A Guide to Mechanical Circulatory Support

A Primer for Ventricular Assist Device (VAD) Clinicians

Scott Stewart
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Foreword

A Guide to Mechanical Circulatory Support: A Primer for Ventricular Assist Device (VAD) Clinicians chronicles the 60-year journey of ventricular assist device (VAD) therapy from the VAD clinician perspective. This guide shepherds VAD clinicians from understanding the pump design, to the care of these complex patients, through information regarding the necessary elements for a sustainable, successful program. The purpose of the book is to provide foundational education for VAD clinicians to ensure a standardized threshold of knowledge exists. The introduction is intended to provide context to this journey and bridge the chapters.

Evolution of Pump Design: Disruptive Changes in the Course of AHF Care

Heart disease remains the leading cause of death worldwide. Advanced heart failure (AHF) carries a poor prognosis and prior to VAD therapy and heart transplantation, there were no options for the treatment of AHF. Patient management focused on palliation of symptoms during the end stage of the disease.

In **1954**, Dr. Walton Lillehei, desperate to surgically correct a congenital anomaly incompatible with life, used a "biologic" oxygenator (the baby's father), so he could cross clamp the baby's heart. Lillehei's solution, albeit creative and hemocompatible, carried the unacceptable risk of a 200% mortality rate as both infant and parent were vulnerable to poor outcomes. The invention of the heart-lung bypass machine in the 1950s opened up the path to surgical interventions for cardiac structural abnormalities including coronary bypass surgery.

In the **1960s**, pioneers in the field considered heart replacement options, heart transplant, and mechanical support. In the **1970s**, the National Institutes of Health appropriated funding to research mechanical heart pump designs. VAD therapy became the disruptive (course changing) technology, creating options for patients dying of AHF by improving survival and quality of life. The advent of effective immunosuppression in the **1980s** made organ transplant the gold standard for end-stage heart failure with survival rates superior to VAD support. The limitation of heart transplant is donor availability. The advantage of VAD therapy is pump supply is theoretically unlimited, and it is immediately available off-the-shelf.

In the **1980–1990s**, pump designs created pulsatile flow to mimic the beating of the human heart. In order to create pulsatility, these large pumps were designed with chambers that would fill and empty rhythmically, via volume displacement, causing forward blood flow. The internal components were in constant contact leading to wear and tear issues and eventual pump failure. The size and durability of the pump limited wide-scale use of these volume displacement systems. This mandated a new pump design but required abandoning pulsatility.

In the **2000s**, smaller, more durable pumps created a second disruption in the trajectory of the evaluation of pump designs catapulting VAD care into the continuous flow (CF) era. Patients with a small body habitus became candidates for implantation and patients on CF pumps can survive for years. The implication of the CF era means we are caring for a rapidly growing patient population living longer, victims of our own success. Pediatric patients are also candidates for durable mechanical support. Age-specific concerns must be addressed by clinicians at pediatric implanting hospitals. Returning to school can be fraught with anxiety over body image issues and adaptation to VAD equipment.

Program Structure: Impacted by Research and Regulations

Arguably as important as mechanical design advances to the evolution of VAD care, regulatory bodies such as the Food and Drug Administration (FDA), European Medicines Agency (EMU), Centers for Medicare and Medicaid (CMS), and regulatory compliance companies such as The Joint Commission (TJC) and Det Norske Veritas (DNV) have played a role in defining programmatic structure. Regulatory approval of the devices, expansion of the indication to Destination Therapy (DT), and permission for discharge in the community, have had an impact on VAD programs, compelling VAD teams to operationalize these mandates into their model of care.

Program structure and processes must be compliant with regulatory standards in order to receive approval for implantation and therefore payment for equipment and services. Regulating bodies mandate that VAD programs design an education plan that defines the learning needs and expectations for every healthcare professional who provides care to ensure patient safety. As VAD volumes grow, the model of care (which clinician provides what care/service to patients) has to evolve. The standards and the growing VAD population inform the structure of VAD programs. This leads to programmatic model iterations: from caring for patients one at a time to (AHF) disease management; to program management; and now population management. Innovations in content and educational platforms have facilitated the dissemination of VAD education. This book is written during the unprecedented times inflicted by the pandemic. Quarantine invoked the use of internet tools for meetings and routine patient visits virtually. Internet tools have become a handy way to remotely educate internal and external stakeholders and likely to be vehicles for mass education moving forward.

Sophisticated clinical trial designs provided data on pump performance and appropriate indications for implantation. The Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (**REMATCH**) study represented a pivotal shift in the definition of equipoise by ensuring that patients randomized to the medical treatment arm received protocol-driven care. This protocol was the precursor for guideline-driven therapy for AHF. In **2001**, the FDA approved the results of the REMATCH trial and defined DT as an approved indication. This essentially established that VAD are used to treat heart failure, a paradigm shift away from limiting implants to patients on the transplant list. The Multicenter Study of MagLev™ Technology in Patient Undergoing Mechanical Circulatory Support Therapy with HeartMate 3™ (MOMENTUM) trial pushed this idea of using VADs to treat heart failure by changing indication-at-implant nomenclature to short-term and long-term support. Other clinical trials investigating the use and outcomes for the HeartMate II and HVAD enhanced the understanding of continuous flow management.

The DT indication permits non-transplant hospitals to implant VADs. This ushered in a change in landscape for the VAD community providing access to the therapy at an increasing number of facilities. To date, there are approximately 185 CMS certified VAD implanting hospitals in the United States.

Over the past several decades, computer databases fostered clinicians' ability to track outcomes through registries. Registries capture outcome data from large numbers of patients suffering from the same disease. Recognizing the need to describe the long-term outcomes of VAD patients post-market approval, the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) registry was established in **2005**. Examination of the data led to the conclusion that sicker patients at the time of implant have worse outcomes, quantifying the assumption VAD clinicians had long held true. INTERMACS profiles classify patients into one of seven acuity categories. INTERMACS profiles became a call to action to work with referring physicians to send patients for evaluation before patients are unsalvageable with mechanical circulatory support.

Team Composition and Patient Management: From Organic to Intentional

In the 1990s, VAD care was driven by the cardiac surgeons on postoperative surgical units with the goal of supporting patients until they were transplanted. Patients remained on VAD support in the hospital until a suitable donor was identified extending the length of stay for months. The FDA approved the Novacor and eXtended Vented Electric (XVE) pumps for use outside the hospital in September **1998**. This approval was a life changing relief for patients who disconnected from their homes and communities in the hospital and allowed them to be discharged. The FDA approval had significant implications for VAD programs requiring the team to expand the scope of services and engage new specialists to provide care in

multiple settings: hospitals, clinics, home, nursing facilities, dialysis centers, and prehospital emergency settings. Subspecialties such as Heart Failure Cardiologists and VAD Coordinators were born out of the need to ensure expert, safe care in these new care settings and for participation in formal clinical trials. Financial coordinators and social workers rapidly became essential to the VAD team to facilitate the transition from candidacy to home on support.

VAD clinicians must deliver care from evaluation for candidacy to end of support. Recognition that the team must support patients through this continuum of care informs the team on composition of members, education to roles and duties, assurance of continuity of care through transitions, and establishment of defined clinical practice guidelines. Administrative support and fiduciary stewardship of resources are essential elements of the viability of the program.

Patients endure a rigorous candidate selection process to ensure that an AHF therapy recommendation can be made that will likely result in a desired outcome. As previously stated, timing to implant is an important determinant of patient outcomes. Referral pathways, community education, and streamlined evaluation timetables will facilitate appropriate timing of implantation.

Empowering patient and caregivers to engage in decision-making and self-care is recognized as a key element in ensuring positive outcomes. It is incumbent on VAD teams to provide patient and caregiver education regarding the risks, benefits, alternatives, equipment management, and quality of life after implantation. VAD clinicians and patients must align care goals during the evaluation process to ensure that patients receive the therapy that achieves their quality and quantity of life goals. Applying adult learning theory and healthcare literacy principles to patient education and consent conversations will ensure their experience matches their expectation. A mismatch in expectations can lead to dissonance between patients and clinicians, and disappointment regarding their decision to go forward with VAD implantation. Patient satisfaction surveys and quality of life tools are utilized by programs to give patients a voice regarding their perceptions of the program and the therapy. Survey scores can be used to make changes at the program level and in the patient education materials.

VAD implant surgery has also evolved. The lateral thoracotomy implant technique is gaining acceptance in appropriately identified patients. This technique spares the patient from a full sternotomy which is beneficial, especially for transplant candidates who will have to have another sternotomy. The drive line exit site location is in the hands of the surgical team. A mutually agreed upon location with the patient improves the patient experience. Attention to the waistline and avoiding exit sites under adipose tissue folds can reduce the risk of infection at the site. Infection remains one of the Achilles heels of the therapy and VAD clinicians are responsible for creating a drive line exit site management plan in an effort to reduce complication burden. Surgical recovery includes successful extubation, mobilization, care and cleaning of surgical incisions, monitoring drain output, hemodynamic monitoring, right ventricular management, and monitoring for arrythmias including augmentation of pacemaker/implantable cardioverter defibrillator settings if present.

The heart failure syndrome affects every system in the body. VADs do not cure heart failure so meticulous patient management, focusing on right ventricular function, volume status, and afterload reduction is necessary to achieve optimal outcomes. Frailty is a consequence of aging and heart failure. Reversing the ravages of frailty requires adequate nutrition and exercise. The multidisciplinary approach to addressing comorbid conditions, nutrition, exercise, and heart failure improves outcomes.

As continuous flow physiology is not found in human nature, clinicians caring for this patient population must apply new principles of assessment and intervention. Vital signs are monitored with telemetry and dopplers to measure heart rate and mean arterial pressure. Caring for VAD patients requires expert understanding of the patient-pump interface and management of CF physiology. Monitoring VAD parameters at a frequency dictated by patients' acuity establishes trends that inform clinicians about pump filling and emptying: flow, power, pulsatile index, peak/trough. As the rotations per minute, speed of the pump, is equivalent to the dose of the therapy, optimization of the speed through routine echocardiograms will ensure adequate offloading of the left ventricle. Iatrogenic valvular complications such as aortic insufficiency (AI) compromise forward flow therefore determination of valve opening during the echocardiogram can assist clinicians in selecting a speed that creates forward flow and intermittent valve opening to reduce the risk of AI. Expertise in obtaining clear echocardiographic images is paramount to speed optimization and detection of structural distortions; therefore, the VAD team has expanded to include echographers. CF and the presence of the titanium pump cause complications unique to VAD support. With all the advances in pump design, hemocompatibility remains a design quest. Currently, the risk of clot formation in the pump is managed with traditional anticoagulation, warfarin with or without antiplatelet therapy. Surveillance for complications directly related to VAD support, with early recognition and treatment reduces the complication burden experienced by VAD patients. Equipment malfunction, bleeding, strokes, pump thrombosis, arrhythmias, right ventricular failure, and infection remain vexing complications.

As the majority of patients care for by VAD programs are outpatient, VAD teams must design a structured approach to managing transitions of care. Safe patient discharges include ensuring patients and caregivers are adequately trained and have a stable living situation. Access to power and phone utilities is mandatory. VAD clinics, equipped with dopplers and monitors, provide outpatient surveillance and support. Distribution of VAD equipment in the clinic must be well planned to include the creation of billing structure to ensure the program is reimbursed for the equipment. When patients live a long distance from the implanting hospital, VAD programs may engage local community providers to assess patients. This requires active engagement by the VAD team to train and communicate with local providers. VAD patients who choose to travel must make additional plans to ensure VAD equipment is packed safely and proper documents are provided to airport security. The VAD community pulls together to provide temporary, emergency care for

out-of-town patients when they are staying close to another implanting hospital. Programs in warmer climates may even serve a seasonal home bases for "snowbird" patients.

Multidisciplinary team members are mandated to provide community preparation to support pulseless, electrically dependent patients in the outpatient setting. Programs must intentionally partner with prehospital providers and outside nursing/dialysis facilities to ensure all clinicians respond appropriately to equipment alarms and patient emergencies. Anecdotal reports of the successful revival of VAD patients with chest compressions led to consensus recommendations for interventions during "cardiac" arrest. VAD clinicians are challenged with the duty to ensure first responders are educated to identify emergencies and proper decision-making regarding chest compressions.

VAD programs care for patients across the continuum and over the course of years. Social workers, psychologists, and supportive care/palliative care specialists are essential team members. Recognition of the importance of patient support at home and in the community to mitigate care burden and improve the quality of life on support are central to optimal outcomes. Psychological stressors can be intensified by critical illness so on-going assessment and interventions are essential. An unfortunate result of extending older VAD patients' lives is the evitability of age-related cognitive decline for both patients and their caregivers. Partnering with community resources, home health services, and long-term care facilities is an emerging focus for VAD programs as we care for patients for a longer duration of support.

In **2013**, CMS mandated that Palliative Care specialists be part of the VAD team and became a standard in TJC Disease-Specific Certification process. By definition, all patients implanted as DT will suffer life ending complications; therefore, the VAD will need to be deactivated. Explicitly defining patient stated goals of care and intentionally managing symptoms related to end-stage heart failure is important as care shifts from VAD support to comfort measures. Palliative care specialists are instrumental in the evaluation process, treating symptoms, and at end of life.

VAD Clinician Professional Development

The AHF/VAD community established several professional organizations to foster the exchange of innovations and educational support. Active participation in professional organizations enhances the positive impact VAD clinician can have and is one of the strongest ways clinicians advocate for patients.

- The International Society for Heart and Lung Transplant (ISHLT) was founded in 1981. ISHLT is a not-for-profit, multidisciplinary, professional organization dedicated to improving the care of patients with advanced heart or lung disease through transplantation, mechanical support, and innovative therapies via research, education, and advocacy.
- The International Consortium of Circulatory Assist Clinicians (**ICCAC**) is a professional mentoring organization of mechanical circulatory assist device

clinicians whose **mission** is to share information, educate, and support individuals in this field to achieve optimal outcomes for patients requiring mechanical circulatory. ICCAC was incorporated in 2007.

The role of the VAD clinician was created to fill the need to coordinate the care of VAD patients throughout the continuum of support. Passionate, committed, accomplished thought leaders in the VAD community have shaped this work into a recognized profession. This role is legitimized by the definition of "expert VAD clinician" through published works such as *A Guide to Mechanical Circulatory Support: A Primer for Ventricular Assist Device (VAD) Clinicians.* The future of the technology looks exciting so the possibilities for the development of the VAD clinician role are promising. Stay calm and pump on!

Washington, DC, USA Tonya Elliot

Acknowledgments

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We wish to dedicate this book to all the VAD coordinators and clinicians who have come before us to trailblaze the field of MCS. Their passion for the pursuit of mechanical treatment of heart failure, innovation, hours of effort, imagination beyond the possible, and relentless discovery has brought us to our current state of knowledge and skill. Perhaps through this compendium of brilliant clinicians we might inspire those who follow to continue innovating and paving the way in this clinical arena.

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Contents

Mechanical Circulatory Support: Evolution and History

Michael Sobieski and Joanne Chichetti

> The positive thinker sees the invisible, feels the intangible and achieves the impossible. (Anonymous)

Advanced heart failure (HF) is estimated to affect over 6.5 million people with 250,000 to 300,000 individuals failing medical management in the United States alone [1, 2]. While heart transplantation remains the gold standard for the treatment of advanced HF, organ availability continues to be the limiting factor for less than 3500 patients receiving this treatment option annually. Additionally, the number of patients dying while on the heart transplant waiting list now exceeds 10% [3, 4].

Advances in medical and surgical treatment options, including durable mechanical circulatory support (MCS) devices, have improved survival and quality of life for this select population. Specifically, the technical and clinical management advances made in the MCS devices arena have significantly altered the clinical paradigm. The current data from the Risk Assessment and Comparative Effectiveness Management in Ambulatory Heart Failure Patients (ROADMAP) study demonstrated a clinically and statistically significant survival benefit to patients being supported by current MCS therapy compared to medically managed patients with advanced HF symptoms (New York Heart Association class III or IV) [4]. Despite this encouraging information, the adverse event rate remained the limiting factor in the adoption of MCS therapy to a wider population. The ROADMAP study was terminated early due in part to the improved outcomes in the MCS arm [4].

The current focus of device design is targeted at improving the adverse event burden. Early MCS device adverse event priorities focused in durability (device

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end-of-life failures) and biocompatibility (heart/pump interface thrombosis), whereas second-generation device adverse event profiles have stroke and hemolysis as the main comorbidities associated with therapy.

