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Pregledni rad

Optimal utilization of mechanical circulatory support and transplant resources in the comprehensive treatment of terminal heart failure

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Abstract Treatment of end-stage heart failure has reached new frontiers. With a scarce availability of hearts, mechanical circulatory support (MCS) has become an integral part of end-stage heart failure treatment and has improved survival. A variety of devices may be instituted either for short or long term support in different clinical indications, such as postcardiotomy circulatory failure, acute cardiogenic shock, chronic heart failure in patients not eligible for a transplant to heart transplant deterioration. Permanent or temporary MCS has emerged as an indispensible treatment for advanced stage heart failure alongside established standard medical procedures. Herein we report brief narrative review of MCS devices used for end-stage heart failure.

Key words heart failure, mechanical circulatory support, ventricular assist device, cardiac transplantation

Background

Epidemiology of heart failure

Due to increased demand for treatment of end-stage heart failure patients, MCS has become a significant therapy tool. Heart failure, the endpoint of progressive disease, has become the leading mortality and morbidity etiopathogenic knot in developed countries with a prevalence of 2.5%.[1,2] By improvement of medical and surgical technology, end-stage heart failure patient population has markedly increased, currently including 17 million Europe and USA citizens, with raising incidence of 500,000 new patients yearly.[3] The estimated 5-year mortality is around 80%. Once patients become dependent on inotropic therapy, their 1-year survival reduces to less than 30%.[4,5] The number of heart transplantations reported to the International Society of Heart and Lung Transplantation (ISHLT) registry worldwide is 3,500-4,000 annually, remaining steady over the past two decades; donor supply has not changed substantially.[6] ISHLT encompasses 66% of heart transplantations performed worldwide. According to the Eurotransplant report, in the year 2012, Eurotransplant region, 569 heart transplantations were performed, with 1235 patients remaining on the active heart waiting list.[7] With a scarce availability of hearts, more patients will lack possibility for heart transplant, thus leading to increased rate of heart decompensation which in turn emphasizes the role of MCS in treatment of end-stage heart failure.

The ideal therapy for management of heart failure refractory to usual medical care continues to be heart transplant. Optimal utilization of resources such as donor availability and developed heart failure programs is mandatory if program sustainability is to be achieved. MCS is rather supplementary, than alternative therapy, although shortage of organs available directs MCS towards alternative therapy. However, there are numerous general factors influencing indication and timing of MCS therapy. Multidisciplinary heart failure teams should be organized and charged with providing comprehensive care from initial referral until support is terminated. This team should be able to perform appropriate patient selection, determine appropriate timing of MCS procedure as well as sufficient perioperative patient management.

Historical overview

The MCS era has its roots in John Gibbon's cardiopulmonary system, successfully used for an atrial septal defect repair.[8] The first steps were taken in the USA with the founding of the Artificial Heart Program in 1964 with the National Institute of Health. Michael DeBakey developed the original pneumatically driven left ventricular assist device (LVAD) prototype and, in 1966, reported the first successful use of the bridge to recovery LVAD in a young woman unable to be weaned from cardiopulmonary bypass.[9] Denton A. Cooley moved the whole process a step further in 1969 with implantation of a pneumatically driven artificial heart into a patient in postcardiotomy

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shock as a bridge to transplant, support lasted 64 hours.[10] Despite promising beginnings, incidence of complications, predominately infectious and thrombo-embolic, led to a moratorium in 1991. However, advances in the technology reversed the whole process in 1994, and the efforts continued.

Types of support

MCS vary in terms of circulatory or combined circulatory and respiratory support, concept of therapy and duration of support;

ECMO/ECLS (Extracorporeal membrane oxygenation, extra-corporeal life support) is a technique of circulatory/respiratory support that ensures adequate heart and lung functioning in patients that are in grave cardiorespiratory insufficiency. ECMO refers to respiratory support, or gas exchange, while ECLS is a broader term, including both circulatory and respiratory measures of treatment.

VADs can be used for isolated left, right or biventricular failure. Most of the VADs are used for isolated left ventricular failure. Those devices are preload dependent, requiring optimal right ventricular function, and afterload independent (not in cases of marked hypertension). They are independent of left-sided contractility and rhythm disturbances. However, right ventricular and biventricular support options are less well established.

