CME

Perioperative Management of the Patient With a Left Ventricular Assist Device for Noncardiac Surgery

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The pandemic of heart failure and the limited options for treatment of end-stage disease have resulted in an increase in the utilization of left ventricular assist devices (LVADs). Improvements in device technology and patient survival have led to an expanding population of patients requiring noncardiac surgery while on LVAD therapy, thus leading to a growing need for familiarity with the physiology of these patients. This review describes the functional mechanics of the most prevalent continuous-flow LVAD, the HeartMate II, and focuses on perioperative anesthetic concerns. (Anesth Analg 2018;126:1839–50)

Heart failure is a formidable global public health problem affecting an estimated 26 million people worldwide[1] including 15 million in the 51 countries represented by the European Society of Cardiology[2] and 6.5 million in the United States.[3] Cardiac transplantation is regarded as the most effective therapy for those with refractory American Heart Association Stage D heart failure with reduced ejection fraction. However, its use has been severely restricted by the limited supply of donor hearts,[4] which has led to a rise in the use of left ventricular assist devices (LVADs) for bridge to transplant (BTT) and for destination therapy (DT), the permanent implantation of a LVAD in those deemed ineligible for cardiac transplantation.[5–7] Approximately 4%–49% of this growing cohort of patients will require noncardiac surgery[8–14] underscoring the importance of understanding device management in the perioperative period.

FUNCTIONAL MECHANICS

Since 2010, >95% of all newly implanted LVADs have been continuous-flow (CF) devices.[7] Presently, the 2 most widely used LVADs are the second-generation HeartMate II (HM II; St Jude Medical, St Paul, MN) and the third-generation HeartWare Ventricular Assist Device (HVAD; HeartWare, Framingham, MA) with 20,000 and 10,000 patients treated worldwide, respectively.[15,16] The HM II is US Food and Drug Administration approved for BTT (2008) and DT (2010), while the HVAD is approved only for BTT (2012).

The HM II and HVAD are CF LVADs that use a magnetic field to rotate an impeller, which directs flow parallel (axial-flow HM II) or perpendicular (centrifugal-flow HVAD) to the axis of rotation[17] (Figure 1, A-C). While centrifugal-flow pumps are more afterload sensitive and preload dependent than axial-flow pumps,[17,19] the basic concepts governing the physiology of both devices are similar. An overview of the HM II will be provided as a general model for the functional mechanics of CF devices.

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Accepted for publication October 16, 2017.

Funding: None.

The author declares no conflicts of interest.

Reprints will not be available from the author.

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DOI: 10.1213/ANE.0000000000002669

Device Design

The HM II is a fully implantable LVAD composed of an inflow cannula that connects to the left ventricular apex, a linear conduit that contains the motor and impeller, and an outflow cannula that connects to a graft sewn to the ascending aorta above the aortic valve (Figure 1D). As the impeller turns, the LVAD draws blood from the left ventricle (LV) into the ascending aorta, reducing the workload of a failing LV and providing cardiac output support to the body. The motor is powered by a percutaneous lead that connects to a system controller and then either to battery packs or to alternating current power. The HM II, as well as the HVAD, can provide up to 10 L/min of support.[17]

Determinants of Flow

The magnitude of blood flow through the HM II is determined by the pressure gradient across the pump and the speed in revolutions per minute (RPM).[20–22]

Pressure Gradient Across the Pump. Pump flow, or the amount of cardiac output support, is inversely proportional to the pressure gradient across the pump. The pressure gradient is defined as the difference between the outlet and inlet pressures of the pump, which correlate physiologically to the aortic and left ventricular pressures, respectively (Figure 2A). Larger pressure gradients result in less pump flow, while smaller pressure gradients result in greater LVAD flow. This phenomenon is apparent on a single-beat basis resulting in increased flow during systole and decreased flow during diastole (Figure 2B, C).

Afterload Sensitivity. The pressure gradient dictating overall flow is determined in part by the patient's outlet aortic pressure making CF LVADs "afterload-sensitive" devices. The hypertensive CF LVAD patient with a high mean arterial pressure (MAP) will receive less cardiac output support due to the increased pressure gradient. Hypotension increases pump flow, but may injure perfusion-dependent organs. Notably, a retrospective study by Mathis et al[24] showed that an intraoperative MAP <70 mm Hg for >20 minutes was strongly associated with acute kidney injury. The inverse relationship between afterload and flow is illustrated in a series of HM II performance curves (Figure 2D). A goal MAP

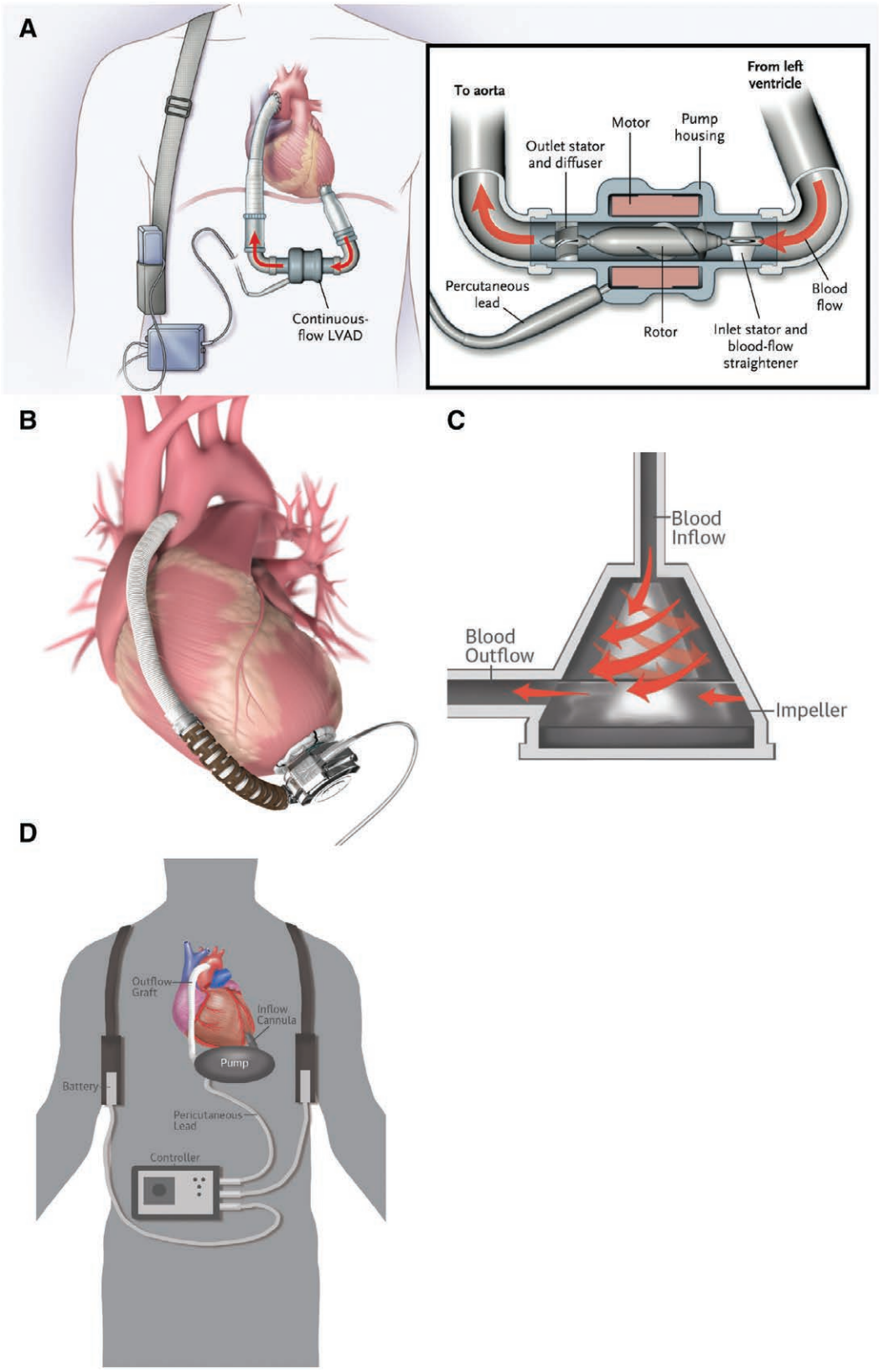

Figure 1. Continuous-flow left ventricular assist devices. A, The HeartMate II, an axial-flow CF LVAD, propels blood parallel to the axis of rotation of the rotor. B, The HeartWare ventricular assist device is smaller than the HeartMate II and attaches directly to the left ventricular apex. It provides centrifugal flow in which inflowing blood is propelled forward in a perpendicular direction, shown in (C). D, Various components of an implantable LVAD, including the inflow cannula and outflow graft, percutaneous lead, system controller, and batteries. Image (A) modified from Slaughter et al.[18] Image (B) courtesy of HeartWare, Framingham, MA. Images (C and D) modified from Mancini and Colombo.[17] All images were used with permission. CF LVAD indicates continuous-flow left ventricular assist device; LVAD, left ventricular assist device.

