br>- VAD (initial 30 days)<br>-MCS with device-related complication<br>-mechanical ventilation<br>- Continuous infusion of single or multiple inotropes in addition to hemodynamic monitoring | Status 1<br>VA ECLS<br>- Nondischargeable BiVAD<br>- MCS with life-threatening arrhythmias | Status 4<br>-VAD malfunction/complications<br>-Mechanical ventilation +inotrope/± tMCS<br>Status 4S<br>-PRA > 80% | HU<br>-Inotrope-dependency<br>-MCS with complications<br>-Short-term MCS | Score:<br>(a) Candidate risk score (0—1151 points)<br>- VA ECLS-<br>-Natriuretic peptides<br>- Renal function<br>- Total bilirubin<br>(b) Exceptions:<br>-durable MCS with device-related complications<br>- uncomplicated BiVAD and TAH.<br>(c) Donor-recipient matching<br>(d) Traveling time | Status 1<br>(a) MCS with at least:<br>- RVAD or BiVAD<br>- LVAD with complications<br>- TAH/complications<br>- IABP<br>- ECLS<br>- Mechanical ventilation + IV inotropes + IABP | Urgency status 0 -dependent on tMCS including ECLS for at least 48 hours (without multi-organ failure)<br>-Durable VAD complications<br>Max time for this grade is limited to 7 days and afterward will downgrade to urgency status 1 | super-urgent heart allocation scheme (SUHAS)<br>-short term MCS<br>-meets criteria for urgent listing but is not suitable for long term VAD and/or other exceptional circumstances |
| Status 1B<br>-Continuous IV inotropes<br>-LVAD/ RVAD | Status 2<br>- Dischargeable LVAD/RVAD/ TAH<br>- Nondischargeable LVAD<br>- IABP or percutaneous MCS<br>- MCS with malfunctioning<br>- Sustained VT/VF | Status 3.5<br>High dose/multiple inotropes in hospital + not a candidate for durable VAD | HU 1A (Only Netherlands)<br>high-dose inotropes + IABP +restored organ function;<br>• patient on medium or long-term VAD + restored organ function in whom support is no longer feasible;<br>• patient listed for an acute re-transplantation due to graft failure <7 day after a previous heart transplant;<br>• Patient with intractable, life-threatening arrhythmia. | | Status 2A<br>- LVAD<br>- IV inotropes<br>- ICD and recurrent malignant ventricular arrhythmias | Urgency status 1<br>Cardiogenic shock requiring requiring -vasoactive drugs and invasive mechanical ventilation, -and/or IABP, and/or long-term VAD; and for arrhythmic storm | urgent heart allocation scheme (UHAS)<br>-dependent on inotropes<br>-VAD with RV failure requiring inotrope; recurrent infection related to VAD/TAH<br>-other complications including VAD/ TAH |
| Status 2<br>All other patient | Status 3<br>- Continuous infusion of single or multiple inotropes in addition to hemodynamic monitoring<br>- 30-days of exception time for LVAD<br>- MCS with complications | Status 3<br>VAD not meeting status 4 criteria<br>Patients on inotrope in hospital, not meeting above criteria<br>Heart-lung candidates<br>Cyanotic congenital heart disease with resting saturation<65%<br>Congenital heart disease pts<br>Adult-sized complex congenital pts with dysrhythmia or failing ventricle | HU 1B (only Netherlands)<br>Stabilized patient still on high dose of inotropes. | | Status 2B<br>- Candidates not with 1 or 2A status | Elective: all others | non—urgent allocation scheme (NUHAS) ≥2 criteria:<br>-persistent NYHA class IV despite optimal therapy<br>-Peak $VO_2$ ≤12 ml/kg/min, or <50% predicted<br>- BNP > 400 pG/ml or NT-proBNP>1600 pG/ml<br>Cardiac index ≤2 L/min/$M^2$<br>≥2 HF related hospitalization in last 12 months<br>Worsening WHO class II pulmonary hypertension<br>-worsening renal function due to cardiorenal syndrome<br>-recurrent ventricular arrhythmia despite optimal therapy<br>-worsening liver function due to right heart failure despite optimal therapy<br>-persistent/recurrent symptomatic |

