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Ventricular Assist Devices

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Abstract

Heart failure is a common and debilitating disease with about 40 million affected worldwide. While there has been some improvement in the optimal medical therapy over the last two decades there is a worldwide stagnation in the number of heart transplantations which is only available to a very few selected patients. The emergence and progress in mechanical circulatory support strategies over the same period has provided a real hope for those patients who have otherwise similar life expectancy to terminal cancer patients. Devices like the IABP have been around for longer but it was the advent of extracorporeal pulsatile and especially the so-called second and third generation ventricular assist devices that provided a real progress in the surgical treatment of heart failure. Devices like the HeartMate II and the HeartWare MVAD found widespread application as intracorporeal continuous-flow left ventricular assist devices. Initially the licences were for bridge to transplantation but more and more patients are now receiving these devices as destination therapy. There are certain specific complications like device thrombosis, bleeding and driveline infection that are related to these devices and are the focus of current research and development so that over the next decade or so that we can anticipate that newer devices may provide a direct alternative to transplantation with the advantage of its availability off the shelf. The ensuing increased usage of these devices will possibly reduce the cost to more affordable rates for the health care providing institutions worldwide which will make them available to millions of patients who have otherwise a very bleak outcome.

Keywords: heart failure, heart transplantation, mechanical circulatory support, ventricular assist devices, VAD complications

1. Introduction

Heart failure (HF) is a common condition affecting 37.7 million people worldwide. In majority of affected patients it can be debilitating chronically if not immediately lethal in some. The burden on the affected individual as well as the wider society is considerable. Currently the best

available treatment for worsening end-stage HF despite optimal medical therapy is considered to be heart transplantation with the caveat that it is available for only very few patients who are deemed eligible to be accepted on the waiting lists and survive long enough without precluding end-organ dysfunction for a suitable organ to become available. For the rest the outcome is very poor with an average survival of 50% at 5 years after diagnosis of HF, rates comparable with the diagnosis of cancer. While early extra-corporeal pulsatile mechanical circulatory support has been around since 1960s, it was the advent of continuous flow intra-corporeal ventricular assist devices (VAD) that made this treatment widely available as longer term option to advanced HF patients. Last decade has seen a worldwide surge in the use of long-term left ventricular assist devices (LVAD) that has given a new hope to patients together with new challenges. These challenges are based around chronic driveline infections, right ventricular failure, neurological events and the dilemma between thrombosis and bleeding. Recently the focus of research and development has shifted towards alleviation of these complications and development of comprehensive strategies and pathways for acute and chronic HF patients.

2. Heart failure

Heart failure (HF) is one of the most common causes of death while it affects about 37.7 million people worldwide and was identified as an epidemic in 1997 [1, 2]. In majority of patients it can have a debilitating effect chronically if the initial insult is survived. The burden on the affected individual as well as the wider society is substantial. Poor exercise tolerance, chronic lethargy and depression with constant anxiety of sudden death together with frequent hospitalizations are among those factors limiting patients' quality of life (QOL). The burden to the society is highlighted by 1–4% of all hospital admissions in Europe and US being due to HF with an average stay of 5–10 days and readmission rates of about 25% within 1 month and 50% within 2 months after discharge [3].

Over the last two decades the management of HF has improved with optimal medical therapy including ACE-Inhibitors, β -Blockers, loop-diuretics and Spironolactone together with implantable defibrillators and resynchronisation devices. However the best available therapy for advanced HF is heart transplantation with the caveat that it is available for only very few patients who are deemed eligible to be accepted on the waiting lists and survive long enough for a suitable organ to become available. For the rest the outcome is very poor with an average survival of 50% at 5 years and 10% at 10 years after diagnosis of HF. This rate has not changed in the last 20 years whereas the survival when diagnosed with cancer has doubled in the last 40 years. Therefore there is much potential for alternative treatment options of which the ventricular assist devices present a real hope.