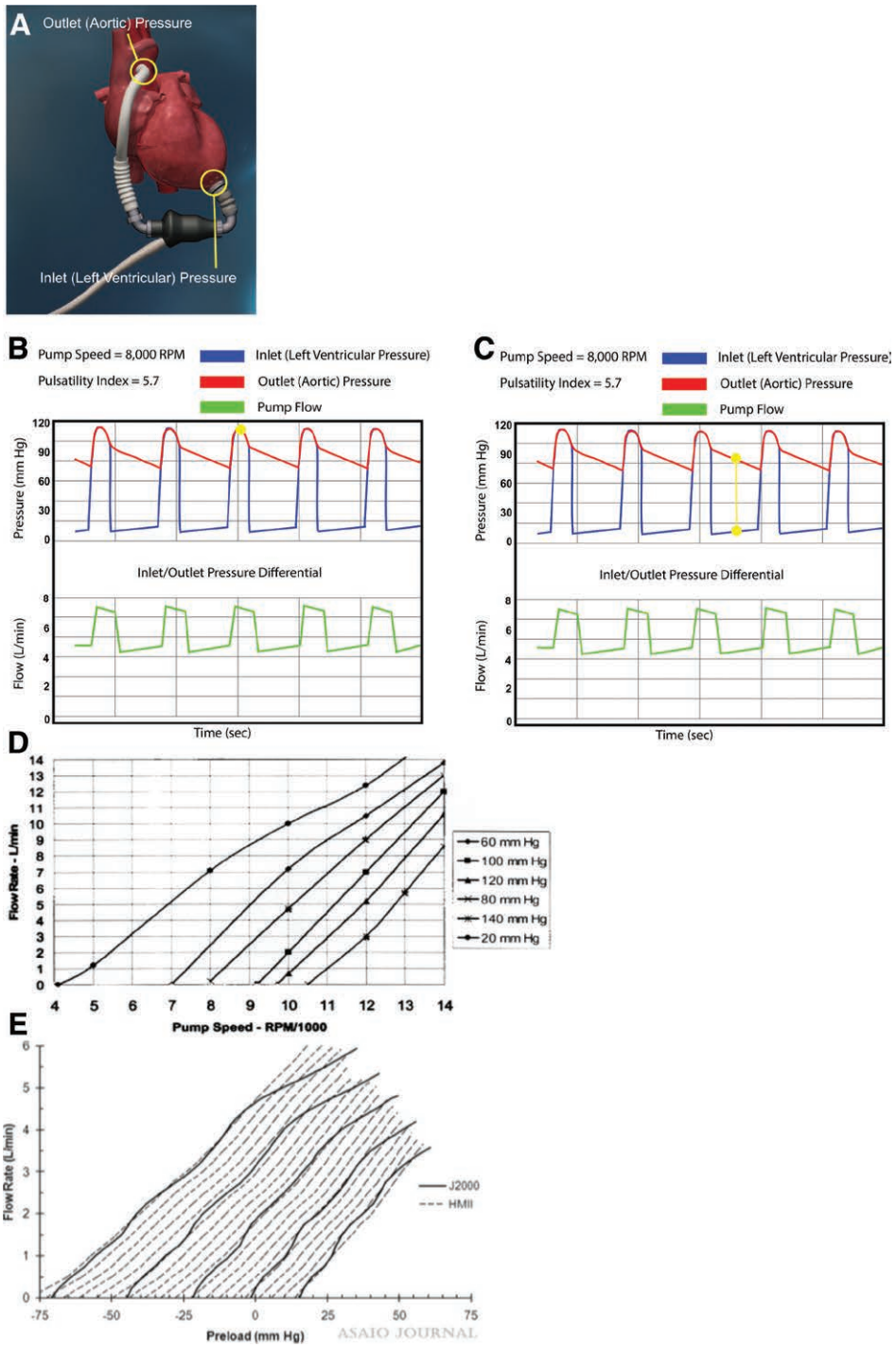

Figure 2. Determinants of flow. A, Locations of the outlet aortic root pressure and the inlet left ventricular pressure. B and C, Simulated HeartMate II waveform monitors demonstrating the variation in pump flow that occurs during the cardiac cycle. In (B), the yellow circle denotes systole during which left ventricular pressure (blue line) becomes identical to aortic root pressure (red line) resulting in a minimal pressure difference across the pump. This results in a relative increase in pump flow (green waveform). In (C), the yellow line marks the maximal difference between the aortic and left ventricular pressures that occurs during diastole. This increased pressure gradient correlates with a relative decrease in pump flow. Images (A–C) modified with permission from St Jude Medical. D, Effects of changes in afterload on the performance of the HeartMate II. Each individual line plots the pump flow at various pump speeds. The family of curves generated from left to right signifies increasing afterload (ie, increasing differential pressures as the outflow resistance is gradually increased in a mock loop). Afterload sensitivity is illustrated by examining the flows achieved at a fixed speed of 12,000 RPM; when the differential pressure increases from 20 mm Hg (top line, circle) to 140 mm Hg (bottom line, star), the flow decreases from ~12 to 3 L/min. Used with permission from Griffith et al.[20]. E, Effects of changes in preload on the performance of the HeartMate II (dotted lines). Each line plots the pump flow according to varying preload in a mock loop with a fixed afterload of 80 mm Hg. The family of curves generated from left to right was produced by increasing RPM in increments of 200 starting from 7000 RPM at the far left. Increases in preload result in increases in flow in a demonstration of preload dependency. The Jarvik 2000 (J2000, solid lines; Jarvik Heart, New York, NY), another continuous-flow LVAD, also demonstrates preload dependency. Used with permission from Khalil et al.[23]. LVAD indicates left ventricular assist device; RPM, revolutions per minute.

of 70–90 mm Hg is recommended as a way to maintain a balance between flow and perfusion pressure.[25,26]

Preload Dependency. The pressure gradient dictating pump flow is also determined by preload, rendering CF LVADs "preload dependent."[23] An increase in LV preload increases inlet left ventricular end-diastolic pressure, which decreases the pressure gradient and increases the pump flow. Conversely, a decrease in LV preload decreases the pump flow. Figure 2E illustrates the direct relationship between preload and flow.

The preload-dependent CF LVAD is limited by the volume available in the LV. Low LV preload can occur from decreased venous return from multiple causes including hypovolemia (eg, overdiuresis or hemorrhage), position changes (eg, reverse Trendelenburg), or mechanical obstructive phenomena (such as tamponade). Low LV preload may also occur as a result of cardiogenic dysfunction, notably right ventricular failure. Adequate right heart function is crucial as successful LVAD pump function depends completely on the ability of the right ventricle (RV) to deliver volume to the LV. Increased pulmonary vascular resistance (PVR) can also limit LV preload.

When LVAD flow exceeds the available LV preload, the walls of the LV can collapse toward the inflow conduit causing a suction event. When this occurs, the HM II temporarily decreases the speed in an attempt to promote LV filling.[25] Suction events can precipitate ventricular arrhythmias,[27] which may be asymptomatic or result in RV dysfunction and hemodynamic deterioration.[28,29] A suction event can occur either from increased LVAD outflow or decreased LV preload.

Speed. Blood flow through the pump is directly proportional to the speed with higher RPMs generating more flow. Figure 3 illustrates the hemodynamic effects of increasing LVAD speed from 8000 to 10,000 RPM. As speed increases, the LV becomes more unloaded resulting in a decrease in LV systolic pressure; this corresponds to a decrease in height of the blue waveform. In addition, the aortic diastolic pressure rises[25] resulting in a rise in mean pressure of the red waveform but also diminution of pulsatility. The occurrence of a narrow pulse pressure may increase the difficulty of palpating a pulse in the CF LVAD patient.

A key point is demonstrated with the waveform illustrations at 8500 and 9500 RPM. At 8500 RPM, the aortic and LV waveforms overlap, which signifies the generation of a LV systolic pressure that exceeds aortic root pressure. In this instance, the aortic valve opens and blood flows through the valve and through the pump (pump flow in parallel). At 9500 RPM, the increase in LVAD support results in a separation of these 2 waveforms as the LV no longer generates a systolic pressure that exceeds the aortic root pressure. The aortic valve remains closed throughout the cardiac cycle; consequently, blood bypasses the valve and flows exclusively through the pump (pump flow in series).