(*continued on next page*)

**Table 3** (*Continued*)

| United StatesPre oct 2018 (3 tier) | United States 6 tier allocation system | Canada | Eurotransplant | France | Italy | Spain | United Kingdom |
|---|---|---|---|---|---|---|---|
| | Status 4<br>- IV inotropes<br>- LVAD, stable<br>- CHD, Restrictive CM, Retransplant | Status 2<br>Inpatient, outpatients on inotrope not meeting above criteria<br>Multiorgan transplantation (other than heart-lung)<br>Adult with cyanotic congenital heart disease with resting saturation 65% to 75%<br>Adult with Fontan palliation with protein losing enteropathy or plastic bronchitis | T<br>Transplantable | | Status 3<br>Inactive on waitlist | | pulmonary edema or serious systemic congestion despite optimal therapy |
| | Status 5<br>Combined organ transplant<br>Status 6: all other patients | Status 1<br>All other out-of-hospital pts | | | | | |

registry, patients undergoing heart transplant (HT) after the revision were more likely to have received tMCS before HT (10% vs 41%). (12) Furthermore, in the year after implementation of the new UNOS donor heart allocation system, tMCS use in patients admitted with ADHF-CS increased in US transplant centers but not in other hospitals.[17]

It appears that of the patients who have received transplants under the new system, 33.0% received IABP, whereas 12.4% received ECLS or other tMCS.[70] The use of IABP has risen >20% and is chiefly responsible for the 31.0% rise in the use of tMCS with new compared to the old allocation system.

## European experience

### Spain

In 2010, the Organización Nacional de Trasplantes (ONT) adopted a 3-tier system with the highest level (ONT status 0) reserved for patients who cannot be weaned from tMCS or those with complications related to durable MCS devices (Figure 1, bottom right). However, IABP was specifically excluded from the status 0 designation. Over the time period 2010 to 2015 across 16 centers in Spain, 291 patients were listed at this critical status and the majority were transplanted within a month, Survival was best for tMCS and lowest for ECLS and biventricular support.[71]

### Eurotransplant

Eurotransplant governs organ allocation for their member states (Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, The Netherlands, and Slovenia). (https://Eurotransplant.org) The details are complex as there is a national and international high urgency status as well as "T" for transplantable and "NT" inactive non−transplantable status (Figure 1 top right). High urgency is restricted to those patients with inotrope dependence with specific criteria for hypoperfusion that must be met. However, Eurotransplant does not assign priority status to VA-ECLS nor temporary support devices (Table 3).[72] In addition, durable MCS including total artificial hearts are not granted high urgency unless there are specific complications, and even in these cases, the patient must be beyond 30 days from implantation to qualify. (https://www.eurotransplant.org/wp-content/uploads/2021/09/H6-EThAS-September-7-2021.pdf) A rotating national board of transplant professionals must approve all initial national high urgency requests. High-urgent status is revoked whenever the clinical status improves (e.g., cessation of inotrope dependency) or deteriorates in a way that would most probably preclude HT (e.g., uncontrolled septicemia, neurologic damage on MCS).

The majority of donors are allocated to high urgent recipients and therefore durable VADs are less likely to receive transplants (unless complications develop). Organs that are turned down for the top 3 patients are distributed by "rescue" allocation and with careful selection, the outcomes appear to be similar.[73]