3. Mechanical circulatory support

3.1. Emergence of ventricular assist devices

The relative short history of mechanical circulatory support in clinical use started with the invention of the cardiopulmonary bypass machine early 1950s that allowed safe operations

on the open heart. The first device to temporarily support the circulation other than for heart operations was reported in 1962 in the form of intra-aortic balloon pump (IABP) [4, 5]. The research into the development of more substantial mechanical circulatory assist devices that was initiated by the National Institutes of Health (NIH) in the US was responsible for most of the progress that followed from the 1960s onwards. Funded by the NIH we had the first reported clinical use of an intra-corporeal and then extra-corporeal ventricular assist devices in 1963 and 1966 respectively by DeBakey's group [6]. A total artificial heart (TAH) was developed in Baylor College of Medicine and then implanted in 1969 by Cooley. Much progress in the following 30 years has been around sizeable extra-corporeal devices that were driven pneumatically with substantial consoles. These were relatively successful so-called first generation short-term devices with pulsatile flow pattern allowing patients in acute heart failure to bridge to recovery or transplantation but were burdened with high rates of mortality and morbidity. Patients were bed-bound, unable to mobilise and could only be supported for few days to weeks. The lack of long-term durability of these devices was the main factor to restrict the use only as a short-term bridge to transplantation.

The next big step towards more usable devices took shape around the millennium with a new so called second generation devices that were smaller therefore implantable and intra-corporeal. These pumps provided a continuous flow (CF) pattern generated by an axial rotor which was suspended mechanically in its casing. The lack of pulse was a shock to the medical community that required some debate and time to get over. These CF VADs also required thinner drivelines that helped to reduce the infections often originating from exit sites of large cannula and drive lines of the first generation devices. To date the most commonly used example of these devices is the HeartMate II which is still used frequently. Other rarely used examples were Jarvik 2000 and Micromed DeBakey VAD.

Another quantum leap happened more recently in the last decade when there was a surge in the number of implanted LVAD's worldwide triggered by both the new licences obtained for destination therapies and particularly with further progress achieved with newer so called third generation devices. These devices introduced substantial progress in further miniaturisation, reliability, durability and noise reduction all of which contributed to the usability and long-term manageability of patients who now tend to envisage living with these devices for the rest of their lives. Primary third generation device example is the HeartWare HVAD with recent addition of HeartMate 3 both of which have a centrifugal pump that is magnetically suspended eliminating wear-out with better durability. Miniaturisation meant that they could be implanted entirely intra-pericardial even on smaller adults and children.

Current research focuses in reducing the much feared morbidities. Driveline infections is one and often cited as the 'Achilles' tendon' of LVADs. Progress in transcutaneous energy transmission systems (TETS) promise to avoid the need for drivelines altogether. Special consideration of the right ventricle (RV) is required as the vast majority of VADs is placed for the support of the left ventricle with early and late post-operative RV failure resulting in significant increase in mortality. Strategies have been developed to predict RV failure, to preventively optimise haemodynamic parameters pre-operatively and to improve management post-operatively. The dilemma between pump thrombosis and bleeding can be very difficult to manage and has to be patient specific. Usual long-term strategy involves a combination of warfarinisation and anti-platelet therapy that allows individual attention to patients'

tendency to either “bleed” or “clot”. Another fascinating area of research is gastro-intestinal AV-malformations and their relationship with von Willebrand factor and CF pattern of these new devices. Newer materials are sought for better biocompatibility and reduced thrombogenic properties.

Due to the unique nature of patients and their LVADs most of established MCS Programs have now comprehensive long-term management protocols involving patients’ families, General Practitioners, local emergency departments and hospitals, ambulance services and local government services.

