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PHYSIOLOGIC EFFECTS OF CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICES

Aaron H. Healy, MD^a, Stephen H. McKellar, MD, MSc^a, Stavros G. Drakos, MD, PhD^b, Antigoni Koliopoulou, MD^a, Josef Stehlik, MD, MPH^b, and Craig H. Selzman, MD^a

Aaron H. Healy: aaron.healy@hsc.utah.edu; Stephen H. McKellar: stephen.mckellar@hsc.utah.edu; Stavros G. Drakos: stavros.drakos@hsc.utah.edu; Antigoni Koliopoulou: antigone.koliopoulou@hsc.utah.edu; Josef Stehlik: josef.stehlik@hsc.utah.edu

^aDepartment of Surgery, University of Utah, 30 North 1900 East, Salt Lake City, Utah, United States of America

^bDepartment of Medicine, University of Utah, 30 North 1900 East, Salt Lake City, Utah, United States of America

Abstract

Background—Within the past ten years, continuous-flow Left Ventricular Assist Devices (LVADS) have replaced pulsatile-flow LVADs as the standard of care for both destination therapy and bridging patients to heart transplantation. Despite the rapid clinical adoption of continuous-flow LVADs, an understanding of the effects of continuous-flow physiology, as opposed to more natural pulsatile-flow physiology, is still evolving.

Materials and Methods—A thorough review of the relevant scientific literature regarding the physiologic and clinical effects of continuous-flow physiology was performed. These effects were analyzed on an organ system basis and include an evaluation of the cardiovascular, respiratory, hematologic, gastrointestinal, renal, hepatic, neurologic, immunologic, and endocrine systems.

Results—Continuous-flow physiology is, generally speaking, well tolerated over the long term. Several changes are manifest at the organ system level, however. While many of these changes are without appreciable clinical significance, other changes, such as an increased rate of gastrointestinal bleeding, appear to be associated with continuous-flow physiology.

Corresponding Author: Craig H Selzman, MD, Division of Cardiothoracic Surgery, University of Utah, 30 N 1900 E, SOM 3C127, Salt Lake City, UT 84132, Ph: +1 801 581 5311, Fax: +1 801 585 3936, ; Email: craig.selzman@hsc.utah.edu

Author Contributions:

Healy: conception and study design, acquisition and interpretation of data, drafting and revising of article, final approval

McKellar: conception and study design, final approval

Drakos: conception and study design, final approval

Koliopoulou: revising of article, final approval

Stehlik: revising of article, final approval

Selzman: conception and study design, interpretation of data, revising of article, final approval

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Conclusions—Continuous-flow LVADs confer a significant advantage over their pulsatile-flow counterparts with regard to size and durability. From a physiologic standpoint, continuous-flow physiology has limited clinical effects at the organ system level. Though improved over previous generations, challenges with this technology remain. Approaching these problems with a combination of clinical and engineering solutions may be needed to achieve continued progression in the field of durable mechanical circulatory support.

Keywords

Cardiac surgery; Heart failure; Left ventricular assist device; Mechanical circulatory support; Physiology

1. Introduction

Heart failure affects 5.7 million Americans and is responsible for more than one million hospital admissions and 58,000 deaths annually [1]. As a means of treating heart failure, efforts to replicate and perfect artificial human circulation have been underway for several decades. The first successful use of mechanical circulation was by John Gibbon in 1954 when he used a heart-lung machine to repair an atrial septal defect [2]. Mechanical circulatory support evolved over the next 30 years to include left ventricular assist devices (LVADs) and permanently implantable artificial hearts [3,4]. In subsequent years, LVADs have advanced to become the predominant form of long-term mechanical circulatory support in use today [5].

The first several iterations of LVADs were volume displacement pumps. These devices were the workhorses of the field for many years and reached their clinical peak when they were approved for use in patients who were ineligible for heart transplantation, also known as destination therapy. The landmark REMATCH trial, published in 2001, demonstrated a profound survival benefit at one (52% vs. 25%) and two years (23% vs. 8%) after device implant compared to patients receiving optimal medical management [6].

Despite the dramatically improved survival offered by the use of these pulsatile-flow devices, there were several disadvantages associated with their use. First, the use of various bearings and valves employed in pulsatile designs were associated with limited durability, requiring many patients to undergo LVAD replacement surgery [7–9]. Second, pulsatile LVADs employed the use of a volume displacement chamber, resulting in a relatively large device. In turn, this required both a patient with a large body habitus and extensive dissection to accommodate implantation [10,11]. Third, owing to the mechanism of the volume displacement chamber, these pumps were often noisy.

In large part due to the limitations of pulsatile-flow designs, the clinical use of LVADs with continuous-flow mechanisms has been widely adopted over the last decade (Figure 1). Research into the use of continuous-flow designs, however, has been underway for more than fifty years. The first report on the development of a continuous flow device occurred in 1960 where it was described as “an ideal heart pump [12].” This claim has since been questioned, in part, because of the lack of pulsatile flow. Despite vastly improved pump designs and ever-increasing human experience, the controversy over the efficacy of

continuous flow devices has remained. At one level, the rapid adoption of continuous flow pumps in the last 10 years makes sense. For anyone who places these devices, the ease of insertion and simplicity of patient management is greatly welcomed. Overlooked in this enthusiasm, however, is deference for the pulsatile circulatory system honed by nature. After a decade of experience with continuous-flow devices, we can conclude that continuous-flow circulation is generally safe and that challenging a human physiology designed for pulsatile flow with a continuous-flow LVAD is appropriate. Herein, we seek to summarize the evidence regarding continuous flow pumps at the level of each organ system to determine if Saxton was correct in his description of “an ideal heart pump.” To accomplish this, we thoroughly reviewed the available literature comparing pulsatile- and continuous-flow LVADs on an organ system basis. The results of these searches are summarized in the following sections.