History of Mechanical Circulatory Support

Since development of the first cardiopulmonary bypass machine (CPB) in 1953 (the Gibbon-IBM heart-lung machine) by Dr. John Gibbon, MCS devices have undergone significant refinements to size, weight, durability, implantability, and clinical outcomes [5]. Currently, the medical field credits many pioneers in the field including Lillehei, Kolff, DeBakey, Cooley, Bernhard, Kirkland, DeWall, Kantrowitz, Frazier, Portner, and Olsen to name a few. The first documented use of a ventricular assist device (VAD) was in 1963 by doctors Michael DeBakey and Domingo Liotta (Fig. 1), which consisted of a pulsatile displacement pump attached from the left atrium to the descending aorta, providing up to 2.5 L/min of augmented flow in a post cardiotomy patient [6–9]. The first total artificial heart (TAH) as a bridge to transplant (BTT) was performed in 1969 by Dr. Denton Cooley with the patient surviving 64 h on pulsatile MCS support until a suitable organ was identified [10]. These early successes with MCS therapy lead to the National Heart, Lung, and Blood Institute (NHLBI) guidelines (1975) for the development of left ventricular assist systems (LVAS). These guidelines established a number of goals including: support up to 10 L/min, durability of 2 years or longer, ease of use control system, reliability, and ability to adjust to various physiologic conditions. The NHLBI also established guidelines for minimizing adverse events specifically, minimizing the risk of hemolysis, thrombosis, clot formation, and device failure [11].

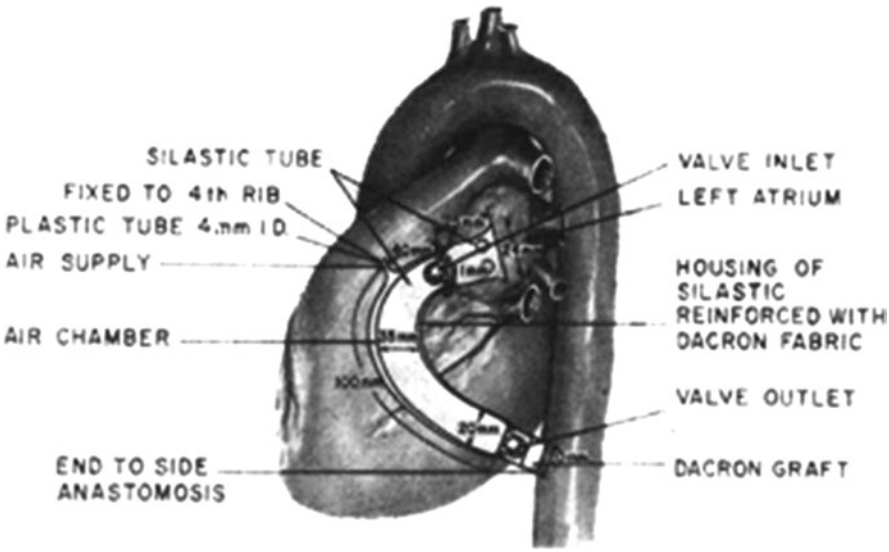

Fig. 1 Drs. Liotta and DeBakey first use of a VAD post cardiotomy

In 1982, Dr. William DeVries implanted the first TAH in a non-heart transplant candidate (destination therapy—DT) using the Jarvik [7] designed by Dr. William Kolff, with the patient surviving 112 days on MCS support [12].

The first successful implant of a left ventricular assist device was the Novacor LVAS (World Heart, Oakland, CA, Fig. 2) an electrically driven, pusher-plate designed to facilitate forward flow in a cyclic manor by allowing blood to enter and exit the device through bioprosthetic valves at the inlet/outlet of the device [13]. The first patient to be implanted with an LVAD and successfully discharged from the hospital did not occur until 1984, when Dr. O.H. Frazier implanted a vented-electric pulsatile device, HeartMate VE (Thermo Cardiosystems, Woburn, MA) [14, 15].

It was the culmination of 30 years of work, beginning in 1964 with the establishment of the NHLBI, to reach clinically relevant MCS systems implanted successfully in multiple patients. All of the first-generation LVADs were volume-displacement pumps designed to generate a pulse, with normal pulse pressures and mimic the systolic/diastolic cycle of the native heart. These systems included the Novacor LVAS [16], HeatMate IP/VE/XVE (TCI, Thoratec, Pleasanton, CA) [17, 18], Thoratec PVAD/IVAD (Thoratec, Pleasanton, CA) [19], and LionHeart LVAD (Arrow International, Reading, PA) [20]. These devices were large (weight up to 2.5 lb, displacement 900 cc) and required venting outside the body habitus, or a compliance chamber, and were subject to mechanical failures. The size of the device required a patient to have a body surface area (BSA) >1.8 m^2 to fit within the body. The most common adverse events were associated with bearing wear, valve dysfunction, or infection.

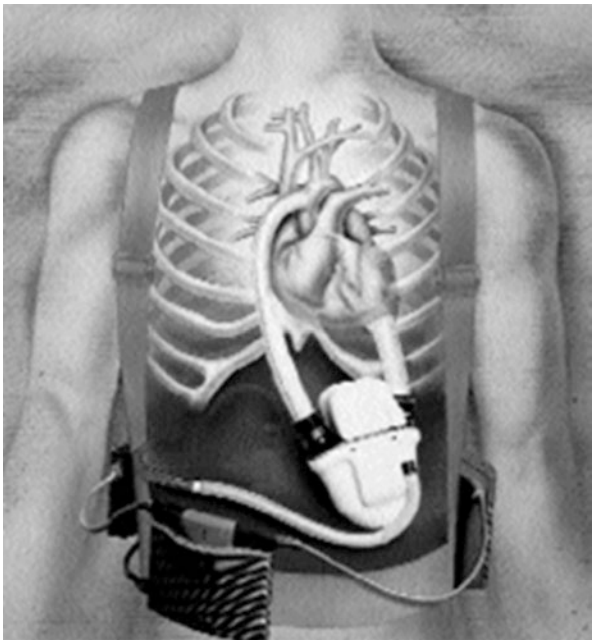

Fig. 2 Novacor LVAS circa 1983

First-generation devices were highly successful as demonstrated by the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart failure (REMATCH) trial [21]. In this trial, the authors determined the use of LVAD therapy provided a clinically meaningful survival benefit and improved the patients' quality of life. It also demonstrated the weaknesses of first-generation devices in noting the device group had a 2.35 times greater risk for serious adverse event (SAE) (Sepsis, LVAD failure or bleeding) compared to the medical therapy group. It was because of these SAEs investigators like Wampler, Dasse, and Larose pursued other device designs.

Overcoming Some of the Hurdles

To overcome these limitations with respect to size, durability, and energy requirement, the MCS field focused on device development of smaller, more reliable, continuous flow concepts. The main benefits of continuous flow technology include size reduction and reliability as fewer moving parts are subject to wear and tear for prolonged periods of time. The second-generation continuous flow devices (Figs. 3, 4, and 5) included the HeartMate II (Thoratec/Abbott Laboratories, Abbott Park, IL), DuraHeart LVAD (Terumo Heart, Ann Arbor, MI), MicroMed Debakey VAD (MicroMed Technology, Houston, TX), HVAD (Heartware/Medtronic, St. Paul, MN), HeartAssist 5 (ReliantHeart, Houston, TX), EvaHeart (Evaheart, Houston, TX), Jarvik 2000 (Jarvik Heart, New York, NY), VentriAssist (VentriCor, Sydney, Australia), and Levacor (WorldHeart, Salt Lake, UT).

"In the early 2000's Heartware team was developing the smallest, wearless LVAD. Being so different there were a lot of sceptics which made fundraising and life difficult.", states Jeff Larose. As key inventor of the Heartware HVAD he continues, "What I have learned from this is if you believe you are doing the right thing then humbly stand your ground and see it through." Device durability was greatly improved due to the smaller (<500 g) size and only one moving part (rotor or impeller). The continuous flow devices are either axial or centrifugal in design and do not provide a pulse, each is affected by preload and afterload for providing forward flow. Because they are valve-less they are susceptible to reverse flow under certain physiologic conditions.

The introduction and acceptance of second-generation LVAD therapy has led to a shift in adverse event profiles from device malfunction to stroke and thrombosis/hemolysis. The impellers on continuous flow devices require a high rotational speed (HeartMate II 7000–12,000 rpm; HVAD 1800–4000 rpm; Reliant Heart 5000–10,000 rpm; Micromed DeBakey 7500–12,000 rpm) to provide volume and pressure unloading of the left ventricle with pump flow of 5–6 L/min. The trade off in engineering design for reliability is a loss of physiologic performance; diminished or absent vascular pulsatility with potentially high sheer stress rates. It is hypothesized the diminished pulse pressure and high sheer stress rate may be associated with the differential adverse events seen with the second-generation LVADs. This was combatted in the adaptation of the "artificial pulse"

Fig. 3 HeartMate II

Fig. 4 Medtronic HVAD

associated with the HeartMate 3 (Abbott Labs, Lake Bluff, IL, Fig. 6). There has been a significant evolution and changes in the clinical paradigm over the past 68 years, and we are currently standing on the shoulders of the pioneers in MCS therapy to develop the future.

Fig. 5 Jarvik 2000

History of the VAD Coordinator Role

Fig. 6 Abbott HeartMate 3

"In the beginning" there were no VAD coordinators. The responsibility to assist in the management of this select population fell on the shoulders of dedicated medical professionals who already were working within the hospital setting; in the operating room, intensive care unit, physician's office, or the physicians themselves. The ventricular assist device (VAD) coordinator has evolved over the years to be an essential member of a complex interdisciplinary team and contributes greatly to the overall success of a VAD program. Coordinators vary widely in their clinical education, background, and include a broad spectrum of professionals; nurses, nurse practitioners (NP), physician assistants (PA), biomedical engineers, perfusionists, and in some smaller programs, physicians. Their position includes many areas of responsibility; clinical, educational, organizational, and regulatory responsibilities [22]. VAD coordinators have provided vital contributions in the areas of research and guideline decision-making development [23]. VAD coordinators provide continuity for the team, the patients, and their families and serve as the program link [22]. Coordinators are responsible for tailoring education to individual patients and their families, enabling out-of-hospital care and device management. This care involves day-to-day management of the device (dressing changes, documentation of vital signs, daily weights, and device settings), as well as troubleshooting any potential problems that may arise. Equally important to the safe transition home is the education of community resources such as police, fire, power companies, and emergency medical service (EMS) that may come in contact with the VAD patient when they are out in the community. The VAD coordinator organizes and presents education and maintains ongoing resources for these entities on a 24/7 bases. A well-designed and executed education plan will allow the VAD patient to integrate safely back into their community, maximizing long-term outcomes [24]. Coordinators oversee the ongoing physical, emotional, nutritional, and financial aspects of their patients and caregivers throughout the continuum of care [23].

As discussed earlier, VAD technology has advanced over the past six decades. During the 1980s and early 1990s, VAD coordinators were the "right hand" of the surgeons, seeing patients during the evaluation process, assisting in the operating room (OR) with device preparation and implantation, and delivering/coordinating post-operative treatment plans. Their experience in patient selection, management, education, data collection, and research have all led to the current success rate in 2-year survival. The VAD coordinator's major concerns pre-and post-implant included nutrition, early mobility, balancing bleeding versus thrombus formation, and infection control [25]. In early 1990s, the FDA approved the Implantable Pneumatic Left Ventricular Assist System (IP-LVAS) as the first VAD system for BTT [26, 24]. These patients were tethered to electrical or pneumatic cords connected to their pump and eventually to a console or controller, which limited their mobility. The VAD had a very large external driveline, and securing this was of major concern to prevent infection [25]. Patients needed to push their electrical consoles to allow them to ambulate. The console's internal battery lasted 30 min before it was needed to be placed back on AC electrical power (T. Buda, M.L. O'Hara, A. Sims, Personal communication, March 2021).

First-generation BTT VAD patients were not allowed to be discharged home prior to their transplant as the IP-LVAS was not FDA approved for hospital discharge. VAD

coordinators were responsible for the procedures required to maintain the proper function of the IP-LVAS throughout the day. This included "venting" the device periodically which stopped the pump for several seconds to replenish the air in the system and recalibrate the stroke sensor (T. Buda, M.L. O'Hara, A. Sims, Personal communication, March 2021). Patient survival was the primary clinical endpoint, and little attention was placed on the patient's quality of life (QOL) [27]. Initially, patients remained in the intensive care unit. With the evolution of the device and improvement of patient management, eventually, stable patients were transitioned to step-down "VAD-trained" telemetry units. Many of these patients were admitted to the hospital for several months, and some for greater than a year. During this time, it was not uncommon for an entire hospital unit to be dedicated to housing VAD patients waiting for heart transplants. The patients looked to each other and the VAD coordinators for support. The patients would develop their own support groups by playing cards, games, and watching movies to pass the time (T. Buda, M. Flannery, M.L. O'Hara, A. Sims, Personal communication, March 2021). Waiting for a suitable donor to be identified was often a long and frustrating ordeal and patients often required counseling from clinical social workers, and mental health providers (T. Martin, Personal communication, March 20, 2021).

In 1991 the Texas Heart Institute implanted the first battery-powered vented electric (VE) LVAD after Thermo Cardiosystems received approval from the US Federal Food and Drug Administration (FDA). The patient was a 33-year-old male with a history of dilated cardiomyopathy. He was implanted with the VE-LVAD on September 3, 1991, as BTT, and was supported for 16 months. The VAD clinical protocol restrictions required the patient to remain in the hospital awaiting his transplant. Due to the significant decrease in his QOL, in August 1992, following an 11-month hospital admission, the clinical protocol was amended to allow the patient to take day trips, which then advanced to overnight stays outside the hospital [15]. The use of battery power provided untethered independence for the patient and improved mobility. The VE-LVAD system required significantly less supervision or intervention from health care providers. The device functioned well, and the external battery life provided 5–8 h of power before needing to be changed [15]. This breakthrough was the first step to allow patients to be discharged home and led to significant improvements in patients' QOL [27].

The introduction of the VE-LVAD led to expansion of the coordinator's role and world of possibilities. The growing population of device-supported patients created a need for additional coordinators to manage the volume and complexity. The coordinator's role evolved and expanded to include completing comprehensive physical assessments, monitoring diagnostic test results, and providing intensive education to patients and their families. During this time many had dual roles as heart transplant coordinators which further expanded the role to include facilitating evaluations for VAD and transplant candidacy in addition to pump prep in the OR, and attending patient procedures outside the OR. At many centers, coordinators were required to stay with the VAD patient in the OR until the device was turned off and explanted at the time of transplant. Post-transplant the coordinators would then manage the patient collaborating with the surgical, medical, and transplant teams. During this early period, it was not uncommon to have a VAD team with only one

person in the role of VAD coordinator. Many of these coordinators worked well into the night, slept in the hospital, often working 24 h straight in supporting ICU staff, acting as a resource until the VAD patient became stable (T. Buda, M.L. O'Hara, T. Martin, A. Sims, Personal communication, March 2021).

With the introduction of second-generation devices, the advent of the home discharge became attainable. The resulting development and initiation of safe discharge protocols fell on the shoulders of the coordinators. In 1994, the HeartMate VE patient home discharge program was initiated. VAD patients were required to meet several strict criteria; surgical and medical stability, minimum hospital stay of at least 30 days post implant, and demonstration of a high level of independence and competence with minimal to no assistance from professional staff for any aspect of their activities of daily living and device care. One main support person was to be identified and trained along side the patient and both were required to pass this training course prior to discharge. This pre-discharge education was provided by and the responsibility of the VAD coordinator. Only after all the criteria were met was the patient allowed to participate in the release program [27]. As part of the release/discharge program, the patient and support person(s) were required to be (1) trained to manage the device, able to troubleshoot and solve basic device problems, and (2) certified in cardiopulmonary resuscitation. (3) The patient had to participate in five trips for less than or equal to 16 h. (4) Then they were required to participate in 3-day trips chaperoned in most cases by the coordinator. At discharge, the patient was provided immediate telephone access to the coordinator. The patient was required to reside within 2 h of travel time to the implanting center, and they needed to keep a written daily log. Patients were contacted by the coordinator at least twice a week [27].