MCS could be instituted as a bridge to decision (BTD), bridge to candidacy (BTC), bridge to transplantation (BTT), bridge to recovery (BTR) and as destination therapy (DT).[11] According to the INTERMACS report, there has been gradual increase in the number of MCS utilization attempts, predominately in the BTT group of patients.[12] Individual factors influencing indication and timing of MCS are not uniform and differ among indication subgroups. In the BTT group, patients rely on suitability for heart transplant candidacy and donor availability. On the other hand, BTC patients have contraindications or risk factors for heart transplantation that can be resolved while on MCS. DT indication is developed for patients not eligible for heart transplant due to previously established contraindications. BTD therapy is applied in patients requiring re-evaluation of their candidacy for heart transplant or the device upgrade after improve of clinical status through MCS. BTR is instituted in patients with the goal to restore myocardial function, usually in non-ischemic heart failure. In those cases, weaning of support remains to be utmost goal.

Long term support

Aside from commonly used heart failure treatment modalities, certain proportion of patients do not respond to, thus requiring either heart transplant or MCS.[13] Still, some patients will never establish candidacy due to numerous contraindications, and will require long term ventricular assist device support as a destination therapy. Some patients, due to their poor physical condition are not liable for any of the previously mentioned treatment possibilities, leaving palliative care as the only definitive treatment method. Palliative care is an important part of treatment when patients are faced with severe symptoms and no other options.

There are quite a few classifications regarding the MCS pumps. Chronologically, pumps could be classified in three classes according to period of utilization.

The first generation mechanical circulatory support pumps were bulky, complex, pulsatile, positive displacement pumps. Main limitations were mechanical failure due to system complexity and limited durability, infections due to percutaneous cannulae, thrombo-embolic complications, very little patient mobility due to device gross appearance and limitation arising from the need for minimum body surface area to be greater than 1.5 m2 which made it impossible for pediatric use. One of the major drawbacks is the requirement of volume compensation. First generation devices such as the Thoratec paracorporeal ventricular assist device (PVAD, Thoratec Corp.), the Berlin Heart Excor (Berlin Heart, Berlin, Germany) and the Toyobo LVAS (Toyobo Co LTD, Osaka, Japan) are paracorporeal devices, in which the blood pump lies external to the patient, appropriate for temporary use for the BTT and BTR indications. The Thoratec PVAD, is probably the most common used pump in the history of mechanical circulatory support. The Toyobo LVAS is the only device approved for use in Japan, a country with a great shortage of donor hearts due to its ethical and social specificity.[14,15] Novacor left ventricular assist system (LVAS, WorldHeart, Salt Lake City, UT, USA) was used as a BTT device in a patient in 1984. Thoratec implantable ventricular assist device (IVAD) is the only implantable mechanical circulatory support device for biventricular support. HeartMate extended vented electric LVAS (HeartMate XVE, today known as HeartMate I, Thoratec), due to its low thrombogenicity, is the only long-term mechanical circulatory support device not requiring systemic anticoagulation, only aspirin antiplatelet therapy. The Randomized Evaluation of Mechanical Assistance in Treatment of Chronic Heart Failure (REMATCH) study compared clinical benefits of HeartMate XVE to medical treatment.[16] The study included 129 patients in NYHA class IV not eligible for heart transplantation. The 1-year survival in the HeartMate XVE group was 52% compared to 25% in the medical therapy group. After two years survival, it was 28% compared to 8%. However, one of the major limitations for its continued use was the infection rate of 41% after 18 months of use and device failure of 17%.[17]

