

Review Article

Mechanical Circulatory Support: Historical Perspective

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Introduction:

“Dear heart, stop getting involved in every emotion, your job is to pump blood and that’s all”. This witty remark is portrayed on a board in the lobby of Chittagong Medical College Cardiac Surgery ICU. Despite being linked to love, hate and other deep human emotions, heart basically is a muscular pump, or more correctly two pairs of pumps connected in a circulatory circuit. It may be estimated that the heart of a 70-year-old individual pumps around 220 million liters or 250000 tons of blood in his or her lifetime. To perform such a towering task, the heart consumes only 250 ml of blood per minute from its own pumped pool. That makes human heart as one of the most efficient pumps working nonstop day and night lifelong. As any mechanical device, human heart is also prone to failure due to various reasons. That’s what makes the requirement of mechanical support devices in addition to lifestyle modifications and pharmacological maneuvers. Introduction of a long-term mechanical circulatory support device or ‘durable LVAD’ has become a celebrated event in Bangladesh recently. This warrants the discussion of the various aspects of mechanical circulatory support devices.

The intra-aortic balloon pump (IABP) is the commonest mechanical support device in use. The IABP balloon supports hemodynamics by diastolic pressure augmentation and improved coronary perfusion. During systole, the balloon shrinks and reduces the afterload. This device has a long history of clinical use since the early 1960s. In

heart failure management, the results are conflicting. It is still an effective first-line treatment. IABP is suitable for short term mechanical support in case of left ventricular failure (LVF). Some of the short term mechanical devices are shown in Table I.

Interest in mechanical circulatory support (MCS) devices advanced concurrently with the interest in cardiopulmonary bypass in the 1950s. Patients with advanced heart failure needing MCS are severely limited with symptoms on minimal exertion or rest, with circulatory insufficiency, on inotropic support or awaiting transplantation. Patients that are deemed ineligible for heart transplantation because of underlying medical conditions related to heart failure may become candidates due to the beneficial effects of MCS. This observation led to blunting of various definitions such as bridge to transplantation (BTT) and destination therapy (DT).

After years of clinical development, durable mechanical circulatory support devices are now widely available for patients with advanced heart failure. Short term devices like IABP and ECMO have been available for quite some time. Availability of continuous-flow left ventricular assist devices (LVADs) for long-term support has changed the face of advanced heart failure care. MCS candidate selection, risk stratification, and management strategies are evolving in tandem with new pump technology, producing a shift in the profiles of patients being considered for MCS.

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Timely referral for MCS evaluation and appropriate implantation now depends on familiarity with recent advances in pump design and clinical outcomes.

Table-I
Devices Available for Short-Term MCS

Device	Mechanism	Duration
IABP	Counter pulsation	Days
ECMO	CPB	Days-weeks
BVS5000, AB5000	Pulsatile	Weeks
Thoratec pVAD	Pulsatile	Weeks
CentriMag	Centrifugal	Weeks
TandemHeart	Centrifugal	Days
Impella	Axial flow	Days

History of Mechanical Circulation:

The application of mechanical circulatory support in animal experiment models can be traced back to the work of the legendary duo Alexis Carrel and Charles Lindberg in the 1930s. The modern era of cardiac surgery began in 1953 with the introduction of cardiopulmonary bypass by John Gibbon, allowing increasingly complex operations and laying the foundation for circulatory assist devices.^{1,2} Soon after its invention, the heart-lung machines were used to support patients with postcardiotomy cardiogenic shock to facilitate recovery. By the 1960s, simple cardiac assist devices began to replace cardiopulmonary bypass for the treatment of post cardiotomy shock. In 1963, Liotta et al., reported the first clinical use of an implantable artificial ventricle.³ This primitive Ventricular Assist Device (VAD) consisted of a pneumatically driven, tubular displacement pump with a valved conduit connecting the left atrium to the descending thoracic aorta. The pump provided partial left ventricular bypass for 4 days after postoperative cardiac arrest before the patient died of multiple organ failure. Inspired by this pioneering work in cardiac surgery and encouraged by results from large animal experiments, the National Institutes of Health (NIH), USA established the Artificial Heart Program in 1964. By 1966, the first successful pneumatic LVAD had been used by DeBakey to support a patient for 10 days after complex cardiac surgery.¹