In 1998 the HeartMate VE LVAS and the Novacor LVAS received FDA approval as BTT, allowing patients to be discharged home without being enrolled in a clinical trial. The FDA did not require any specific length of stay in the hospital post-implant and did not dictate patient education requirements [27]. As VAD patient discharges increased, so did the role of the VAD team and coordinators. The coordinator's role expanded to provide the primary care required for the clinical management and safety. Preparing for life outside the hospital setting required proper training to allow for a smooth transition, and improvement in the patients' QOL. The success of VAD therapy focused on adequate physical rehabilitation, the patient's ability to perform activities of daily living and self-care, evaluation of discharge into a safe environment, and outreach to community services and first responders. Long-term clinical management of VAD patients by the coordinator was and continues to be critical for successful outcomes. The VAD team members and VAD coordinators provided the continuity needed to assure positive outcomes [28].

In order to streamline the education process as the number of implants continued to double annually, in some high-volume hospitals, group patient education classes were held. Patients were required to pass a written test and practical return demonstration on emergency procedures. The coordinator's role expanded to include 24 h 7-day on-call telephone coverage for VAD patient emergencies. Patients were required to have 24 h 7-day caregiver availability in case of a VAD emergency. Community VAD education was also expanded. Coordinators would travel to the patient's community

to provide VAD education to hospital emergency departments, police, and fire departments as well as the patient's community physicians. Depending on the distance, some coordinators traveled out of state to perform their educational duties. They notified electric companies concerning the need for uninterrupted electrical power and performed home safety inspections, including checking electrical sockets to assure proper amperage and grounding to support the device (T. Buda, M. Flannery, M.L. O'Hara, T. Martin, A. Sims, Personal communication, March 2021).

In 2002, the FDA approved the HeartMate XVE LVAD as a permanent support device for patients ineligible for heart transplantation as destination therapy (DT) or permanent alternative cardiac support. This approval led to support for Medicare-approved national insurance coverage for use of the HeartMate XVE for DT. At the same time, Joint Commission (JC) initiated a dialogue with the Centers for Medicare and Medicaid Services to develop a disease-specific certification for DT VAD centers. This ultimately led to the implementation of standardized processes, best clinical practice guidelines, and evidence-based practice [29, 30]. Since the approval of the HeartMate XVE LVAD, technology has evolved into smaller devices that are simpler to surgically implant, more durable, reliable, and have improved patients' QOL. The first-generation complications of device failure have been significantly reduced by the introduction of second- and third-generation devices but bleeding, thrombosis, and infection remain a significant post-operative concern [28].

With the evolution of device designs, expansion of technology acceptance, and increased number of implants, VAD coordinators identified a need for the revision of standardization and protocols for the management of patients with mechanical circulatory support (T. Martin, Personal communication, March 20, 2021). In 2007, the incorporation of the International Consortium of Circulatory Assist Clinicians (ICCAC) began, expanding the community of VAD coordinators and mechanical circulatory assist device clinicians to collaborate at an international level. Their goal is the continuing improvement of care for patients with mechanical circulatory support through clinical protocols, research, interdisciplinary networking, and VAD coordinator certification (https://iccac.global/).

By the early 2000s, the volume of discharged patients significantly increased, and the various multiple types of devices led to coordinators identifying gaps in EMS first responder community training. A multicenter initiative led to the development of EMS field guides and quick reference cards. These guides assist EMS providers to respond appropriately when they encounter VAD patients. MyLVAD.com, a website created for the LVAD community posted these EMS guides on the website as a reference [31]. ICCAC and the EMS field guides are only two examples of the ongoing collaborating efforts of VAD coordinators and MCS clinicians.

In the future, remote monitoring of VAD pump parameter trends will allow VAD coordinators to manage patients using log files downloaded from a patient's device. These files would allow coordinators to identify pump malfunction, and other significant problems [22]. As VAD therapy continues to evolve, so will the scope of the VAD coordinator's role. The anticipation of the fully implantable left ventricular assist device (FILVAS) technology will require rigorous trials. Coordinators will need to change their patient education focus from external equipment management

and troubleshooting to the concept of completely implantable and wireless components (A. Sims, Personal communication, March 2021).

The Future

Currently, in development at the time of this publication, are a number of new and innovative pump designs with the potential to address the limitations of the current third-generation systems. These include: Medtronic (Heartware) MVAD and tMAVD, Oregon Heart TAH, CarMat TAH, Rienheart TAH, and NuHeart.

Kurt Dasse who has been instrumental in bringing a number of currently used clinical devices to the bedside states, "The past four decades have been associated with incredible breakthroughs to overcome the challenges facing mechanical circulatory support community. Breakthroughs including improved clinical management, hemocompatibility, wireless transcutaneous energy transfer, rotary blood pump technology, magnetic levitation, and wireless communication for analysis of pump performance have all led to improved survival and quality of life for patients supported with MCS devices." Although it has been a long haul, the field has greatly benefited from technological advances that required time and brilliance to develop. One can only imagine what the next four decades will bring, changing the lives for the better in patients with end-stage heart and lung disease.

> Imagination will often carry us to worlds that never were. But without it we go nowhere. (Carl Sagan)

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Pump Design and Mechanics

Kathy Princer

Pump Design and Mechanics

Ventricular assist devices (VADs) can be categorized into two groups, pulsatile and non-pulsatile. While each group has several different devices from various manufacturers that fit into these two categories, they all follow many of the same characteristics of their respective groups. Pulsatile devices mimic the natural blood flow from the native heart, while non-pulsatile devices have a continuous flow that is like that of a garden hose. This chapter will examine the unique features of pulsatile and non-pulsatile devices, discuss some of the common features between both groups and share future design possibilities.

Pulsatile VAD Designs

The first-generation VADs were pulsatile in nature. Much like replicating a heart [1], the VAD generates its' own systolic and diastolic phases. These phases are independent of the patient's native heart but occur based on programming of the VAD. Some VADs are programmed to run at a fixed rate, pumping at whatever rate is programmed into the device, regardless of blood volume. Other VADs are programmed to run in an automatic mode, where the device enters systole once the VAD has reached a set volume threshold. Most automatic modes can revert to a fixed mode in the event of the loss of the sensing trigger.

Pulsatile VADs provide a pump stroke volume with each beat of the VAD. The pump output can be calculated by multiplying the VAD rate, measured in beats per minute by the stroke volume, measured in mL to calculate the VAD output as liters per minute.

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$$\text{VAD output}\left(\text{LPM}\right) = \text{VAD rate}\left(\text{BPM}\right) \times \text{Stroke volume}\left(\text{mL}\right)$$

The two main designs for pulsatile VADs involved a pusher plate technology and a blood sac or bladder technology. In both cases, a compliance chamber is needed within the pump to accommodate the displacement as the pump goes in and out of systole. With a pusher plate technology, the pusher plate can be moved through pneumatic actuation, as was seen with the Heartmate Pneumatic VAD or by an electrical motor, as used in the Heartmate XVE VAD. With a blood sac technology, such as the Thoratec pVAD or iVAD, a console generated compressed air to collapse the blood sac or bladder and applied a vacuum to fill the sac.

In both the pusher plate and blood sac designs, the VAD has an inflow and outflow valve within the pump. These valves ensure uni-directional flow [1]. The valves can be either tissue or mechanical. Tissue valves can have challenges with infection and degradation and mechanical valves can have issues with thrombus formation.

For pneumatic actuation, there must be an external driver or console that contains a compressor. The words console and driver can be used interchangeably. Many of the drivers for use within the hospital have more programming capabilities, so they may have more than one compressor. While many portable drivers that allow for use outside of the hospital may have only one compressor and fewer programming capabilities.

The pneumatic drivers require a programmed amount of time that is spent in systole. Some devices do this as a set time measured in milliseconds and some do it as a percentage of the whole pump cycle as measured as a percent systole. The remainder of the cycle will be spent in diastole. To control pneumatic actuation, the VAD console can be adjusted to exert a drive pressure to the blood sac of the pump. The amount of drive pressure will depend if the VAD is placed on the right side or the left side and the associated resistance (i.e., right-side PVR, left-side SVR). Drive pressure should be optimized to ensure that the blood is fully ejected from the pump to avoid risk of thromboembolism. However, care must be maintained to ensure the patient is not experiencing hemolysis due to too high of drive pressure. The VAD console may also be adjusted to control the amount of vacuum applied to fill the blood sac. The vacuum will create a negative pressure inside the blood sac to allow the blood sac to fill during pump diastole. Care must be used while the patient has an open chest as there may be a risk of pulling an air embolism into the pump through the suture lines.

With an electrical motor, the motor drives cams that push against the pusher plate. As it pushes against the pusher plate, the VAD ejects the blood. Once the blood has been ejected, the cams fall to a neutral position, waiting for the next cycle of blood to fill the pump (Fig. 1). In addition, a type of large-diameter percutaneous lead for venting air [2] is needed to dispel the compliance chamber which is on the motor side of the pump.

Fig. 1 Heartmate XVE

Cannulas and VAD Placements

Cannulas are tubes that attach the VAD to the heart. Cannula placement will depend on whether the device is being used on the right side, the left side, or bi-ventricularly. If the device is being used on the right side, the inflow cannula (inflow to the VAD) can be cannulated in the right atrium or the right ventricle. The outflow cannula (outflow from the VAD) will be placed into the pulmonary artery. For left-sided VADs, the inflow cannula can be placed into either the left atrium or left ventricle and the outflow cannula can be placed in the ascending or descending aorta. The VAD itself may be placed internally or externally (Figs. 2 and 3).

Handpump

Depending on the design of the pulsatile pump, there may be a handpump that can be used to manually pump the VAD in the event of a failure of the VAD or the external driver. The handpump allows the user to maintain circulation of the patient until the situation can be fixed [3]. When using the handpump it is important that the user

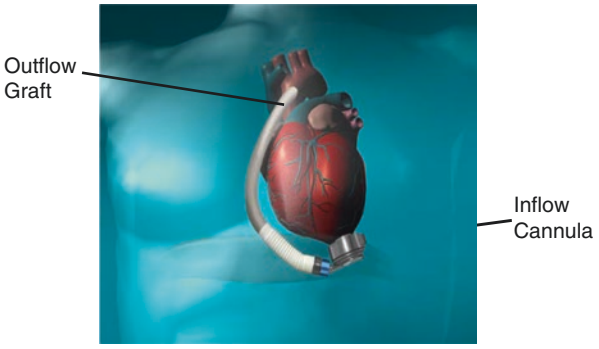

Fig. 2 Implant configuration-Heartmate 3

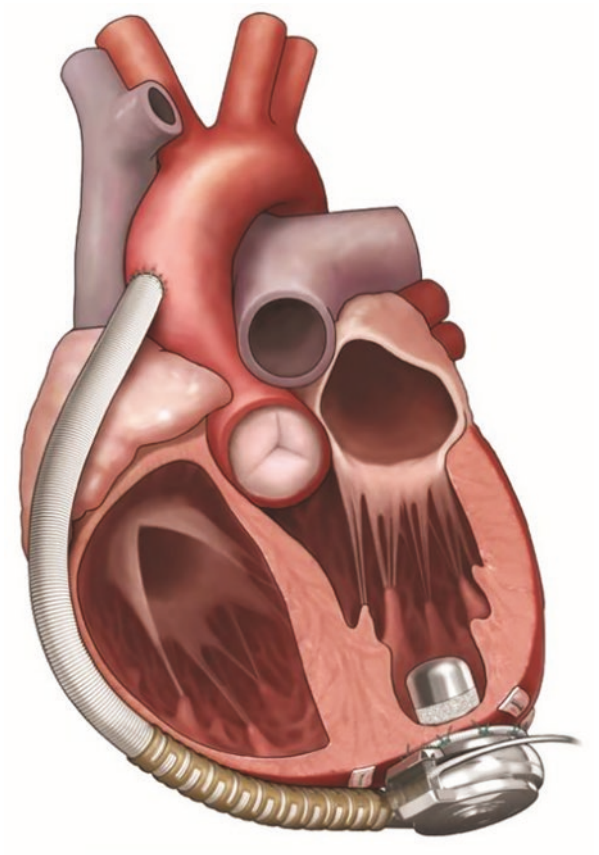

Fig. 3 Heartware HVAD pump and left ventricular cannulation

pumps it fast enough to ensure an adequate pump output for the patient, but not too fast that the VAD does not have enough time to fill.

Pulsatile Waveforms

Depending on the design of the VAD, there can be an opportunity to view waveforms that indicate the filling and emptying of the device. The goal is to have incomplete fill and complete ejection. Incomplete fill allows a mechanical device to have an artificial "stretch" that mimics the Starling law. By allowing room for an increase in blood volume during times of increased venous return, the pump can accommodate increases and fluctuations to this volume. Complete ejection is important to ensure that there are not stagnant areas of blood flow within the pump. These stagnant areas can lead to thrombus formation.

Non-Pulsatile VAD Designs

The design of pulsatile VADs reached a point where they could no longer be reduced in size due to the need for a compliance chamber. Size can be an area of concern as it restricts implants into smaller patients, including women and children. There were also mechanical complications associated with pulsatile devices, therefore the need to create smaller non-pulsatile pumps arose [2]. Clinical studies proved over time that patients could survive and achieve end-organ perfusion with the use of a non-pulsatile device [4]. Non-pulsatile devices no longer have a strong systolic and diastolic phase, rather the device has continuous forward flow. There can be increases and decreases in flow due to the systolic and diastolic contributions of the native heart. These contributions from the native heart create a change in flow through the VAD that can be seen on an arterial waveform that appears as a dampened systolic and diastolic wave with diminished pulse pressure.

Non-pulsatile VADs may also be called continuous flow VADs. These two terms can be used interchangeably. Due to the continuous flow characteristics of these pumps, there are no valves in the design of the pump. As the pump always has flow going through, the valves are not needed to control systolic and diastolic phases. However, since there are no valves, there is the possibility of retrograde flow. If the VAD is pumping and there is not too much afterload, there should be forward flow. But in the case of very high afterload and low flow conditions, the pressure gradient across the pump may be too high and prevent forward flow. Also, if the VAD stops pumping, since the aortic pressure is greater than the ventricular pressure, blood will flow from the aorta back to the ventricle. The concern is that this retrograde flow could back fill the left ventricle, flood the lungs and lead to further clinical decline. At the time of transplant, when the VAD is going to be stopped, it is important to put a cross-clamp on the outflow graft to prevent retrograde flow.

Non-pulsatile VADs can either be an axial, such as the Heartmate II or a centrifugal design, such as the Heartware HVAD or the Heartmate 3. An axial design

uses a rotor, a stator, and bearings. The rotor is designed to rotate, while the stator is designed to be stationary. The bearings are used to allow the rotor to be able to spin. These types of bearings are called mechanical or pivot bearings [5]. When selecting bearings, it is important that the bearing is designed to very tight specifications such that there are no knicks or crevasses that could lead to thrombus formation. Bearings also need to be made of a biomaterial that does not create heat, as heat also leads to thrombus formation. Typically, these bearings are made of jewels or ceramics. Axial flow technology moves the blood by pushing it out, like a propeller in a pipe [5].

Centrifugal flow uses a floating rotor called an impeller. All impellers are rotors, but not all rotors are impellers. Impellers is the term that is used in centrifugal pumps as it pulls the blood into the pump by sucking it in and throwing it out along the blades. The impeller can either be lifted on blood (hydrodynamic bearing), be suspended by magnetic force (electromagnetic/position sensor) or permanent magnets or a combination of any of these [5]. These types of bearings are designed for long life as there are no touching parts. When the impeller is designed it is important to that the gap for blood flow be great enough to prevent hemolysis and thrombus build up (Fig. 4).

Flow through non-pulsatile pumps can be measured through a mechanical flow probe. However, the challenge is that most flow probes only last for about 1–2 years. VADs need to last much longer than 1–2 years, especially in the Destination Therapy population. Therefore, many companies are not relying on the flow probe technology, but rather on creating algorithms that reliably estimate the flow through

Fig. 4 Heartware-open view of HVAD pump

the pump. The known measurements on a VAD are the speed of the pump (speed at which the rotor or impeller spin) and the power that the pump needs to deliver that speed. From these two known measures, the VAD estimates the other measurements.

For flow, it is a measure of the speed of the rotor and the power. Depending on the pump, there are different algorithms to calculate the flow. Some of the pumps also add a third parameter to the algorithm. The pump has the user input a hematocrit value into the monitor and this value is used to determine how viscous the blood is, which can affect the flow in relation to the speed and power. The hematocrit allows the algorithm to be more accurate. The user will find that for the same speed and power an increase in the hematocrit entry will make the flow decrease. Entering the hematocrit value into the monitor does not truly change the flow through the pump, it just helps the algorithm estimate the flow more accurately. Also, it is important for the user to remember that this hematocrit value that is entered is a static value, dependent on that moment of time. Therefore, if a patient has a change in clinical condition, such as bleeding or receiving a unit of blood, the hematocrit may clinically be changed in a patient and that change needs to be reflected in the monitor.