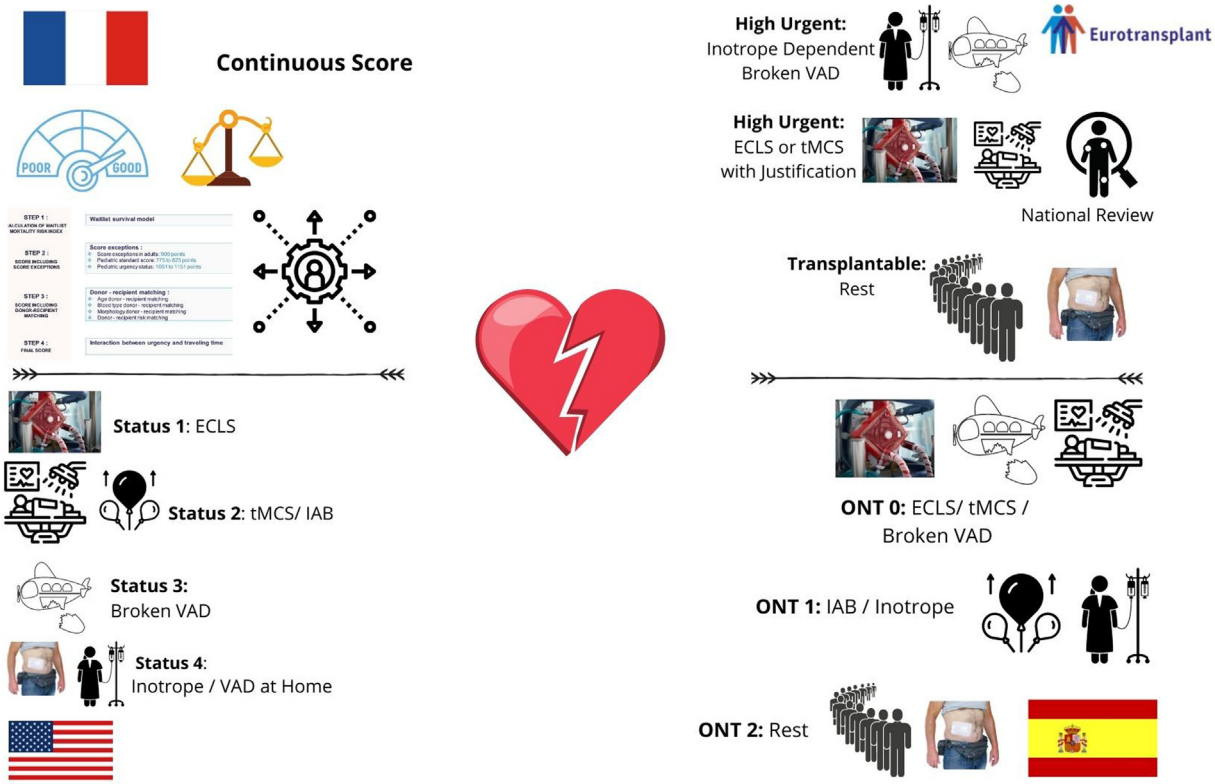


**Figure 1** Organ allocation policy is illustrated for 4 countries (clockwise from the top left). France, EuroTransplant, Spain and the United States. France has a complex system of points awarded based on donor and recipient characteristics including points for ECLS. Eurotransplant grants high urgency to proven inotrope requiring patients as well as durable MCS patients with specific complications. ECLS or tMCS patients only qualify for high urgency with an exception request. The United States has a 6 tier system, with use of ECLS at highest priority followed by tMCS such as IABP. Durable MCS is status 4, as is continuous home inotrope infusion. Spain's system grants highest priority to ECLS and tMCS as well as MCS with complications, and lower priority to IABP or inotrope patients. Durable MCS patients have the lowest priority.

While initially introduced as a rare exception to bypass the regular waiting list to allow transplantation within a period of days to a few weeks, the number of simultaneous HU status patients has increased tremendously. Due to the growing number of patients on HU-status and the decline in organ donation, currently the majority of cardiac transplants are performed for HU-status patients.[74] This in turn, has resulted in a higher mortality while waiting for a suitable donor and is compounded by an ever-increasing number of high-urgency candidates and longer waiting times.

## Germany

To mitigate risk and optimize outcomes, an attempt is being made to create a suitable scoring system for the allocation of hearts. In Germany (currently a member of Eurotransplant), a combined benefit model, the cardiac allocation score (CAS), has been under construction since 2011 and aims to select patients in a severe, urgent condition with a good transplant prognosis.[75-77] Risk of mortality on the waiting list is measured based on the Seattle heart failure model (SHFM) and post-transplant outcomes are predicted by the Index for Mortality Prediction After Cardiac Transplantation score (IMPACT score) and the combination is adjusted to yield a maximum value of 100. High values identify patients with a high predicted mortality risk while on the waiting list and high predicted probability of survival after an HT. The idea of a benefit score was bolstered by the observation that after establishment of the lung allocation score, waitlist mortality was effectively reduced whereas post-transplant outcomes remained stable.[78,79]

