Mechanical Circulatory Support

Principles and Applications

David L. Joyce
Lyle D. Joyce

OXFORD

MECHANICAL CIRCULATORY SUPPORT

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PRINCIPLES AND APPLICATIONS

SECOND EDITION

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Contents

Preface

It has now been a little over eight years since publishing the first edition of *Mechanical Circulatory Support: Principles and Applications*. The world has changed a great deal in that time, but perhaps nowhere has this been more pronounced than in the field of mechanical circulatory support. Durable LVAD outcomes now rival those of cardiac transplantation, short-term devices are changing the landscape in cardiogenic shock, and perioperative decision-making has now benefited from over three decades of experience. It has been an exciting time to be a part of this journey, and we have been truly blessed to join with some of the most well-established thought leaders in the field to develop a reference that we hope will synthesize this wisdom in a way that is accessible to all who participate in the care of patients with advanced heart failure.

The second edition could never have taken place without substantial contributions from a very large team of supporters. We would like to specifically thank Craig Panner, William Allen, and the rest of the team at Oxford University Press for their tremendous partnership throughout this effort.

This project was officially launched in May 2017 as part of a much larger vision on the part of Drs. Paul Pearson and Doug Evans when they placed their bets for the heart transplant and MCS program at the Medical College of Wisconsin on a father/son team from the Mayo Clinic. We remain immensely grateful to them for inviting us to join in this adventure, supporting us on projects like this, and dreaming with us on what comes next. In the words of Lin-Manuel Miranda in *Hamilton*, "There's a million things [we] haven't done . . . but just you wait!"

Editing a textbook of this magnitude could never be accomplished by two busy cardiac surgeons without the commitment of very talented colleagues, especially Chris Quandt, Jodi Burgess, and Tom Lang, who not only kept us on schedule but demanded excellence in the final product. We also appreciate the tremendous effort put forth by each of the authors.

Of course, those who pay a huge toll are our families, who have spared us the time to complete this task. We are most grateful to Tina (Mom/wife), Joyce (wife/daughter-in-law), and Lyle and Lucia (children/grandchildren).

Our desire is that you will find this book useful at whatever level of heart failure patient care you are providing and that it will serve as a handbook at the bedside as well as a thought provoker when studying some of the most complex physiological challenges that this exciting frontier provides.

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MECHANICAL CIRCULATORY SUPPORT

1 A Historical Perspective on the Development of Mechanical Circulatory Support Devices

O. H. FRAZIER

Introduction

The cardiac surgical field has progressed from a belief that the heart was an untouchable organ to the reality that it is an organ that can be surgically repaired, supported, and even replaced with great success. The invention and development of mechanical circulatory support devices has led the way in this endeavor. The first attempts were to replicate the pulsatile human heart. The first permanent implant of the Jarvik 7 total artificial heart (TAH) implant by Devries and Joyce in 1982, under a clinical trial directed by the Food and Drug Administration (FDA), opened the door for the investigation of not only TAHs but also multiple left ventricular assist devices (LVAD). The Jarvik 7-70 TAH first implanted in a woman by Joyce in 1985 is the same pump still used today, giving it the longest track record of any manufactured implantable support device. The field has turned to continuous-flow devices (axial and centrifugal) for the most part because of durability issues, but the long-term impact that this change in physiology has on the body remains only partially understood.

The History

The evolution and subsequent development of the field of mechanical cardiac assist and replacement for the failing heart has been indelibly linked to similar advances in the evolution of open heart surgery and, subsequently, cardiac transplantation. The first successful use of the heart-lung machine by Dr. John Gibbon for open cardiac repair in 1953 was initially viewed as being of limited value, as it was successful in only one case of a simple secundum atrial-septal defect (ASD) repair. John Lewis at the University of Minnesota had already performed the first successful case of intracardiac surgery on September 2, 1952.[1] He closed a secundum ASD in a 5-year-old girl utilizing inflow stasis and total body hypothermia. Dr. Gibbon, in fact, did not want to report his initial experience with the heart-lung machine, as he thought the heart itself was irreversibly injured and the idea of surgical correction of a "sick heart" without hope of meaningful recovery, in spite of successful anatomic correction, would limit the application of this technology. Dr. Walter Lillehei, with Lewis at the University of Minnesota, had encouraged Dr. Gibbon to report his case, which he ultimately did.[2] As a result, this important historic event was first recorded only locally in a regional publication, the *Minnesota State Medical Journal*.