A state of diminished pulsatility has been implicated in a number of long-term sequelae including aortic valve thrombosis,[17,25,30–33] the development of aortic insufficiency (AI), which creates a futile circuit as LVAD flow regurgitates back into the LV rather than moving forward as effective cardiac output,[34–37] and the formation of arteriovenous malformations, which appear to partially account for the increased incidence of gastrointestinal bleeds (GIBs) in the HM II population.[38–40] For these reasons, a state of pulsatility and regular opening of the aortic valve is desirable, which informs the upper limit of RPM. Some patients have oversewn aortic valves, which render them completely device dependent.

ANTICOAGULATION, BLEEDING, AND THROMBOSIS

Patients implanted with the HM II are typically anticoagulated with warfarin and aspirin to reduce the risk of thrombosis; center-specific practices may augment antiplatelet therapy with dipyridamole. CF LVAD patients appear to have much higher rates of hemorrhagic compared with thrombotic complications.[41] Boyle et al[42] assessed 956 HM II outpatients, finding only 0.07 thrombotic events/patient-year (embolic stroke, pump thrombosis) but 0.72 hemorrhagic events/patient-year (hemorrhagic stroke, bleeding requiring surgery or transfusion).

Hemorrhagic complication rates in HM II patients beyond the immediate perioperative period appear to range from 22% to 44% with GIB cited as the most prevalent bleeding site (accounting for 45%–70% of bleeding events).[40–43] Overall GIB rates are reported at 9%–40%[38–46] with approximately 30%–60% thought to be caused by arteriovenous malformations.[38–40] Consequently, upper and lower endoscopies have become frequent procedures in this patient population.[24,47]

The increased propensity to bleed in HM II patients may also be due to the development of an acquired type 2A von Willebrand disease. Von Willebrand factor, a large multimeric glycoprotein, promotes primary hemostasis by binding to collagen in damaged endothelium and to platelets. CF LVADs create a high-shear environment, which may induce glycoprotein unfolding and enzymatic cleavage by the metalloprotease ADAMTS-13 resulting in loss of the highest molecular weight multimers (HMWMs).[48–51] These HMWMs are the most hemostatically active; hence, the reduced ability to form a platelet plug is a possible contributor to the increased bleeding seen in HM II patients. Interestingly, this acquired coagulation defect can occur in other scenarios involving high shear such as aortic stenosis.[52]

Loss of these multimers occurs in all patients implanted with a HM II[43,53–55] within minutes of LVAD implantation[56] and resolves after device explantation or heart transplantation[43,53,54,57]; multimer loss also occurs in patients implanted with the HVAD.[58,59] Despite the universal onset of this acquired von Willebrand disease, not all HM II patients develop hemorrhagic complications suggesting a multifactorial etiology.[54,60]

Our understanding of the risk of thrombosis is continuing to evolve, as well. Data from the Interagency Registry for Mechanically Assisted Circulatory Support initially showed the overall risk of confirmed or suspected pump thrombosis requiring LVAD exchange to be 5.5% between 2008 and 2012.[61] However, 3 institutions reported an increase in their pump thrombosis rate from 2.2% to 12.2% between 2011 and 2013.[62,63] This finding was reflected in the larger Interagency Registry for Mechanically Assisted Circulatory Support population, but the trend then appeared to partially reverse by 2014.[64] Thrombotic risk appears to be

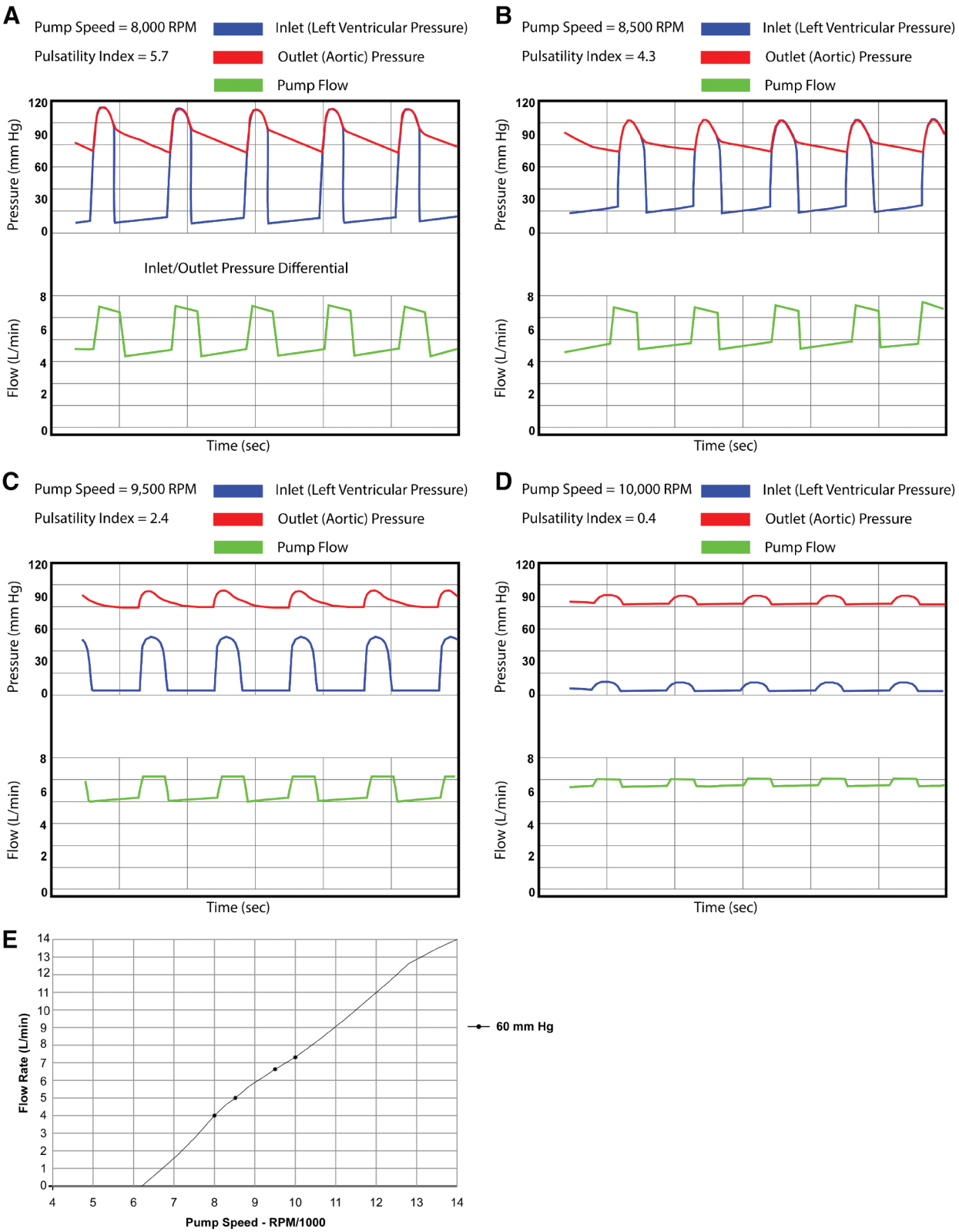

Figure 3. Hemodynamic effects of increasing LVAD speed. A–D, Illustration of the effects of increasing speed (8000, 8500, 9500, and 10,000 RPM) on aortic (red waveform) and left ventricular (blue waveform) pressures, as well as on the pulsatility of pump flow (green waveform) in association with changes in the pulsatility index. See text for explanation. Modified with permission from St Jude Medical. E, These speed changes coincide with the flow trajectory of a single performance curve at constant afterload from Figure 2D. Adapted from Griffith et al.[20] RPM indicates revolutions per minute.

decreased by specific surgical implant techniques, heparin bridging, and the avoidance of pump speeds <8600 RPM[65] and increased with active infection.[66] Low levels of hemolysis typically occur during normal pump function but elevation of lactate dehydrogenase >600 IU/L is concerning for thrombosis.[61,64,66,67]

PREOPERATIVE ASSESSMENT

Preoperative evaluation of the CF LVAD patient presenting for noncardiac surgery includes several questions beyond the usual anesthetic assessment. The type of LVAD implanted should be clarified. Knowledge of the therapeutic strategy (BTT versus DT) may inform the decision to transfuse in scenarios exclusive of life-threatening bleeding. Blood products are typically minimized in the BTT population to decrease alloimmunization, especially in those with panel reactive antibodies that increase the difficulty of a donor organ match. The designation of DT, however, may be misleading in certain patients who are initially labeled as such but then thrive on device therapy and are subsequently bridged to candidacy en route to becoming a full BTT.