3.2. Current devices

The vast majority of currently used LVADs are the HeartWare HVAD and HeartMate 3. Both are miniaturised and fully implantable into the pericardial cavity and by the use of a centrifugal pump that is magnetically levitated they avoid mechanical wear-out therefore more durable and less thrombogenic. The HVAD has a centrifugal pump that is magnetically levitated with hydrodynamic bearings avoiding mechanical interface resulting with only one moving part that is the pump which is driven by two motors providing a continuous flows of blood. The HVAD System weighs at 160 g and is small enough to fit intra-pericardial in most patients with dilated cardiomyopathy. There have been reports of two pumps for bi-ventricular support and some paediatric use to ages below 10 years all of which placed fully intra-pericardial [7–9]. Only some restrictive cardiomyopathy and smaller children present a challenge due to lack of intra-pericardial space. The HeartMate 3 is similar in design and function with certain differences. These include full magnetic levitation without hydrodynamic bearings allowing for the rotor to operate in wider RPM ranges which in turn allows flows between 2.5 and 10.0 L/min and larger gaps between the rotor and the casing reducing the haemolysis and shear stress to the blood. There is also an attempt to address the concerns about CF in regards to its causative effects on AVM’s by incorporating a degree of pulsatility to the flow profile. The Abiomed Impella device is a different approach which includes the option of percutaneous insertion and placement across the aortic valve with blood inlet area in the LV cavity and outlet area in the ascending aorta reaching flows up to 5 L/min. An axial rotor is positioned at the outlet area. Common complications include haemolysis, device thrombosis, bleeding, vascular injury and arrhythmia [10, 11]. There are numerous other short- and long-term ventricular assist devices available however these are less frequently used by the majority of centres specialising in MCS.

3.3. Patient selection

Each patient in heart failure requires individualised assessment for suitability for MCS implantation which proposes only one aspect of patient management. Patient and device choice depend on the indication and purpose of the MCS implantation. Statistically over the last decade the majority of patients treated with assist devices fall in to Intermacs classes 1–4. **Table 1** describing severity of heart failure according Intermacs classification (Interagency Registry for Mechanically Assisted Circulatory Support) and expected survival of patients in each category which helps to determine the urgency of the intervention as well as its type.

Intermacs level	Short code	Definition	Expected survival: action required
Level 1	“Crash-and-burn”	Critical cardiogenic shock, oliguria/anuria, rising lactate levels and liver function tests	Hours/days: immediate intervention required
Level 2	“Sliding fast”	Progressive decline despite inotropic support	Days/weeks: intervention within days
Level 3	“Hospital bound”	Stable but inotrope dependent	Weeks/months: elective MCS vs. Transplant within weeks
Level 4	“Frequent flyer”	Resting symptoms, frequent hospitalisation with decompensation	Months/year: elective MCS vs. Transplant
Level 5	“House bound”	Comfortable at rest, intolerant to minimal activity of daily living	Year/s: elective MCS vs. transplant depends on other parameters
Level 6	“Walking wounded”	Exertion intolerant, can only manage normal activity of daily living	Year/s: elective MCS vs. transplant depends on other parameters
Level 7	NYHA III	Advanced NYHA III	Years: medical management, MCS or transplant not indicated

Table 1. Intermacs classification with definitions and management strategies.

Level 1: patients in this category usually present with fulminant myocarditis or more commonly after complicated myocardial infarction when primary PCI failed to restore the resulting acute loss of pump function of the heart. If there is sufficient evidence that the individual would be suitable transplant candidate than a longer term MCS could be considered but in reality in this emergency setting this evidence is lacking so that in most cases short-term MCS device is chosen as salvage and bridge to decision. Devices to consider for these patients include intra-aortic-balloon-pump (IABP), extra-corporeal-membrane-oxygenator (ECMO) or more recently the Impella device or TandemHeart. While the application of ECMO usually requires a dedicated centre, the insertion and management of IABP or Impella is less cumbersome but only provide partial support of the circulation. Occasionally the Impella device is also used for right ventricular support either in addition to the left sided support or in isolation. There are reports from highly specialised ECMO centres achieving relatively high survival rates for ECMO application on patients with out-of-hospital-cardiac-arrest (OOHCA) and ongoing CPR [12].