Second generation mechanical circulatory support devices are constructed of rotary, axial-flow pumps, with contact bearings, producing well tolerated continuous pulseless blood flow, suited for high flows at low pressures differences. They were introduced from 1998 to 2000.[18] Major steps forward were diminished blood trauma, lower anticoagulation requirements, less hemorrhagic complications, smaller size and better patient mobility. Single moving rotors and no seals minimized previously high device failure rate.[19] Commonly used doyens of this generation are Jarvik 2000 (Jarvik Heart, Inc.; New York, NY), HeartMate II (Thoratec Corp.) and MicroMed DeBakey VAD (MicroMed Technologies, Woodlands, TX, USA). All of them are long term support devices, fully implantable, some of them implantable intraventricularly, such as Jarvik 2000, and others implantable intraabdominally. HeartMate II can be used as a left and right ventricular assist device. This is important since 30% of the patients requiring long-term ventricular support

also develop right ventricular failure.[20] HeartMate II is intended to provide hemodynamic support in patients who have established heart transplant candidacy, as a BTT, who will become candidates after long term support, BTC, whose recovery is delayed or in patients with absolute contraindications for heart transplantation, therefore are used as a permanent destination therapy, DT. Notably, the HeartMate II is the only second generation FDA approved device for BTT and DT. Second-generation superiority is demonstrated by a randomized trial comparing the HeartMate XVE and HeartMate II. Survival at 2 years in the HeartMate II group was 46% compared to 11% in the HeartMate XVE group. Moreover, the device-replacement rate was also significantly lower in the second generation group, 10% versus 36%. In a study published by Miller et al. 83% HeartMate II patients improved from NYHA IV to NYHA I or II class 3 months after implantation. Only one day after implantation, cardiac index increased from 2.0 L/min/sqm to almost 3.0 L/min/sqm on average.[21] Continuous blood flow increases thrombogenicity, and strict anticoagulation is required. The risk of hemorrhagic and thrombo-embolic complications was similar in both groups.[22] The rearmost ratio is changing owing to improved anticoagulation regimes. In the second generation device group, infection, owing to percutaneous drivelines, is a major survival limiting factor.[23, 24] Infection is most common within first 3 months after device implantation. HeartMate II showed decreased risk of infection, probably due to a smaller driveline diameter. 75% of patients with percutaneous lead infections survived 1 year versus 89% of patients without lead infections during LVAD support.[25] Risk infection is a multifactorial phenomenon, depending not only on the type and place of implantation, but patient status and comorbidities.

Third generation ventricular assist devices are just like the second-generation, providing continuous blood flow generated either by axial or centrifugal rotary blood pump. The main difference is the implementation of electromagnetic or hydrodynamic forces for suspension of the rotor in the device, without contact bearings. In such a manner, the number of moving parts is reduced to one, allowing longer durability, and decreasing device size. Some of those devices are approved for use; others are still undergoing clinical investigation. In Europe, the Berlin Heart Incor (Berlin Heart, Berlin, Germany), the HeartWare HVAD (HeartWare International, Inc, Framingham, MA, USA) and the Terumo DuraHeart (Terumo Heart Inc, Ann Arbor, MI, USA) are approved for use. The HeartWare HVAD size allows it to be fully implanted in the pericardial sac, decreasing invasiness and associated surgical morbidity.

The standard route of implantation for these long term devices is via median sternotomy using cardiopulmonary bypass. Prior to the implantation and systemic heparinization, the pump pocket is created, depending on the type of implant. Cannulation is performed paying special attention to cannula positioning, leaving enough space for subsequent cannulation during heart transplantation. Cross clamping is avoided, if possible, to protect the right ventricle. Adueqate maintenance of preload and afterload is mandatory.