Perioperative Anticoagulation

The perioperative anticoagulation plan for the HM II patient should balance the risk of excessive intraoperative bleeding with the risk of thromboembolic complications. Manufacturer guidelines suggest maintaining an international normalized ratio of 2.0–3.0,[68] but there are no clear guidelines on the management of anticoagulation in the perioperative period during noncardiac surgery. Expert consensus opinion from the International Society for Heart and Lung Transplantation states that "for non-emergent procedures, warfarin and antiplatelet therapy may be continued if the risk of bleeding associated with the procedure is low. If therapy needs to be stopped, warfarin and antiplatelet therapy should be held for an appropriate period of time as determined by the type of procedure being undertaken and risk of bleeding. Bridging with heparin or heparin-alternative while a patient is off warfarin may be considered."[69]

There is considerable interinstitutional variability on the management of anticoagulation in the perioperative period for the elective case. Practices range from holding aspirin and warfarin from 2 to 7 days before surgery,[9,10,13] maintaining aspirin therapy but discontinuing warfarin 5 days before surgery with heparin bridging reserved for patients with additional indications for anticoagulation,[12] and maintaining anticoagulation at the lower level of manufacturer recommendations unless the patient undergoes a procedure with a high risk of bleeding such as with neurosurgical or ophthalmological surgeries.[47] In a study of 68 endoscopies in patients with CF LVADs, warfarin was stopped in those presenting for an emergency procedure due to bleeding but was continued in those presenting electively for diagnostic procedures.[70]

Intraoperative packed red blood cell (PRBC) transfusion rates for noncardiac surgery in the CF LVAD population have been reported to range from 15% to 38%,[10–12,47,71] though it is difficult to disentangle the role of multiple variables in these small studies. In the largest retrospective analysis of CF LVAD patients undergoing noncardiac surgery, Mathis et al,[24] who studied 702 noncardiac surgeries (92% of 246 patients had CF devices), reported a mean preoperative international normalized ratio of 1.7 and the use of a preoperative heparin bolus or infusion in 28% of the cases; only 6.7% of cases were emergent and 1.1% designated as American Society of Anesthesiologists status V. In this setting, 1.4% of procedures had an intraoperative estimated blood loss >500 mL and 6.4% (45 cases) required exogenous transfusion (PRBC, fresh frozen plasma, platelets, desmopressin, factor VIIa) with 4.2% requiring intraoperative PRBC transfusion. Those 45 cases included 7 endoscopies for GIB and 30 major noncardiac cases, the most common of which were general surgical, neurosurgical, and vascular procedures. Device thrombosis occurred in 0.6%.[24]

Emergent cases may require reversal of anticoagulation with fresh frozen plasma, prothrombin complex concentrate or vitamin K taking into consideration its slower onset of action.[69] Ultimately, the perioperative anticoagulation regimen may need to be tailored to the type of surgery (major or minor), the timing (elective or emergent), and to a particular individual's history (eg, recurrent GIB versus embolic stroke or deep vein thrombosis/pulmonary embolism) and risk factors (ie, presence of mechanical valves, atrial fibrillation with or without additional risk factors for stroke, or an inherited or acquired hypercoagulable state).[13]

Preoperative RV Assessment

Function of the unsupported RV should be known. Echocardiographic data may be helpful, as well as the history of hospitalizations and therapies for RV failure (ie, need for inotropes or devices in the past). A greater severity of preexisting RV dilation and dysfunction suggests less reserve, a greater need for RV protective strategies, and sets a higher pretest probability for the possibility of intraoperative RV failure. This knowledge is particularly pertinent in surgeries with a high risk of bleeding where a balance must be struck between under- and over-resuscitation, both of which can result in inadequate LV preload, low flow/power, and suction events. Over-resuscitation can result in low LV preload when RV distension limits RV stroke volume and decreases right-sided output; a dilated RV can also limit LV filling and stroke volume due to ventricular interdependence.[72] Hence, differentiating the causes of low flow/power in the context of low pulsatility (see Pulsatility Index below) can be crucial for dictating management, as low LV preload due to hypovolemia warrants volume therapy while low LV preload due to RV failure may require, among other therapies, judicious fluid administration or even cessation of resuscitation and diuresis.[73,74]

Assessing the optimal degree of resuscitation may require invasive monitors, the usage of which varies between series (central venous pressure [CVP], 0%–27%; pulmonary artery catheter, 0%–16%; transesophageal echocardiography [TEE], 1.1%–19%).[10–12,24,47,71,75] One study reported that 51% of cases had a preoperative central venous line, peripherally inserted central catheter, or midline in place.[71] The CVP, when elevated, may aid in the recognition of right ventricular volume overload or dysfunction. Pulmonary artery catheters allow for monitoring of pulmonary artery pressures, assessment of cardiac output by thermodilution, and determination of mixed venous oxygen saturation (Svo_2), though the latter 2 parameters will be depressed with

both hypovolemia and RV dysfunction; however, access to thermodilution and Svo_2 may be useful when additional corroborating data are required beyond the trend of displayed ventricular assist device (VAD) parameters. TEE provides direct visual assessment of right-sided function. Arterial catheter utilization is discussed in Intraoperative Management.

In the 2 largest retrospective studies of noncardiac surgeries in the CF LVAD population, the most common cases were found to be endoscopies, tracheostomies, and vascular access procedures[47] and cardiology and gastroenterology cases.[24] Reported rates of general anesthesia versus monitored anesthesia care range from 19% to 88% and 11% to 81%, respectively.[10,24,71] In 1 study, 93% of endoscopies were performed with monitored anesthesia care.[70] Regional block and neuraxial anesthesia rates have been reported at 0.2%–2.7% and 0%, respectively[24]; 2 studies each reported single instances of spinal anesthesia.[10,71]

Location and Staffing

The noncardiac surgery of a LVAD patient would ideally take place in the implanting center or in a hospital with personnel familiar with LVADs, as the input of a cardiothoracic surgeon or VAD nurse or perfusionist can be invaluable, recognizing that travel and emergency situations may obviate such intents. Increasing familiarity with LVAD technology and rising case loads have led to the growing involvement by noncardiac anesthesiologists. Care by noncardiac anesthesiologists has been reported to range from 21% to 100%[11,12,70,71,75] with trends toward increased involvement over time noted by Stone et al[47] (who have implemented formal didactic LVAD training at their institution since 2001) as well as by Mathis et al,[24] who reported noncardiac anesthesiologist involvement rising from 43% in 2004–2010 to 67% in 2011–2015, although they noted case clustering with gastroenterology procedures.[24]

Evans and Stone[76] have called for a systematic approach to staffing noncardiac surgeries in the LVAD population, suggesting that the appropriately trained noncardiac anesthesiologist may, with the immediate availability of a knowledgeable colleague, provide care for the LVAD-supported patient without major comorbidities undergoing a minor procedure, and that these may be performed in their out-of-operating room locations. They suggest that a cardiac anesthesiologist become involved when the patient is on pharmacological support, has significant comorbidities, or is undergoing a major procedure.[76]

As with any patient undergoing general anesthesia, an assessment of the suitability of the out-of-operating room environment for a given patient with a LVAD should be made, particularly with regard to adequacy of space and presence of needed equipment. Similarly, depending on institutional resources and patient considerations, prior communication with a cardiac surgeon to ensure preprocedural knowledge of the location, date, and nature of the intervention may be prudent.

INTRAOPERATIVE MANAGEMENT

Power Source

The patient's holster holds 2 batteries, which together provide 6–10 hours of power (14-V lithium-ion batteries at 12,000 RPM utilizing 10 W[77]). The patient should be changed to an alternating current source to avoid the possibility of battery depletion. Batteries should be available in the event of a power failure.

Monitoring VAD Monitor

LVAD variables may be accessed through the patient controller or with a HM II monitor, which continuously displays speed, power, flow, and pulsatility index (PI). The set speed is displayed in RPMs, with typical settings between 8600 and 9800 RPM (range, 6–15,000 RPM).[25,78,79] The power utilized by the pump is a directly measured parameter that, at typical RPM settings, normally spans 4–9 W (range, 0–25.5 W).[25,78,79] Power usage is increased by higher RPMs or with greater flow through the pump. Power increases >10–12 W at stable RPMs are concerning for the development of thrombus on the rotor causing an increase in drag.[79]

In contrast to these directly measured parameters, flow is calculated from RPM and power,[25,78] with higher RPMs and power resulting in higher displayed flows. Calculated flow tracks correctly with actual pump flow when changes in power are a result of adjustments to speed or shifts in the pressure differential, but will register erroneously high if an increase in power is actually due to thrombus on the rotor. Calculated flows are imprecise when <3 L/min.[25]

Pump flows should not be used as an absolute measure of the patient's cardiac output. At normal flows between 4 and 6 L/min, the displayed flow and the actual flow through the outflow graft as measured with an ultrasonic flow probe may differ by as much as 20% or up to 1 L/min.[80] Also, flow estimates alone will not capture total cardiac output if pump flow is in parallel with significant native circulation through the aortic valve. While the displayed flow may not be completely accurate, the trend can be useful; though imperfect, alterations in displayed flow may be easier to intuit than alterations in power when assessing a patient's condition.