2.1 Cardiovascular System

Unloading of the left ventricle and reestablishing normal cardiac output are primary reasons for implantation of an LVAD. While pressure unloading has been shown to be similar when comparing pulsatile- and continuous-flow LVADS, significantly greater volume unloading has been observed in pulsatile-flow devices, whether measured by either device flow rates or left ventricular end diastolic dimension (LVEDD) [13,14]. There is some conflicting evidence in this area, however, as other studies that show better unloading with pulsatile devices using a decrease in LVEDD on echocardiography could not confirm this finding with right ventricular catheterization [15]. Still other analyses showed no difference in pressure and volume unloading when comparing continuous- and pulsatile-flow LVADs [16]. A possible explanation for this discrepancy is the use of different continuous flow devices in the studies. Either way, left ventricular unloading using continuous-flow devices is sufficient enough to be associated with aortic valve commissural fusion of at least a mild degree in 48–89% of patients [17,18].

Examining the effect of continuous-flow LVADs on left ventricular unloading naturally leads to questions regarding how this type of flow affects myocardial recovery, particularly when compared to pulsatile-flow LVADs. Pulsatile flow devices have been associated with improved ejection fraction, with one study showing an improvement in average ejection fraction from 21% to 33%, while the ejection fraction of patients supported with continuous-flow devices remained static at 17% [19]. Similarly, a single-center, retrospective review evaluating factors associated with weaning from LVAD support showed a nearly three-fold increased probability of weaning in patients supported with pulsatile-flow LVADs [20]. The reasons for the observed differences in progression to myocardial recovery in patients supported with LVADs are unclear. Hypotheses include decreased coronary blood flow and myocardial atrophy [21,22], though the latter theory has largely been debunked [23,24].

Right ventricular dysfunction has historically occurred in approximately 40% of patients with LVADs and is a risk factor for increased mortality [25,26]. That being the case, there is some evidence to suggest that patients with continuous-flow LVADs may experience less right heart failure than patients with pulsatile-flow devices. A study of the HeartMate II LVAD (Thoratec Corporation, Pleasanton, CA) bridge to transplantation clinical trial showed

only a 20% incidence of right ventricular failure among the study population, defined as insertion of a right ventricular assist device (6%), 14 or more days of inotropic support after implantation (7%), or inotropic support starting more than 14 days after implantation (7%) [27]. The randomized trial comparing continuous-flow and pulsatile flow pumps for destination therapy found that right heart failure managed with the extended use of inotropes was less in patients with continuous-flow devices (27% vs. 20%, $p < 0.001$). However, there was no difference in the incidence of right heart failure that was managed with a right ventricular assist device [28]. For patients with right ventricular (RV) dysfunction prior to continuous-flow LVAD implantation, it has been shown that RV function does not worsen after implantation of the LVAD and may actually improve [29,30]. Another study, which was a retrospective analysis of RV function and tricuspid regurgitation after continuous-flow LVAD implantation, found improvement in both parameters (Table 1) [31]. These improvements likely occurred as a result of decompression of the pulmonary vascular bed with a resultant drop in pulmonary vascular resistance.

Further, in patients with intractable pulmonary hypertension, both pulsatile- and continuous-flow LVADs have been shown to alleviate pulmonary hypertension to a level that is compatible with heart transplant eligibility [31–34]. A retrospective study comparing the two flow types found that continuous-flow devices were associated with a greater decrease in pulmonary artery systolic pressure than pulsatile-flow devices [35]. No differences were found between the two groups with regard to right ventricular ejection fraction, grade of tricuspid insufficiency, or tricuspid annular plane systolic excursion.

The long-term effects of continuous-flow physiology on vessel morphology are unknown. Studies in a goat model showed diminished arterial constriction and aortic wall thickness in animals supported with continuous-flow physiology [36,37]. A comparison of aortic wall tissue at the time of insertion of a continuous-flow LVAD and at the time of transplantation/autopsy in humans showed increased foci of medial degeneration, smooth muscle cell depletion, elastic fiber fragmentation, medial fibrosis and atherosclerotic changes, but no difference in mean medial thickness [38]. At the time of transplantation, hearts supported with a continuous-flow LVAD had a reduction in the volume density of elastin and mucinous ground-substance, along with an increase in collagen, compared to hearts that were not supported with an LVAD prior to transplant [39]. These changes do not appear to be manifest at the end-organ level, however, as evidenced by a lack of difference in the vasculature with regard to perivascular infiltrates, intravascular infiltrates, wall thickness, thrombosis, endothelial cell swelling, vessel wall necrosis, or perivascular fibrosis [40]. However, larger vessels, such as the brachial artery, have been shown to have reduced flow-mediated vasodilation in patients with continuous flow LVADs compared to control patients without LVADs [41]. These differences could also be observed with regard to changes in vessel diameter (Figure 2). These different findings between the vasculature at the arterial and end organ levels may be due to the possibility that even in pulsatile-flow physiology, perfusion at the end-organ level has been sufficiently dampened by the arterioles to be essentially continuous. Therefore, the end-organ vasculature may not be experiencing any significant differences in flow type when a continuous-flow pump is placed in a patient accustomed to pulsatile physiology. Conversely, a recent study using a chronic ischemic heart failure bovine model found that end organ perfusion was improved when pulsatility

was integrated into a continuous-flow LVAD by using variable speeds compared to the use of a constant speed [42]. In summary, what clinical significance, if any, changes to the arterial vasculature signify remains to be seen.

2.2 Respiratory System

The effect of non-pulsatile flow on pulmonary circulation has been clinically studied in the setting of Fontan procedures. Fontan physiology, a pulseless pulmonary circulation, is well tolerated. Studies of continuous-flow physiology in newborn lambs shows that non-pulsatile circulation is associated with a smaller decrease in pulmonary vascular resistance as flow rates are increased compared to pulsatile flow physiology [43]. Pulsatility loss in a porcine model is associated with pulmonary hypertension and increased pulmonary resistance [44]. Hemodynamic changes in pulmonary and systemic circulation during non-pulsatile flow don't seem to affect gas exchange or intrapulmonary shunt ratio [45].

From a purely clinical standpoint, the type of flow has little to no clinical effect on the rate of respiratory complications. A single center retrospective review of 182 patients found that there was no difference in the rate of prolonged intubation after LVAD placement (defined as 6 or more days of ventilator support), reintubation, or tracheostomy in patients with continuous flow LVADs compared to those with pulsatile flow LVADs [46]. Likewise, no difference was observed in the rate of respiratory failure when devices with the two flow types were compared in a randomized, controlled trial of destination therapy LVAD patients [28].