Short term support

Acute cardiorespiratory disorders encompassing respiratory, cardiac or combined failure, cardiac surgery complications and transplant rejection sometimes merit therapy that goes beyond conservative measures. Extracorporeal circulatory support has become standard treatment for patient in end stage heart failure and/or postreanimation treatment as a bridge to recovery or bridge to definite treatment/transplant. Sometimes, it is used to provide protection during high-risk procedures. There are two basic operational modalities: V-V (venous-venous) modality that replaces insufficient lung functions, and V-A (venous-arterial) modality that replaces both heart and lung functions. It is possible to introduce the ECMO/ECLS machine either through central cannulation (through median sternotomy and direct cannulation, most often as postcardiotomy support) or peripheral blood vessel cannuation, predominately using Seldinger's technique, most often as primary support. In peripheral cannulation, the risk of peripheral limb ischemia should be taken into account. Vascular complication reports range from 11.5% to 28 %.[26-28] ECLS/ECMO encompasses basic principles of cardiopulmonary bypass. However, one of the main differences is duration of support. The system consists of a centrifugal, afterload dependent pump, membrane oxygenator and heat exchanger. The support is temporary (days to weeks), avoids ongoing iatrogenic injury, sustaining life while bridging to organ recovery or replacement. This concept, known as „bridge-to-decision" or „bridge-to-bridge" may optimize patient survival. The ideal indications for ECMO/ECLS are isolated severe heart failure (one organ failure), refractory to conventional therapy or cardiac arrest undergoing cardiopulmonary resuscitation. However, common indications are multiple, ranging from acute, severe, cardiac or pulmonary failure unresponsive to optimal management, with expected recovery in days to weeks (predominately pulmonary failure). The main principle for ECMO/ECLS institution is introduction prior to multiorgan failure onset and an established exit strategy. Approximately 2-6% of surgically treated patients require postoperative ECMO/ECLS support for refractory cardiopulmonary dysfunction. ECMO has been utilized to obtain rapid resuscitation, stabilization, and subsequent triage to a more permanent treatment strategy. In postcardiotomy patients, ECMO/ECLS can be applied in mode of "extended perfusion" to improve patient survival.

Compared to other available systems, ECMO/ECLS support is associated with high morbidity and mortality. The long term survival in different clinical scenarios (30 days after successful weaning) lingers around 25-36%.[29-32]

Intra Aortic Balloon Pump (IABP) is easily available, easy to implant, relatively inexpensive support, recommended for use up to a few days in acute heart failure settings. The IABP increases blood pressure and flow during inflation by creating an additional perfusion event to both the central and the peripheral circulation during diastole. In the IABP-SHOCK II randomized clinical trial intraaortic balloon pump support did not reduce 30-day mortality. The study involved patients with cardiogenic shock complicating acute myocardial infarction, when early revascularization was planned. At 30 days, 39.7% in

the IABP group and 41.3% patients in the control group had died.[33]

The Levitronix CentriMag (Levitronix; Waltham, MA, USA) is a continuous-flow centrifugal, paracorporeal ventricular assist device used in postcardiotomy patients or in patients with refractory primary cardiogenic shock as a bridge to a more permanent solution of the hemodynamic collapse.[34, 35] It is designed as a bridge-to-recovery, bridge-to-decision, bridge-to-bridge or as a bridge-to-transplantation device. Due to its improved technical design, absence of seals, bearings and valves, a magnetically levitated rotor not in contact with the housing of the device, the Levitronix CentriMag can provide longer circulatory support and less blood trauma. In salvage postcardiotomies, it can be attached to cardiopulmonary bypass cannulas already in situ. Moreover, it has been used for the purpose of extracorporeal membrane oxygenation.[36] Although it is more expensive, it is very effective in either univentricular or biventricular support.

Patient selection

The decision to institute MCS is often difficult, the criteria vary among hospitals, but however helpful priciples have been discussed. Typical heart failure signs are the basic step in further decision making: cardiac index <2.0 L/min/sqm, systolic blood pressure <80 mmHg and pulmonary capillary wedge pressure >20 mmHg, leading to multiple organ failure. All of these criteria should be present despite optimal medical therapy.

In order to collect all information about increasing use of MCS devices, scientific data and results, databases were established. The first was founded in 2006 by National Heart Lung and Blood Institute (NHLBI) - the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS). This database collects information on mechanical circulatory support devices implants in the USA. Since its beginning, more than 6800 implantations have been registered. Reported survival is 80% at 1 year and 70% at 2 years, considering continuous flow devices (account for more than 95% of adult primary LVAD implants) (12). EUROMACS was established in the 2009, in order to collect data from the European centres.

INTERMACS developed patient profiles in order to improve clinical characterization of MCS recipients (Table 1).[37] Patients are grouped into 7 clinical profiles according to their clinical presentation and medical management. INTERMACS profiles 1 to 5 reflect NYHA IV class, while patients in INTERMACS profiles 6 and 7 actually correspond to NYHA III or IIIb[14].