Pulsatility Index. The PI is a dimensionless measure of pulsatile flow through the pump. It can be conceptualized as follows:

$$\frac{Q_{max} - Q_{min}}{Q_{avg}} \times 10$$

where Q_{max} is maximum pump flow, Q_{min} is minimum pump flow, and Q_{avg} is the average pump flow over a cardiac cycle,[20] though it is actually calculated by power pulses (highest W − lowest W divided by average W × 10).[78] The magnitude of these pulsations is measured and the PI is calculated, averaged over 15 seconds, and then displayed. The PI can range between 1 and 10, but typically spans 3–6 during clinical use.[25,81] A PI <3 generally warrants investigation.

As shown earlier in Figure 2B and C, the native heart contributes to pulsatile flow when the LV contracts and increases LV systolic pressure. Pulsatility is influenced by the magnitude of LVAD support compared with this native heart function. Relative increases in LVAD support or decreases in native heart contribution result in less pulsatile flow and decreased PIs.

For example, Figure 3 demonstrates the relationship between speed and PI. Augmentation of LVAD support from 8000 to 10,000 RPM results in a decrease in the pulsatility of pump flow (green waveform). The difference between

the maximum and minimum flow becomes attenuated resulting in smaller PIs. The lowest PI at 0.4 signifies the least pulsatile flow and is associated with the highest level of LVAD support. Decreased pulsatility can also occur at a stable RPM when drops in afterload promote greater LVAD unloading of the LV or when low LV preload (resulting in less Frank-Starling augmentation of contractility) results in a reduction in the generated LV systolic pressure.[25,26,81,82] In general, a low PI may be viewed as resulting from conditions that create a more decompressed LV.

The PI can be a useful parameter to follow in the perioperative setting. It should not be utilized as a sole dictate of management but can contribute to the overall picture provided by signs, symptoms, information from other monitors, and clinical context. Assuming no changes in RPM or intrinsic contractility, a decreased PI can signal 2 important pathological processes: low afterload or low LV preload.[22] Low afterload is associated with high pump flow/power, while low LV preload is associated with low pump flow/power; this is similar to non-LVAD patients who can be in a high output state from vasodilatory processes (eg, sepsis) or a low-flow state from a preload or cardiac etiology. As stated earlier, when low LV preload is suspected due to a low PI with low flow/power, differentiation between hypovolemia and RV failure is essential. As continuously displayed variables, the PI and flow/power can be monitored for changes and responses to treatment.[83,84] The differential diagnosis for a low PI assuming stable RPM is shown in Figure 4. Much of this algorithm overlaps with the approach to hypotension in the LVAD patient with the exception of a low PI induced by increased RPM, which generally increases flow and blood pressure.

Monitoring Pulse Oximeter

Depending on the RPM as well as the preload, afterload, and native contractility at a particular moment, the patient implanted with a CF LVAD may exhibit anywhere from minimal to significant pulsatility. Decreased pulsatility may affect the reliability of the pulse oximeter, which requires a change in blood volume adequate to differentiate the light absorbance of arterial blood from venous blood.[85] The use of a cerebral oximeter, which does not require a pulse and provides a regional measurement of venous-weighted oxyhemoglobin saturation,[86] has been reported both as an adjunct to the pulse oximeter[75,82,87,88] as well as a gauge of cardiac output.[89] Arterial blood gas analysis can be used to assess oxygenation when noninvasive modalities fail or are unavailable.

Monitoring Blood Pressure

The degree of pulsatility also affects the odds of successful noninvasive blood pressure (NIBP) cuff use in the CF LVAD patient. Bennett et al[90] assessed the performance of various NIBP modalities in patients with the HM II, and found that Doppler ultrasound was the most reliable technique with a 94% success rate. The NIBP was successful only 53% of the time but when obtained, was accurate when compared with arterial line systolic and mean pressure; notably, 41% of the time, only a single mean value was displayed.

Lanier et al[91] corroborated these findings by showing success rates of 100%, 63%, and 91% with Doppler, NIBP, and the Terumo Elemano BP monitor (Terumo Medical Corporation, Somerset, NJ), a slow-deflation double cuff that is able to detect blood pressure in patients with a reduced pulse pressure; interestingly, they found that a 9 mm Hg increase in arterial line pulse pressure correlated with a 300% increase in the odds of NIBP success. These measurements all showed strong correlation with arterial line blood pressures. Lanier et al[91] also found that Doppler correlated more closely with systolic blood pressure (SBP) rather than MAP, particularly in pulsatile patients; in patients with diminished pulsatility, Doppler measurements of SBP tended to be more similar to MAP due to the small pulse pressure. Interpretation of Doppler-derived measurements must be done with care given the potential for mistaking SBP for MAP in the pulsatile patient.

Several studies have found the intraoperative use of the NIBP to be sufficiently reliable as the sole source of blood pressure monitoring,[14] particularly in 1 series of 68 endoscopies.[70] Arterial line utilization rates of 0%–72% have been reported[11,12,14,70,71,75] and reports of decreased usage over time[24,47] are also suggestive of the success of various centers

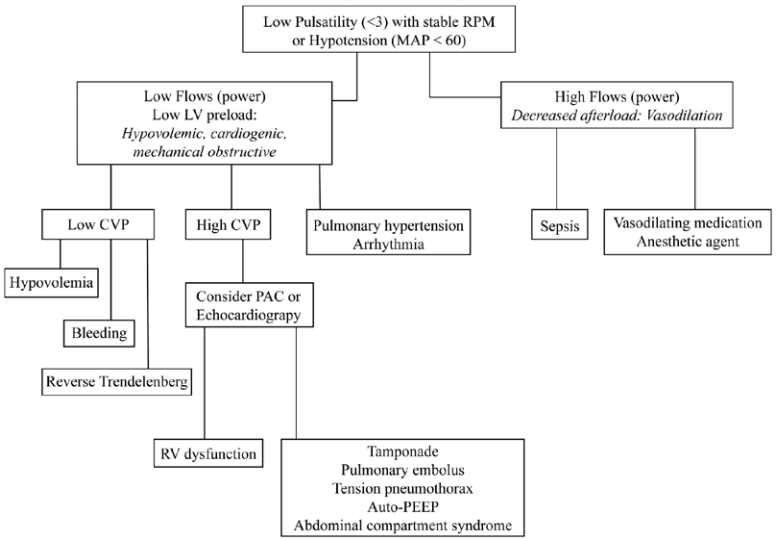

Figure 4. The differential for low PIs in the setting of stable RPMs. This algorithm also represents the approach to hypotension in the patient with a continuous-flow LVAD. Adapted from Feldman et al.[69] The differential for high PIs (not shown) depends on the presence of low flow/power (increased afterload, decreased speed) or high flow/power (increased myocardial contractility from recovery, inotropes or exercise[22] or greater LV filling resulting in Frank-Starling augmentation of contractility[81]). CVP indicates central venous pressure; LV, left ventricle; LVAD, left ventricular assist device; MAP, mean arterial pressure; PAC, pulmonary artery catheter; PEEP, positive end-expiratory pressure; PI, pulsatility index; RPM, revolutions per minute; RV, right ventricle.

in using the NIBP in CF LVAD patients. Mathis et al[24] found a decrease in arterial line usage from 31% to 16%, but also found that 55% of patients undergoing noncardiac surgery demonstrated monitoring gaps >20 minutes.

It appears that the NIBP may be successfully used in the CF LVAD patient; its use should be seriously considered, particularly in BTT patients in whom repeat surgery is anticipated, as these patients may benefit from minimizing arterial cannulations, which can lead to scarring and subsequent difficulty of access. However, depending on the surgery and the patient, arterial monitoring may be of greater benefit than risk, particularly given the possibility of decreased organ reserve and greater sensitivity to hypotension in the CF LVAD patient as well as the potential for fluctuations in pulsatility that may result in the erratic performance of noninvasive monitors. Furthermore, intraprocedural placement of an arterial line may be challenging if the absence of a palpable pulse requires ultrasound or Doppler for localization of an arterial vessel.