2.3 Hematologic System

Given the devastating consequences of bleeding and thromboembolism (TE), the hematologic effects of LVAD support are a major concern. Continuous-flow VADs require anticoagulation and are prone to thrombus formation in the pump housing chamber. Rate of TE events vary among different technologies. Pulsatile VADs with mechanical valves required high levels of anticoagulation while the HeartMate XVE (Thoratec Corporation, Pleasanton, CA) needed only anti-platelet therapy. Data from the HeartMate II bridge to transplant trial reported event/rates per patient year as follows: bleeding requiring surgery = 0.78, bleeding requiring 2 units of packed red blood cells = 2.09, ischemic stroke = 0.13, hemorrhagic stroke = 0.05, transient ischemic attack = 0.10, peripheral nonneurologic thromboembolism = 0.15, and device thrombosis = 0.05 [47]. Over the next few years following this study, clinicians perceived an increase in the rate of pump thrombosis of the HeartMate II device, prompting a formal analysis of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS). This showed that freedom from device exchange or death due to thrombosis at 6 months after device implant had decreased from 99% in 2009 to 94% in 2012 [48]. Overall survival in patients with the HeartMate II was 80% at one year after device placement.

Owing to the mechanism of a rapidly spinning axial/centrifugal rotor in continuous-flow devices, hemolysis is found in a greater degree than in patients with pulsatile-flow LVADs. Fibrinolytic markers such as D-dimer, fibrinogen, plasma-free hemoglobin, and red blood cell sedimentation rate are generally highest just after implant of continuous-flow devices

and then undergo a relative decrease with ongoing VAD support [49]. Despite laboratory evidence of increased hemolysis with the use of continuous-flow LVADs, most patients are not clinically affected. An analysis of the INTERMACS registry using 4,850 patients found that freedom from clinically significant hemolysis, defined as a plasma-free hemoglobin greater than 40 mg/dL in setting of clinical evidence of hemolysis occurring more than 72 hours after device implantation, was 91% at two years. For those patients who did experience hemolysis, it was associated with higher rates of device malfunction, device exchange, and mortality [50]. Further, lactate dehydrogenase and plasma-free hemoglobin levels have been shown to be significantly elevated in patients who were being admitted for LVAD thrombosis [51].

2.4 Gastrointestinal System

The most common adverse event associated with continuous-flow LVAD support is bleeding [52]. Gastrointestinal bleeds, in particular, occur in 15–30% of continuous-flow LVAD patients at a rate of 0.45 events/patient-year [53,54] and are a major driver of readmission and thromboembolic events [55–58]. The reasons for increased rates of gastrointestinal bleeding are likely multifactorial and include chronic anticoagulation, mucosal ischemia, loss of von Willebrand factor activity, and an increased rate of angiodysplasia [59]. Acquired von Willebrand syndrome, due to proteolysis of von Willebrand factor secondary to sheer stress, has even been observed in short-term support using continuous-flow LVADs [60]. Interestingly, a higher pulsatility index – which is a measure of the degree of residual pulsatility present in patients with continuous flow LVADs, has been shown to be associated with a lower rate of nonsurgical bleeding (Figure 3).

A study of post-implantation nutritional status comparing the HeartMate XVE and HeartMate II demonstrated that patients with the HeartMate II had higher albumin levels after 6 months of support [61]. It was suggested that this might be the result of early satiety due to the larger size of the HeartMate XVE and the pressure effect on the stomach and upper GI tract.

2.5 Renal System

Several groups have studied kidney function in continuous-flow LVAD patients. A comparison of pre- and post-implant levels of serum urea nitrogen and creatinine demonstrated that kidney function was either maintained or improved in patients awaiting transplantation [53,62]. In a cohort of continuous-flow LVAD patients supported for at least one year, creatinine and blood urea nitrogen levels initially declined, then gradually increased over the following year. The values at one year, however, remained significantly lower than their baseline values [63]. Other studies that directly compared pulsatile- and continuous-flow LVADs have used serum urea nitrogen, creatinine, creatinine clearance, and glomerular filtration rate as outcomes. They uniformly demonstrated that there was no difference in kidney function between the two groups [64–66]. Conversely, a randomized, controlled evaluation of continuous- and pulsatile-flow devices for use in destination therapy showed a significantly lower rate of post-implant renal failure in patients with continuous-flow devices [28]. Long-term data from the INTERMACS registry also describes an

approximately 50% reduction in the rate of renal dysfunction in patients with continuous-flow LVADs compared to pulsatile-flow LVADs [52].

2.6 Hepatic System

Studies of hepatic function in continuous flow LVAD patient populations have produced similar results to those of renal function. Using total bilirubin, serum glutamico-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), alanine aminotransferase (ALT), and aspartate aminotransferase (AST), it has been shown that hepatic function is improved or maintained over the duration of continuous-flow LVAD support [53,62]. Direct comparisons of liver perfusion using continuous- and pulsatile-flow LVADs have used albumin, total bilirubin, SGOT, SGPT, AST, and ALT as outcome measures but have not shown any difference between the two groups [64,66]. INTERMACS data describes the rate of hepatic dysfunction in continuous flow device patients as 0.60/100 patient-months compared to a rate of 1.32 events/100 patient-months in patients with pulsatile-flow devices [52]. In patients supported with a continuous-flow device for a year, total bilirubin declined continuously over the course of LVAD support [63]. In addition, synthetic function of the liver was observed to improve, as evidenced by a continuously increasing serum albumin level.

2.7 Neurologic System

Effects on the neurologic system can be divided into two categories, those that are the direct result of continuous-flow per se and those that are secondary effects due to having a continuous flow device. Regarding the former category, there are a few studies performed during the early clinical application of continuous-flow devices that do shed some light on the subject. Using markers of brain injury such as protein S-100B and neuron-specific enolase, it has been shown that there is no difference in continuous and pulsatile-flow LVADs in the first fourteen days of support [67]. Interestingly, while microembolic signals detected using transcranial Doppler were shown to be predictive of thromboembolic events in patients with pulsatile Novacor LVADs [68] there is no correlation between microembolic signals and thromboembolic events in patients with continuous-flow DeBakey LVADs [69]. It is not known whether these findings apply to the current widely used continuous flow LVADs.