Following the historic first human heart transplant operation in Cape Town by Dr

Christiaan Barnard in 1967, the use of artificial ventricle technology became necessary as a mechanical bridge to support patients with postcardiotomy shock until a donor organ could be available. In 1969, Cooley et al., reported the first use of a total artificial heart as a bridge to transplant (BTT).⁴

Despite the early promise of human heart transplantation in the 1970s, high mortality rates further spurred on the development of MCS. However, the first generation LVADs of the 1970s could only support for a few days. These pumps had a traumatic blood interface leading to hemolysis and thrombosis, as well as inadequate power supply, faulty control mechanisms, and prohibitive cost. These limitations prompted the NIH to issue another series of initiatives in the late 1970s to develop component technology for deployment in durable implantable assist devices intended for use in chronic heart failure.

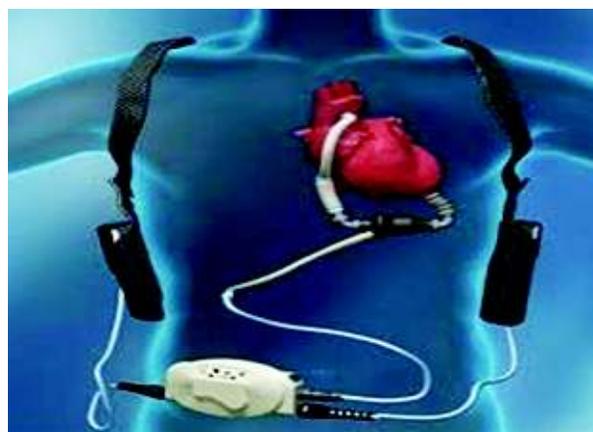


Fig-1: *Left ventricular assist device (LVAD).*

The apogee of popular interest in mechanical circulatory replacement came in 1982 after Barney Clark, a Seattle dentist, received the Jarvik-7 total artificial heart (TAH). This was the first device intended for permanent circulatory support and allowed the recipient to survive 112 days before dying of sepsis.⁵ TAH development eventually stalled because of high rates of infection, pump thrombosis, and stroke. Then the MCS community redoubled efforts to design simpler, single chamber pumps that could act as assist devices in series with the native ventricle.

Thanks to the research work of Norman Shumway, cardiac transplantation experienced a renaissance

with the approval of cyclosporine by US FDA in 1983. Improved immunosuppression featuring a calcineurin inhibitor contributed to a sharp increase in graft survival and a rapid expansion in the number of heart transplant programs in the United States.⁶ Hopes for artificial circulation persisted with the collaborative efforts of intrepid surgeons, innovative engineers, and courageous patients. The NIH-sponsored programs for long-term support bore fruit in 1984 with successful deployment of the electric, pulsatile Novacor LVAD as a BTT. That same year the centers for Medicare and Medicaid Services codified distinct strategies for mechanical support to guide device development and regulatory approval. By the mid-1990s, FDA had approved multiple pulsatile platforms allowing patients to recover from post cardiomy shock or bridge to cardiac transplant.⁷ The expansion of durable LVAD options for patients with advanced heart failure came just as the significant shortage of donor hearts was becoming apparent. In USA, <2300 donor hearts are available for 250,000 advanced heart failure patients. Although LVAD technology was invented in the bridge setting, development began to be targeted toward devices capable of long-term or permanent circulatory support (Fig-1).^{1,8}

Revolution in pump design

Through extensive research works over the past three decades, a series of revolutions in pump design and pivotal clinical trials have changed the face of advanced heart disease care. The landmark FDA approval of the HeartMate XVE (HM XVE) for permanent destination therapy in 2003

uncoupled access to durable MCS from transplant eligibility. As VAD therapy entered the mainstream, the collaborative Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) was established in 2006 to map the evolution of durable MCS. Since the approval of the continuous-flow HeartMate II (HM II) for DT in 2010, a 10-fold increase is observed in approved LVADs implanted for lifelong support in transplant-ineligible patients.⁹ With 1-year survival now at >80% by the approved continuous-flow LVADs, the promise of half a century's work has been realized, and "the decade of the ventricular assist device" seems to have arrived.¹⁰