Hemodynamic Goals and Assessment of Pulsatility

The intraoperative management of the CF LVAD patient undergoing noncardiac surgery should focus on maintaining afterload (MAP 70–90 mm Hg), providing adequate preload and incorporating strategies to prevent iatrogenic strain on the right heart. In addition, the patient's pulsatility should be monitored. The CF LVAD patient will likely exhibit dynamic changes in their PI during the normal course of an anesthetic due to events such as medication boluses and surgical stimulation. However, significant losses of pulsatility (PI <3) that are sustained and unexplained should be noted, as treatment for detrimental changes in afterload, preload, or right heart function may be required. The baseline pulsatility should be taken into consideration, as some patients with chronic RV dysfunction may reside at a low PI. Decreases in pulsatility may be accompanied by loss of fidelity of the pulse oximeter or decreased success of the NIBP; conversely, monitoring reliability may be restored with maneuvers that restore pulsatility. Cerebral oximetry can provide supplementary data during brief periods of diminished pulsatility.

Iatrogenic RV strain should be avoided by minimizing PVR. Spontaneous ventilation attenuates PVR so long as hypoxia and significant hypercarbia are limited. When positive pressure ventilation is required, ventilator settings should be optimized to avoid high tidal volumes and high positive end-expiratory pressure, although some positive end-expiratory pressure may be required to prevent atelectasis, which also increases PVR.[73,92] The risk of RV distension can be minimized by avoiding overaggressive fluid resuscitation in the patient who is not volume responsive and is without preload-recruitable RV cardiac output.[73,74]

RV failure is most directly diagnosed via TEE, but can be inferred by a high CVP coupled with a low PI with low flow/power and signs of shock such as hypotension or escalating pressor requirements, low cardiac output, low Svo_2, and lactate production. Treatment may require pulmonary vasodilation by nitric oxide or prostaglandin therapy; inotropic support with milrinone, dobutamine, or epinephrine; vasopressor therapy to prevent right ventricular ischemia; and control of RV overload.[73] In several studies, intraoperative use of vasoactive medications beyond phenylephrine appears rare,[24,70,71] suggesting that RV failure may be an uncommon cause of low LV preload.

Other Perioperative Issues

The role of von Willebrand factor repletion in the setting of significant bleeding has not been clarified. It is unclear whether endogenous release by desmopressin or exogenous repletion by Humate P (von Willebrand factor/factor VIII concentrate; CSL Behring, Melbourne, Australia) or Wilfactin (von Willebrand factor concentrate; LFB Group, Les Ulis, France) would be effective in these patients who likely have ongoing degradation of HMWMs. However, there are, intriguingly, case reports of patients with refractory GIBs who were successfully treated with these agents without thrombotic complications.[93–95] The reported rate of desmopressin usage is quite low at 0.3%.[24]

Intraoperative malignant arrhythmias are uncommon, occurring in 1.2% of patients.[24] In addition to evaluating for general precipitating factors (electrolyte derangements, inotropic medication, etc), the possibility of a suction event as a cause should be considered. Management can be pharmacologic or by external cardioversion or defibrillation.

Device failure is a rare but disastrous complication of LVAD therapy with an intraoperative occurrence reported at 0.1%.[24] Unless the patient has recovered myocardial function, a pump stop may require pharmacologic temporization of acute unstable heart failure with vasopressors and inotropes until definitive surgical therapy can be achieved. Treatment will likely be complicated by retrograde flow through the device, similar to AI, at rates of 1–2 L/min due to the lack of valves.[25]

The occurrence of hemodynamically unstable events may require advanced cardiac life support, whose execution may be complicated by lack of a detectable pulse. Manufacturer guidelines state that the use of chest compressions is concerning for dislodgement of LVAD cannulae but that clinical judgment should be used in deciding whether or not to initiate them.[79] A recent consensus statement from the American Heart Association asserted that withholding compressions may cause more harm than the potential to dislodge the device in patients in circulatory failure (defined as MAP <50 mm Hg and/or intubated end-tidal CO_2 <20 mm Hg in the unresponsive or altered LVAD patient[29]).

HEARTMATE III

The HeartMate III (HM III; St Jude Medical, St Paul, MN) is a third-generation CF LVAD[17,96] that is emerging in prominence in Europe, where it is already approved for BTT and DT (2015), as well as in the United States, where it is currently undergoing evaluation in the MOMENTUM 3 trial. The interpretation of the PI in the HM III has not yet been established (D. Abate, personal communication; St Jude Medical, St Paul, MN). Unique characteristics of the HM III include full magnetic levitation (rather than mechanical contact bearings) and wide flow gaps, which not only minimize friction and stasis but also allow for the sharp speed changes that produce an artificial pulse every 2 seconds (2000 RPM decrease for 0.15 seconds, 4000 RPM increase for 0.2 seconds then a return to set speed).[97,98] It remains to be seen whether these design elements will preserve HMWMs

by reducing shear stress, decrease thrombosis due to better blood flow around the impeller, and mitigate the risk of GIB and AI with induced pulsatility.

CONCLUSIONS

The use of durable, implantable CF LVADs for the treatment of refractory end-stage heart failure is rising. As such, anesthesiologists must continue to cultivate their working knowledge of the altered physiology of these patients. Challenges in the care of these patients include management of afterload sensitivity and preload dependency, nonpulsatility and its effect on the reliability of noninvasive monitoring, altered coagulation, assessment of the risk of intraoperative bleeding and thrombosis, and decisions regarding the need for invasive monitoring.

ACKNOWLEDGMENTS

The author thanks David Abate (St Jude Medical) and David Chung for their assistance.

DISCLOSURES

Name: Mabel Chung, MD.
Contribution: This author helped design, prepare, and review the manuscript.
This manuscript was handled by: W. Scott Beattie, PhD, MD, FRCPC.

REFERENCES

1. Ambrosy AP, Fonarow GC, Butler J, et al. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. *J Am Coll Cardiol*. 2014;63:1123–1133.
2. Dickstein K, Cohen-Solal A, Filippatos G, et al; ESC Committee for Practice Guidelines (CPG). ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the task force for the diagnosis and treatment of acute and chronic heart failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). *Eur J Heart Fail*. 2008;10:933–989.
3. Benjamin EJ, Blaha MJ, Chiuve SE, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2017 update: a report from the American Heart Association. *Circulation*. 2017;135:e146–e603.
4. Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the international society for heart and lung transplantation: thirty-second official adult heart transplantation report—2015; focus theme: early graft failure. *J Heart Lung Transplant*. 2015;34:1244–1254.
5. Peura JL, Colvin-Adams M, Francis GS, et al; American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology; Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Cardiovascular Disease in the Young; Council on Cardiovascular Nursing; Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia. Recommendations for the use of mechanical circulatory support: device strategies and patient selection: a scientific statement from the American Heart Association. *Circulation*. 2012;126:2648–2667.
6. Kirklin JK, Naftel DC, Kormos RL, et al. The fourth INTERMACS annual report: 4,000 implants and counting. *J Heart Lung Transplant*. 2012;31:117–126.
7. Kirklin JK, Naftel DC, Pagani FD, et al. Seventh INTERMACS annual report: 15,000 patients and counting. *J Heart Lung Transplant*. 2015;34:1495–1504.
8. Ahmed M, Le H, Aranda JM Jr, Klodell CT. Elective noncardiac surgery in patients with left ventricular assist devices. *J Card Surg*. 2012;27:639–642.
9. Arnaoutakis GJ, Bittle GJ, Allen JG, et al. General and acute care surgical procedures in patients with left ventricular assist devices. *World J Surg*. 2014;38:765–773.
10. Bhat G, Kumar S, Aggarwal A, et al. Experience with noncardiac surgery in destination therapy left ventricular assist devices patients. *ASAIO J*. 2012;58:396–401.
11. Barbara DW, Wetzel DR, Pulido JN, et al. The perioperative management of patients with left ventricular assist devices undergoing noncardiac surgery. *Mayo Clin Proc*. 2013;88:674–682.
12. Morgan JA, Paone G, Nemeh HW, et al. Non-cardiac surgery in patients on long-term left ventricular assist device support. *J Heart Lung Transplant*. 2012;31:757–763.
13. McKellar SH, Morris DS, Mauermann WJ, Park SJ, Zietlow SP. Evolution of general surgical problems in patients with left ventricular assist devices. *Surgery*. 2012;152:896–902.
14. Nelson EW, Heinke T, Finley A, et al. Management of LVAD patients for noncardiac surgery: a single-institution study. *J Cardiothorac Vasc Anesth*. 2015;29:898–900.
15. Thoratec Corporation. HeartMate II Left Ventricular Assist System: Healthcare Professionals. Available at: http://heartmateii.com/. Accessed February 20, 2017.
16. HeartWare. HeartWare: Clinicians. Available at: https://www.heartware.com/clinicians. Accessed February 20, 2017.
17. Mancini D, Colombo PC. Left ventricular assist devices: a rapidly evolving alternative to transplant. *J Am Coll Cardiol*. 2015;65:2542–2555.
18. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med. 2009;361:2241–2251.
19. Sladen RN. New innovations in circulatory support with ventricular assist device and extracorporeal membrane oxygenation therapy. *Anesth Analg*. 2017;124:1071–1086.
20. Griffith BP, Kormos RL, Borovetz HS, et al. HeartMate II left ventricular assist system: from concept to first clinical use. *Ann Thorac Surg*. 2001;71(3 suppl):S116–S120.
21. Chung M, Sobol J, Sladen, RN. Ventricular Assist Device Classification and Basic Functional Mechanics. In: High K and Pulido JN, eds. *Mechanical Circulatory Support: Ventricular Assist devices (VADs) and Extracoporeal Membrane Oxygenation (ECMO):* A Society of Cardiovascular Anesthesiologists Monograph. Chicago, IL: Society of Cardiovascular Anesthesiologists; 2014:16–30.
22. Lim HS, Howell N, Ranasinghe A. The physiology of continuous-flow left ventricular assist devices. *J Card Fail*. 2017;23:169–180.
23. Khalil HA, Cohn WE, Metcalfe RW, Frazier OH. Preload sensitivity of the Jarvik 2000 and HeartMate II left ventricular assist devices. *ASAIO J*. 2008;54:245–248.
24. Mathis MR, Sathishkumar S, Kheterpal S, et al. Complications, risk factors, and staffing patterns for noncardiac surgery in patients with left ventricular assist devices. *Anesthesiology*. 2017;126:450–460.
25. Slaughter MS, Pagani FD, Rogers JG, et al; HeartMate II Clinical Investigators. Clinical management of continuous-flow left ventricular assist devices in advanced heart failure. *J Heart Lung Transplant*. 2010;29:S1–S39.
26. Wilson SR, Givertz MM, Stewart GC, Mudge GH Jr. Ventricular assist devices the challenges of outpatient management. *J Am Coll Cardiol*. 2009;54:1647–1659.
27. Vollkron M, Voitl P, Ta J, Wieselthaler G, Schima H. Suction events during left ventricular support and ventricular arrhythmias. *J Heart Lung Transplant*. 2007;26:819–825.
28. Nakahara S, Chien C, Gelow J, et al. Ventricular arrhythmias after left ventricular assist device. *Circ Arrhythm Electrophysiol*. 2013;6:648–654.
29. Peberdy MA, Gluck JA, Ornato JP, et al. Cardiopulmonary resuscitation in adults and children with mechanical circulatory support: a scientific statement from the American Heart Association. *Circulation*. 2017;135:e1115–e1134.
30. Demirozu ZT, Frazier OH. Aortic valve noncoronary cusp thrombosis after implantation of a nonpulsatile, continuous-flow pump. *Tex Heart Inst J*. 2012;39:618–620.
31. Shah S, Mehra MR, Couper GS, Desai AS. Continuous flow left ventricular assist device related aortic root thrombosis complicated by left main coronary artery occlusion. *J Heart Lung Transplant*. 2014;33:119–120.