A more recent study evaluated the effect of sympathetic activation during tilt-table testing among patients with continuous- and pulsatile-flow LVADs. Those patients with continuous-flow LVADs had marked increases in sympathetic activation, thought to be due to baroreceptor unloading. These authors speculated that chronic sympathetic activation may contribute to decreased end organ function over the long term [70]. Autoregulation of cerebral perfusion does not appear to depend on flow type, despite a noted reduction in pulsatility among patients with continuous-flow LVADs compared to patients with pulsatile-flow LVADs [71].

With regard to secondary effects of continuous-flow physiology, most clinical events are consequences of LVAD management – the balance between bleeding and thrombosis. That being the case, rates of neurologic dysfunction are lower over long-term follow-up in

continuous-flow LVAD patients than in pulsatile-flow patients according to INTERMACS data [52]. Prospective studies of neurologic outcomes in LVAD patients are sparse, though the HeartMate II Destination therapy trial found no difference in stroke rate when comparing continuous- and pulsatile-flow LVAD patients. There was also no difference between the two groups when strokes were subdivided into ischemic and hemorrhagic categories [28].

2.8 Immunologic System

Whereas LVADs are frequently used to bridge patients to transplantation, any effect that flow physiology may have on the immunologic system can have considerable relevance. To this end, a retrospective comparison of pulsatile- and continuous flow patients who were bridged to transplant evaluated post-transplant incidence of treated rejection and the mean number of rejection episodes per patient. No differences were observed by either measure [72]. Other studies have found different results. Our group has previously demonstrated that patients transplanted after being bridged with a continuous-flow LVAD have similar overall rejection rates as patients bridged with pulsatile-flow LVADs, but have a lower rate of clinically relevant rejection according to the International Society for Heart and Lung Transplantation revised cardiac allograft rejection scale (Table 2) [73,74]. Conversely, another retrospective study found that episodes of severe rejection were significantly more frequent in patients who were bridged to transplant with a continuous-flow LVAD compared to those who were bridged with a pulsatile-flow LVAD [75].

2.9 Endocrine System

Most studies of endocrine function associated with continuous-flow physiology come from research involving cardiopulmonary bypass. Studies show variable changes to the function of the adrenocortical system. For example, evidence exists of a reduction in cortisol secretion during non-pulsatile bypass that can be corrected through the use of pulsatile bypass [76]. In contrast, other studies comparing hypothermic pulsatile and nonpulsatile cardiopulmonary bypass found no differences between the two groups with regard to cortisol, renin, or adrenocorticotrophic hormone levels [77,78]. Evidence of the effect of continuous-flow physiology using durable LVADs is limited, though at least one study exists evaluating the administration of hypothalamic releasing hormones in continuous-flow LVAD patients. This demonstrated a normal response of adrenocorticotrophic hormone, thyroid-stimulating hormone, luteinizing hormone, and prolactin, and a slightly diminished response of growth hormone [79]. Though other studies of this area are lacking, and absence of evidence is not evidence of absence, it seems reasonable to conclude that given the widespread use of continuous-flow LVADs in the treatment of modern heart failure, the effects of continuous-flow physiology on endocrine function are clinically negligible.

3.1 Conclusions

Over the last 10 years, continuous-flow LVADs have become the standard of care when long-term mechanical support is required. They have several mechanical advantages over pulsatile-flow devices, including decreased size, increased durability, and ease of implantation. From a physiologic standpoint, continuous-flow is generally well tolerated, even over extended periods of several years. Though some differences exist among various organ system parameters (Table 3), most of these differences likely have minimal clinical

significance. In a minority of situations, such as with gastrointestinal bleeding, continuous-flow physiology presents challenges that are not seen as frequently as in patients with pulsatile-flow. Effective treatment and prevention of these events mark some the current clinical difficulties in managing patients with continuous-flow physiology.

While continuous-flow LVADs clearly have several mechanical advantages over pulsatile LVADs, it may well be that a hybrid approach would provide the most optimal patient outcomes. For example, a combination of continuous-flow pump design with software algorithms to generate pump speed variations to create pulsatility may prove to be advantageous. The needed frequency of pulsatility to optimize outcomes, whether similar to the human heart or just a few times per minute, is not known. What is clear is that despite the significant benefit that continuous-flow technology has provided to patients with end-stage heart failure, some large clinical hurdles remain and will be the subject of considerable research in the coming years.

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References

1. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics – 2015 update. *Circulation*. 2015; 131:e29. [PubMed: 25520374]
2. Gibbon JH. Application of a mechanical heart and lung apparatus to cardiac surgery. *Minn Med*. 1954; 37:171. [PubMed: 13154149]
3. DeBakey ME. Left ventricular bypass pump for cardiac assistance. Clinical experience. *Am J Cardiol*. 1971; 27:3. [PubMed: 5538711]
4. DeVries WC, Anderson JL, Joyce JL, Joyce LD, Anderson FL, Hammond EH, et al. Clinical use of the total artificial heart. *N Engl J Med*. 1984; 310:273. [PubMed: 6690950]
5. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED, et al. Sixth INTERMACS annual report: a 10,000-patient database. *J Heart Lung Transplant*. 2014; 33:555. [PubMed: 24856259]
6. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, et al. Long-term use of a left ventricular device for end-stage heart failure. *N Engl J Med*. 2001; 345:1435. [PubMed: 11794191]
7. Pagani FD, Long JW, Dembitsky WP, Joyce LD, Miller LW. Improved mechanical reliability of the HeartMate VXE left ventricular assist system. *Ann Thorac Surg*. 2006; 82:1413. [PubMed: 16996944]
8. Dowling RD, Park SJ, Pagani FD, Tector AJ, Naka Y, Icenogle TB, et al. HeartMate VE LVAS design enhancements and its impact on device reliability. *Eur J Cardiothorac Surg*. 2004; 25:958. [PubMed: 15144995]
9. Dembitsky WP, Tector AJ, Park S, Moskowitz AJ, Gelijns AC, Ronan NS, et al. Left ventricular assist device performance with long-term circulatory support: lessons learned from the REMATCH trial. *Ann Thorac Surg*. 2004; 78:2123. [PubMed: 15561049]
10. Frazier OH, Rose EA, Oz MC, Dembitsky W, McCarthy P, Radovancevic B, et al. Multicenter clinical evaluation of the HeartMate vented electric left ventricular assist system in patients awaiting heart transplantation. *J Thorac Cardiovasc Surg*. 2001; 122:1186. [PubMed: 11726895]
11. El-Banayosy A, Arusoglu L, Kizner L, Tenderich G, Minami K, Inoue K, et al. Novacor left ventricular assist system versus HeartMate vented electric left ventricular assist system as a long-