Level 2: these patients are deteriorating despite escalating inotropic support and usually show end-organ dysfunction and not expected to survive more than days or weeks. They are either unfit for transplantation due to end-organ dysfunction or not expected to survive long enough for a suitable donor-heart to become available. Considerations for Level 2 patients include destination therapy or bridge to either decision or candidacy/transplantation. Devices for this category include HVAD or HM3 among other less often used devices as well as even less commonly used total artificial heart systems (TAH). More common than TAH is the temporary support of the right ventricle with extra-corporeal CentriMag in addition to an LVAD. If there is complicating respiratory dysfunction, it is easy to add an oxygenator to the CentriMag circuit and await recovery.

Level 3 and 4: these patients have a very poor quality of life being either hospital bound or admitted frequently. They also often have end-organ dysfunction that precludes them from listing for transplantation. If they are suitable for transplantation and have preferable blood group/typing and body weight and if the geographical donor pool is preferable making heart transplantation likely within few weeks or months then waiting for transplantation may be a good option. However in reality in most centres in the world overcoming all of these postulations and receive a successful heart transplantation is preserved to a very few lucky ones. In vast majority patients at this level of disease progression present considerable disease burden and require MCS in an elective fashion. Left ventricular support with HVAD and HM3 are most commonly used. In patients with concomitant right ventricular dysfunction there are different approaches available. Mostly, pre- and post-operative optimisation and attentive management of the body fluid equilibrium are sufficient to prevent right ventricular failure. Sometimes a temporary RVAD with CentriMag is required to overcome the immediate intra- and post-operative insult to the right ventricle. A right sided Impella is also an option in this setting.

Level 5 and 6: patients at these levels of disease progression are usually stable in the short and medium term period therefore could be placed on heart transplant waiting lists with close follow up to early pick up any sign of deterioration or end-organ dysfunction. Some patients in this category present or develop pulmonary hypertension precluding them from listing for transplantation which can be improved with an LVAD therapy rendering them into a candidacy position. Generally these patients are not considered for MCS as the heart failure burden is comparable with the burden of any type of mechanical support is often accompanied. In the coming years this cohort of patients will become increasingly the focus when we can significantly reduce the frequently observed complications related to MCS.

3.4. Peri-operative management

End-stage heart failure with diminished organ perfusion has a detrimental effect to most of organ systems of the body. Renal dysfunction due to reduced cardiac output, liver dysfunction due to cardiac output as well as congestion, nutritional depletion due to dysfunctional gastrointestinal absorption as well as liver dysfunction causing physical debilitation, respiratory dysfunction due to congestion as well as pulmonary hypertension, upwards regulation of the systemic inflammatory responses, cognitive impairment due to hypoxia and psychological implications due to constant anxiety and burden of the disease all contribute to push the individual into a vicious circle and downwards spiral of end-stage heart failure. Any MCS system aiming to alleviate the underlying cardiac dysfunction is bound to fail if these organ systems are not concomitantly addressed.

Aggressive fluid removal with high dosages of loop-diuretics and/or renal replacement therapy in form of haemofiltration may be required on top of optimal medical therapy which includes β -Blockers, ACE-Inhibitors and Spironolactone. The achievement of the ideal fluid equilibrium sets the right ventricle in a best possible starting position to overcome the strains of the operation and the increased cardiac output that will be provided by the LVAD. The use of infused phosphodiesterase inhibitors and inhaled nitric oxide can support the right

ventricle in this immediate post-operative period. Cardiac arrhythmia needs to be treated aggressively for the same purpose.

Intensive input from the dietitian as well as physiotherapist and psychologist represent cornerstones of optimal pre- and post-operative management of patients receiving MCS.

3.5. Surgical techniques

The urgency of the procedure and the type of MCS together with the individual clinicians and units experience determines the technique of implantation. Of course there are different approaches to the implantation technique including bilateral small thoracotomies, avoidance of the CPB, using more distal aortic sites for outflow-graft anastomosis and exit point of the drive-line. We will however only discuss the most common approaches of the techniques related to the implantation of the most commonly used devices.