The first open heart surgery, however, was actually performed by Dr. Clarence Dennis et al. in April 1951, again at the University of Minnesota, for what was thought to be a secundum ASD, but in fact proved to be a more complicated A-V canal anomaly, and the patient died intraoperatively.[3] A second case less than one month later died of a massive intraoperative air embolism. Contributing to the mortality of both patients was the large amount of return of intracardiac blood flow in the open heart. This obscured the pathology in both cases and was a primary factor in the early mortality of these two patients.

Dr. Lillehei was an important early contributor to the success of open-heart surgery; in fact, he was considered the most important by all of the pioneers interviewed by this author. His studies of the survival of anesthetized dogs with only azygos blood flow indicated that the normal resting blood flow in anesthetized humans was not required for survival in open heart surgery.[4] This seminal observation

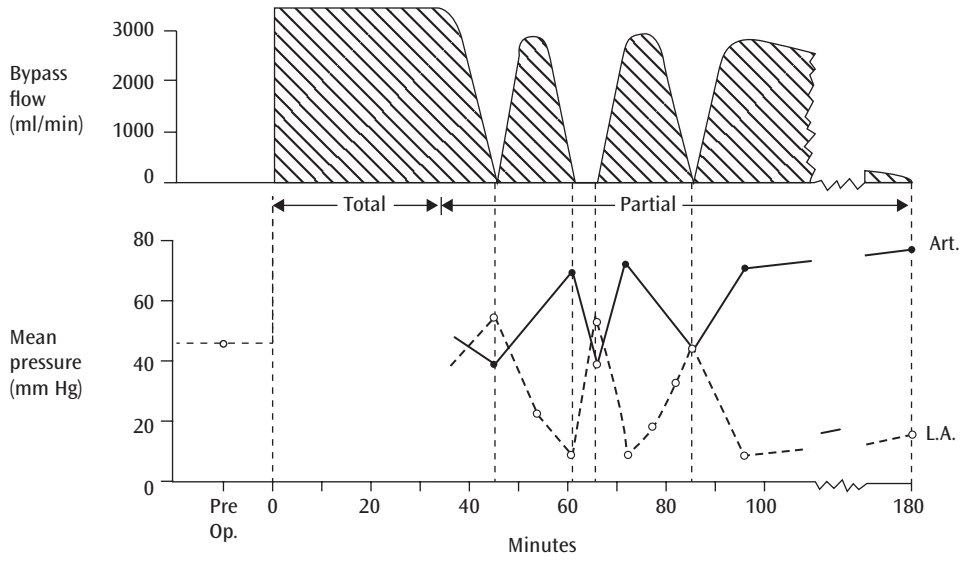

Figure 1.1. *Effect of resting the failing heart on cardiopulmonary bypass when unable to wean after initial operation.* Reprinted from DeBakey ME, Left ventricular bypass pump for cardiac assistance, *American Journal of Cardiology* 1971;27:3–11, with permission from Elsevier.

was fundamental for the subsequent success of open heart surgery because in patients perfused at baseline physiologic flows, the blood return to the open heart on the heart-lung machine (as in Dennis's experience) was too high to allow adequate visualization and successful correction of an intracardiac defect. By utilizing the azygos low flow concept, the actual successful repair of intracardiac (ventricular) defects was initiated by Dr. Lillehei by applying minimal support with cross circulation.[3] The evolution and subsequent successful open heart surgery by the use of the cardiopulmonary bypass machine by Dr. Denton Cooley in Houston, and Dr. Lillehei and Dr. John Kirklin in Minnesota, led to a meaningful application and expansion of cardiac surgery.[5,6,7]

In the early 1960s Dr. Michael DeBakey also became active in the field of open-heart surgery. He was particularly intrigued with the possibility of longer-term support of patients who could not be weaned from the heart-lung machine. While he was at Tulane, Dr. DeBakey had worked with Dr. George Burch, who had applied complete bed rest with subsequent heart rest as a therapy for chronic heart failure. Dr. DeBakey began investigating a similar approach of resting, with a true LVAD, the heart of patients who could not be weaned from the heart-lung machine. Dr. Domingo Liotta, who had worked on the TAH with both Dr. William Kolff and Dr. Tetsuzo Akutsu, was recruited in 1961 by Baylor College of Medicine to work with Dr. DeBakey in the Baylor Research Labs. The efforts of Dr. Liotta were focused on the development of both a device for total heart replacement and a device for left ventricular assistance following failure to wean from cardiopulmonary bypass. This author was introduced to the field as a student by Dr. Domingo Liotta and Dr. DeBakey and made it his professional research effort from this time (1963). Dr. DeBakey observed clinically that a patient who could not be weaned from the heart-lung machine could occasionally recover enough to be weaned by simply resting the heart longer, with longer support on cardiopulmonary bypass[8] (Figure 1.1). This case was the stimulant to pursue longer-lasting support with a true LVAD.