- term mechanical circulatory support device in bridging patients: a prospective study. *J Thorac Cardiovasc Surg.* 2000; 119:581. [PubMed: 10694620]
12. Saxton GA Jr, Andrews GB. An ideal heart pump with hydrodynamic characteristics analogous to the mammalian heart. *Trans Am Soc Artif Intern Organs.* 1960; 6:288. [PubMed: 13746986]
 13. Klotz S, Deng MC, Stypmann J, Roetker J, Wilhelm MJ, Hammel D, et al. Left ventricular pressure and volume unloading during pulsatile versus nonpulsatile left ventricular assist device support. *Ann Thorac Surg.* 2004; 77:143. [PubMed: 14726050]
 14. Thohan V, Stetson SJ, Nagueh SF, Rivas-Gotz CR, Koerner MM, Lafuente JA, et al. Cellular and hemodynamics responses of failing myocardium to continuous flow mechanical circulatory support using the DeBakey-Noon left ventricular assist device: a comparative analysis with pulsatile-type devices. *J Heart Lung Transplant.* 2005; 24:566. [PubMed: 15896754]
 15. Drews T, Jurmann M, Michael D, Miralem P, Weng Y, Hetzer R. Differences in pulsatile and non-pulsatile mechanical circulatory support in long-term use. *J Heart Lung Transplant.* 2008; 27:1096. [PubMed: 18926400]
 16. Garcia S, Kandar F, Boyle A, Colvin-Adams M, Liao K, Joyce L, et al. Effects of pulsatile- and continuous-flow left ventricular assist devices on left ventricular unloading. *J Heart Lung Transplant.* 2008; 27:261. [PubMed: 18342746]
 17. Mudd JO, Cuda JD, Halushka M, Soderlund KA, Conte JV, Russell SD. Fusion of aortic valve commissures in patients supported by a continuous axial flow left ventricular assist device. *J Heart Lung Transplant.* 2008; 27:1269. [PubMed: 19059105]
 18. Hata H, Fujita T, Ishibashi-Ueda H, Nakatani T, Kobayashi J. Pathologic analysis of the aortic valve after long-term left ventricular assist device support. *Eur J Cardiothorac Surg.* 2014; 46:193. [PubMed: 24335262]
 19. Kato TS, Chokshi A, Singh P, Khawaja T, Cheema F, Akashi H, et al. Effects of continuous-flow versus pulsatile-flow left ventricular assist devices on myocardial unloading and remodeling. *Circ Heart Fail.* 2011; 4:546. [PubMed: 21765125]
 20. Krabatsch T, Schweiger M, Dandel M, Stepanenko A, Drews T, Potapov E, et al. Is bridge to recovery more likely with pulsatile left ventricular assist devices than with nonpulsatile-flow systems? *Ann Thorac Surg.* 2011; 91:1335. [PubMed: 21444064]
 21. Ootaki Y, Kamohara K, Akiyama M, Zahr F, Kopcak MW Jr, Dessoffy R, et al. Phasic coronary blood flow pattern during a continuous flow left ventricular assist support. *Eur J Cardiothorac Surg.* 2005; 28:711. [PubMed: 16198117]
 22. Kinoshita M, Takano H, Taenaka Y, Mori S, Takaichi S, Noda H, et al. Cardiac disuse atrophy during LVAD pumping. *ASAIO Trans.* 1998; 34:208. [PubMed: 3196510]
 23. Drakos SG, Kfoury AG, Hammond EH, Reid BB, Revelo MP, Rasmusson BY, et al. Impact of mechanical unloading on microvasculature and associated central remodeling features of the failing human heart. *J Am Coll Cardiol.* 2010; 56:382. [PubMed: 20650360]
 24. Diakos NA, Selzman CH, Sachse FB, Stehlik J, Kfoury AG, Wever-Pinzon O, et al. Myocardial atrophy and chronic mechanical unloading of the failing human heart: implications for cardiac assist device-induced myocardial recovery. *J Am Coll Cardiol.* 2014; 64:1602. [PubMed: 25301465]
 25. Fitzpatrick JR, Frederick JR, Hiesinger W, Hsu VM, McCormick RC, Kozin ED, et al. Early planned institution of biventricular mechanical circulatory support results in improved outcomes compared with delayed conversion of a left ventricular assist device to a biventricular assist device. *J Thorac Cardiovasc Surg.* 2009; 137:971. [PubMed: 19327526]
 26. Drakos SG, Janicki L, Horne BD, Kfoury AG, Reid BB, Clayson S, et al. Risk factors predictive of right ventricular failure after left ventricular assist device implantation. *Am J Cardiol.* 2010; 105:1030. [PubMed: 20346326]
 27. Kormos RL, Teuteberg JJ, Pagani FD, Russell SD, John R, Miller LW, et al. Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. *J Thorac Cardiovasc Surg.* 2010; 139:1316. [PubMed: 20132950]

28. Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med*. 2009; 361:2241. [PubMed: 19920051]
29. Maeder MT, Leet A, Ross A, Esmore D, Kaye DM. Changes in right ventricular function during continuous-flow left ventricular assist device support. *J Heart Lung Transplant*. 2009; 28:360. [PubMed: 19332263]
30. Morgan JA, Paone G, Nemeh HW, Murthy R, Williams CT, Lanfear DE, et al. Impact of continuous-flow left ventricular assist device support on right ventricular function. *J Heart Lung Transplant*. 2013; 32:398. [PubMed: 23402946]
31. Atluri P, Fairman AS, MacArthur JW, Goldstone AB, Cohen JE, Howard JL, et al. Continuous flow left ventricular assist device implant significantly improves pulmonary hypertension, right ventricular contractility, and tricuspid valve competence. *J Card Surg*. 2013; 28:770. [PubMed: 24118109]
32. Haddad H, Elabbassi W, Moustafa S, Davies R, Mesana T, Hendry P, et al. Left ventricular assist devices as bridge to heart transplantation in congestive heart failure with pulmonary hypertension. *ASAIO J*. 2005; 51:456. [PubMed: 16156313]
33. Salzberg SP, Lachat ML, von Harbou, Zünd G, Turina MI. Normalization of high pulmonary vascular resistance with LVAD support in heart transplantation candidates. *Eur J Cardiothorac Surg*. 2005; 27:222. [PubMed: 15691674]
34. Etz CD, Welp HA, Tjan TD, Hoffmeier A, Weigang E, Scheld HH, et al. Mechanically refractory pulmonary hypertension: treatment with nonpulsatile left ventricular assist devices. *Ann Thorac Surg*. 2007; 83:1697. [PubMed: 17462383]
35. Ozturk P, Engin AY, Nalbantgil S, Oguz E, Ayik F, Engin C, et al. Comparison of continuous-flow and pulsatile-flow blood pumps on reducing pulmonary artery pressure in patients with fixed pulmonary hypertension. *Artif Organs*. 2013; 37:763. [PubMed: 24033601]
36. Nishimura T, Tatsumi E, Nishinaka T, Taenaka Y, Masuzawa T, Nakata M, et al. Diminished vasoconstrictive function caused by long-term nonpulsatile left heart bypass. *Artif Organs*. 1999; 23:722. [PubMed: 10463496]
37. Nishimura T, Tatsumi E, Taenaka Y, Nishinaka T, Nakatani T, Masuzawa T, et al. Effects of long-term nonpulsatile left heart bypass on the mechanical properties of the aortic wall. *ASAIO J*. 1999; 45:455. [PubMed: 10503625]
38. Segura AM, Gregoric I, Radovancevic R, Demirozu ZT, Buja LM, Frazier OH. Morphologic changes in the aortic wall media after support with a continuous-flow left ventricular assist device. *J Heart Lung Transplant*. 2013; 32:1096. [PubMed: 23968812]
39. Ambardekar AV, Hunter KS, Babu AN, Tudor RM, Dodson RB, Lindenfeld J. Changes in aortic wall structure, composition, and stiffness with continuous-flow left ventricular assist devices: a pilot study. *Circ Heart Fail*. 2015; 8:944. [PubMed: 26136459]
40. Potapov EV, Dranishnikov N, Morawietz L, Stepanenko A, Rezai S, Blechschmidt C, et al. Arterial wall histology in chronic pulsatile-flow and continuous-flow device circulatory support. *J Heart Lung Transplant*. 2012; 31:1171. [PubMed: 22995552]
41. Witman MA, Garten RS, Gifford JR, Groot JH, Trinity JD, Stehlik J, et al. Further peripheral vascular dysfunction in heart failure patients with a continuous-flow left ventricular assist device: the role of pulsatility. *JACC Heart Fail*. 2015; 3:703. [PubMed: 26277768]
42. Soucy KG, Giridharan GA, Choi Y, Sobieski MA, Monreal G, Cheng A, et al. Rotary pump speed modulation for generating pulsatile flow and phasic left ventricular volume unloading in a bovine model of chronic ischemic heart failure. *J Heart Lung Transplant*. 2015; 34:122. [PubMed: 25447573]
43. Johnson EH, Bennett SH, Goetzman BW. The influence of pulsatile perfusion on the vascular properties of the newborn lamb lung. *Pediatr Res*. 1992; 31:349. [PubMed: 1570201]
44. Henaine R, Vergnat M, Bacha EA, Baudet B, Lambert V, Belli E, et al. Effects of lack of pulsatility on pulmonary endothelial function in the Fontan circulation. *J Thorac Cardiovasc Surg*. 2013; 146:522. [PubMed: 23219498]
45. Boldt J, Zickmann B, Dapper F, Hempelmann G. Does the technique of cardiopulmonary bypass affect lung water content? *Eur J Cardiothorac Surg*. 1991; 5:22. [PubMed: 2018644]