The simple percutaneous insertion of IABP does not require much attention due to its common use and familiarity. The Impella device is inserted percutaneously through the femoral or subclavian/axillary arteries with the help of Fluoroscopy and cardiac catheterisation techniques. The blood inlet area is at the tip of the device which is positioned across the aortic valve in the left ventricular outflow tract well away above the papillary muscles and the outlet area is positioned well above the aortic valve at the level of the sino-tubular junction. Transoesophageal Echocardiographic images help exactly position the inlet and outlet areas.

For the implantation of the HVAD the patient is positioned supine and draped exposing the entire front of the trunk including cranially the jugular notch and medial two thirds of the clavicles for the exposure of the subclavian vessels, laterally along the anterior axillary line down to the anterior superior iliac spinosus and further down the lateral thigh and caudally just above the patella. The groins are kept prepared in case femoral cannulation is required for ECMO or additional RVAD support. Standard median sternotomy and ascending aortic and right atrial cannulation is performed for cardiopulmonary bypass (CPB). Techniques avoiding median sternotomy therefor avoiding the need for re-do sternotomy for eventual heart transplantation includes left anterior thoracotomy at the apex which can be localised with TTE, and right parasternal thoracotomy at 2nd ICS can be used with or without CPB. The LV apex is examined and the dimple identified to centre the sewing ring around just lateral to the distal LAD. We use 16 pledged 4/0 Prolene sutures in a horizontal mattress fashion and a layer of sealant to secure the sewing ring in position. Then while the heart is fibrillated a cross incision with a blade is made and the coring device provided in the implantation pack is used to remove a cylindrical piece of myocardium within the sewing ring. The HVAD device is then inserted into the sewing ring and fastened with the screw driver provided. The inflow cannula is oriented directly pointing to the middle of the mitral valve which is confirmed with TOE images. The outflow graft is left open momentarily for de-airing. The outflow graft is then sutured with continuous 5/0 Prolene sutures just like any other top-end anastomosis right laterally onto the ascending aorta above the ST junction and above the SVC using a side-biting clamp. The clamp on the graft can again be released momentarily before tying the knot for further de-airing of the LV. The driveline can now be tunnelled across the abdominal wall with three exit points in a Z-shaped or V-shaped course initially sub-fascial then subcutaneous. The final exit point is at the level lateral and below the

umbilicus either on the right or the left flank depending on patients' handedness and preference which is usually determined pre-operatively if possible. After the driveline is connected to the driver CPB is discontinued slowly and the HVAD started and RPMs set that allow the inter-ventricular septum to be straight and neither bulged to the left nor to the right. TOE is used to assess the septum as well as right ventricular function and aortic valve opening. Volume load, inotropic support, especially Milrinone, inhaled nitric oxide and setting of the RPMs of the LVAD can help to fine tune the patients' haemodynamic equilibrium and prevent RV failure. This is usually the timing for the decision to add an RVAD is made. The implantation of the HM3 is very similar with that of the HVAD with only little differences owing to the design of the pump.

If there is the need for temporary RVAD then CentriMag is often used as extracorporeal centrifugal VAD using the femoral venous cannulation for inflow and a Gore-Tex vascular graft onto the pulmonary artery and tunnelled through the left second intercostal space parasternally and above the pectoral muscle with any aortic cannula attached as outflow. If a more long-term RVAD is required then another HVAD can be used in intra-pericardial position using inferior RV wall or the RA as inflow access and the PA as outflow. The use of TAH could also be considered however the evidence for long-term TAH is scanty.

3.6. Complications

We will investigate not the common complications related to any heart surgery but only those particular to VADs. These include drive-line infections (DLI), pump thrombosis (PT), GI-bleeding, cerebral vascular incidents, right ventricular failure and aortic valve insufficiency.