The rest-and-recovery approach to this problem with an LVAD soon became Dr. DeBakey's main goal. He utilized this in the first successful case of bridge-to-recover utilizing an LVAD, performed in September 1966 (Figure 1.2).

Dr. DeBakey's role was pivotal in the effort to develop mechanical circulatory cardiac devices, not only in his initial clinical application of devices, but more importantly, in his efforts to achieve National Institutes of Health (NIH) funding for this research in this difficult, demanding, and time-consuming field. This was achieved at the urging of Dr. DeBakey and the support of President Lyndon B. Johnson and philanthropist Mary Lasker in the early 1960s (Figure 1.3).

At that time, the National Heart and Lung Institute, now known as the National Heart, Lung, and Blood Institute, began dedicating significant research funds, which were essential for the further advancement of this field.

The cardiac surgery field was further impacted at this time with the initiation of cardiac transplantation by Christiaan Barnard in December 1967.[9] Although Dr. Christian Barnard, following Dr. Norm Shumway and Dr. Richard Lower's pioneering research, had initiated cardiac transplantation, a significant number of these early transplants were in fact performed in Houston by Dr. Cooley. Dr. Liotta began visiting

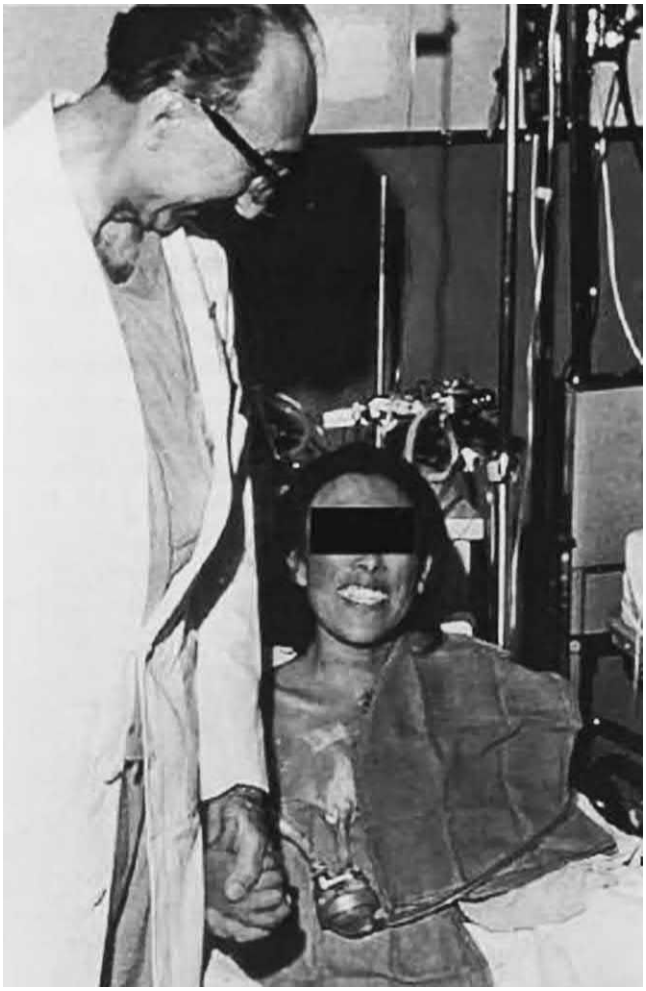

Figure 1.2. *Dr. DeBakey's first patient, who was successfully bridged to recovery with a left ventricular assist device.* Reprinted from DeBakey ME, Left ventricular bypass pump for cardiac assistance, *American Journal of Cardiology* 1971;27:3–11, with permission from Elsevier.

Figure 1.3. *Dr. DeBakey and President Lyndon Johnson after signing the bill to create the US Artificial Heart Program in 1964.*
Photo downloaded from http://resource.nlm.nih.gov/101676363.

Dr. Cooley in December 1968 to encourage him to consider use of the total heart replacement device he had fabricated as a bridge to transplant (BTT), and perhaps saving a patient facing imminent death who could not be weaned from the heart-lung machine. This was in fact undertaken by Dr. Cooley in April 1969.[10] The Liotta total heart replacement gave short-term support to a patient suffering certain, imminent death from heart failure after unsuccessful resection of a left ventricular aneurysm. Dr. Cooley implanted this pump in only 34 minutes. The patient recovered from this surgery, and his circulation was successfully maintained by the Liotta heart. In retrospect, however, he was grossly over-immune suppressed and subsequently prematurely transplanted (despite a white blood count of <2,000 at the time of transplant). He died quickly of subsequent overwhelming sepsis. The first implantation of an artificial heart (better defined as a biventricular replacement by pneumatically activated dual cardiac support devices) did show success, however, in supporting this patient. The field of transplantation was plagued with poor results during this initial experience, so that in the United States programs in 1972 were restricted to a research program at Stanford with Dr. Shumway and a similar program at the Medical College of Virginia with Dr. Lower.