## France

Similarly, the new French heart allocation system incorporates a candidate risk score based on hemodynamic markers of severity (short-term MCS use and natriuretic peptides) and markers of end-organ dysfunction (glomerular filtration rate and total serum bilirubin level) along with other criteria such as exceptions and donor-recipient matching.[72] However, the long-term utility of such scoring systems is not entirely clear. (Figure 1, top left)

## England

Before 2016, in the United Kingdom there were 2 active transplant waiting list categories (urgent and non−urgent) with inotrope dependent and tMCS patients in the urgent category. Based on long waiting times and waitlist mortality concerns, a third category was added (Super-Urgent

Heart Allocation Scheme - SUHAS) which was for patients on tMCS and must be re-certified monthly.[80] In addition, IABP was moved to urgent from super-urgent priority in 2017 due to a high number of requests for such listing. If a center would like super urgent status for an IABP patient, an appeal to the National Adjudication Panel is required. With the introduction of SUHAS, mortality on the waiting list, and waiting time have been reduced, while maintaining post-transplant survival.[80]

## Putting it all together

The variety of allocation schema in use worldwide is a testament to the fact that there is no perfect way to allocate scarce resources particularly in life threatening situations such as organ transplantation. *Figure 2* is a graphic illustration of some key considerations regarding heart organ allocation. There are 5 elements.

## Comprehensive formula

While easier said than done, an approach (illustrated by the calculator in the figure) which combines several factors is preferable to one which is simpler but driven by therapeutic choices (i.e., IABP = Status 2). The allocation system in France is an example of this model.[72] Their scheme provides a high number of points for certain therapies such as ECLS but not others, and includes donor and recipient factors. In addition, the comprehensive nature of the score reduces the chance that clinicians can choose support therapies to modify the transplant wait list time directly (given the morbidity associated with ECLS as a support strategy).

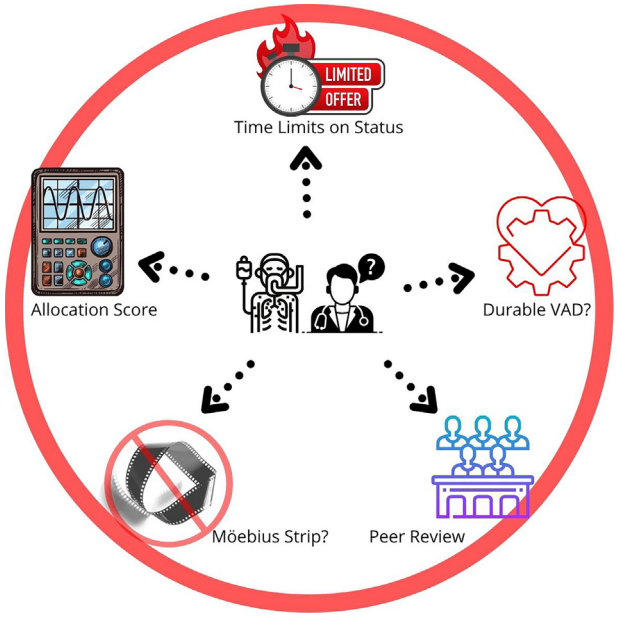


**Figure 2** This graphically illustrates 5 key issues to consider with organ allocation. Clockwise from the top left are the calculator representing the need for comprehensive systems which account for several variables and don't immediately set priority on 1 basis (such as device placement). Next the "Limited offer" stopwatch which implies that organ priority should be time limited to avoid "crowding" at super urgent status. Next is the durable MCS option which should be considered as a proven modality to manage patients with end stage heart failure in need of heart replacement. Next, the "jury" figure is intended to signify peer review of exceptions which is necessary to maintain fair usage of allocation policy when circumstances warrant a deviation from standard rules. Lastly is the Möbius strip made of film. When durable MCS no longer leads to organ transplantation, the concept of bridge to transplantation no longer exists and this affects usage of MCS as well as patients negatively.