Non-pulsatile VADs have a way of monitoring the pulsatility of the native heart. Some VADs, like the Hearmate II and 3 do this through a measure called a Pulsatility Index (PI) and some, like the Heartware HVAD do this through a waveform with a peak, trough, and pulse pressure to measure how pulsatile the native heart is. If the pulsatility number or waveform is low, it can be indicative of several things such as hypovolemia, right heart failure, too high of a speed, arrhythmias, or poor native heart contractility.

HQ Curves

HQ curves are very helpful to understand and explain non-pulsatile pumps. The H represents the pressure gradient, also known as the pressure drop or pressure differential across the pump. This is the difference between the inflow and outflow of the pump and is measured by subtracting the left ventricular pressure from the aortic pressure. The Q represents the rate of blood flow through the VAD. HQ curves demonstrate that for a specific speed (RPM), flow decreases as the pressure gradient increases. These curves also show that for a specific pressure gradient, the flow increases as the speed increases [6]. Another concept for HQ curves is the head curve of the pump (Fig. 5).

Centrifugal pumps have a flatter head curve than axial pumps, this means that for centrifugal pumps they operate over a large range of flows for very small changes in the pressure differential across the pump [7]. Axial flow pumps have a much steeper head curve. These HQ curves are also important in the presence of low flow situations. A centrifugal pump, having a flatter head curve, will be less susceptible to suction events than an axial pump will be.

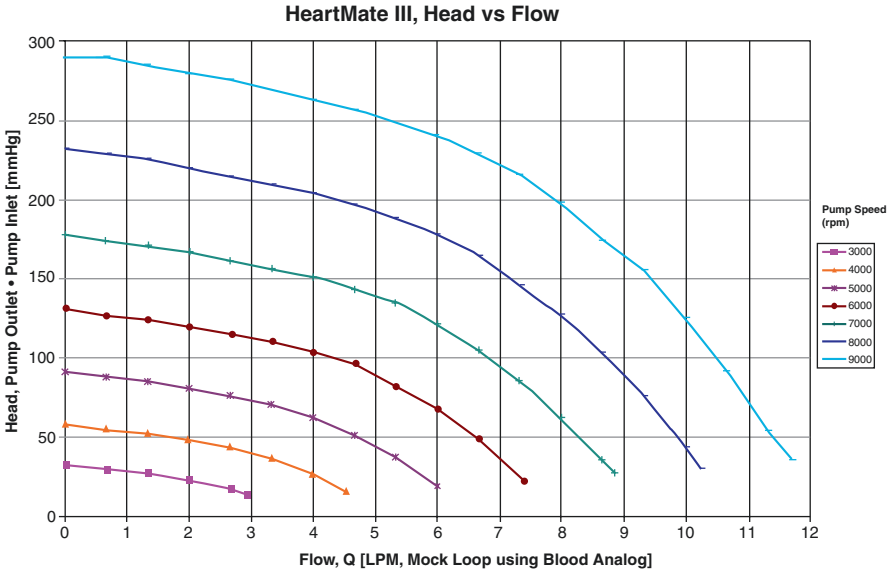

Fig. 5 Heartmate 3 HQ curves

Suction Events

Suction events can happen with either axial flow or centrifugal flow VADs. Suction events happen when the flow into the pump is too low, but the VAD continues to pull blood in. This can lead to the cavitation of the left ventricle onto the inflow conduit of the VAD. Axial flow VADs have a greater affinity to suction events at low flows than centrifugal VADs do [5]. Suction events can also lead to arrhythmias as the inflow touches the heart wall. Also, arrhythmias may lead to suction events as there will be a decrease in blood volume.

Artificial Pulse

Some of the VADs have an artificial pulse. Initially, this was thought to create more of a pulsatility for clinical care but was really determined to provide a better wash of the pump. Studying computational fluid dynamics, which is a mathematical model to examine fluid flow, it was found that an artificial pulse produces good washout because it creates rapid variations in the flow velocity in the pump [8]. It also increases turbulence which likely helps reduce thrombus also (Fig. 6).

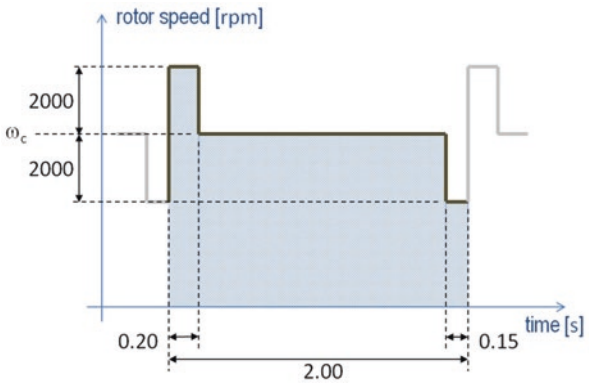

Fig. 6 Heartmate 3 artificial pulse

Non-Pulsatile Waveforms

Data can be downloaded from the patient's controller, typically through a monitor to either a thumb drive or other memory device. This data can then be sent to the company for further analysis. The company can inform the clinician as to any issues with power, the driveline, the controller, or the pump itself. They can also help determine if the mechanics are sound, but that there could be a clinical situation such as high afterload and hypovolemia.

Common Components for Pulsatile and Non-Pulsatile Devices

Percutaneous Lines

For pneumatic actuation, there is a pneumatic driveline that exits the body and connects to the pneumatic driver. Compressed air and vacuum travel through these drivelines to eject the blood sac. If the patient has both a right- and left-sided device these pneumatic drivelines are typically color-coded to indicate right and left sides. In addition, the drivelines are usually keyed in such a way that the right side cannot be connected to the left side of the driver and the left driveline cannot be connected to the right side. Due to the large difference in drive pressure needed to drive the right and left VADs, it is very important to not connect the left driveline to the right VAD and vice versa.

For electrical actuation, there is a driveline that exits the body of the patient and connects to a controller. Electricity is carried through this driveline to the motor inside of the VAD. Typically, there are redundant wires imbedded in the driveline, such that if one wire breaks, there are back-ups that can work. If the driveline has

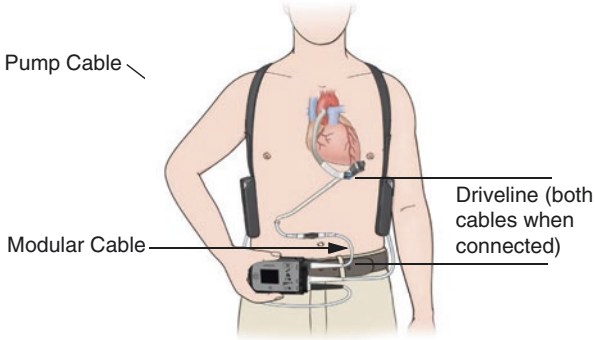

Fig. 7 Heartmate 3 modular cable/driveline

superficial cracks to the outer driveline, rescue tape can be applied to place a temporary fix to the driveline. Over time that rescue tape may need to be replaced or further repaired. If the driveline suffers significant damage or the wires are compromised enough to create an alarm, there are some devices, such as the Heartmate 3 that have a modular portion of the driveline that allows the user to replace the section of driveline that may be causing the problem (Fig. 7). If switching out the modular piece does not fix the problem, then the technical staff from the device company can come to the hospital to splice a new driveline onto the old one. The VAD will be stopped for a brief time, while the technician cuts the existing driveline and solders on a new driveline. If this repair does not work or if the damage is inside of the patient's body or near the skin, the patient may need a device exchange.

With drivelines, it is very important that during device implant and during controller exchanges the ends of the driveline stay clean. Residue that gets on the ends of the driveline can cause issues either immediately or over time.

Controllers

The patient will always wear a controller, attached to their driveline and powered by either AC or DC power. This controller is essentially the minicomputer that controls the speed of the pump, delivers the electricity to the driveline, and displays the VAD parameters. The controller has a "fuel gauge" to display how much power is currently available to the controller. The controller also displays and annunciates all alarms. Most controllers have a display that explains what the alarm is and how to troubleshoot it. Alarms are available for low or disconnected power sources, low clinical values such as low flow, controller fault, driveline issues, and any pump stoppage.

Some controllers have a back-up controller system built into the primary controller. Some controllers also have a locking mechanism that allows the controller to be locked onto the driveline. Care must be used when switching out the controller during troubleshooting, as once the controller is disconnected the VAD is no longer

Fig. 8 Heartmate 3 controller

Fig. 9 Heartware controller

running. Patients should always carry a back-up controller in case he/she needs to switch the controller out in an emergency (Figs. 8 and 9).

Power Sources

VADs will operate by either AC power or DC power. AC power typically comes from a bedside console that plugs into the wall and then connects to the VAD through a long power cable. Some of these consoles have a built-in back-up battery and some do not.

DC power can be through batteries or through an AC/DC converter such as an adaptor in a car. Most batteries are lithium-ion, however there are also some lead-acid batteries that can serve as a back-up power source in the AC power consoles. Care needs to be taken when shipping the lithium-ion batteries, as lithium-ion batteries are at risk for explosion. Also, the patient should never store the batteries in his/her car as they may not work after being exposed to very hot or very cold temperatures (Figs. 10 and 11).

The batteries have fuel gauges. These fuel gauges have two purposes, one is to tell the user how much charge is still in the battery while it is attached to the controller. However, most users look at the controller for this information. The second purpose is that the user can check the status of the extra batteries that they are carrying to determine which ones are fully charged and which ones are depleted. Patients should always carry extra batteries for when the batteries need to be switched out.

Some batteries have the connections to the controller molded into the battery assembly and some have an extra clip that must be attached to the battery to

Fig. 10 Heartmate 3 Battery Image

interface to the controller. These battery connections should be periodically cleaned according to device manufacturers to ensure good contact.

Battery Chargers

The batteries for the VAD will need to be recharged after use. The system will have a battery charger included in its' fleet of accessories. These battery chargers should be housed in a location that is easily accessible to the patient. The battery charger usually has a color system to indicate the charge status of each battery. Each battery charges independently of the others in the charger, such that one may be charging while another is already full. Some battery chargers "top off" the battery periodically. Some battery chargers also provide the ability to calibrate the battery by a process that fully discharges the battery and then fully recharges it (Fig. 12).

Monitors

Each VAD will have a monitor that allows the user to program settings for the controller or pump. Settings can include the speed, the low limit, the hematocrit, and

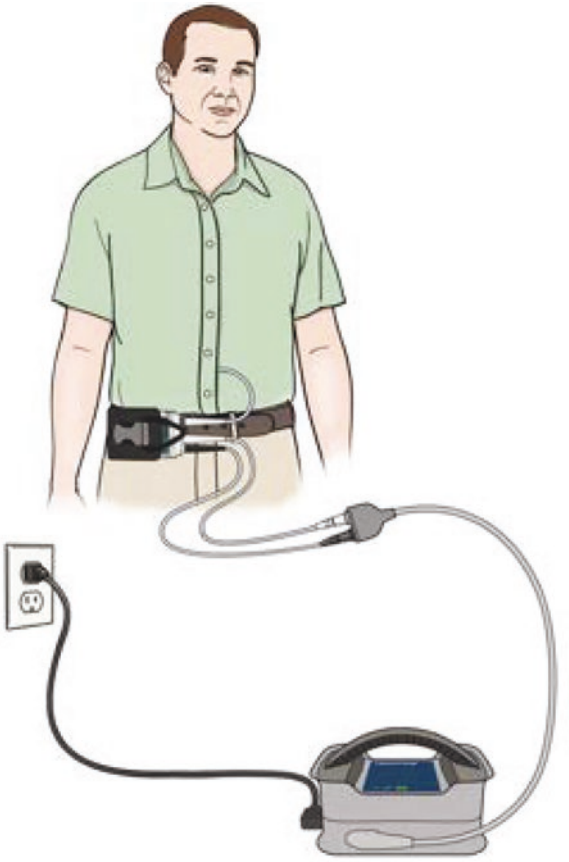

Fig. 11 Heartmate 3 Power Sources

Fig. 12 Heartware battery charger

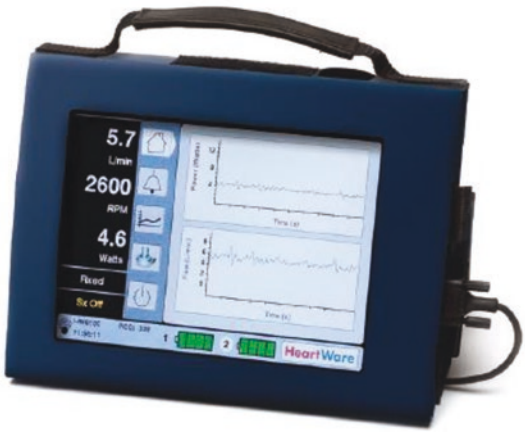

Fig. 13 Heartware monitor

alarm limits. Some monitors, such as the Heartware monitor, have password protection to some of the key screens for programming. This is a safety feature to protect settings from being accidentally changed (Fig. 13).

Blood Contacting Surfaces/Biomaterials

When designing VADs and VAD components, it is very important to acknowledge the human/mechanical interactions. The materials need to be conducive to being used in the body, including preventing thrombus build-up and heat generation.

An area of re-design involved the inflow cannula. Companies worked to determine the optimal shape, how deep into the ventricular cavity the inflow should go and if the inflow should be sintered or not. Sintering is a process where small titanium beads are attached to the titanium surface of the inflow cannula. These beads are designed to form a matrix for tissue to incorporate, thus limiting the growth of the tissue around the inflow cannula [9].

Outflow grafts are typically made of a woven polyester graft and are very commonly a graft that is already used in cardiac surgery. Some grafts need to be preclotted while in the surgical case and some come ready to be implanted. Some outflow grafts need to be connected to the outflow assembly while some come preassembled. It is always imperative to make sure that the user knows what type of graft is used for the specific VAD and what precautions and preparations must be in place. Use of quick reference guides and surgical checklists can help with surgical preparation before implant.

Many outflow grafts also have an outflow graft bend relief. Any kink in the outflow graft can appear as an increase in afterload to the VAD and can decrease flow through the VAD. If there is an outflow graft bend relief with the pump, it is highly encouraged to add it during the implant to prevent any kinks and to help avoid the outflow graft from twisting.

When designing VAD components and the pump, it is important that the parts that are designed can withstand the sterilization procedures necessary to ensure sterility.

FDA Monitoring

All VADs go through extensive testing with animal and clinical trials. After a device is approved by the Food and Drug Administration (FDA), the device is still monitored for ongoing issues. The FDA can require a VAD manufacturer to send device recalls or urgent medical device notifications to implanting hospitals. It is the role of the VAD team to follow the directions in these recalls and notifications, to keep the patient safe. For example, in June 2021 Medtronic sent an urgent medical device notification indicating that physicians should immediately stop new implants of the Heartware HVAD system. The VAD team needed to remove stock, inform stakeholders in the hospital and educate and ensure existing patients that they will continue to be supported. This is further discussed later in chapter "Regulatory Agencies Impacting Mechanical Circulatory Support Programs".

Future VAD Designs

In future designs of the VADs, one goal is to alleviate the need for any percutaneous lines. These lines can be potential sites for infection and can be damaged over time. Designs for transcutaneous energy transmission (TETs) will allow energy to be transferred across the skin to an internal coil. This coil will then provide power to the VAD [1].

In the future, there will likely be more sensors that are built into the pump. These sensors will likely measure the pressure drop across the pump. Sensors could also be added to measure inflow and outflow obstructions.

VADs will need to continue to improve over time to decrease the adverse events associated with this technology. Much attention will be given to improving the hemocompatability of the device as many adverse events are associated with the human/blood interface. While VADs have improved substantially over the years, progress still needs to be made to ensure this will continue to be a viable option for long-term care of end-stage heart failure patients.

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Mechanical Circulatory Support Indications and Patient Selection

Tiffany Buda and Karen Meehan

Introduction

Patients suffering from end-stage heart failure who are failing medical therapy should be considered for advanced therapies such as a heart transplant or placement of durable mechanical circulatory support (MCS) device to prolong life. Guidelines published by heart failure, transplant, and surgical societies have been developed to aid clinicians with determining patient candidacy for MCS placement. In addition to meeting the clinical criteria for durable MCS, adherence to reimbursement criteria established by government and commercial payers must be considered. This chapter will discuss the indications for durable MCS placement from the clinical as well as the reimbursement perspectives and patient selection criteria.