46. Yuan N, Arnaoutakis GJ, George TJ, Allen JG, Ju DG, Schaffer JM, et al. The spectrum of complications following left ventricular assist device placement. *J Card Surg.* 2012; 27:630. [PubMed: 22978843]
47. Miller LW, Pagani FD, Russell SD, John R, Boyle AJ, Aaronson KD, et al. Use of a continuous-flow device in patients awaiting heart transplantation. *N Engl J Med.* 2007; 357:885. [PubMed: 17761592]
48. Kirklin JK, Naftel DC, Kormos RL, Pagani FD, Myers SL, Stevenson LW, et al. Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) analysis of pump thrombosis in the HeartMate II left ventricular assist device. *J Heart Lung Transplant.* 2014; 33:12. [PubMed: 24418730]
49. Slaughter MS, Sobieski MA, Gallagher C, Graham J, Brandise J, Stein R. Fibrinolytic activation during long-term support with the HeartMate II left ventricular assist device. *ASAIO J.* 2008; 54:115. [PubMed: 18204326]
50. Katz JN, Jensen BC, Chang PP, Myers SL, Pagani FD, Kirklin JK. A multicenter analysis of clinical hemolysis in patients supported with durable, long-term left ventricular assist device therapy. *J Heart Lung Transplant.* 2015; 34:701. [PubMed: 25582036]
51. Bartoli CR, Ghotra AS, Pachika AR, Birks EJ, McCants KC. Hematologic markers better predict left ventricular assist device thrombosis than echocardiographic or pump parameters. *Thorac Cardiovasc Surg.* 2014; 62:414. [PubMed: 24995532]
52. Kirklin JK, Naftel DC, Kormos RL, Stevenson LW, Pagani FD, Miller MA, et al. Fifth INTERMACS annual report: risk factor analysis from more than 6,000 mechanical circulatory support patients. *J Heart Lung Transplant.* 2013; 32:141. [PubMed: 23352390]
53. John R, Kamdar F, Liao K, Colvin-Adams M, Boyle A, Joyce L. Improved survival and decreasing incidence of adverse events with the HeartMate II left ventricular assist device as bridge-to-transplant therapy. *Ann Thorac Surg.* 2008; 86:1227. [PubMed: 18805167]
54. Stulak JM, Lee D, Haft JW, Romano MA, Cowger J, Park SJ, et al. Gastrointestinal bleeding and subsequent risk of thromboembolic events during support with a left ventricular assist device. *J Heart Lung Transplant.* 2014; 33:60. [PubMed: 24021944]
55. Letsou GV, Shah N, Gregoric ID, Myers TJ, Delgado R, Frazier OH. Gastrointestinal bleeding from arteriovenous malformations supported by the Jarvik 2000 axial flow left ventricular assist device. *J Heart Lung Transplant.* 2005; 24:105. [PubMed: 15653390]
56. Hasin T, Marmor Y, Kremers W, Topilsky Y, Severson CJ, Schirger JA, et al. Readmissions after implantation of axial flow left ventricular assist device. *J Am Coll Cardiol.* 2013; 61:153. [PubMed: 23219299]
57. Forest SJ, Bello R, Friedmann P, Casazza D, Nucci C, Shin JJ, et al. Readmissions after ventricular assist device: etiologies, patterns, and days out of hospital. *Ann Thorac Surg.* 2013; 95:1276. [PubMed: 23481701]
58. Wever-Pinzon O, Selzman CH, Drakos SG, Saidi A, Stoddard GJ, Gilbert EM, et al. Pulsatility and the risk of nonsurgical bleeding in patients supported with the continuous-flow left ventricular assist device HeartMate II. *Circ Heart Fail.* 2013; 6:517. [PubMed: 23479562]
59. Islam S, Cevik C, Madonna R, Frandah W, Islam E, Islam S, et al. Left ventricular assist devices and gastrointestinal bleeding: a narrative review of case reports and case series. *Clin Cardiol.* 2013; 36:190. [PubMed: 23378047]
60. Davis ME, Haglund NA, Tricarico NM, Keebler ME, Maltais S. Development of acquired von Willebrand syndrome during short-term micro axial pump support: implications for bleeding in a patient bridged to a long-term continuous-flow left ventricular assist device. *ASAIO J.* 2014; 60:355. [PubMed: 24614358]
61. Mason NO, Phelps K, Madsen CN, Khodaverdian RA, Long JW. Nutrition in HeartMate XVE and HeartMate II LVAD patients. *ASAIO J.* 2008; 54:30A.
62. Letsou GV, Myers TJ, Gregoric ID, Delgado R, Shah N, Robertson K, et al. Continuous axial-flow left ventricular assist device (Jarvik 2000) maintains kidney and liver perfusion for up to 6 months. *Ann Thorac Surg.* 2003; 76:1167. [PubMed: 14530006]

63. Deo SV, Sharma V, Altarabsheh SE, Hasin T, Dillon J, Shah IK, et al. Hepatic and renal function with successful long-term support on a continuous flow left ventricular assist device. *Heart Lung Circ.* 2014; 23:229. [PubMed: 23992754]
64. Radovancevic B, Vrtovec B, de Kort E, Radovancevic R, Gregoric ID, Frazier OH. End-organ function in patients on long-term circulatory support with continuous- or pulsatile-flow assist devices. *J Heart Lung Transplant.* 2007; 26:815. [PubMed: 17692785]
65. Sandner SE, Zimpfer D, Zrunek P, Dunkler D, Schima H, Rajek A, et al. Renal function after implantation of continuous versus pulsatile flow left ventricular assist devices. *J Heart Lung Transplant.* 2008; 27:469. [PubMed: 18442710]
66. Kamdar F, Boyle A, Liao K, Colvin-Adams M, Joyce L, John R. Effects of centrifugal, axial, and pulsatile left ventricular assist device support on end-organ function in heart failure patients. *J Heart Lung Transplant.* 2009; 28:352. [PubMed: 19332262]
67. Potapov EV, Loebe M, Abdul-Khaliq H, Koster A, Stein J, Sodian R, et al. Postoperative course of S-100B protein and neuron-specific enolase in patients after implantation of continuous and pulsatile flow LVADs. *J Heart Lung Transplant.* 2001; 20:1310. [PubMed: 11744415]
68. Nabavi DG, Stockmann J, Schmid C, Schneider M, Hammel D, Scheld HH, et al. Doppler microembolic load predicts risk of thromboembolic complications in Novacor patients. *J Thorac Cardiovasc Surg.* 2003; 126:160. [PubMed: 12878951]
69. Thoennissen NH, Allroggen A, Ritter M, Dittrich R, Schmid C, Schmid HH, et al. Influence of inflammation and pump dynamic on cerebral microembolization in patients with continuous-flow DeBakey LVAD. *ASAIO J.* 2006; 52:243. [PubMed: 16760711]
70. Markham DW, Fu Q, Palmer MD, Drazner MH, Meyer DM, Bethea BT, et al. Sympathetic neural and hemodynamic responses to upright tilt in patients with pulsatile and nonpulsatile left ventricular assist devices. *Circ Heart Fail.* 2013; 6:293. [PubMed: 23250982]
71. Cornwell WK 3rd, Tarumi T, Aengevaeren VL, Ayers C, Divanji P, Fu Q, et al. Effect of pulsatile and nonpulsatile flow on cerebral perfusion in patients with left ventricular assist devices. *J Heart Lung Transplant.* 2014; 33:1295. [PubMed: 25307621]
72. Garatti A, Bruschi G, Colombo T, Russo C, Lanfranchi M, Milazzo F, et al. Clinical outcome and bridge to transplant rate of left ventricular assist device recipient patients: comparison between continuous-flow and pulsatile-flow devices. *Eur J Cardiothorac Surg.* 2008; 34:275. [PubMed: 18375138]
73. Healy AH, Mason NO, Hammond ME, Reid BB, Clayson SE, Drakos SG, et al. Allograft rejection in patients supported with continuous-flow left ventricular assist devices. *Ann Thorac Surg.* 2011; 92:1601. [PubMed: 21944258]
74. Stewart S, Winters GI, Fishbein MC, Tazelaar HD, Kobashigawa J, Abrams J, et al. Revision of the 1990 working formulation for the standardization of nomenclature in the diagnosis of heart rejection. *J Heart Lung Transplant.* 2005; 24:1710. [PubMed: 16297770]
75. Klotz S, Stypmann J, Welp H, Schmid C, Drees G, Rukosujew A, et al. Does continuous flow left ventricular assist device technology have a positive impact on outcome pretransplant and posttransplant? *Ann Thorac Surg.* 2006; 82:1774. [PubMed: 17062246]
76. Taylor KM, Wright GS, Reid JM, Bain WH, Caves PK, Walker MS, et al. Comparative studies of pulsatile and nonpulsatile flow during cardiopulmonary bypass. II. The effects on adrenal secretion of cortisol. *J Thorac Cardiovasc Surg.* 1978; 75:574. [PubMed: 642552]
77. Kono K, Philbin DM, Coggins CH, Slater EE, Triantafillou A, Levine FH, et al. Adrenocortical hormone levels during cardiopulmonary bypass with and without pulsatile flow. *J Thorac Cardiovasc Surg.* 1983; 85:129. [PubMed: 6294418]
78. Pollock EM, Pollock JC, Jamieson MP, Beastall GS, Wright C, Torsney B, et al. Adrenocortical hormone concentrations in children during cardiopulmonary bypass with and without pulsatile flow. *Br J Anaesth.* 1988; 60:536. [PubMed: 2837262]
79. Wieselthaler GM, Riedl M, Schima H, Wagner O, Waldhäusl W, Wolner E, et al. Endocrine function is not impaired with a continuous MicroMed-DeBakey axial flow pump. *J Thorac Cardiovasc Surg.* 2007; 133:2. [PubMed: 17198773]