## Time limits

If a patient is severely ill such that they are prioritized ahead of those with longer wait times, then there should be a limit on the time in this privileged status. The limits are commonly placed on the number of days at a high urgent status, but an alternative is to limit the number of organ offers in such a way as to increase the utilization of available organs. In the US, centers set criteria for allowable organ offers on a per patient basis (choosing age, and size minimums and maximums for example). Clinicians could set the criteria for organ offers, and then know in advance how many potential offers at most would be received before the patient dropping in priority.

## Mechanical circulatory support

Regardless of future developments and organ donation advocacy, there will always be an imbalance between the demand for donor hearts and availability. Durable MCS advances will be critical to meeting the need of patients. While the third generation of durable MCS therapy has achieved excellent intermediate term results,[81] longer term issues remain including accumulating complications, late right ventricular failure,[82,83] and limitations of quality of life.[84-86] Continued robust research programs leading to refinement of these devices will be absolutely critical in the years ahead to drive adoption and manage the patients who do not qualify for emergent transplantation.

## Avoid the möebius strip

In mathematics, a Möbius strip is a surface with only 1 side and only 1 boundary curve. In organ allocation, the analog is placement of a durable MCS device as a bridge to transplantation. Durable MCS patients are placed at low priority for transplantation, and often only receive high priority when complications develop (which may worsen their post-transplant outcome). While there is no proven way to predict complications, most accumulate over time. In many countries, there is no crossover from the stable VAD pathway to availability of a suitable organ for transplantation, rendering "bridge to transplant" as a false promise and an infinite path on a Möbius strip. It is imperative that some aspect of waiting time is integrated into allocation policy so that patients may recover fully on durable MCS therapy and then receive transplantation (without suffering complications) if that is deemed the best final therapy by the care team.

## Peer-review

The fifth aspect that is critical to organ allocation is peer review. While many allocation bodies have peer-review processes, this is often reserved for exceptional cases due to the volume of work and outside clinical duties. One issue is whether the reviews are done locally or by unrelated distant parties. In the United States, review of allocation exception requests was previously with local peers but was changed in 2018 to be anonymous distant groups. This has resulted in widespread acceptance of most exception requests, with anonymity and the tendency to "give the benefit of the doubt" to colleagues.[87] Further work needs to be done to reduce exceptions so that the access to transplantation is governed by uniform policy. Ideally, deviations from policy would be exceptional, rather than exceptionally common.

On the other hand, if a tMCS patient is not suitable for durable MCS and a suitable donor is not located then broadening donor acceptance criteria may be warranted. It is noteworthy that even when hearts from donors who are older, more hypertensive, and have diabetes mellitus, hepatitis C, illicit drug use, mild cardiac hypertrophy and severe renal dysfunction are used, overall recipient survival continues to improve.[88,89]

## Conclusions

Short term percutaneous and surgical mechanical circulatory support has evolved over time, with improved outcomes and hence, provides an attractive approach to bridge sick patients awaiting heart transplantation. However, the ability to select patients who are most likely to benefit from this approach remains uncertain and warrants systematic study. While the waitlist mortality and post-transplant outcomes of patients on temporary support is acceptable, the preferential donor allocation to mechanically bridged patients penalizes more stable patients with increased wait time and suboptimal donor availability. As such, allocation of fundamentally limited donor hearts is variable across the world, and represents a challenge to patients, providers and regulators alike. An allocation system which gives weighting to objective markers of severity of illness, chronologic wait time, likelihood of favorable post-transplant outcome, and optimization of the logistics of a match (distance to the donor site) may represent the ideal way forward.

## Disclosure statement

Dr Baran reports consulting for Abiomed, Getinge, Livanova and Abbott. He is a speaker for Pfizer. He is on the Steering Committee for Procyrion, and CareDx. Dr Jaiswal- consulting fee from Novartis in past. Dr Hennig- Travel grants for meeting attendance from BioVentrix and Xvivo Perfusion Dr Potapov- Consulting for Abbott, Abiomed and Medtronic. Advisory Boards for Abbott and Medtronic

## Author contributions

Drs Baran and Potapov conceived of the article topic. Drafts from all 4 authors were combined and edited by Dr Baran with multiple joint rounds of revision by all authors. All authors have reviewed and agree to submit the manuscript for publication.

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