3.6.1. Driveline infections

Overall DLI incidence is around 10–20% with higher rates observed with devices requiring a pump-pocket or has larger diameter drivelines [13]. This rate is also dependent on patient and procedure risk factors including hygiene, nutritional status, diabetes, urgency of the procedure and implantation technique. Prolonged subcutaneous course is thought to prevent speedy up-migration of potential DLI towards the pump itself with severe consequences however at the same time it increases the potential infection sites by increasing the number of skin breakages to allow the long course. The use of antibiotic containing products deposited at the exit site may also help reduce the infection rate. The burial of the Dacron part of the DL below the skin allowing only silicone-skin interface as well as perpendicular exit of the DL as supposed to lying on the skin can further help reduce the DLI rates. Treatment includes targeted antimicrobial therapy and surgical exploration with debridement and re-routing of the DL. Long-term suppressive antimicrobial therapy is a not too unfeasible option to control and contain infections that are difficult to eradicate or too close to the pump and carry high risk for operative approach.

3.6.2. Anticoagulation

Patients present with different levels of general coagulability, which is why there are rather non-scientific terms like "clotter" and "bleeder" in existence and in use in the clinical arena. The general state of the patients nutrition and rates of systemic inflammatory response to

heart failure as well as to the operative insult has surely more influence to the coagulation tendencies. The resistance to acetylsalicylic acid (ASA) is another more scientific explanation why some patients do not respond to platelet inhibition with Aspirin therefore more prone to thrombosis. Previous events of thrombi especially in the left ventricular cavity or in the left atrium predispose to pump thrombosis. Device type also seems to influence the rates of thrombosis although not proven to be statistically significant. Increased thrombosis is also seen if for clinical reasons lower pump-flow rates are sought with corresponding low RPMs of the device. Consideration to all of the above together with a thrombophilia workup will allow an individualised anticoagulation regimen that requires close monitoring with the available methods. The usual anticoagulation regimen that can be the basis includes initial heparinisation started after 12–24 h postoperative depending on chest tube drainage. Heparinisation is guided by activated clotting time (ACT) at 160–220 s. On postoperative day one Aspirin at around 150 mg can be introduced and later increased to 300 mg per day in single or divided doses. Aspirin response can be measured and monitored with serum anti-Xa levels with a therapeutic target range of 0.5–1.0. Aspirin can be supplemented or replaced with Clopidogrel for resistance or allergy. Dipyridamol is often added to this anti-platelet regimen. Warfarin is introduced on day three or later depending on chest tube drainage and presence of epicardial pacing leads which require removal. The recommended target INR is between 2.0 and 3.0 for most devices.

Surveillance of anticoagulation is routinely done by INR measurements complemented by platelet count and serum LDH. However some centres advocate more detailed assessments including platelet function tests, anti-Xa levels and thromboelastogram (TEG).

3.6.3. Pump thrombosis

The diagnosis of pump thrombosis is suspected primarily if there is increase in pump power with or without pump flow changes. This is due to the fact that the driver has to spend more power to achieve same speed of the rotor which is impeded by the presence of the thrombus either reducing the blood inflow into the cannula or through the pump or the outflow graft or indeed mechanically impeding the rotation of the rotor inside the pump in areas of the rotor bearings. Further diagnostic test is the serum LDH levels which increase relative to baseline surveillance levels. Clinical signs i.e. haematuria, of or laboratory tests for haemolysis the likes of haptoglobin, plasma-free haemoglobin, bilirubin and fibrinolysis products can aid the diagnosis. If the pump thrombosis is large enough to cause reduction of pump output signs of heart failure can resurface. Cardiac imaging with Echocardiogram and/or CT Thorax for visualisation of the thrombus in the ventricular cavity as well as assessment of ventricular filling together with manipulation of the pump speed can be carried out for further differentiate the diagnosis.

Treatment of device thrombosis depends on the severity of the thrombus and its haemodynamic and device related complications. This would include up-regulation of anticoagulation, intravenous heparinisation, systemic thrombolysis or device exchange if the former interventions are not successful. New approaches with intra-ventricular and/or intra-pump thrombolysis and washout are being assessed for safety and effectiveness.