Figure 1.
Use of Durable Mechanical Circulatory Support Devices in Adults by Type Over Time.
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Figure 2.

Brachial Artery Flow-Mediated Dilation in New York Heart Association Functional Class II Heart Failure Patients, Class III/IV Heart Failure Patients, Class III/IV Heart Failure Patients Post-LVAD Implantation, and Healthy Control Subjects. * denotes a significant difference compared to controls, while † denotes a significant difference from the Class II Heart Failure Group. HFrEF = Heart Failure with Reduced Ejection Fraction. Reproduced from Witman, et al, [41] with permission.

Figure 3. Survival Free from Non-surgical Bleeding in Continuous-flow Left Ventricular Assist Device Patients. PI = Pulsatility Index. Reproduced from Wever-Pinzon, et al, [58] with permission.

Table 1

	Pre-Operative (n = 114)	3-Month Follow-Up (n = 71)	6-Month Follow-Up (n = 63)	12-Month Follow-Up (n = 52)	P = (Post-Op vs. Pre-Op)
Right ventricular dysfunction (all patients)	2.09 ± 0.64	1.67 ± 0.77	1.36 ± 0.88	1.64 ± 0.79	0.001
Right ventricular dysfunction (pre-op moderate or severe, n = 58)	2.46 ± 0.49	1.79 ± 0.74	1.48 ± 0.80	1.75 ± 0.80	<0.00001
Tricuspid regurgitation (all patients)	1.48 ± 0.75	1.05 ± 0.53	1.04 ± 0.42	0.75 ± 0.58	0.001
Tricuspid regurgitation (pre-op moderate or severe, n = 59)	2.17 ± 0.28	1.14 ± 0.61	1.17 ± 0.47	0.71 ± 0.57	<0.000001

Mean Preoperative, Immediate Postoperative, and Follow-Up Right Ventricular Dysfunction and Tricuspid Regurgitation Following Continuous Flow Left Ventricular Assist Device Implant. 0 = none, 1 = mild, 2 = moderate, 3 = severe. Reproduced from Atturi, et al, [31] with permission.

Table 2

Rejection	Pulsatile (n = 77)	Continuous (n = 34)	p Value
1R-3R	2.00 ± 1.43	1.50 ± 1.16	0.076
2R-3R	0.49 ± 0.72	0.12 ± 0.33	<0.001

Cardiac Allograft Rejection Rates in the First Year After Transplantation in Patients Who Received an LVAD as a Bridge to Transplantation. Rates are episodes per year as determined by pathologic tissue analysis. 1R = Mild Rejection, 2R = Moderate Rejection, 3R = Severe Rejection, LVAD = Left Ventricular Assist Device. Reproduced from Healy, et al, [73] with permission.

Table 3

<u>Organ System</u>
Cardiovascular <ul style="list-style-type: none"> • CF and PF devices have similar pressure unloading, but volume unloading may be better in PF devices • Possibly higher rates of progression to myocardial recovery with PF LVADs • Possibly lower rates of right heart failure in patients with CF LVADs • Comparable alleviation of pulmonary hypertension in CF and PF LVADs • Increased degeneration of aortic wall tissue in CF LVADs, significance unknown
Respiratory <ul style="list-style-type: none"> • Pulseless pulmonary circulation is well tolerated • No difference in rates of post-operative respiratory complications
Hematologic <ul style="list-style-type: none"> • Pump thrombosis a concern with particular CF LVADs • Higher degree of hemolysis with CF LVADs, usually not clinically significant
Gastrointestinal <ul style="list-style-type: none"> • Relatively high rate of gastrointestinal bleeding with CF LVADs
Renal <ul style="list-style-type: none"> • Comparable improvement in preoperative renal dysfunction after device placement • Decreased rates of renal dysfunction in patients with CF LVADs after device placement
Hepatic <ul style="list-style-type: none"> • Comparable improvement in preoperative hepatic dysfunction after device placement • Decreased rates of hepatic dysfunction in patients with CF LVADs after device placement
Neurologic <ul style="list-style-type: none"> • Little evidence that continuous-flow per se affects neurologic function • No difference in stroke rates between CF and PF LVADs • Possibly lower rates of neurologic dysfunction in patients with CF LVADs
Immunologic <ul style="list-style-type: none"> • Possibly lower rates of clinically significant rejection in patients with CF LVADs
Endocrine <ul style="list-style-type: none"> • Little evidence available; likely no difference

Summary of Differences in Physiology Depending on Flow Type. CF = Continuous-Flow, LVADs = Left Ventricular Assist Devices, PF = Pulsatile-Flow