The INTERMACS data show that the patients with the least favourable INTERMACS level 1 have the highest mortality. This relationship has prompted a shift in utilization with a decrease in durable pump implants in INTERMACS 1 and INTERMACS 2 patients and greater rates in INTERMACS level 3. INTERMACS level 1 patients are being treated with less invasive and less expensive temporary devices in order to allow organ function recovery. The percentage of patients with progressive cardiac decompensation (Level 2) or cardiogenic shock (Level 1) at the time of implantation has decreased from approximately 64% in 2011 to less than 54% in 2012. Patients with ongoing cardiac decompensation or shock (INTERMACS Profile Levels 1 and 2) continue to show worse survival rates compared to more stable patients, with decrease of approximately 5–8% in 1-year survival (12). It is imperative that the mechanical circulatory support is instituted before malperfusion and irreversible organ changes occur.

Table 1. INTERMACS level of limitation at time of implant [37]

INTERMACS profile descriptions	Time frame for intervention
Profile 1: Critical cardiogenic shock	Definitive intervention needed within hours.
Profile 2: Progressive decline	Definitive intervention needed within few days.
Profile 3: stable but inotrope dependent	Definitive intervention elective over a period of weeks to few months.
Profile 4: Resting symptoms	Definitive intervention elective over period of weeks to few months.
Profile 5: Exertion intolerant	Variable urgency, depends upon maintenance of nutrition, organ function, and activity.
Profile 6: Exertion limited	Variable, depends upon maintenance of nutrition, organ function, and activity level.
Profile 7: Advanced NYHA III	Transplantation or circulatory support may not currently be indicated.

The survival of patients aged older than 70 years is mildly decreased compared to younger groups. However, they have less tolerance for additional risk factors. Bridge to transplant therapy group has shown modestly increased survival rates when compared to destination therapy group. This is probably due to absence of device-related complications. Worsening renal dysfunction and right ventricular dysfunction are major predictors of significantly reduced long term survival[12].

Adverse event rates are being reduced with novel continuous-flow pumps. Incidence of device malfunction, bleeding, infection, neurological, hepatic and renal dysfunction has decreased. Improved outcomes and access have helped in the utilization of MCS in ever-growing number of countries worldwide.

Mechanical circulatory support at University Hospital Center Zagreb

MCS has stepped up from a last resort therapy to a well established alternative for many heart failure patients. Our first successful use of MCS was in 1987 for a postcardiotomy indication. One year after, we began the heart transplant programme, as pioneers in southeast Europe, on September 30th, 1988. From then on, in the past 25 years, we performed 207 consecutive heart transplants. Although in the beginning the number of transplantations per year oscillated, since 2010 it stabilized at 18-24 heart transplants per year. It is worthwhile to mention that Croatia is among leading countries in heart transplantat programme with 44 heart transplant per 4.3 mil citizens in 2012. With 24 heart transplants in 2012 at our institution and a mortality rate of 20% among heart transplant waiting list candidates, MCS has become an integral part of end-stage heart failure treatment and has improved survival. No MCS backup was used from 1988 to 2008 for preoperative stabilization of heart failure patients as a bridge to transplant or as a postoperative support in case of primary graft failure or refractory heart failure following other conventional cardiac surgery procedures. Our first elective MCS device was instituted in 2008 resulting in first successful BTT. The first long term mechanical circulatory support device, HeartMate II was implanted in 2009. The patient was successfully discharged home. In the past 5 years, 93 adult patients and

Table 2. Classification of adult patients according to INTERMACS registry and procedural outcome, overall and within profile groups, at University Hospital Center Zagreb

		Procedural success	Procedural failure
INTERMACS PROFILE	n (%)	n/group (%)	n/group (%)
PROFILE 1	61 (65.5%)	26/61 (42.6%)	35/61 (57.4%)
PROFILE 2	18 (19.3%)	12/18(66.6%)	6/18 (33.3%)
PROFILE 3	5 (4.8%)	3/5 (60.0%)	2/5 (40.0%)
PROFILE 4	9 (9.6%)	9/9 (100%)	-
OVERALL	93 (100%)	50/93 (53.7%)	43/93 (46.2%)