The initial failure of the use of the application of cardiac transplantation was an important impetus to further research in mechanical support and replacement of the heart. In 1972 a meeting was held with the experts in the field of heart failure at the NIH, and this panel initiated research development of a long-term implantable LVAD. This was not for a BTT (as transplants were not routinely performed); rather, the device to be developed was the final goal of the therapy. This goal was further supported with generous research funding. Successful operation for 2 years was the arbitrary endpoint of the program. The application of this support led to the development of the implantable pulsatile LVAD. Two devices, the Novacor and the TCI HeartMate pumps, were both introduced clinically as a bridge-to-transplant device in the mid-1980s. This became feasible with the renewal of cardiac transplantation by the discovery of an improved immunosuppressant cyclosporine in 1982. Prior to the introduction of cyclosporine, three bridge-to-transplant operations had been performed, all at the Texas Heart Institute: one with an LVAD (as it was the only device available at that time) functioning as a total heart replacement[11] (in a patient suffering from a post-cardiotomy

Table 1.1 • Two-Stage Cardiac Replacement: Texas Heart Institute

Patient	Diagnosis	Date	Procedure	Duration
47-year-old man	CAD, LVA	4/4/1969	TAH	64 hours
		4/7/1969	OHTx	32 hours
21-year-old man	SBE, MR, AR, stone heart	2/9/1978	LVAD	5 days
		2/14/1978	OHTx	14 days
36-year-old man	CAD	7/23/1981	TAH	54 hours
		7/25/1981	OHTx	7 days

Abbreviations: AR, aortic regurgitation; CAD, coronary artery disease; LVA, left ventricular aneurysm; LVAD, left ventricular assist device; MR, mitral regurgitation; OHTx, orthotopic heart transplant; SBE, subacute bacterial endocarditis; TAH, total artificial heart

"stone heart"), the other two with total (biventricular) heart replacements. The patient with the LVAD acting as total support received a heart-kidney transplant after five days of successful support. This was the first such dual-organ transplant (Table 1.1).[11]

Although the pumps worked well in all cases, the patients all died of overwhelming sepsis post-transplant. This seemed to be a finite barrier of this device application (BTT) as long as the pan-immune suppressant azathioprine was the primary immune drug therapy. The development of cyclosporine, a more forgiving immunosuppressant which spared the non-specific immune system, was the key both to successful heart transplants and to patients who had a previous device implant. This drug allowed the successful application of transplantation even to patients who were markedly septic.[12] In particular, the successful transplantation of a young woman suffering from Streptococcal and Staph sepsis was the case that opened the possibility of the use of pulsatile LVADs as a BTT. Although the devices proved important as a life-saving device for patients facing imminent death from heart failure, their limited duration of 2 years of function or thereabouts (in most cases, due to fatigue of the flexing membranes) and the large size of the pulsatile implantable LVADs limited their practical application to that of a rescue device for larger patients that could subsequently be bridged to transplant. The REMATCH trial compared the pumps' use as destination (solo) therapy to a randomized medical cohort. The patients treated with the pumps had a statistically superior survival to the medical group, but the limited survival at 2 years of both groups trivialized the epidemiologic impact of the pulsatile pumps. With this in mind, and with recognition of the limitations, this author began solo the development of implantable continuous-flow pumps as potentially a smaller and more durable approach. The first continuous-flow pump to be used with any short-term success was the Biomedicus pump. This constrained vortex centrifugal flow pump was