Indication for MCS

Intentions for Treatment

Durable MCS is considered for those patients with chronic end-stage systolic heart failure as well as those presenting with an acute event who likely will not survive without MCS. The indications for MCS are described by intention to treat and clinical criteria.

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Intention to treat indications include bridge to recovery (BTR), destination therapy (DT), bridge to candidacy (BTC), and bridge to transplant (BTT) [1–3]. Clinical factors define each indication and guide device selection [3].

The BTR indication includes patients presenting with an acute event (i.e., myocardial infarction, myocarditis) in cardiogenic shock failing medical management requiring escalation of care with a short-term MCS device. This indication allows time to assess for myocardial recovery or demonstrate the need for advanced therapies [1–3]. Evaluation for next-level therapies should be ongoing while monitoring for recovery.

Patients who are unable to be listed for transplant however meet the criteria for durable MCS are designated as DT candidates. This designation indicates patients will remain on durable MCS for the remainder of their life. BTT indication includes those patients that have been evaluated and listed for heart transplant at the time of device implant [3]. Patients with reversible contraindications to transplant (i.e., actively smoking, organ dysfunction) may be placed in the BTC indication as opposed to DT given the potential for transplant once the contraindication is resolved [3].

Further definition of the indications for MCS must include a discussion of the clinical criteria. The clinical criteria are outlined by both a regulatory and clinical perspective. The clinical criteria defined by regulatory bodies are connected to reimbursement and will be discussed first.

Reimbursement Indications

Reimbursement for placement of MCS in the United States (US) is regulated by the Centers for Medicare and Medicaid Services (CMS). CMS requires institutions to be credentialed as an implanting center by either The Joint Commission or the Det Norske Veritas (DNV) Healthcare VAD (ventricular assist device) Credentialing Program [4–6]. Institutions in the United States must adhere to both CMS and their chosen credentialing organization's requirements to obtain and then remain certified by CMS. Incorporating the indications and patient selection requirements in the institution's clinical practice guidelines will assist with meeting specified criteria.

Clinical requirements for MCS institutions are outlined by CMS in their National Coverage Determination (NCD) [4]. The NCD was recently updated (December 2020) and removes the intention to treat requirement [4]. This means determining BTT or DT candidacy prior to implant is no longer necessary. The clinical criteria outlined in the NCD have provisions for both end-stage heart failure patients and those presenting with acute processes. Despite this removal, VAD programs still often discuss patients based on implant indication.

CMS requires potential MCS patients to have an ejection fraction (EF) of ≤25% and be exhibiting New York Heart Association (NYHA) functional class IV symptoms [4]. Additionally, CMS requires that patients must demonstrate either inotrope dependence or demonstrate a low output state evidenced by a cardiac index <2.2 L/min/m^2 despite treatment with guideline-directed medical therapy for a minimum of

45 out of 60 days [4]. To assist with provisions for those patients presenting more acutely or unable to meet the 45 of 60-day requirement, patients may qualify for MCS if they have exhibited advanced heart failure for the last 14 days and are dependent on either an intra-aortic balloon pump or other short-term MCS device for 7 days [4].

Having reviewed the regulatory requirements of CMS, further explanation of the clinical requirements is necessary, specifically, those failing optimal medical management. Despite utilization of guideline-directed medical therapy, advanced heart failure eventually becomes refractory to angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, angiotensin receptor-neprolysin inhibitors, beta-blockers, and mineralocorticoid receptor antagonists [7, 8]. Over time, patients frequently also require an increased diuretic dose to remain euvolemic with advancing disease. Patients suffering with NYHA IIIb–IV symptoms who have functional limitations despite medical therapy often experience frequent hospital readmissions for decompensated heart failure. Patients may also require initiation of inotropic therapy to either aid in diuresis or to improve cardiac function during a decompensated state [9].

Frequent hospitalization with NYHA class IV symptoms is an indicator of worsening heart failure and the need for MCS when on guideline-directed medical therapy. Additional clinical indications include a combination of the following: intolerance to neurohormonal antagonist, increasing diuretic requirements, symptomatic despite cardiac resynchronization therapy, inotrope dependence, low peak VO_2 (<12–14 or 50% of age predicted), and/or end-organ dysfunction attributable to low cardiac output [2, 3, 7, 9–11].

Contraindication for MCS

There are both absolute and relative contraindications to durable MCS. Table 1 summarizes this list. Absolute contraindications to MCS implantation include those patients with irreversible end-organ dysfunction/failure (renal, hepatic), active untreated infection, severe psychosocial limitations, and some institutions include medical non-adherence [1, 10]. Illnesses such as malignancies with a life expectancy of less than 2 years with or without systemic organ involvement are also believed to be an absolute contraindication [2, 11].

Table 1 Contraindications to MCS support [1, 2, 10–16]

Absolute contraindications	Relative contraindications
• Irreversible renal or hepatic disease • Active untreated infection • Severe psychosocial limitations • Any illness with a life expectancy less than 2 years • Right ventricular or biventricular failure if DT LVAD planned	• Age • BMI • Substance abuse • Psychiatric disorders • Limited social support • Non-compliance with medical regimen

DT destination therapy, *LVAD* left ventricular assist device, *BMI* body mass index

Relative contraindications to MCS implant may vary by institution and have been the source of some debate. Patient age, body mass index (BMI), active or recent history of substance use/abuse, psychiatric disorders, and available social support are often more fluid and evaluated on a case by case basis within an institution. Some institutions suggest an age cutoff of 75 years, as recent studies demonstrate a higher mortality post implantation in patients greater than 75 years of age [12]. There is growing evidence that preoperative frailty assessment aids in the decision-making process. Preoperative assessment of hand grip strength has been shown to provide some prognostic value during the evaluation of appropriate MCS candidates [13].

Obesity has also sparked some debate when determining a BMI parameter for VAD implantation. Obesity, defined by a BMI of greater than 35, may be considered a relative contradiction at some centers, with some citing concern for poor outcomes. However, it was found that even patients with a BMI of 40 or greater (extreme obesity) show no difference in survival at 30 days and 1 year post-implant, suggesting BMI remains a relative contraindication [14].

Psychosocial factors are highly debated when determining MCS candidacy. Impaired cognitive function, active substance abuse, unmanaged psychiatric disorders, and/or lack of social support may be prohibitive for safe MCS implantation [10]. Life for a patient post-implant requires ongoing, daily self-care related to equipment maintenance, adherence to a complex medical regimen including proper dosing of anticoagulation, ongoing wound care using sterile technique, frequent lab monitoring, and frequent office visits all in order to ensure the MCS device is adequately supporting the patient. An extensive psychosocial assessment of a patient's cognitive status, psychopathology, social support, and past adherence to medical regimens is part of the process to determine candidacy for MCS placement [15, 16].

Patient Selection

Understanding the regulatory as well as the clinical indications, along with both the absolute and relative contraindications for MCS placement will help guide patient selection. To determine candidacy for MCS placement, patients undergo a thorough evaluation based on the presenting comorbidities along with age-related risk factors [17]. Table 2 outlines the suggested routine age-related and comorbidity testing to be considered. Risk assessment is needed to assist the multidisciplinary team with making a decision for MCS placement [11, 17]. Clinical risks will be discussed followed by psychosocial risks.

While durable MCS is specific to left ventricle support, evaluation of right ventricular function is also required to determine the risk of right heart failure following placement of the device and to plan if biventricular support is needed. Right heart catheterizations along with echocardiography help to provide an assessment of the right ventricle [1, 2]. Right atrial pressure, right ventricular stroke work index (RVSWI), tricuspid annular plane systolic excursion (TAPSE), and pulmonary artery pulsatility index (PAPI) are objective methods for assessment of RV function [2, 3,

Table 2 Evaluation checklist [1–3, 11, 12, 15–17]

- Laboratory assessment
  - Complete metabolic panel
  - Complete blood count
  - Prothrombin time/international normalized ratio
- Chest X-ray
- Electrocardiogram
- Assessment of NYHA class and INTERMACS profile
- Echocardiogram
- Cardiopulmonary exercise stress test (unless on inotrope or on short-term MCS)
- 6-minute walk test
- Hemodynamic assessment with pulmonary artery catheter/right heart catheterization
- Coronary angiogram as indicated
- Computed tomography of chest (non-contrast)
- Internal cardiac defibrillator check
- Spirometry ± bronchodilator
- Complete abdominal ultrasound (assess liver, spleen, kidneys, pancreas, abdominal aorta)
- Bilateral carotid artery ultrasound/duplex
- Bilateral lower extremity peripheral vascular study (ankle-brachial index)
- Consults:
  - Social work for psychosocial assessment
  - Dietician for nutritional assessment
  - Cardiothoracic surgeon
  - Palliative care
  - Other consults as presentation dictates
    - Endocrinology
    - Pulmonology
    - Hematology
    - Hepatology
    - Neurology
    - Nephrology
    - Bioethics
- Additional testing as indicated
  - Neuropsychology testing
  - Urine toxicology screen
  - Wellness testing (if time permits and patient's condition)
    - Dental
    - Colonoscopy (age and comorbid condition dependent)
    - Female patients: Mammogram and pap smear (as indicated by age)
    - Male patients: Prostate specific antigen (as indicated by age)

Note: Not all testing is indicated. Testing based on institution's requirements, patient's age, and comorbidities. Additional testing may be needed based on findings

17]. A right heart catheterization provides intracardiac and pulmonary artery pressures. Findings of pulmonary hypertension may rule out transplant candidacy but MCS may be an option. The echocardiogram reveals right and left ventricular dimensions and function, in addition to the structure of the aortic, mitral, tricuspid, and pulmonic valves. Evidence of aortic, mitral, and/or tricuspid regurgitation or stenosis deserves further attention to determine if valve repair or replacement is needed at the time of MCS implant [1, 18]. Additional surgery at the time of MCS placement adds complexity to the surgery and must be included in the risk assessment [1, 18].

For patients with prior cardiac surgery, a computed tomography (CT) of the chest helps determine re-entry risk, and provides further information about the condition of the aorta. These also assist with determining overall surgical risk [1]. A coronary angiogram will determine if corrective measures for heart failure are possible or determine the need for concomitant surgery at the time of MCS implant [1, 18]. For patients having had prior aortic valve replacement with a mechanical aortic valve, replacement with a bioprosthetic valve should be considered at the time of MCS placement taking into consideration the cumulative risk [18].

Many patients with chronic heart failure present with atrial and/or ventricular arrhythmias, some already having had an ablation(s), a pacemaker, or internal cardiac defibrillator. Patients with pre-MCS history of atrial fibrillation and ventricular tachycardia are at risk for post-MCS implant atrial fibrillation and ventricular tachycardia. Atrial arrhythmias are not a contraindication to MCS, but attention is focused on rate control with medications. If atrial arrhythmias are problematic, an electrophysiologist should be consulted to determine whether an ablation is warranted [1, 17, 18]. Consideration may be given to ligating the left atrial appendage at the time of MCS implant [1]. Ventricular arrhythmias pre-MCS are more problematic, and require specific attention. In addition to the use of antiarrhythmics, hemodynamic optimization may decrease the incidence of ventricular arrhythmias for those patients found to be in decompensated heart failure. Coronary ischemia should be considered for those patients exhibiting persistent ventricular tachycardia despite treatment warranting a left heart catheterization, especially for those patients with known coronary artery disease [1]. Attempts are made to decrease the burden of ventricular arrhythmias pre MCS implant in an effort to prevent the need for a right ventricular support device post implant if ventricular arrhythmias persist despite left ventricular unloading [1].

A history of chronic lung disease, smoking history, or use of oxygen at the time of evaluation warrant further investigation. Baseline pulmonary function testing will determine the degree of pulmonary dysfunction in patients with lung disease and should be completed to assess potential issues with weaning from mechanical ventilation following surgery [1, 3]. Further testing may be needed depending on the results. Patients on mechanical ventilation prior to MCS support are at increased risk for adverse events [3].

A history of gastrointestinal bleeding prior to MCS requires further investigation to determine the cause, due to the need for anticoagulation following MCS implant. A baseline colonoscopy may be required and should be considered for age-related wellness testing if not previously completed to rule out malignancy [1–3].

Further investigation of the renal and hepatic systems is warranted with any abnormal blood tests and/or imaging. Renal failure post implant complicates the patient's postoperative course and may not provide the quality of life the patient is seeking. Patients should understand their risks prior to implant [1–3]. Chronic dialysis is a contraindication for MCS in many institutions [2]. Abnormal liver function tests that do not resolve with improved cardiac output should be further investigated. Cirrhosis is a contraindication to MCS support [1].

Patients presenting with a history of a cerebrovascular accident (CVA) require further investigation that at a minimum requires a baseline head CT and carotid ultrasound [1]. Formal assessment of residual deficits and neurocognitive function are needed to determine the patient's ability to manage the MCS device. Additionally, patients should understand the risk of a stroke with MCS as part of making an informed decision. Patients with severe neurocognitive deficits or demonstrate an inability to care for self is a contraindication to MCS [1, 3].

Other comorbidities to be taken into consideration include rehabilitation ability for those with peripheral vascular disease or chronic back, knee, or hip issues. Peripheral vascular studies are indicated for patients with neuropathy or known circulation issues [1, 3, 18].

A full psychosocial evaluation is completed similar to evaluation for a heart transplant, and is needed to identify risk factors for post implant care [15, 16]. Understanding a patient's past compliance with medical care, social support, substance use, and psychiatric history is relevant for assessing patient's risk for recidivism and failure post implant. Further testing is warranted if there are signs of neurocognitive issues [3]. Efforts are made to mitigate risks to improve patient outcomes [15]. As stated previously, classification of psychosocial issues as relative or absolute contraindications continues to be an area of debate for MCS placement.

Once the evaluation is completed, patients are presented to a multidisciplinary advanced heart failure team for decisions regarding candidacy. Typically, these teams consist of cardiac surgeons, advanced heart failure cardiologists, MCS coordinators, social workers, dieticians, a member of the palliative care, and ideally a team member from bioethics, case management, physical and occupational therapists [11]. Patient demographics, history of present illness, past medical history, pre MCS testing, psychosocial evaluations, and assessment of the patient's support system are presented. The multidisciplinary team discusses any potential barriers they foresee postoperatively and determine a plan for mitigation of risks to promote good patient outcomes. Team members then make recommendations weighing the risks and benefits of MCS therapy specific to the patient. The presentation should acknowledge whether the patient meets CMS and institutional criteria with findings clearly documented in the patient's medical record.

The last phase of the patient selection process is to obtain insurance approval for MCS placement. CMS criteria have previously been discussed above. For those patients with commercial insurance, it is necessary to understand the payers' criteria for device placement. In the current environment, most payers in the United States continue to require the designation of BTT or DT. With the indication for device therapy defined, patients will need to meet these specific designation requirements. For example, if the device is being placed as BTT, the patient will need to be listed for transplant prior to device implant as required by the payer. It is essential for each MCS program to work closely with their finance department or pre-authorization department to fully understand the various payers served and those payers' individual patient-specific selection criteria.

The indications, contraindications, and relative contraindications of MCS guide clinicians to understand the appropriateness of completing a full evaluation for

MCS. After a full evaluation is completed, the multidisciplinary team decides candidacy for MCS device placement based on patient selection criteria specified by the institution, government, and commercial payers. Patient selection criteria should be included in each institution's clinical practice guideline to remove selection bias as well as to inform patients.

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Patient Optimization Prior to MCS

Brittany Rhoades, Holly Hamm, and Scott Stewart

Introduction

Typically, those selected for left ventricular assist device (LVAD) implantation have progressed to end-stand heart failure (HF) and have estimated 1-year mortality >50% with medical therapy [1]. These individuals may be at home slowly declining on current medical therapy or entering the acute care facility in acute cardiogenic shock, commonly referred to as "Crash and burning." This chapter will provide guidelines and considerations for optimization before LVAD implantation.