3.6.4. *Gastro-intestinal bleeding*

Intractable epistaxis is mentioned but not further discussed here as often this can be managed successfully with the input of ENT Surgeons. There are several reports and studies investigating bleeding from the entire gastro-intestinal tract (GIT). Obvious predisposing risk factors include reflux oesophagitis, gastritis or inflammatory diseases like Crohn's or Colitis which may present themselves as contraindication for VAD therapy as they will be very difficult if not impossible to manage with full anticoagulation. More intriguing concept in continuous flow (CF) LVAD therapy is the often encountered arteriovenous-malformations (AVM) that seems to be associated with von Willebrand factor (vWF) deficiency. There are theoretical and conceptual suggestions that the continuous flow pattern of these devices are at least partially responsible for development of AVM's in the GIT. Simultaneously the accelerated speed of the blood through the rotors of these CF pumps is said to be responsible for high shear forces active on the high molecular weight vWF causing distortions/breakages leading to qualitative changes with subsequent reduction of function in relation to platelet aggregation. This combination of AVM's with vWF deficiency gives rise to intractable bleeding occasionally leading to surgical intervention.

3.6.5. *Cerebral vascular incidents*

Intracerebral events are feared for the reason that they are often fatal. They can be of two sometime overlapping pathophysiology namely embolic or haemorrhagic of nature. Embolic events are more often encountered peri-operatively due to particulate matter or air from the operative field reaching cerebral vasculature causing ischaemia. The particulate emboli can originate from preexisting thrombi from the LV or LA cavity, atherosclerotic debris from the aortic manipulation during cross clamping or graft anastomosis or paradoxical thrombi crossing across an undiagnosed ASD. Therefore great care is taken in pre-operative workup to identify these risk factors. Air emboli can be avoided with appropriate and assiduous de-airing manoeuvres aided by CO₂ insufflation of the operative cavity. Later in the follow up period haemorrhagic intracerebral events predominate in frequency and lethality although often overlapped with embolic events that transform into haemorrhagic lesions.

3.6.6. *Right ventricular failure*

Management of the right ventricle in patients receiving LVADs can present itself like a manoeuvre 'between Scylla and Charybdis'. Bi-ventricular assist device implantation has reportedly high mortality therefore efforts are focused into avoidance of RVAD in addition to LVAD therapy if at all possible [14–17]. Strategies have been developed over the last decade that include optimisation of hydrostatic status of the heart failure patients including oral and intravenous pharmacological as well as renal replacement therapies. This effort aims to set the right ventricular filling pressures into the optimal position on the Frank-Starling Curve with the best possible contractility resulting from the actin-myosin relationship. In practice this means to aim to decrease the central venous pressure down to single figures i.e. below 10 mmHg prior to the procedure if there is sufficient time available. Further fluid can be

removed using haemofiltration during cardiopulmonary bypass if used. Other peri-operative measures include off-pump and minimally invasive techniques to minimise systemic inflammatory response to the procedure, TOE guided optimisation of the position of the ventricular septum by manipulation of the LVAD speed and the use of pulmonary arterial pressure attenuating pharmacology including intravenous phosphodiesterase inhibitors and inhaled nitric oxide. Comprehensive heart rhythm management including resynchronisation and anti-arrhythmic strategies are required to avoid the undesirable effects of arrhythmia to RV function. Hybrid approaches of endocardial and epicardial ablation for supra-ventricular or ventricular arrhythmias may represent a feasible option in some centres. Continued effort is necessary in the long-term follow up of these patients focussing on hydrostatic optimisation if the right ventricular function is to be kept under control.

3.6.7. Aortic valve insufficiency

The evidence is mounting that show the adverse effect of the continues flow LVADS to the aortic valve [18–22]. Constant closure of the valve during LVAD support encourages fusion of the leaflets leading to stenosis. More importantly the lack of physiological movements of the leaflets during the cardiac cycle leads to worsening of mild to moderate regurgitation with increased morbidity. Over time an increasing portion of the pump flow returns back to the LV cavity creating a short circuit with resulting peripheral hypo-perfusion and LV filling pressures consequently return of heart failure symptoms. Manipulation of pump speeds to achieve sufficient aortic valve opening is proposed by large MCS Centres. Bioprosthetic aortic valve replacement for more than mild aortic regurgitation at the time of LVAD implantation has been advocated by experts more frequently in recent years.