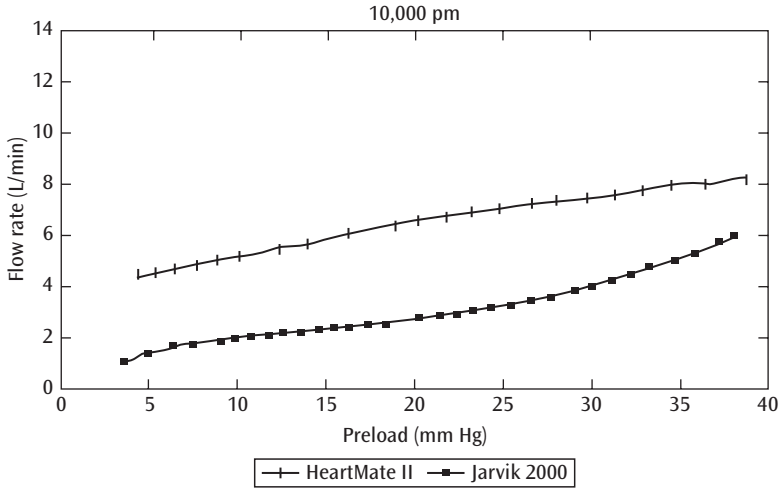

Figure 1.4. *Starling-like response of the HeartMate II and Jarvik 2000 to preload changes without making speed changes.* Reprinted by permission from Springer Nature, *Mechanical Circulatory Support: Principles and Applications*, Morgan JA, Civitello AB, Frazier OH, eds., 2018.

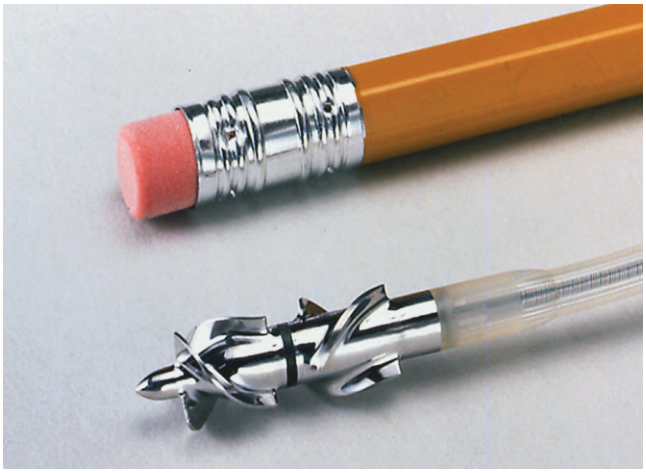

Figure 1.5. *The Nimbus Hemopump impeller.*
Reprinted by permission from Springer Nature, *Mechanical Circulatory Support: Principles and Applications*, Morgan JA, Civitello AB, Frazier OH, eds., 2018.

Figure 1.6. *First clinical patient saved by Hemopump. Dr. Bud Frazier (left); patient (center); Dr. Rich Wampler (right).*
Photo courtesy of Dr. O. H. Frazier. Reprinted by permission from Springer Nature, *Mechanical Circulatory Support: Principles and Applications*, Morgan JA, Civitello AB, Frazier OH, eds., 2018.

a valuable adjunct for short-term external support, both in extracorporeal membrane oxygenation (ECMO) and as temporary LVAD support as a bridge-to-recovery. Not only was the smaller size of the non-pulsatile pumps appealing, but the inherent Starling-like flow response of continuous-flow pumps to elevated inflow pressure would balance automatically the disparate flow between the right and left ventricles (due to bronchial flow) in a total heart replacement (Figure 1.4). This was an important challenge and a potential limitation to the totally implantable pulsatile flow artificial heart.

An additional virtue of a continuous-flow pump is that its smaller size would allow its use in smaller adult patients and even in children. The application of a centrifugal type continuous-flow pump as a right-sided support was also important. The bulky pulsatile devices were anatomically not satisfactory for even short-term use as right-sided support due to the presence of the liver. The first implanted right-sided pump was the Jarvik pump at the Texas Heart Institute in 2003.[13]

The problem with implantation of a continuous-flow pump, however, was challenging from both mechanical and physiologic aspects. The chief mechanical limitation of a continuous-flow pump was twofold: that the RPM required to produce a significant amount of flow with the implantable continuous-flow pump in the bloodstream would be so high that inevitable destruction of blood cells by the device would limit its application, even for short-term use. The other limitation seemed to be a complete barrier. It was an obvious problem in the early 1980s that the only implantable continuous-flow pump designs in use were those that involved axial flow. These devices would require a bearing, and a bearing, of course, requires lubrication, and the lubrication of a bearing in the blood flow path was not thought to be possible. There were numerous assumed physiologic limitations, particularly that of the baroreceptors and their adjustment to a decreased pulsatility. The concern was that this would result in physiologic feedback to decreased pulsatility and hypotension (i.e., vasoconstriction), and the sympathetic response would increase the likelihood of the complications of hypertension seen so commonly in the era prior to antihypertensive medications, particularly both ischemic vasospastic strokes and their possible conversion to hemorrhagic strokes, which were generally fatal. We also would face the barrier of the decreased pulsatility being perceived by the kidneys as renal artery obstruction and this causing an increase in renin output with resultant renal hypertension. With these barriers, both physiologic and mechanical, we nonetheless proceeded with research in the application of the continuous-flow pump as a mechanical support to the heart.