STS INTMERMACS® Score

The Society of Thoracic Surgeons (STS) Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS®) was established in 2005 at the University of Alabama at Birmingham and became part of the STS National Database on January 1, 2018 [2]. INTERMACS® is a North American registry for clinical outcomes of patients who receive an FDA-approved mechanical circulatory support device to treat advanced heart failure. The INTMERMACS® profiles of advanced heart failure shown in Table 1 demonstrate the grading

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Table 1 INTERMACS® profiles of advanced heart failure and modifiers of the INTERMACS® patient profiles

INTERMACS® profiles of advanced heart failure		
Level	**Description**	**The time frame for intervention**
1. *Critical cardiogenic* "Crash and burn."	• Life-threatening hypotension or rapidly escalating inotropic pressure support. • Critical organ hypoperfusion is often confirmed by worsening arrhythmia (A) or Temporary Circulatory Support (TCS).	Within hours
2. *Progressive decline* "Sliding on inotropes."	• Demonstrated "dependence" on inotropic support but has shown no additional signs of continuing deterioration in nutrition, renal function, fluid retention, or other major status indicators. • Refractory volume overload, perhaps with evidence of impaired perfusion, in whom inotropic infusions cannot be maintained due to tachyarrhythmias, clinical ischemia, or other intolerance. • This patient can have an arrhythmia (A) or Temporary Circulatory Support (TCS) modifier.	Within days
3. *Stable, but inotrope dependent* "Dependent stability."	• Stable on mild-moderate doses of intravenous inotropes (or has a temporary circulatory support device) after repeated documentation of failure to wean without symptomatic hypotension, worsening symptoms, or progressive organ dysfunction (usually renal). • Located at home or in the hospital. • This patient can have an arrhythmia (A) modifier, and if in the hospital with circulatory support, can have a Temporary Circulatory Support (TCS) modifier. If the patient is at home most of the time on outpatient inotropic infusion, he or she can have a modifier FF if he frequently returns to the hospital. • *Note*: It is critical to monitor nutrition, renal function, fluid balance, and overall status carefully to distinguish between a patient who is stable at Patient Profile 3 and a patient who has unappreciated decline rendering them Patient Profile 2.	Elective over weeks to months

Table 1 (continued)

4. *Resting symptoms* "Frequent flyer."	• At home on oral therapy but frequently has symptoms of congestion at rest or with activities of daily living (ADL). Symptoms may include but are not limited to shortness of breath during dressing or bathing, gastrointestinal symptoms (abdominal discomfort, nausea, poor appetite), ascites, or severe lower extremity edema. • Modifiers A and FF are applicable.	Elective over weeks to months
5. *Exertion intolerant* "Housebound."	• Comfortable at rest but unable to engage in any activity, living predominantly within the house or housebound. • No congestive symptoms, but may have chronically elevated volume status, frequently with renal dysfunction, and may be described as exercise intolerant. • Modifiers A and FF are applicable.	Variable urgency, dependent on nutrition and organ function
6. *Exertion limited* "Walking wounded."	• Comfortable at rest without evidence of fluid overload, but who can do some mild activity. ADLs are comfortable, and minor activities outside of the home, such as visiting friends or going to a restaurant, can be performed, but fatigue results within a few minutes of any meaningful physical exertion. • Occasional episodes of worsening symptoms and may have had a hospitalization for heart failure within the past year. • Modifiers A and FF are applicable.	Variable urgency, dependent on nutrition and organ function
7. *Advanced NYHA Class 3* "Placeholder."	• Clinically stable with a reasonable level of comfortable activity, despite a history of a previous decompensation that is not recent. The patient is usually able to walk more than a block. • Modifiers A only is applicable. • *Note*: Any decompensation requiring intravenous diuretics or hospitalization within the previous month should make this person a Patient Profile 6 or lower.	No currently indicated

(continued)

Table 1 (continued)

Modifiers of the INTERMACS® patient profiles		
	Applicable profile	**Description**
A—Arrhythmia	All INTERMACS® Patient Profiles	Recurrent ventricular tachyarrhythmias have recently contributed substantially to the overall clinical course. This includes frequent shocks from ICD or the requirement for an external defibrillator, usually more than twice weekly.
TCS—Temporary Circulatory Support	INTERMACS® Patient Profiles 1, 2, and 3	This modifier applies only to patients who are confined to the hospital. Additionally, a patient listed as Patient Profile 3 stable on inotropes who has been at home until elective admission for implantable VAD cannot have a TCS modifier. Temporary circulatory support includes, but is not limited to, IABP, ECMO, TandemHeart, Levitronix, BVS 5000 or AB5000, Impella.
FF—Frequent Flyer	INTERMACS® Patient Profiles 3, 4, 5, and 6	Frequent Flyer is designated for a patient requiring frequent emergency visits or hospitalization for intravenous diuretics, ultrafiltration, or brief inotropic therapy. Frequent would generally indicate at least two emergency visits/admissions in the past 3 months or three times in the past 6 months. This modifier is primarily used for Patient Profiles 4, 5, and 6; however, it can modify Patient Profile 3 if usually at home (frequent admission would require escalation from Patient Profile 7 to Patient Profile 6 or worse). *Note*: If admissions are triggered by tachyarrhythmias or ICD shocks, then the modifier to be applied to would be A, not FF.

INTERMACS®, Interagency Registry for Mechanically Assisted Circulatory Support

process for VAD patients in level of severity along with appropriate comorbid modifiers [3]. It is understood that patients who are in higher numerical values typically have improved quality of life and survival than those in lower categories. Focusing on optimization pre-VAD has the ability to alter a patient category to enhance outcomes.

Preoperative Concerns and Comorbidities

Malnutrition

Protein malnutrition is present if albumin levels (less than 3.5 g/dL) and edema will be present if albumin levels are below 2.7 g/dL. Decreased hemoglobin below 12 g/dL for women and less than 13.5 g/dL for men may indicate a lack of iron or protein, resulting in decreased oxygen perfusion. Individuals should be encouraged to increase their protein intake as higher levels improve wound healing such as sternal incisions and the LVAD driveline exit site. Preoperative consultation with a dietician is recommended if malnutrition is identified to improve preoperative caloric intake. This may include providing nutritional support enterally (e.g., Enterostomal tube or Nasoenteric tube) or parenterally if critically ill or unable to meet nutritional needs. Conceding during nutritional assessment is examination for wounds and consultation with a wound care specialist if available should be considered if both conditions are present [4].

Anemia

Individuals advanced in age experience chronic inflammation, infection, renal failure, and malignancy and may experience anemia associated with chronic disease. Symptoms include fatigue, weakness, dyspnea on exertion, and anorexia. Monitor hemoglobin and hematocrit levels, treat associated diseases, and provide nutritional support. Epogen helps increase red blood cell production and reduces the need for blood transfusions but should be considered cautiously given the risk of prothrombotic effects [5].

Hematologic Disorders

Individuals that have hematologic conditions such as idiopathic thrombocytopenic purpura (ITP); Factor V Leiden, elevated Factor VIII; heparin-induced thrombocytopenia (HIT); or undefined hypercoagulable state have increased risks for bleeding, thrombotic complications, or neurologic events during LVAD therapy [6]. Argatroban is adequate anticoagulation preoperatively, intraoperatively, and postoperatively for patients with HIT. Monitor these individuals closely for bleeding complications postoperatively. Surgical techniques aimed at reducing

hematologic stasis within the device may also be utilized [7]. For patients with hematological disorders, pre-implant guidance should be provided by a hematology consultation.

Diabetes Mellitus (DM)

Glycemic control is directly associated with morbidity and mortality of individuals with heart failure therefore tight glycemic control is crucial. A diabetic treatment plan should be individualized based on the duration of DM, hypoglycemia awareness, age, comorbid conditions, and individual patient considerations. Target levels include HbA1c <7%, pre-prandial capillary plasma glucose 70–130 mg/dL, and peak postprandial capillary plasma glucose <180 mg/dL [8]. Endocrinology should be involved in the management of HF patients with DM and continually follow the patient in the clinic setting.

Peptic Ulcer Disease

Heliobacter pylori (*H. pylori*) should be considered when evaluating a patient for peptic ulcer disease as it carries a high incidence rate. Medications also contribute such as nonsteroidal anti-inflammatory drugs (NSAIDs), acetylsalicylic acid (ASA), glucocorticoids as well as lifestyle factors such as smoking. Symptoms include gnawing epigastric pain, relief with eating (duodenal ulcers), or pain that worsens (gastric ulcers). Individuals may present with gastrointestinal (GI) bleeding (e.g., melena, hematemesis, or coffee-ground emesis) and from mild epigastric tenderness to severe epigastric pain or other signs of an acute abdomen. VAD clinicians should regularly monitor complete blood count (CBC), consider *H. pylori* testing, treatment with an H2 receptor antagonist or proton pump inhibitor (given 30 min before meals), and endoscopy after 8–12 weeks of treatment [8]. Patients with severe disease should be considered for preoperative implant endoscopy.

Hepatitis

Individuals may present with liver inflammation resulting in liver dysfunction because of viral hepatitis (hepatitis A, B, C (non-A, non-B), D, E, G), an autoimmune disorder, or alcohol. Symptoms include fatigue, malaise, anorexia, nausea, and vomiting (n/v), headache, aversion to smoking and alcohol (pre-icteric) or weight loss, jaundice, pruritis, right upper quadrant pain, clay-colored stool, and dark urine (icteric). Monitor the following labs: white blood count (WBC), urinalysis (UA), elevated aspartate aminotransferase (AST) and alanine transaminase (ALT), lactate dehydrogenase (LDH), bilirubin, alkaline phosphatase, and PT lab values should. Administer hepatitis antibodies and provide supportive care with

fluids and hydration, avoid alcohol or drugs detoxified by the liver, no/low protein diet, vitamin K for prolonged PT (>15 s), lactulose for elevated ammonia levels, and administration of antiviral drugs [4]. Given advancement in medication therapy, curative treatment for hepatitis C should be considered preoperatively pending time.

Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS)

Individuals may experience flu-like symptoms to fever, night sweats, and weight loss. AIDS is recognized by CD4 <200 cells/μL and the presence of an opportunistic infection. Perform HIV antigen/antibody testing, and monitor CD4 lymphocyte count and viral load. A viral load of "zero" or "undetectable" is ideal. Therapy should include antimicrobials as needed and Pneumocystis jiroveci pneumonia prophylaxis. Individuals should be started on combination therapy as a standard of care [Active Antiretroviral Treatment (AART)] and monitored for drug resistance throughout therapy [8]. Many centers will consider implantation with low to absent viral loads but consultation with infectious disease should be considered for patients with uncontrolled viral loads or in patients who have progressed to AIDS.

Arrhythmias/ICD Shocks

As HF progresses, arrhythmias can develop or increase in frequency. Rhythm control therapies, as well as rate control, should be implemented. For patients that experience frequent ICD shocks, consult electrophysiology for cardiac mapping and possible intervention [8]. While not specifically a contraindication to LVAD therapy, it is important to control ventricular arrhythmias to preserve right ventricular function. Consideration for atrial arrhythmias is important for pre/postoperative thromboembolic CVA. Consideration for left atrial appendage clipping during the implant procedure should be considered.

Sleep Apnea

Apnea, cessation of breathing for greater than 10 s, and hypopnea, decrease in airflow for greater than 10 s with an oxygen reduction, are associated with hypertension, arrhythmias, and the development of HF. Treatment includes continuous positive airway pressure (CPAP) or Bi-level positive airway pressure (Bi-level PAP) to maintain the airway patent during sleep [8]. Sleep apnea may contribute to cardiac dysfunction post VAD specifically creating RV function stress therefore addressing preoperatively is important for device therapy success.

Chronic Obstructive Pulmonary Disease (COPD)

Cigarette smoking is the most common cause of COPD. When combined, COPD and HF are associated with poor outcomes. Therapy for COPD and HF includes beta-agonist and beta-blockers, respectively. Beta-blocker therapy is not contraindicated in stable COPD, and selective beta-1 blockade can be used safely in HF patients with the respiratory disease [8]. Ensuring stability of COPD status prior to intubation for VAD implant is important for postoperative extubation challenges that may arise and therefore clearance from a pulmonologist is recommended for these patients.

Coronary Artery Disease (CAD)

Non-invasive imaging for ischemia includes exercise stress testing, pharmacologic stress testing, myocardial perfusion imaging, stress echocardiography, and cardiac CT. Use coronary angiography in individuals with exertional angina or equivalent, suspected ischemic LV dysfunction, a vital risk factor for CAB, or those not responding to medical treatment [8]. For LVAD patient specifically, evaluation of the right coronary artery for intervention pre-implant has been considered.

Peripheral Vascular Disease (PVD)

Symptoms of PVD include shiny/hairless skin, cyanosis, ulcerations, and reduced pulses. Doppler ultrasound, ankle-brachial index (ABI), and arteriography help diagnose PVD. Awareness of severity of PVD is important during the evaluation of VAD given the changes from pulsatile flow to a continual flow state as patients with severe PVD may have worsening symptoms. Severe PVD may also hinder postoperative rehabilitation.

Renal Dysfunction

Renal function is closely tied to cardiac support due to regulation of sodium retention and fluid excretion. Increased intravascular filling pressures create elevated blood pressure and thus contribute to increased afterload and LV hypertrophy, furthering the exacerbation of systolic function. Heart failure treatment is focused on the renin-angiotensin-aldosterone pathways and consideration of medication titration is focused to ensure appropriate renal function. Cardiorenal syndrome surrounds increased fluid buildup surrounding the kidneys which improves with diuretic therapy and LV unloading. It is key for VAD clinicians to work closely with nephrology for evaluation of acute and chronic kidney disease. Renal failure requiring dialysis is extremely challenging to manage post VAD insertion and is associated with worse outcomes therefore this risk must be weighed prior to implanting the device.

Obesity

Many centers will consider this a relative contraindication as experiences with higher BMI have not been shown to dramatically affect outcomes [9]. Some LVAD programs will evaluate individuals for surgical weight-loss interventions with LVAD placement [10].

Depression and Anxiety

Psychological conditions are common in patients suffering from cardiovascular conditions [8]. Depression and anxiety increase sympathetic nervous system stimulation, atherosclerotic process, autonomic changes, cardiac electrical instability, elevated biomarkers, and plaque rupture/thrombosis. Tools for depression assessment include PHQ-2, PHW-9, and Beck Depression Inventory. Management includes pharmacologic therapy with anti-depressant drugs including serotonin reuptake inhibitors (SSRI), cognitive behavior therapy, and increasing physical activity (i.e., exercise) [8]. Patients at risk should have consultation with psychiatry for evaluation of mental health disorder post VAD.

Psychosocial Readiness for LVAD Implant

The thorough psychosocial assessment of patients undergoing evaluation for MCS implantation has become the standard of care. It is vital to understand the patient's support systems, commonly employed coping mechanisms, financial resources, home environment, and individual investment in complying with the prescribed medical plan prior to determination of the appropriateness of MCS candidacy. Generally, a licensed medical social worker or a licensed psychiatrist performs a comprehensive psychosocial assessment during the MCS evaluation, but each program will define who will conduct the assessment depending on their staffing structure.

The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT), Psychosocial Assessment of Candidates for Transplant (PACT), Montreal Cognitive Assessment (MoCA), and the Mini-Mental State Examination (MMSE) and the CAGE Assessment for Alcohol Abuse or the Patient Health Questionnaire [11] are useful for the psychosocial evaluation.

The goals of the evaluation process are to (1) identify any potential psychosocial risks for poor outcome after MCS, including risks related to the individual's psychiatric history or social stability; (2) ensure that the prospective MCS recipient comprehends the risks, benefits, and implications of device implantation to the patients and caregiver; (3) determine the patient's and caregiver's ability to cope with major surgery and the requirements of life with an MCS device; (4) determine that support systems are in place and ensure a realistic plan for recovery and living with the device [11].

The objective of the assessment is not to place barriers for moving forward with MCS therapy but to identify gaps and appropriate resources that can guide therapy and help the patient be successful post-implant. The following provides critical elements of a comprehensive psychosocial evaluation [11] and guidance on how each of the above elements can affect postoperative success:

- Cognitive evaluation
- Screen for psychiatric illness
- Evaluate for a history of alcohol, tobacco, and substance abuse
- Evaluate the history of compliance with medical therapies and recommendations
- Evaluate psychosocial obstacles that would limit the chance of a successful outcome
- Assess the level of family/caregiver support and presence of caregiver burden
- Verify an adequate level of health insurance or ability to obtain it

Cognitive Evaluation

Complete a formal cognitive assessment to assess the patient's current behavior and coping skills and how they have managed previous life or health-related stressors. Neurocognitive testing might also be helpful to assess a patient's memory attention, concentration, problem-solving, and ability to multi-task and focus.