Pulsatile versus continuous pumps

Following the invention of a smaller high speed, rotary impeller pump, continuous flow VADs with enhanced durability and near silent operation became available. The transition from pulsatile technology toward continuous flow has been remarkably swift. Before 2008, all VADs implanted in the United States outside the clinical trial setting delivered pulsatile flow via an electrically (Novacor, HeartMate XVE) or pneumatically (HeartMate IP, Thoratec IVAD/PVAD) driven volume displacement pump. However, after FDA approval of the HM II for BTT and then DT, by the first half of 2010, 98% of all LVADs implanted in the United States were of continuous flow Type.¹¹

The rapid rise of continuous flow pumps has been propelled by their significant survival and performance advantage over older, pulsatile

Table-II
Some Devices for Long-Term Mechanical Circulatory Support

Device	Mechanism	Indications
Thoratec pVAD	Pulsatile	Bridge to transplant, Bridge to recovery
Novacor	Pulsatile	Bridge to transplant, Destination therapy
Heartmate XVE	Pulsatile	Bridge to transplant, Destination therapy
Heartmate II	Axial flow	Bridge to transplant, Destination therapy
Abiomed TAH	Pulsatile	Bridge to transplant
CardioWest TAH	Pulsatile	Bridge to transplant
Berlin EXOR Pediatric	Pulsatile/pneumatic	Bridge to transplant
DeBakey Child	Continuous	Bridge to transplant, Bridge to recovery

devices. The randomized HM II DT study enrolled NYHA class IV patient ineligible for transplant and directly compared flow profiles. Superior survival was seen with the continuous (HM II) in comparison with pulsatile (HM XVE) VAD at both 1 year (68% vs 55%) and 2 years (55% vs 24%).¹¹ The INTERMACS registry confirmed the superior survival with continuous versus pulsatile flow LVADs at 1 year (83% vs 67%) and 2 years (75% vs 45%), with an overall $P < 0.0001$.⁹

Smaller rotary pumps

Smaller rotary pumps like the HM II have some unique benefits beyond improved survival. The lower pump profile allows preperitoneal abdominal implantation in somewhat smaller patients, including women and adolescents. Before the HM II, patients with small body surface area relegated to an extracorporeal pump as a BTT and had no approved DT option that could safely fit in their abdomen. Smaller pump profiles also have been linked to earlier postoperative recovery and enhanced comfort due to less crowding. The newer HeartWare VAD (HVAD), Jarvik 2000 which were under investigation few years back but now in use, are small enough to allow intrapericardial implantation, which may further enhance comfort.¹² The Jarvik 2000 has got FDA approval for both BTT and DT in 2012. Jarvik 2000 for DT, which uses a unique behind-the-ear power cable and has no pump pocket, is superior to HM II, which uses an abdominal cable and pump pocket and can be implanted through thoracotomy. It requires practically no care of the cable exit site and unlike abdominal cables, does not require frequent dressing with sterile bandages that may require expensive home nursing. Jarvik 2000 patients with the behind-the-ear connector may shower and bath normally and can even go swimming. Jarvik 2000 for BTT, has a power cable that exits the abdominal wall-same like HM II and HVADs. JARVIK HEART is continuing research on new developments including child size and tiny infant size pumps with the support of the National Institutes of Health under the “PumpKIN” program (Pumps for Kids, Infants, and Neonates). The HeartWare HVAD has a centrifugal-flow design, with a smaller more compact profile than the HeartMate II (160g vs 375g) respectively. The impeller is suspended via a combination of

magnetic and hydrodynamic forces and flows as high as 10L/min and got FDA approval in 2012 for BTT and in 2017 for DT. It can also be implanted via thoracotomy. This implant approach has been shown to lead to shorter hospital stays. The near silent operation of nonpulsatile technology also makes these pumps less intrusive for patients and their caregivers, particularly in quiet public places.