3.7. Long-term management

The patient population with long-term LVAD therapy has been increasing due to the improved technology and the management strategies of the complications. More patients are now receiving LVADs as de-facto destination therapy as there is no other promising treatment option available for patients who do not belong to the lucky few transplant recipients. This increasing population require close and continued care that is very distinct and individualised. A great number of regional health care services, social services and potentially family and friends need to be involved in the care of these patients. Local emergency services and hospitals need to be familiarised with the specific patient profiles. They need not to panic and commence CPR if there is no pulse. They need to know that some arrhythmia is better tolerated than without an LVAD, that deranged anticoagulation does not always require immediate counter measures, that any infection/sepsis can have amplified detrimental effects on RV function and anticoagulation and that their hydrostatic equilibrium may have a very small margin of safety. Social services and local council authorities have to facilitate emergency measure for power cuts. Relatives and friends or carers need to familiarise themselves with the LVAD driver connections to the drive-line, batteries and power cables and what certain alarms mean and how to contact the appropriate MCS Centre. This close monitoring and cooperation can only be achieved with dedicated VAD coordinators taking on a central role

between the patient and their carers, the clinicians and local emergency and social services. Well thought through protocols taking into account the geographic particularities and circumstances are required to accommodate the needs of this distinct group of patients that is certain to grow in numbers in the not so far future.

4. Future developments

The technology around mechanical circulatory support is evolving with an exponential speed which makes any prediction beyond few years futile. We can however look into current work that is focusing in the alleviation of VAD complications and is promising to become clinical practice in foreseeable future. One of these is contactless energy transfer that is combined with subcutaneous implantable batteries allowing transcutaneous energy transfer (TET) and avoid the driveline passing through the skin eliminating the 'Achilles' heel' of MCS Systems [23]. Further work involves strategies aiming for early and more sensitive recognition and treatment of certain complications especially the likes of pump thrombosis. These techniques use remote monitoring systems with in-time assessment and intervention of pump readings and parameters to more finely tune the VAD therapy [24]. Improved biocompatibility of materials used and rotor design will surely be helpful to reduce thrombosis risk as well as to reduce shear forces affecting blood components. Further miniaturisation and less invasive techniques of implantation can be expected to become more common place in the near future and will allow to expand the age spectrum of the recipients. Better understanding and management of right ventricular dysfunction may be coupled with more intuitive bi-ventricular support in order to achieve better and sustainable results. With improved results and better control of complications one can expect to broaden the spectrum of recipients to less sick patients and include Intermacs classes 5 and above to preemptively avoid end-organ dysfunction of heart failure patients.

5. Conclusions

Within a relatively short period of emergence the implantation of left ventricular assist devices have made a huge impact in treatment of end-stage heart failure patients. The development of a new treatment method inevitably brings with it new challenges that limit its spectrum of utilisation. LVAD specific challenges which represent the limiting factors are mainly driveline infections, anticoagulation balances, cerebral incidents and right ventricular dysfunction. We can be optimistic that current research will lead to progress in tackling of these challenges so that we will be able to claim that this therapy method represents a first line management plan for HF patients. Notwithstanding the recent encouraging attempts of widening the donor pool to donation after circulatory death, the number of heart transplantation worldwide has reached a plateau and is only available to very few select types of patients. The prospect of much improved mechanical support methods for the circulation with better manageability represents a real hope for patients in wider age spectrum as well as in earlier phases of disease

progression. Sooner or later MCS Systems that are available off the shelf and adaptable to each patients needs have the potential to replace heart transplantation for end-stage heart failure. However we may want to mention here that in parallel there are endeavours in bio-engineering and gene-manipulation which could allow speculations into the 'off-the-shelf' availability of authentic spare organs for each person.

Conflict of interest

The authors have no conflicts of interest to declare.

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