Baseline demographic information such as educational level, living situation, cultural background, religious beliefs and practices, significant relationships, employment, lifestyle, community activities, and legal history are essential to the overall psychological picture of the patient. The ability to operate and care for the device is also a vital assessment factor that should include any sensory or physical impairments or disabilities.

Psychiatric Illness

The most challenging elements to assess for, especially on a short timeline, is psychiatric illness such as depression, anxiety disorder, schizophrenia, and other mood disorders, which are not uncommon in patients with chronic illness. Psychiatric illness is manageable with the proper resources; the critical factor is the patient's psychiatric stability and coping ability [11]. Timing of the evaluation for MCS can play a significant role in a patient's response to the idea of MCS therapy, especially when they are acutely ill, INTERMACS® Profile 1 or 2. Establishing care with a mental health provider before implant when possible is necessary to treat pre-existing psychiatric conditions, help the patient cope, aid in a smooth pre- and post-op recovery, and allow the patient quality of life.

Alcohol, Tobacco, and Substance Abuse

An assessment of alcohol and substance use is an essential factor to consider during the psychosocial evaluation. Abuse of any substance can affect a patient's current or future candidacy for transplant as well as their ability to adhere to medical guidelines post-implant. Excessive alcohol or drug abuse should be a contraindication to elective device implantation. Each center may have different standards as to what level of alcohol or drugs use is acceptable, but guidelines should be in place. The use of social contracts might be necessary to assist the patient to connect with the resources necessary to be successful with their care after VAD. Social contracts can also be a method of accountability to the patient's goals leading to the best chance of quality life with a VAD.

Adherence to Medical Therapies

Determining a patient's history of adherence to medical therapy can be crucial in predicting how compliant they might be post-implant. Keeping appointments, taking medications as instructed, and following diet and exercise recommendations are among the things to note. If nonadherence is present before implant, with the added stress of the LVAD evaluation and the implant itself, medical adherence post-implant will be much more challenging. Social contracts may help improve nonadherence.

Family/Caregiver Support

Social support is one of the essential parts of the psychosocial evaluation. A higher level of caregiver support may mitigate non-adherent behaviors and lead to better outcomes. The caregiver will be actively involved in almost every aspect of the patient's journey to LVAD implant and after including clinic visits, medication adherence, education on the LVAD device and accessories/equipment, dressing changes, and 24/7 support when needed. The patient's social support network becomes even more critical should complications arise post-implant.

Caregiver burden is a popular term when speaking about MCS therapy and must be discussed and recognized with the patient's support system. Identifying caregivers and obtaining informed caregiver consent is as vital as patient informed consent due to the long-term care commitment and continuous care requirement once discharged home. The essential caregiver requirements can impose significant physical, psychological, and financial strain on caregivers. Additionally, caregivers describe the fear of device emergencies, depression, anxiety, and posttraumatic stress disorders [12]. For this reason, a substantial caregiver burden may occasionally become the reason to forgo LVAD surgery for the patient. The decision not to

proceed with LVAD therapy is not uncommon for elderly patients who rely on their spouses for help and often have their own medical problems. MCS programs should therefore have support mechanisms in place for caregivers of MCS patients. Support groups are a common way to assist the patient and caregiver with caregiver strain.

Financial Support

A financial assessment should be part of the evaluation process for LVAD implants. The patient needs to have the ability to handle financial obligations pre- and post-implant and ensure that financial stability. A financial coordinator may assist with assessing current insurance coverage for the hospitalizations and outpatient expenses. This role may also assist with additional government and community resources such as disability insurance assistance, medication assistance, and transportation.

Increasing Physical Conditioning Pre and Post MCS

Frailty is a clinically recognizable state of increased vulnerability resulting from decline across multiple physiologic systems and is generally associated with the following specific signs of physical dysfunction: unintentional weight loss, poor grip strength, slow gait speed, and low physical activity [13]. Frailty directly contributes to poor health outcomes, including falls, disability, increased hospitalization, and mortality. Historically, VAD programs have used a subjective provider assessment (SPA) or "eye-ball" test to assess physical conditioning before device implant. Several frailty measures have been applied to heart failure or surgical populations [13] and include the following assessments: cognitive, mobility or physical activity, mood, and social support. The primary outcomes evaluated by the assessment tools include postoperative complications, length of stay, rehospitalization, and mortality. Two more common frailty measures are The Fried criteria and the Short Physical Performance Battery [13]. Both measures are highly predictive of adverse outcomes in a variety of populations. These assessments may lead to enhanced pre-surgical interventions aimed to improve post-surgical outcomes.

Prehabilitation or "Prehab" seeks to optimize patients before surgery to enhance general health and wellbeing before surgery [14] which increases an individual's "physiological reserve' to buffer the surgical stress response [15]. Prehabilitation requires multidisciplinary team involvement to address the following pre-surgical risk factors: physical inactivity and poor fitness, hazardous health behaviors (e.g., smoking, alcohol use), nutrition, and psychological factors [16]. Prehab interventions include combined aerobic and resistance training, individual objective fitness assessment, structured inspiratory muscle training program to reduce perioperative pulmonary complications, lifestyle modification resources and counseling (e.g., smoking cessation, alcohol specialist services), identification of macro-and micronutrient deficiencies, protein supplementation if protein intake is less than 1.5–2.5 g/

kg daily and after exercise training sessions, and counseling or psychological interventions to control anxiety and depression [16].

Engaging prehab efforts can also inform the postoperative therapy interventions. Cardiac rehabilitation (CR) is the standard of care following surgery, the key to enhancing health for individuals post-surgery, and ideally suited to counteract poor preoperative frailty and improve an individual's functional status following surgery [17]. The critical components of CR include the following: baseline patient assessments, nutritional counseling, aggressive risk factor management (i.e., lipids, hypertension, weight management, diabetes control, and smoking), psychosocial and vocational counseling, and physical activity and exercise training in conjunction with the appropriate clinical management of heart failure and use of cardioprotective drug therapy [18]. CR has demonstrated improvements in cardiorespiratory fitness, muscle strength, and KCCQ scores in patients with continuous-flow LVADs [17].

Hemodynamic Optimization Before MCS Implant

Preoperative optimization is key to a successful intraoperative and postoperative course for the LVAD patient. Pulmonary artery pressure (PAP)-guided HF management using CardioMEMS™ can be used for hemodynamic optimization before LVAD implant in ambulatory individuals [19]. HEMO-VAD pilot study demonstrated more significant increases in quality of life (QoL) measures (EQ-5D-5L and PHQ-9 questionnaires, and 6-min walking distance [6-MWD]) between baseline and 3 months post-LVAD than those not hemodynamically optimized pre-LVAD [20].

Unless contraindicated, all patients should receive a right heart catheterization before implant with an indwelling pulmonary artery catheter to assess hemodynamics up until the time of implant and after that. Hemodynamics can then be used to guide the following clinical goals preoperatively:

- Achieve optimal fluid balance using diuretics and ultrafiltration if necessary
- Avoid persistently elevated left-sided filling pressures that can lead to elevated TPG and PVR; the use of oral, inhaled, or IV pulmonary vasodilators may be considered
- Achieve optimal end-organ perfusion
- Correction of acute kidney injury due to cardio-renal syndrome
- Decompression of the liver, kidneys, and intestines as evidenced by normal liver enzymes, kidney function, and nutritional lab values
- Maximize heart function and blood pressure with the use of inotropes [21]

When warranted, temporary mechanical support such as an intra-aortic balloon pump, Impella, or extracorporeal membrane oxygenation is helpful for further optimization. These devices provide an enhanced cardiac output, restore renal and liver function, and provide excellent hemodynamic support, allowing patient extubation and assessment of full neurological status. These devices also have adequate

durability allowing time for correction of multiorgan failure prior to implantation of a durable device.

All patients should have an echocardiogram to assess right heart function, LV function, valvular, and other structural abnormalities that can be optimized or surgically repaired before or during LVAD implant. These items should be included during the pre-implant meeting with the entire multidisciplinary team to review.

Perform a final assessment of right heart function before implant. A thorough analysis of right ventricular function is critical to maintaining optimal LVAD support. Postoperative right ventricular failure has persisted as a complication and barrier to LVAD success and is associated with increased mortality and morbidity [12, 22–24]. Risk scores can aid clinicians in quantifying the risk of RV failure, such as the Michigan RVF Risk Score, Utah RVF risk score, Pittsburgh Decision Tree, and the EuroMACS-RHF risk score. Various components comprise these scores, such as laboratory data, medications, hemodynamic data, and echocardiographic measurements. Despite the risk score used, judicious patient selection is vital in preventing right ventricular failure in patients undergoing LVAD implantation; particularly in patients undergoing LVAD implant as long-term support. Patients at high risk for right ventricular failure intraoperatively or postoperatively can have a planned RVAD support strategy going into surgery.

Right ventricular function, volume, and oxygen delivery should be closely monitored before LVAD implant using monitoring devices such as a central venous catheter, arterial lines, and echocardiogram. If acute coronary ischemia is present, revascularization may restore RV cardiac function. Other precipitating causes such as arrhythmias, irregular heart rates, hypercapnia, or hypoxemia should be corrected. Preserved systemic blood pressure should (i.e., alpha-adrenergic agents) optimize RV preload (i.e., gentle fluid administration in acute RV infarction) and reduce RV afterload (i.e., diuresis in decompensated and dilated RV). Nitric oxide, prostanoids, and PDE5 inhibitors are beneficial in improving afterload in acute RV failure. Agents such as PDE3 inhibitors (i.e., milrinone) should be used to improve contractility [25]. Epinephrine should be used with caution as it may lead to tachycardia.

Infection Control

Chronic heart failure can result in an increased risk of infection due to inflammation, immunosuppression, and malnutrition. Many patients with heart failure evaluated for MCS therapy have had prolonged hospitalizations resulting in an increased risk for colonization with an infection from antibiotic-resistant organisms. Furthermore, peripherally inserted central catheter (PICC) lines, central venous catheters, indwelling urinary bladder catheters, intra-aortic balloon pumps, and endotracheal tubes represent ongoing infectious risks to the patient. Remove all unnecessary lines before implant. Indwelling lines required for the patient's clinical stability or safety should be inspected and changed with cultures drawn if there are

any signs of infection, such as elevated white blood cell count or fever. Suppose as time and clinical status permit, a preoperative dental assessment for all patients is warranted [24].

Assess all individuals' signs of infection before LVAD implant and aggressively treat with antimicrobial therapy. An active infection can increase morbidity at implantation, resulting in the seeding of the device that is rarely eradicated, even with prolonged and aggressive antibiotic therapy [24]. It may be helpful in these cases to have the assistance of an infectious disease specialist to manage the antibiotic recommendations. Patients should also have a nasal swab to screen for methicillin-resistant staphylococcus aureus (MRSA) and receive topical treatment with antibacterial ointment to the nares if positive before LVAD implant. Wash individuals with chlorhexidine alcohol the evening before surgery to prevent the colonization of hospital organisms on the skin. The skin is also prepped with chlorhexidine-alcohol and povidone-iodine in the operating room before incision.

All patients should receive perioperative prophylactic antibiotic treatment. The regimen will vary from center to center, but a process should be in place to ensure all patients receive their antibiotics dosed appropriately to the patient's renal function and timed to be most efficacious with the upcoming surgery. Perioperative antibiotics typically consist of gram-positive coverage and broad-spectrum gram-negative coverage based on known epidemiological data, risk of infection with these pathogens, colonization rates, and individual optimization [24]. High-risk patients may also require antifungal coverage. Infectious disease experts may be consulted for recommendations when variations from the standard of care are deemed necessary.

Conclusion

Left ventricular assist devices have become an integral therapy for individuals suffering from advanced heart failure. INTERMACS profiles provide a standard scale to identify the clinical severity, ranging from 1 to 7, with one being the sickest patient requiring mechanical circulatory support. While preoperative comorbidities are not absolute contraindications to LVAD therapy, they directly impact morbidity and mortality postoperatively. To gain the most benefit of LVAD therapy, assess preoperative comorbidities and optimize as time allows. In addition to clinical concerns, perform a thorough psychosocial assessment before the LVAD implant. The goal of this assessment is to identify barriers to LVAD therapy and success long-term. Often these barriers can be overcome through the collaboration of the multidisciplinary LVAD team. Physical strength and conditioning should be optimized both pre-LVAD and post-LVAD through rehabilitation and cardiac rehab, respectively. Lastly, immediately before LVAD implantation, individuals should be optimized hemodynamically, and any risks for infection should be addressed and empirically treated with antimicrobial medications.

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Surgical Insertion of a Ventricular Assist Device

George Batsides and Anja Strehlow

Preoperatively

It is beneficial to schedule a pre-surgical meeting the day or two prior to scheduled insertion to review the patient case. Participants from all departments who will be in the OR should attend, including surgeon(s), surgical assistant, cardiac anesthesiologist, perfusion, MCS coordinator, and OR nurse. During this meeting it is pertinent to review any medical issues, surgical approach, concomitant procedures needed, ECHO/cath/CTs, concerns, etc. Relevant medical history includes CAD/ischemia, PHTn, PVD/PAD, renal disease, hepatic disease, ICD, prior cardiothoracic procedures, prior epicardial ablation, prior abdominal surgery, LV issues (thrombus, aneurysms), and RV function. Also discussion should be the location of the driveline exit site based on patient body habitus and hand dominance.

Upon completion of all preoperative evaluations and work-up by the multidisciplinary VAD team, informed consent is obtained. Informed consent should include the typical cardiac surgery complications including potential for bleeding, stroke, death, reoperation, infection, and myocardial infarction. The patient and family should be made aware of the general acute high-risk nature of surgery in patients with failing hearts. The team should also cover topics of potential right ventricular failure and therapeutic options that may be required during the intraop and immediate post-operative period. The potential for future complications like driveline infection, mucosal and gastrointestinal bleeding, and anticoagulation

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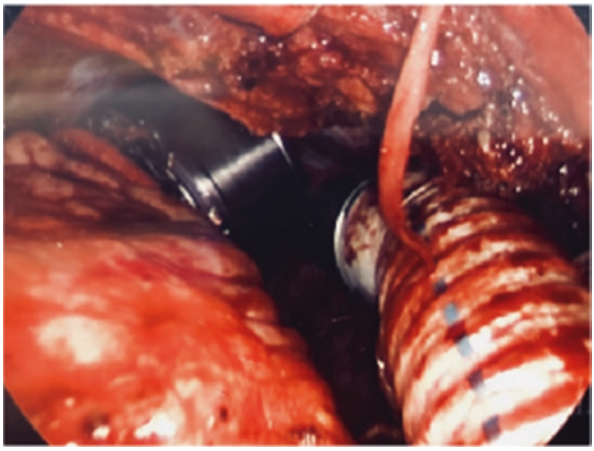

Fig. 1 HeartMate III inserted at apex of left ventricle

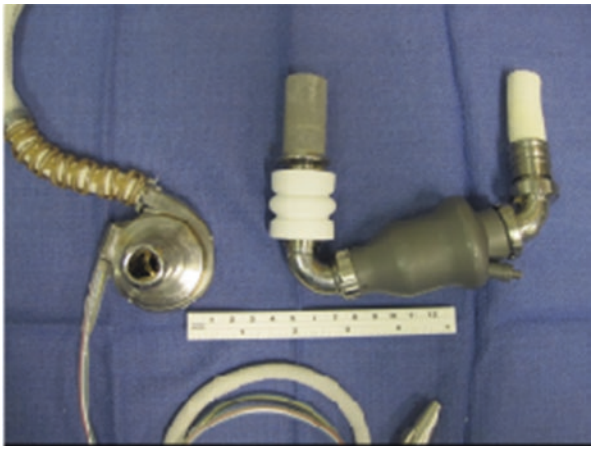

Fig. 2 Left: HeartMate III centrifugal flow pump, right: HeartMate II axial flow pump

strategies need to also be discussed. The type of device to be implanted should be discussed with the VAD team during this pre-implantation meeting. Figures 1 and 2 highlight VAD pumps that may be considered.

Operative Techniques

Standard cardiac surgery arterial monitoring, central venous access, and urinary catheter are employed. Pulmonary artery catheter insertion and standard cardiac general anesthesia induction strategies are utilized. Transesophageal echo (TEE) is performed and diagnoses are confirmed. The TEE should also focus on the presence of patent foreman ovale, evaluation of atrial septal defect, left ventricle apical thrombus, and left atrial appendage thrombus. The degree of mitral regurgitation and aortic insufficiency is also accessed. (Please see outline attached). *Note, PFO/ASD's should be closed and LV thrombus removed during the procedure*.