Complications

All MCS devices are subject to complications resulting from the complex interplay between pump and patient. Although device durability has been dramatically enhanced with continuous flow pumps, stroke and infection remain substantial risks, and unanticipated hazards specific to rotary VADs have been recognized. Mechanical failure of first-generation electric and pneumatically driven pulsatile pumps frequently resulted in reoperation for device exchange or even death. In REMATCH, 35% of HM XVE recipients experienced component failure within 24 months.¹ Similarly, in the HM II DT study, 20 of 59 patients randomly assigned to HM XVE required 21 device replacements and 2 device explants because of bearing wear and valve dysfunction.²⁶ By contrast, current continuous-flow LVADs like the HM II are designed with only a single, nearly frictionless moving part and do not have a pusher plate or artificial valves. In the pivotal HM II DT trial, the rate of pump replacement was only 0.06/patient-year for HM II in comparison with 0.51/patient-year for HM XVE ($P < 0.001$).^{1,12}

Although LVAD durability has been greatly extended, the inherent risks of bleeding, stroke, and infection remain. On June 3rd 2021 HVAD system was recalled from market by FDA due to increased neurological adverse events. LVAD patients and their families require intensive education before implant and especially postoperative management (device alarm trouble shooting, battery changes, and driveline care) to prepare them for life outside the hospital.

The TAH offers full circulatory replacement therapy for patients with irreversible biventricular failure, although only 2% to 3% of current MCS implants are TAHs.⁹ The pneumatically driven SynCardia TAH was FDA approved for BTT in 2004, and received centers for Medicare and

Medicaid Services coverage in 2008 (Fig-3). Device malfunction, along with bleeding, stroke, and infection, remain concerns with TAH technology.¹



Fig-2: Total Artificial Heart (SynCardia) both internal part (upper) and external part (lower).

Miniaturization and modern machines

Another important trend in pump development has been miniaturization, even at the expense of flow rate. HeartMate III heart pump (weight 200g, measuring 50.3mm in diameter and 55.8mm in height, including inflow cannula) has fully levitated, self-centering, bearing less rotor using magnetic levitation (Full MagLev™ Flow Technology), has its own intrinsic pulsatility which reduces stasis and minimize thrombus, able to fit

intrapericardially and has less chance of pump failure with a remarkable 79% 2 year survival rate in long term MOMENTUM-3 study. Heartmate III got FDA approval for DT (Destination Therapy) in October 2018. Implantable miniature pumps may be able to deliver long-term partial circulatory support to allow recovery of ventricular function after an acute insult or provide durable assistance.

Every therapy designed to increase survival must be judged in part not only by those events or complications that diminish survival but also by those that help define the quality of life anticipated. For device therapy, the critical adverse events include device malfunction or failure, neurologic events, and infections. From the early analyses, about 10% of patients developed significant device malfunction within the first 6 months. The most frequent causes implicated in deaths were cardiovascular failure, central nervous system events, infection, liver failure, and respiratory failure. It is hoped that the precision and consensus underlying these definitions will level the playing field and accelerate the reduction of complications for current and future device development.¹³

Circulatory Assist/ Support Devices and Bangladesh:

The circulatory assist/ support devices have little application in Bangladesh so far. NICVD had a Datascope IABP machine since the 1990s. The first reported use of this device was performed in early 1997. French surgeon Dr Akter Ali Rama visited Bangladesh and demonstrated the first cases of Off Pump CABG here. One of the patients had



Fig 3: HeartMate III

postoperative low output syndrome and IABP was used. IABP became available in most major cardiac surgery centers these days. The first ECMO in Bangladesh was procured in 2013. ECMO is now available in four different centers, three in Dhaka and one in Sylhet. In addition, a CentriMag device is now also ready for use in a Dhaka hospital. The first long term mechanical circulatory support device (durable LVAD) of Bangladesh was implanted in United Hospital Dhaka on the 2nd of March 2022. A Heartmate III device was successfully implanted in a 42-year-old Bangladeshi patient. The patient was discharged home in good health on 24th March 2022.

Conclusion:

The rapid progress of MCS technology in recent years has extended survival and improved quality of life for selective patients with advanced heart failure. Indeed, mechanical support has become central to the evidence based care of chronic, refractory heart failure. For the first time, there is a meaningful option for lifelong support even in patients who are not candidates for transplantation. Novel pump design has improved clinical outcomes, altered the profile of MCS candidates, and changed the structure of advanced heart disease programs. With these advances have come new challenges and opportunities.

Conflict of Interest - None.

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