32. Fried J, Han J, Naka Y, Jorde UP, Uriel N. Myocardial infarction after left ventricular assist device implantation: clinical course, role of aortic root thrombus, and outcomes. *J Heart Lung Transplant*. 2014;33:112–115.
33. Nakajima S, Seguchi O, Murata Y, et al. Left coronary artery occlusion caused by a large thrombus on the left coronary cusp in a patient with a continuous-flow ventricular assist device. *J Artif Organs*. 2014;17:197–201.
34. 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;27:1269–1274.
35. Pak SW, Uriel N, Takayama H, et al. Prevalence of de novo aortic insufficiency during long-term support with left ventricular assist devices. *J Heart Lung Transplant*. 2010;29:1172–1176.
36. Frazier OH. Unforeseen consequences of therapy with continuous-flow pumps. *Circ Heart Fail*. 2010;3:647–649.
37. Jorde UP, Uriel N, Nahumi N, et al. Prevalence, significance, and management of aortic insufficiency in continuous flow left ventricular assist device recipients. *Circ Heart Fail*. 2014;7:310–319.
38. Demirozu ZT, Radovancevic R, Hochman LF, et al. Arteriovenous malformation and gastrointestinal bleeding in patients with the HeartMate II left ventricular assist device. *J Heart Lung Transplant*. 2011;30:849–853.
39. Crow S, John R, Boyle A, et al. Gastrointestinal bleeding rates in recipients of nonpulsatile and pulsatile left ventricular assist devices. *J Thorac Cardiovasc Surg*. 2009;137:208–215.
40. Wever-Pinzon O, Selzman CH, Drakos SG, 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;6:517–526.
41. Boyle AJ, Russell SD, Teuteberg JJ, et al. Low thromboembolism and pump thrombosis with the HeartMate II left ventricular assist device: analysis of outpatient anti-coagulation. *J Heart Lung Transplant*. 2009;28:881–887.
42. Boyle AJ, Jorde UP, Sun B, et al; HeartMate II Clinical Investigators. Pre-operative risk factors of bleeding and stroke during left ventricular assist device support: an analysis of more than 900 HeartMate II outpatients. *J Am Coll Cardiol*. 2014;63:880–888.
43. Uriel N, Pak SW, Jorde UP, et al. Acquired von Willebrand syndrome after continuous-flow mechanical device support contributes to a high prevalence of bleeding during long-term support and at the time of transplantation. *J Am Coll Cardiol*. 2010;56:1207–1213.
44. Harvey L, Holley CT, John R. Gastrointestinal bleed after left ventricular assist device implantation: incidence, management, and prevention. *Ann Cardiothorac Surg*. 2014;3:475–479.
45. Morgan JA, Paone G, Nemeh HW, et al. Gastrointestinal bleeding with the HeartMate II left ventricular assist device. *J Heart Lung Transplant*. 2012;31:715–718.
46. Stern DR, Kazam J, Edwards P, et al. Increased incidence of gastrointestinal bleeding following implantation of the HeartMate II LVAD. *J Card Surg*. 2010;25:352–356.
47. Stone M, Hinchey J, Sattler C, Evans A. Trends in the management of patients with left ventricular assist devices presenting for noncardiac surgery: a 10-year institutional experience. *Semin Cardiothorac Vasc Anesth*. 2016;20:197–204.
48. Tsai HM, Sussman II, Nagel RL. Shear stress enhances the proteolysis of von Willebrand factor in normal plasma. *Blood*. 1994;83:2171–2179.
49. Dong JF. Cleavage of ultra-large von Willebrand factor by ADAMTS-13 under flow conditions. *J Thromb Haemost*. 2005;3:1710–1716.
50. Jilma-Stohlawetz P, Quehenberger P, Schima H, et al. Acquired von Willebrand factor deficiency caused by LVAD is ADAMTS-13 and platelet dependent. *Thromb Res*. 2016;137:196–201.
51. Bartoli CR, Restle DJ, Zhang DM, Acker MA, Atluri P. Pathologic von Willebrand factor degradation with a left ventricular assist device occurs via two distinct mechanisms: mechanical demolition and enzymatic cleavage. *J Thorac Cardiovasc Surg*. 2015;149:281–289.
52. Vincentelli A, Susen S, Le Tourneau T, et al. Acquired von Willebrand syndrome in aortic stenosis. *N Engl J Med*. 2003;349:343–349.
53. Meyer AL, Malehsa D, Bara C, et al. Acquired von Willebrand syndrome in patients with an axial flow left ventricular assist device. *Circ Heart Fail*. 2010;3:675–681.
54. Crow S, Milano C, Joyce L, et al. Comparative analysis of von Willebrand factor profiles in pulsatile and continuous left ventricular assist device recipients. *ASAIO J*. 2010;56:441–445.
55. Geisen U, Heilmann C, Beyersdorf F, et al. Non-surgical bleeding in patients with ventricular assist devices could be explained by acquired von Willebrand disease. *Eur J Cardiothorac Surg*. 2008;33:679–684.
56. Van Belle E, Rauch A, Vincentelli A, et al. Von Willebrand factor as a biological sensor of blood flow to monitor percutaneous aortic valve interventions. *Circ Res*. 2015;116:1193–1201.
57. Klovaite J, Gustafsson F, Mortensen SA, Sander K, Nielsen LB. Severely impaired von Willebrand factor-dependent platelet aggregation in patients with a continuous-flow left ventricular assist device (HeartMate II). *J Am Coll Cardiol*. 2009;53:2162–2167.
58. Meyer AL, Malehsa D, Budde U, Bara C, Haverich A, Strueber M. Acquired von Willebrand syndrome in patients with a centrifugal or axial continuous flow left ventricular assist device. *JACC Heart Fail*. 2014;2:141–145.
59. Birschmann I, Dittrich M, Eller T, et al. Ambient hemolysis and activation of coagulation is different between HeartMate II and HeartWare left ventricular assist devices. *J Heart Lung Transplant*. 2014;33:80–87.
60. Crow SS, Joyce DD. Are centrifugal ventricular assist devices the answer to reducing post-implantation gastrointestinal bleeding? *JACC Heart Fail*. 2014;2:146–147.
61. Kirklin JK, Naftel DC, Kormos RL, 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;33:12–22.
62. Starling RC, Moazami N, Silvestry SC, et al. Unexpected abrupt increase in left ventricular assist device thrombosis. *N Engl J Med*. 2014;370:33–40.
63. Mehra MR, Stewart GC, Uber PA. The vexing problem of thrombosis in long-term mechanical circulatory support. *J Heart Lung Transplant*. 2014;33:1–11.
64. Kirklin JK, Naftel DC, Pagani FD, et al. Pump thrombosis in the Thoratec HeartMate II device: an update analysis of the INTERMACS registry. *J Heart Lung Transplant*. 2015;34:1515–1526.
65. Maltais S, Kilic A, Nathan S, et al; PREVENT Study Investigators. PREVENtion of HeartMate II pump thrombosis through clinical management: the PREVENT multi-center study. *J Heart Lung Transplant*. 2017;36:1–12.
66. Uriel N, Han J, Morrison KA, et al. Device thrombosis in HeartMate II continuous-flow left ventricular assist devices: a multifactorial phenomenon. *J Heart Lung Transplant*. 2014;33:51–59.
67. Shah P, Mehta VM, Cowger JA, Aaronson KD, Pagani FD. Diagnosis of hemolysis and device thrombosis with lactate dehydrogenase during left ventricular assist device support. *J Heart Lung Transplant*. 2014;33:102–104.
68. Russell S, Slaughter M, Pagani F, Moore S, Idrissi K, Klodell C. HeartMate II LVAS: patient management guidelines. 2006. Available at: https://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4333b2-20-%209_4%20HM%20II%20Patient%20Management%20Guidelines.pdf. Accessed March 11, 2017.
69. Feldman D, Pamboukian SV, Teuteberg JJ, et al; International Society for Heart and Lung Transplantation. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant*. 2013;32:157–187.
70. Goudra BG, Singh PM. Anesthesia for gastrointestinal endoscopy in patients with left ventricular assist devices: initial experience with 68 procedures. *Ann Card Anaesth*. 2013;16:250–256.
71. Degnan M, Brodt J, Rodriguez-Blanco Y. Perioperative management of patients with left ventricular assist devices undergoing noncardiac surgery. *Ann Card Anaesth*. 2016;19:676–686.
72. Haddad F, Doyle R, Murphy DJ, Hunt SA. Right ventricular function in cardiovascular disease, part II: pathophysiology, clinical importance, and management of right ventricular failure. *Circulation*. 2008;117:1717–1731.