In 1986 we began working on both the short-term Hemopump, which was developed by Dr. Rich Wampler working for the Nimbus Corporation, while simultaneously working with Dr. Rob Jarvik on a continuous-flow pump that would, in fact, be a long-term implantable device. Our animal research was particularly encouraging with the Hemopump because we found that even with RPMs up to 27,000 with this small pump implanted in vivo as a temporary support, significant hemolysis was avoided (Figure 1.5). Long-term pump research with Dr. Jarvik proved more of a challenge. In fact, the early pumps with a non-lubricated bearing in the bloodstream did prove unsuccessful in the initial in vivo testing. In the first animal tested, the pump worked only about three days. However, Dr. Jarvik continued to work diligently on this bearing problem over the ensuing years, and by the early 1990s this technology showed the potential for long-term successful implantation.

The clinical introduction of the Hemopump in April 1988 was an important step in the development of this technology. The patient was dying of rejection following cardiac transplant. Although his cardiac function had deteriorated below what we would expect for survival, we were able to revive this patient with the insertion of a Hemopump. Reversal of the rejection was achieved by the use of the immune suppressant OKT 3 over a period of five days of Hemopump support. The pump was removed and the patient subsequently successfully discharged (Figure 1.6).

A multi-institutional study of the Hemopump's efficacy was then instituted. In this study, 41 study group patients were enrolled with excellent efficacy. However, as this was the first implantable continuous-flow pump to be presented to the FDA, and the entry criteria were a broad amalgam of heart failure patients from a variety of etiologies, the FDA understandably requested more data with more precise entry-group criteria. However, the financing of this study was from the capricious efforts of venture capitalists who then withdrew funding, and there was no way to complete the study. Shortly after it became obvious that we were not going to carry forward this technology, I contacted Helmuth Reul, who was a pioneer in the field of biomedical engineering. He had trained in Houston and was a long acquaintance. I made him aware of the virtue of this technology and he and colleagues, then working in Aachen, Germany, successfully turned this technology into a device that is now the most widely used temporary support pump in both Europe and the United States (the Impella pump). The Jarvik pump required solving other problems of commercialization before moving into clinical utilization. Dr. DeBakey had reviewed one of Dr. Jarvik's applications for an NIH grant and, although he turned it down, shortly after his review he introduced his own modification of an axial flow pump. This pump was the DeBakey or Micromed pump. Although it is no longer in use, it accelerated the introduction of the Jarvik pump. Implanted first at the Texas Heart Institute in April 2000, the Jarvik pump remains in clinical use. The work of Dr. Wampler in demonstrating the tolerance of the circulation to a high RPM pump and that of Dr. Jarvik in mastering the blood immersed-bearing problem are the two most important contributions in the initiation of the field of continuous-flow cardiac support devices, as their genius and diligence overcame what were perceived as finite barriers to the use of this technology.

The next pump to be introduced clinically was also an axial flow device. This pump was a modification of the Hemopump into a long-term implantable device. This author was the medical advisor for both the Jarvik and the Nimbus companies, as there was no widespread clinical interest in an implantable continuous-flow blood pump at that time. The engineer at Nimbus, John Moise, a very capable PhD in biomedical engineering from Cal Tech, was attempting to magnetically spin the rotating portion of the intended implantable long-term axial-flow modification of the Hemopump. I told him of our success with Jarvik's blood-washed bearings, but he was skeptical as he recited the conventional view that blood-washed non-lubricated bearings were not feasible. I told him that long-term animal survival with a blood-washed bearing had already been achieved in our lab. This was a virtue of the limited interest in this technology. With that in mind, work was then directed for the HeartMate II axial flow pump with blood-washed bearings. Following the company's dissolution in the mid-1990s, this technology underwent further modification by Thoratec and TCI (Thermocardio System, Inc.), the developer of the HeartMate I pump. This pump was only then designated as the HeartMate II. It was initially implanted in Europe with poor results. Initially sintered titanium was placed on the inner aspect of the pump, similar to its application in the pulsatile vented electric HeartMate. However, in the small clearance of the blood-flow pathway of the HeartMate II, this was an impediment to the function and predisposed this pump to clot formation. This reflects the minute details involved in the success of this life-saving technology. The sintered titanium was removed and the first clinical HeartMate II was implanted at the Texas Heart Institute in November 2003. An advantage of the HeartMate II is the restriction of inflow generated by the cannula not being incorporated with the pump. This ensures the presence of an adequate blood reservoir. This of course also resulted in more early complications, related particularly to hypertension. We also discovered that if the aortic valve was not opening, blood pressure could not be measured with the usual pressure cuff. We presented this to company and cardiology leaders in 2006 and as a result instituted a policy in all clinical centers of using the Doppler device to measure the blood pressure and in controlling the blood pressure to a much lower level. This resulted in a marked decrease in the incidence of strokes and allowed us to move forward with the rapid expansion of the use of this important technology.