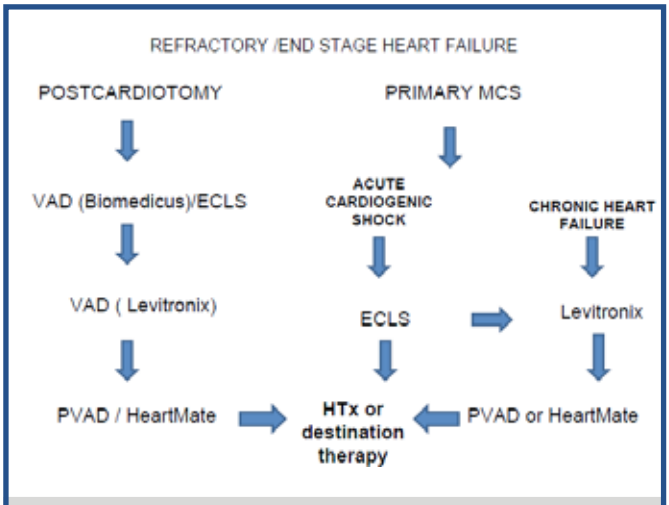

Figure 1. Mechanical circulatory support device selection algorithm at University Hospital Center Zagreb

5 paediatric patients were treated with mechanical circulatory support, 110 procedures were performed, as some of the patients had multiple procedures. In the same period, 98 patients underwent heart transplantation. Mechanical circulatory support procedures were considered as single procedures if they included only one type of device. Upgrade, considered as device substitution, or addition of another device was considered as a multiple procedure. A variety of devices were used from the onset of the mechanical circulatory support program. Short and long term support was instituted for different clinical indications, ranging from postcardiotomy circulatory failure, acute cardiogenic shock, chronic heart failure in patients not eligible for a transplant to heart transplant deterioration.

The device selection algorithm was developed at University Hospital Center Zagreb. Mechanical circulatory support indications are divided into two arms – primary and postcardiotomy. The treatment usually starts with short circulatory support, depending upon the clinical scenario and upgrading to a more complex and expensive mechanical circulatory support devices (Figure 1).

Indications for primary mechanical circulatory support included: acute exacerbation of chronic heart failure predominately, acute cardiogenic shock. Altogether, procedural success was accomplished in 60% of patients. 56.2% patients were treated with ECMO, 34.2% LVAD, 7.9% RVAD, and 5.2% with BiVAD. Mechanical circulatory support efficiently bridged 15 patients with heart failure to heart transplantation. 19 patients were supported with long term support, either as a destination therapy or as a bridge to heart transplant; of those, 17 patients received HeartMate II, and 2 patients received HeartWare HVAD. Postcardiotomy mechanical circulatory support was used in 34.4% patients. Observed patient clinical outcomes after 30 days were: alive 21.5%, alive on support 15.0% or dead 63.4%. In the paediatric group, 3/5 patients were bridged to recovery. Most common perioperative complication was renal failure, in 44.0% of patients. Classification of adult patients according to INTERMACS registry and procedural outcome, overall and within profile groups, is shown in Table 2.

Furthermore, mechanical circulatory support for acute and severe respiratory failure, in the form of V-V ECMO, was applied in three patients. One patient with severe respiratory failure was bridged to lung transplantation. The patient was successfuly transported on extracorporeal life support from Zagreb to Vienna in 2010, where subsequent lung transplantation was performed. This cross institutional accomplishment was achieved using portable V-V ECMO.

Our single-center experience with the mechanical circulatory support and transplantation resources has provided us with important information concerning complex heart failure problem issues. We have learned that proper interdisciplinary patient management is crucial in improving patient outcome. Success is time and team dependent and requires individual device and patient management.

The country's health program is currently planning a rapid onset of mechanical circulatory support for patients in outlying medical facilities. The aim is to provide sufficient ECMO/ECLS network that will sufficiently deploy the ECMO/ECLS support all over the country.

Discussion

Improved medical care and developed prevention system contribute to ageing population. Technological improvements in design and surgical techniques, lead to expanding mechanical circulatory support indications and utilization. Technological advancements allow for ease on implantation. Novel devices are smaller, more durable, and more easily implantable; some of them may be implanted without cardiopulmonary bypass. Still, major drawbacks such as bleeding and thrombo-embolic complications are associated with adverse outcomes and should inevitably be considered. Artificial surfaces that come into contact with blood induce coagulation and require systemic anticoagulation therapy. No protocol has been established and room for improvement is evident in anticoagulation and anti-platelet protocols as well as in technical performance. The second drawback is the need for external sources of energy. Due to this factor, the incidence of infections, although diminished compared to older devices still remains one of the main limiting factors for long term survival. Hence, the transcutaneous transmission of energy from an external source is a promising idea current under development.