73. Fischer LG, Van Aken H, Bürkle H. Management of pulmonary hypertension: physiological and pharmacological considerations for anesthesiologists. *Anesth Analg*. 2003;96:1603–1616.
74. Haddad F, Couture P, Tousignant C, Denault AY. The right ventricle in cardiac surgery, a perioperative perspective: II. Pathophysiology, clinical importance, and management. *Anesth Analg*. 2009;108:422–433.
75. Sheu R, Joshi B, High K, Thinh Pham D, Ferreira R, Cobey F. Perioperative management of patients with left ventricular assist devices undergoing noncardiac procedures: a survey of current practices. *J Cardiothorac Vasc Anesth*. 2015;29:17–26.
76. Evans AS, Stone ME. A patient safety model for patients with ventricular assist devices undergoing noncardiac procedures. *Am J Med Qual*. 2014;29:173–174.
77. Thoratec Corporation. Resource library: HeartMate 14 Volt Li-Ion battery: instructions for use (103770.C). 2011. Available at: http://www.thoratec.com/_assets/download-tracker/HMII/103770/103770_C_14V-Battery-ENGLISH.pdf. Accessed March 26, 2017.
78. Lund LH, Gabrielsen A, Tirén L, Hallberg A, El Karlsson K, Eriksson MJ. Derived and displayed power consumption, flow, and pulsatility over a range of HeartMate II left ventricular assist device settings. *ASAIO J*. 2012;58:183–190.
79. Thoratec Corporation. HeartMate II LVAS left ventricular assist system operating manual. 2007:111. Available at: https://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4333b2-18-%209_2%20HM%20II%20Operating%20Manual.pdf. Accessed March 10, 2017.
80. Slaughter MS, Bartoli CR, Sobieski MA, et al. Intraoperative evaluation of the HeartMate II flow estimator. *J Heart Lung Transplant*. 2009;28:39–43.
81. Thunberg CA, Gaitan BD, Arabia FA, Cole DJ, Grigore AM. Ventricular assist devices today and tomorrow. *J Cardiothorac Vasc Anesth*. 2010;24:656–680.
82. Ficke DJ, Lee J, Chaney MA, Bas H, Vidal-Melo MF, Stone ME. Case 6-2010: noncardiac surgery in patients with a left ventricular assist device. *J Cardiothorac Vasc Anesth*. 2010;24:1002–1009.
83. Chacon MM, Hattrup EA, Shillcutt SK. Perioperative management of two patients with left ventricular assist devices presenting for noncardiac surgery in the prone position. *A A Case Rep*. 2014;2:70–73.
84. Khemees TA, Shabsigh A. Feasibility of robotic-assisted laparoscopic nephroureterectomy in left ventricular assist device patient. *Case Rep Urol*. 2012;2012:282680.
85. Chan ED, Chan MM, Chan MM. Pulse oximetry: understanding its basic principles facilitates appreciation of its limitations. *Respir Med*. 2013;107:789–799.
86. Bickler P, Feiner J, Rollins M, Meng L. Tissue oximetry and clinical outcomes. *Anesth Analg*. 2017;124:72–82.
87. Oleyar M, Stone M, Neustein SM. Perioperative management of a patient with a nonpulsatile left ventricular-assist device presenting for noncardiac surgery. *J Cardiothorac Vasc Anesth*. 2010;24:820–823.
88. Slininger KA, Haddadin AS, Mangi AA. Perioperative management of patients with left ventricular assist devices undergoing noncardiac surgery. *J Cardiothorac Vasc Anesth*. 2013;27:752–759.
89. Argiriadou H, Anastasiadis K, Antonitsis P, et al. Use of cerebral oximetry for monitoring cardiac output during off-pump implantation of Jarvik 2000 left ventricular assist device. *Artif Organs*. 2010;34:267–271.
90. Bennett MK, Roberts CA, Dordunoo D, Shah A, Russell SD. Ideal methodology to assess systemic blood pressure in patients with continuous-flow left ventricular assist devices. *J Heart Lung Transplant*. 2010;29:593–594.
91. Lanier GM, Orlanes K, Hayashi Y, et al. Validity and reliability of a novel slow cuff-deflation system for noninvasive blood pressure monitoring in patients with continuous-flow left ventricular assist device. *Circ Heart Fail*. 2013;6:1005–1012.
92. Haddad F, Couture P, Tousignant C, Denault AY. The right ventricle in cardiac surgery, a perioperative perspective: I. Anatomy, physiology, and assessment. *Anesth Analg*. 2009;108:407–421.
93. Hollis IB, Chen SL, Chang PP, Katz JN. Inhaled desmopressin for refractory gastrointestinal bleeding in a patient with a HeartMate II (R) left ventricular assist device. *ASAIO J*. 2016;63:e47–e49.
94. Cushing M, Kawaguchi K, Friedman KD, Mark T. Factor VIII/von Willebrand factor concentrate therapy for ventricular assist device-associated acquired von Willebrand disease. *Transfusion*. 2012;52:1535–1541.
95. Fischer Q, Huisse MG, Voiriot G, et al. Von Willebrand factor, a versatile player in gastrointestinal bleeding in left ventricular assist device recipients? *Transfusion*. 2015;55:51–54.
96. Farrar DJ, Bourque K, Dague CP, Cotter CJ, Poirier VL. Design features, developmental status, and experimental results with the HeartMate III centrifugal left ventricular assist system with a magnetically levitated rotor. *ASAIO J*. 2007;53:310–315.
97. Bourque K, Cotter C, Dague C, et al. Design rationale and preclinical evaluation of the HeartMate 3 left ventricular assist system for hemocompatibility. *ASAIO J*. 2016;62:375–383.
98. Pagani FD. Continuous-flow rotary left ventricular assist devices with "3rd generation" design. *Semin Thorac Cardiovasc Surg*. 2008;20:255–263.