The next important advance in this field was the development of a magnetically levitated centrifugal force continuous-flow pump. This work was initiated in 1994, working again with Dr. Wampler. The pump evolved into what is now known as the HeartWare device. The appeal of this approach would be the potential of only requiring a hydrodynamic bearing, or possibly not requiring any bearing at all. Although we were confident the axial flow pumps would be more durable than the pulsatile pumps, we did not envision the long-term durability that we would eventually achieve with these blood-washed bearings. There is always a potential for bearing wear and failure. Another very important advantage of the flat surface of the centrifugal continuous-flow pump was its potential for intrapericardial placement. This made it ideal for right ventricular support. The flat surface of the pump allowed easy placement on the anterior diaphragmatic surface of the right ventricle. The company that was originally formed was called

Kriton Medical, but for financial reasons it was reformed under the name HeartWare, Inc., in 2000. This pump was eventually brought to clinical fruition and was implanted in Australia and in Europe in 2005. We began implanting the HeartWare pump in the United States in 2008. Both the HeartMate II and the HeartWare pumps have been approved by the FDA as both bridge-to-transplant and destination therapy devices.

In 1994, after working with Victor Poirier and Kurt Dasse for more than 20 years, I suggested that they start working on a totally magnetically suspended pump with no bearings. They were leaders in the development of the pneumatic and vented electric HeartMate pumps. This work came to fruition about 20 years later with the successful FDA approval of the HeartMate 3 implantable pump as a long-term device and a short-term extracorporeal pump that was further developed by Kurt Dasse (the Centrimag pump). This evolved into an important short-term, external pump that is widely used today. Both pumps were subsequently developed and brought to market by Thoratec Corporation.

As of January 2019, roughly 60,000 pumps have been implanted: the HeartMate II has been implanted in over 26,000 patients, the HeartMate 3 in over 4,000, the HeartWare in over 17,000 patients, and the Jarvik in over 10,000. Hence, the use of these pumps is widespread and the pulsatile LVAD pumps have not been made since 2012. These pumps are in use in over 500 hospitals throughout the United States and in other countries, and the durability of these pumps (one of the main reasons for pursuing their use) has certainly been proven. The data on the HeartMate II alone has shown patients implanted for up to 14 years with one device. There have been 6 such patients with this pump alone for over 7 years, and over 110 patients have had one pump for over 10 years, and more than 300 over 8 years. We have solved the dilemma of the 2-year durability limitation that the pulsatile pumps demonstrated. In 2016, the number of continuous-flow pumps implanted was twice that of heart transplants.

However, these pumps have numerous problems that may be related to this abnormal physiology that we have introduced. It must be recalled that the technologies (valves, pacemakers, circulation, etc.) that we have introduced surgically in cardiovascular disease have in general mimicked the physiology of the natural heart and circulation. Even the pulsatile pumps we developed worked to mimic the functioning left ventricle, pumping one-third systole and two-thirds diastole. The problems that we have seen with the continuous-flow pump may be tied to the role of this altered physiology. This remains to be properly investigated. We have permanently altered diastolic flow from passive to active through the cardiac cycle. This could affect some of the complications we see with the technology. Certainly, there was a relationship to the strokes and the elevated blood pressure, as well as the difficulty with obtaining proper blood pressure levels by the conventional method. This still has not been extensively investigated by cardiovascular physiologists. We must try to see if even more precise data can be related to the pressure and its subsequent complications that we see. The problems that we have seen with the continuous-flow pumps, such as gastrointestinal (GI) bleeding and hemorrhagic strokes, in particular, have not been approached in a disciplined physiologic manner. The proper pressure is still in question, particularly in nonpulsatile flow (the aortic valve not opening).

In 1963 Drs. DeBakey and Liotta began working to develop an artificial heart. In 1965 Dr. DeBakey stated that by 1980, there would be "a hundred thousand Americans with a functional artificial heart." Likewise, NIH studies from the late 1960s predicted that a clinically practical artificial heart would be in widespread use by the mid-1980s. But the problems associated with developing such a device proved to be far more formidable than was commonly assumed, based on the perception at the time that an artificial heart could be a simple pump. The continuous-flow pumps now in widespread use as LVADs also may offer the best answer to total heart replacement. Many patients still would benefit from TAH technology. In the 1970s, we developed a plutonium-powered internal battery that could power a 50-watt pump for more than 82 years. Obviously, this was not pursued because we did not have a pump that would last more than 2 years. These continuous-flow pumps, however, have not yet been pumped to mechanical failure, and their long durability evidences their potential as meaningful long-term pumps.