Optimal timing of mechanical circulatory support implementation and patient selection strategies are currently being widely discussed. Initially, it was thought that mechanical circulatory support was the only exit strategy when all other medical methods are exhausted. Nowadays, the increasingly accepted opinion is that mechanical circulatory support must be implanted before permanent end-organ damage occurs, improving patient recovery odds.

Further development of mechanical circulatory support technology may upgrade it from an adjunct to a viable alternative to heart transplant in particular for patients that do not meet transplant criteria. Heart transplant and MCS are inextricably associated and present two complementary ways in heart failure treatment.

Integration of circulatory support and heart transplantation programs increases the availability of heart transplantation procedures, however, it increases complexity and cost.

Permanent or temporary mechanical cardiac support has emerged as an irreplaceable treatment for advanced stage heart failure alongside established standard medical procedures. Success of treatment depends on patient selection, timing, and routine practice experience with mechanical circulatory systems.

References

1. Giamouzis G, Kalogeropoulos A, Georgiopoulou V et al. Hospitalization epidemic in patients with heart failure: risk factors, risk prediction, knowledge gaps, and future directions. J Card Fail 2011; 17:54–75.
2. Giamouzis G, Triposkiadis F, Butler J, Westermann D, Giannakoulas G. Heart failure. Cardiol Res Pract 2011; 2011:1596-08.
3. Lloyd-Jones D, Adams RJ, Brown TM et al. Executive summary: Heart disease and stroke statistics—2010 update: a report from the American Heart Association. Circulation 2010; 121:e46-e215.
4. Ammar KA, Jacobsen SJ, Mahoney DW et al. Prevalence and prognostic significance of heart failure stages: application of the American College of Cardiology/American Heart Association heart failure staging criteria in the community. Circulation 2007; 115:1563–70.
5. Hershberger RE, Nauman D, Walker TL, Dutton D, Burgess D. Care processes and clinical outcomes of continuous outpatient support with inotropes (COSI) in patients with refractory endstage heart failure. J Card Fail 2003; 9:180–7.
6. Christie JD, Edwards LB, Kucheryavaya AY et al. The Registry of the International Society for Heart and Lung Transplantation: 29th adult lung and heart-lung transplant report-2012. J Heart Lung Transplant 2012; 31:1073-86.
7. EUROTRANSPLANT. Eurotransplant International Foundation Annual Report 2012. Available from: http://www.eurotransplant.org
8. Gibbon JH. Application of a mechanical heart and lung apparatus to cardiac surgery. Minnesota medicine 1954; 37:171–185.
9. DeBakey ME. Development of mechanical heart devices. Annals of Thoracic Surgery 2005; 79:S2228–S2231.
10. Gemmato CJ, Forrester MD, Myers TJ, Frazier OH, Cooley DA. Thirty-five years of mechanical circulatory support at the Texas Heart Institute: an updated overview. Tex Heart Inst J 2005; 32:168–177.
11. McMurray JJ, Adamopoulos S, Anker SD et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Eur J Heart Fail 2012; 33:1787–847.
12. Kirklin JK, Naftel DC, Kormos RL et al. Fifth INTERMACS annual report: risk factor analysis from more than 6,000 mechanical circulatory support patients. J Heart Lung Transplant 2013; 32:141-56.
13. Strüber M, Meyer AL, Malehsa D, Kugler C, Simon AR, Haverich A. The current status of heart transplantation and the development of artificial heart systems. Dtsch Arztebl Int 2009; 106:471–477.
14. Saito S, Nishinaka T, Yamazaki K. Long-term support with a left ventricular assist device therapy in Japan. Circ J 2010; 74:624-625.