In 2005 at the Texas Heart Institute, we replaced the ventricles in an experimental animal with two continuous-flow pumps. We repeated these experiments numerous times and found that animals with continuous-flow pumps performed well, grew normally, and had a normal activity response on the treadmill; many of them survived long term (para 90 days). We began working in 2012 with an investigator in Australia, Daniel Timms, who had devised a continuous-flow TAH. This pump is small but can produce up to 20 L of flow if needed. It has only one moving part, which is magnetically levitated. It perfuses both the pulmonary and systemic circulation simultaneously. We have demonstrated the feasibility of this pump in experimental animals and have even showed a Starling response, much like the normal heart, without changing the pump speed, when calves implanted with this pump are on the treadmill. This technology offers great promise for the future and for the meaningful prevention of premature death from the loss of natural heart function.

Finally, the concept of continuous flow stems from short-term use of low flows on the early patients who could not be weaned from the heart-lung machine. The first pulsatile devices introduced for this support in the 1980s were, in fact, left ventricular replacement devices. With both the TCI pump and the Novacor device in the normal operating

mode, the aortic valve never opened. The non-pulsatile device, however, is best suited as a true assist device; that is, the lowest flow possible to allow normalization of function to the native heart should be sought. The entire function of the left ventricle can be successfully achieved by these pumps, but this should only be used if clinically necessary. Minimization of complications can be optimized by preservation of pulsatility.

The present movement is clearly in the direction of continuous flow, and thousands of lives are being successfully prolonged. However, it must be reiterated that this represents a unique physiology never before encountered in mammalian species. We have patients doing well who have not had a pulse in more than 11 years and yet are totally asymptomatic. We must, however, study and address the complications and the role played by the altered physiology seen with the use of this technology, in both its short-term and long-term application, to optimally benefit the heart failure patient.

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2 Indications for Mechanical Circulatory Support

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Indications for Mechanical Circulatory Support (MCS) Therapy

Identifying and selecting optimal patients is key for success with MCS. Understanding the indications can help.[1,2,3] But patient selection goes well beyond a list of indications. It encompasses multiple factors that must be carefully balanced.

The key elements around selecting patients can be summarized as the following:

1. **Survival:** Will the patient's survival be better with or without MCS? What tools are available to help us estimate his or her odds of survival?
2. **Quality of Life (QOL) and Risks for Complications:** Will the patient's life be better from MCS? What is the likelihood of a good outcome vs. a life-limiting complication?
3. **Timing:** What is the appropriate timing? Should MCS be implanted early? What are the risks in delaying implant?
4. **Shared Decision-Making:** How do we optimally engage patients in the decision-making process?

Each of these elements is very complex. Some data are available but much of it is retrospective and observational. Ultimately, teams are tasked with using the data plus a large degree of clinical expertise ("expert opinion") to make these complicated decisions. This chapter will lay out the principles upon which both referring and implanting clinicians can build for mature decision-making.

Referral for Evaluation for MCS

A robust list of indications includes features that could suggest an adverse prognosis. These are helpful to decide which patients should be referred (and when) for evaluation. These are summarized in Table 2.1. Patients with one or more of these clinical features are at risk for adverse outcomes and should be considered for MCS.

A practical guide to referral is as follows:

1. *Persistent symptoms*: Either the patient or the physicians are not happy with how the patient is doing based on the patient's symptoms or inability to tolerate disease-modifying heart-failure treatments.
2. *An adverse trajectory*: Is this a patient who is improving, stable, or likely to worsen?[2] MCS and goals of care should be explored for those with an adverse trajectory.
3. *High-risk clinical features*: Does the patient have one or more clinical features that have demonstrated a risk for decline and adverse outcome (as in Table 2.1)?

Standard Indications for MCS

Traditionally MCS has been divided into categories:[3]

- *Bridge to Transplant (BTT)* = Patients being implanted to be able to get to a heart transplant.
- *Destination Therapy (DT)* = Patients who do not meet criteria for heart transplant but could have good survival with MCS. The goal is to improve longevity and quality of life.
- *Bridge to Candidacy (BTC)* = Patients for whom the MCS is implanted who do not currently meet BTT criteria. These patients start as DT, but with the hope that they could cross over to the BTT category.

These divisions are somewhat artificial. Patients in the Momentum 3 Trial were not enrolled based on these