15. Saito S, Matsumiya G, Sakaguchi T et al. Fifteen-year experience with Toyobo paracorporeal left ventricular assist system. J Artif Organs 2009; 12:27-34.
16. Rose EA, Gelijns AC, Moskowitz AJ et al. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med 2001; 345:1435-43
17. Hunt SA. Mechanical circulatory support: new data, old problems. Circulation 2007; 116:461-2.
18. Kirklin JK, Naftel DC. Mechanical circulatory support: Registering a therapy in evolution. Circ Heart Fail 2008; 1:200–205
19. Pagani FD, Miller LW, Russell SD et al. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. J Am Coll Cardiol 2009; 54:312-21.
20. Kolff WJ. Total artificial hearts, LVADs or nothing? And muscle and air-powered LVADs. Akutsu T, Koyanagi H, eds. Heart replacement. Tokyo: Springer, 1993: 3-11.
21. Miller LW, Pagani FD, Russell SD et al. Use of a continuous-flow device in patients awaiting heart transplantation. N Engl J Med 2007; 357:885–96.
22. Slaughter MS, Rogers JG, Milano CA et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med 2009; 361:2241-51.
23. Holman WL, Kirklin JK, Naftel DC et al. Infection after implantation of pulsatile mechanical circulatory support devices. J Thorac Cardiovasc Surg 2010; 139:1632-6.
24. Martin SI, Wellington L, Stevenson KB et al. Effect of body mass index and device type on infection in left ventricular assist device support beyond 30 days. Interact Cardiovasc Thorac Surg 2010; 11:20-3.
25. John R, Pagani FD, Naka Y, et al. Post-cardiac transplant survival after support with a continuous-flow left ventricular assist device: Impact of duration of left ventricular assist device support and other variables. J Thorac Cardiovasc Surg 2010; 140:174–81.
26. Foley PJ, Morris RJ, Woo EY, et al. Limb ischemia during femoral cannulation for cardiopulmonary support. J Vasc Surg 2010; 52:850-853.
27. Hendrickson SC, Glower DD et al. A method for perfusion of the leg during cardiopulmonary bypass via femoral cannulation. Ann Thorac Surg 1998; 65:1807-8.
28. Zimpfer D, Heinisch B, Czerny M, et al. Late vascular complications after extracorporeal membrane oxygenation support. Ann Thorac Surg 2006; 81:892-895.
29. Jaski BE, Ortiz B, Alla KR, et al. A 20-year experience with urgent percutaneous cardiopulmonary bypass for salvage of potential survivors of refractory cardiovascular collapse. J Thorac Cardiovasc Surg 2010; 139:753-7.
30. Magovern GJ Jr, Magovern JA, Benckart DH, et al. Extracorporeal membrane oxygenation: preliminary results in patients with postcardiotomy cardiogenic shock. Ann Thorac Surg 1994; 57:1462-8.
31. Ko WJ, Lin CY, Chen RJ, Wang SS, Lin FY, Chen YS. Extracorporeal membrane oxygenation support for adult postcardiotomy cardiogenic shock. Ann Thorac Surg 2002; 73:538-45.
32. Goldstein DJ, Oz MC. Mechanical support for postcardiotomy cardiogenic shock. Semin Thorac Cardiovasc Surg 2000; 12:220-8.
33. Thiele H, Zeymer U, Neumann FJ et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med 2012; 367:1287-96.
34. Bhama JK, Kormos RL, Toyoda Y, Teuteberg JJ, McCurry KR, Siegenthaler MP. Clinical experience using the Levitronix CentriMag system for temporary right ventricular mechanical circulatory support. J Heart Lung Transplant 2009; 28:971-6.
35. Haj-Yahia S, Birks EJ, Amrani M, et al. Bridging patients after salvage from bridge to decision directly to transplant by means of prolonged support with the CentriMag short-term centrifugal pump. J Thorac Cardiovasc Surg 2009; 138:227-30.
36. Aziz TA, Singh G, Popjes E, et al. Initial experience with CentriMag extracorporal membrane oxygenation for support of critically ill patients with refractory cardiogenic shock. J Heart Lung Transplant 2010; 29:66-71.
37. Stevenson LW, Pagani FD, Young JB, et al. INTERMACS profiles of advanced heart failure: the current picture. J Heart Lung Transplant. 2009; 28:535-41.