After confirming diagnosis, TEE is then focused on right ventricular function including measurement of the tricuspid annual plane systolic excursion (TAPSE) and wall motion abnormalities along with evaluation of tricuspid regurgitation. To assist in the evaluation of RV function, central venous pressure (CVP), pulmonary artery pressures, and pulmonary artery pressure index (PAPI) score are also noted. The PAPI is calculated by (systolic PA − diastolic PAP/CVP).

The degree of aortic valve insufficiency (AI) should be closely evaluated. Trace to mild AI can be left alone, however, mild to moderate and moderate to severe AI should be treated at the time of LVAD implantation (Fig. 3). This can be accomplished by aortic valve plication (Park stitch) or aortic valve replacement with a bioprosthetic valve (Fig. 4). Mechanical valves are not recommended as thrombus can form due to lack of opening. It is generally accepted that mitral regurgitation can be left alone.

The degree of tricuspid valve regurgitation (TR) in LVADs is an often debated topic. The causes of TR need to be as clearly defined as possible (i.e., secondary to pacer/defibrillator wires, dilated annulus/functional). Frequent practice is to repair moderate to severely regurgitant valves. This can be achieved relatively quickly using an annuloplasty ring without cardioplegic arrest.

Special consideration to intra-operative left atrial appendage ligation/clipping, dealing with LA thrombus if present as with prior mitral clips should be planned out preoperatively. Mitral clips that are not well placed or fixed should be removed via the ventriculotomy.

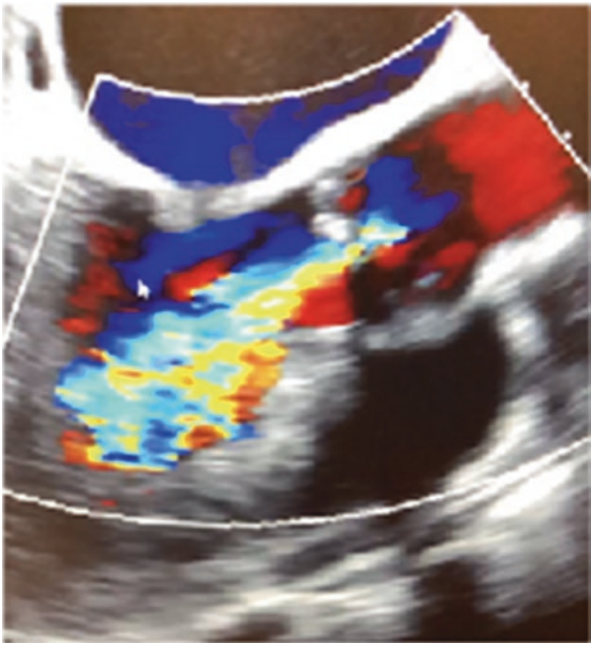

Fig. 3 Severe aortic insufficiency on echo

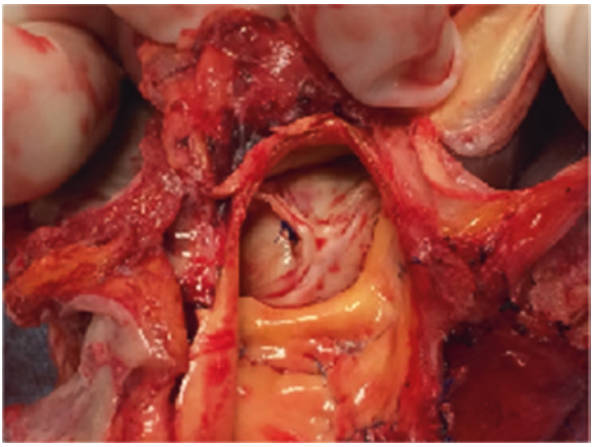

Fig. 4 Park stitch technique in LVAD patient visualized at time of cardiac transplantation

Procedure

Different LVAD implant techniques have evolved over the years. The primary used approach is the standard full sternotomy approach. It is important to note that some implanting centers have adopted a mini-sternotomy/L mini-thoracotomy and sternal sparing R mini-thoracotomy/L min-thoracotomy approaches (Fig. 5). For simplicity, we will focus on the basic inflow and outflow insertion techniques via a full sternotomy and central cannulation for cardiopulmonary bypass (CPB).

Full sternotomy is the most widely used exposure for LVAD insertion. It allows access to the entire heart and ascending aorta. If multiple procedures are needed to be performed this is the ideal exposure. After the sternotomy is performed, the pericardium is opened widely in an inverted T fashion. Pericardial sutures are then placed. It is important to note that the left side of the inverted T needs to be extended as wide as possible and often extends into the pleural space. This allows for optimal positioning of the VAD (specifically for HeartMate III and HVAD). HeartMate II requires a pump pocket to be developed below the rectus muscle (Fig. 6). This is achieved by opening the rectus sheath like an envelope thus placing it on top of the posterior sheath but below the rectus muscle. This pocket often times crosses the midline to the right side. Although HeartMate II is less widely used at the time of this publication, there are certain patients/situations that it is still implanted such as device exchange for thrombosis/malfunction. Creation of this pocket should be prior to administration of heparin. As can be seen in the photo the pump sits nicely in the pocket on the edge of the diaphragm, as if it were on a shelf, with the inlet cannula pointing down into the LV apex.

As a practice when opening the pericardium superiorly, it is recommended to take down the pericardial reflection off the aorta exposing some of the undersurface of the aortic arch. This is to ensure aortic cannulation is performed high, leaving room for a partial occlusion clamp for the outflow graft and other necessary

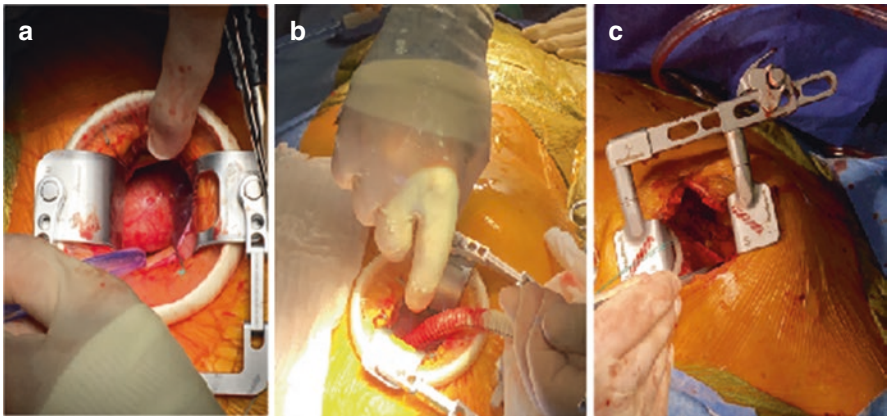

Fig. 5 Surgical Implantation. (**a**) Ascending aorta exposed via right mini thoracotomy. (**b**) Aortic outflow graft sewn to ascending aorta. (**c**) LV apex exposed via left mini thoracotomy

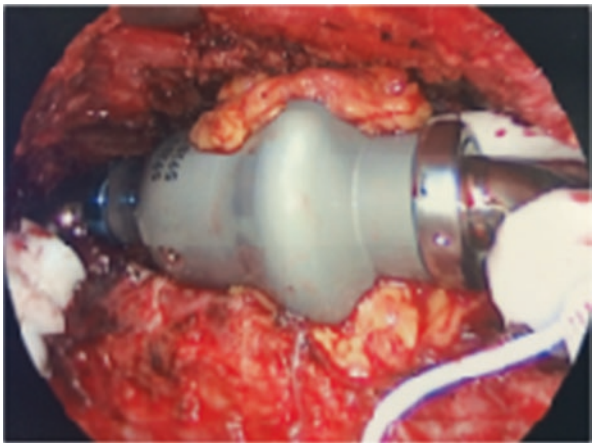

Fig. 6 HMII seated in pocket, with omental pedical covering an old extracorporeal LVAD rectus exit site

procedures (i.e., aortotomy for valve repair or room for proximal vein graft to the right coronary artery).

At this point any lysis of adhesions is performed and the aorta is separated from the main PA, allowing room for clamping. The patient is fully heparinized for a target-activated clotting time (ACT) of >450 s. Subsequently, the aorta and right atrium are cannulated forcardiopulmonary bypass (CPB) (cannulation of superior vena cava and inferior vena cava may be needed for PFO closure and tricuspid work). An aortic root vent is placed and the LVAD pump is set up and primed on the back table by perfusion or VAD coordinator.

When ready, cardiopulmonary bypass is instituted. In general, there is no need to cross-clamp the aorta and arrest, but rather stay warm. Otherwise cooling is

performed to the surgeon's temperature preference. CO_2 is used to flood the field to minimize O_2 embolization. Often times the lungs are kept ventilated at low tidal volumes.

The patient is placed into trendelenburg position and multiple wet lap pads are placed behind the heart elevating the LV apex. Next the true apex of the LV is identified using digital pressure and echo guidance (Fig. 7). The direction of the operator's index finger is toward the mitral valve and not the septum. This point cannot be over-emphasized; the direction needs to be confirmed prior to sewing the cuff and/or coring the apex. Time is taken to ensure perfect apical positioning and the area is marked. Once confirmed the sewing cuff is brought up and positioned accordingly. For the HeartMate III and HVAD the cuff is then sutured first with four tacking sutures (knots tied over a pledget away from the cuff).

Now using a running 3-0 proline suture with healthy bites of muscle, the cuff is sewn to the apex. Again prior to coring, testing with digital pressure is performed to ensure optimal position, as at this point it can still be corrected. When satisfied with appropriate positioning, the coring device is brought to the field and the apex is cored out with the root vent off (if placed) (Fig. 8). A floppy sucker is placed in the LV to assist in visualization and any trabeculae that would impede the inflow cannula are cut and removed. Apical clot is removed at this time as well. The pump is locked into place and the lap pads are all removed, dropping the heart carefully back to normal position in the pericardium. Echo confirms the inflow cannula positioning. Prior to moving on to the next step, it is key to ensure good hemostasis at the apical cuff/LV suture interface. This area may need to be reinforced (with felt or glue) especially in patients with prior/recent anterior wall infarcts as the tissue may be friable.

Next the bend relief is secured and the driveline is tunneled out through the rectus to the anterior abdominal wall near the costal margin in the anterior axillary line. The exit site should be marked and reviewed preoperatively with the patient. One must take into consideration where the patient's belt line will fall so the exit site is not too lateral or posterior. Ideally, this location should be marked prior to implant in discussion with VAD team and patient input. The driveline tends to exit out on the

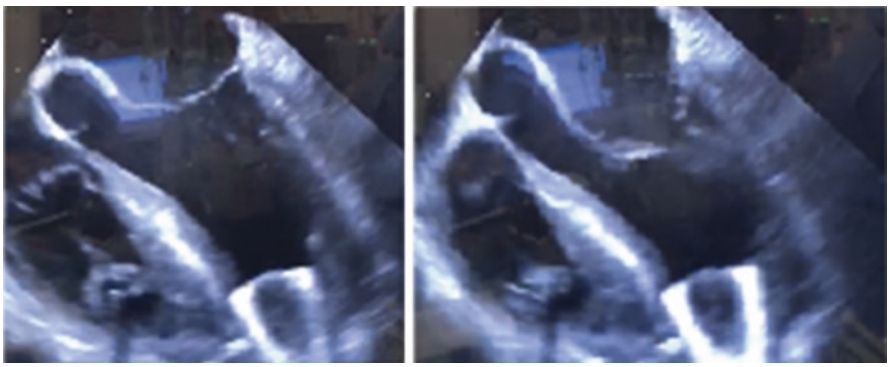

Fig. 7 Echo showing proper inflow orientation towards mitral valve

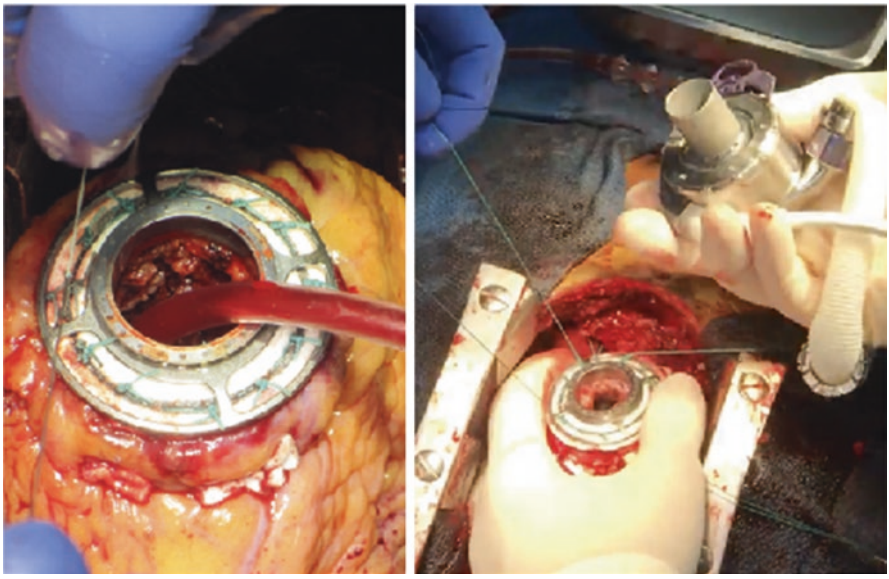

Fig. 8 Attaching the sewing cuff to the apex

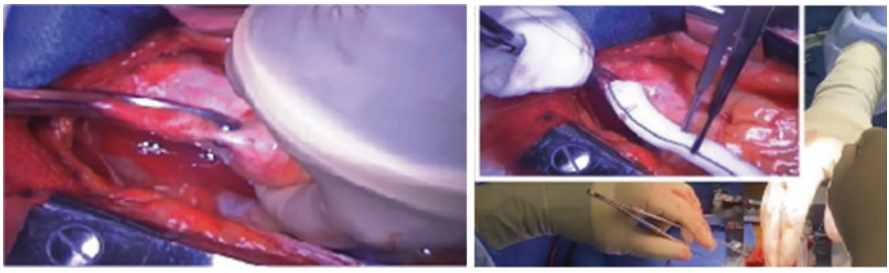

Fig. 9 Partial occlusion clamp being applied to ascending aorta and outflow graft being sewn

left but has on occasion gone to the right due to patient preference (side sleeper or dominant handedness). The pump is then connected and ready to be turned on once the outflow graft is completed.

The outflow graft is now tended to. The graft is stretched and brought to the ascending aorta and trimmed accordingly (Fig. 9). This step is also of utmost importance, as leaving the graft too short or too long can cause kinking. To obtain optimal length; volume is left in the heart and the distended graft (with a vascular clamp applied to the end) is draped along the acute margin with some slack allowing it to fall in the gutter adjacent and lateral to the right atrium and on to the greater curvature of the aorta. The graft then trimmed and beveled. Now with the CPB machine at transiently lower flow a partial clamp is placed on the ascending aorta along the greater curvature. Pump flow is restored and a small aortotomy is

made and extended, the superior and inferior margins are opened up with a 4.0 punch. This will help ensure an open anastomosis. The anastomosis is created with a running 4-0 prolene.

Upon completion and prior to removing the clamp de-airing is performed either with a vent placed in the ascending aorta above the clamp and/or one in the outflow graft based on the surgeon's preference (Fig. 10). Once the clamp is removed, further de-airing will need to be completed once the pump is turned on. Careful de-airing of the LV and LVAD will take some time. Great care is taken to avoid cerebral embolization of air as well as embolization down the right coronary artery as this will transiently affect RV function.

With vents on and volume left in the heart the LVAD is now turned on. Once de-aired, the weaning process is started. Appropriate inotropic and pressor support is added by the anesthesia team. In choosing pressor doses be mindful that norepinephrine can be more of a pulmonary vasoconstrictor and vasopressin is often needed in chronic heart failure patients. Lung tidal volumes are brought back to normal range in preparation for weaning from CPB. Volume is left in the heart slowly and LVAD revolutions per minute (RPM) are slowly elevated. This weaning process differs for surgeons and is tailored accordingly on a case-by-case basis. Special attention is given to hemostasis prior to complete weaning, any repair sutures needed should ideally be done prior to full wean. Special attention is also given to the status of the right ventricle and the pulmonary pressures. Milrinone/epinephrine and nitric oxide are added as needed. In general, weaning from CPB with a higher MAP (75-80 mmHg) for RV support is ideal. This can be allowed to drive back to the 65–75 mmHg range later dependent on the RV function. Once fully off CPB the systolic blood pressure and RV function are closely monitored. In

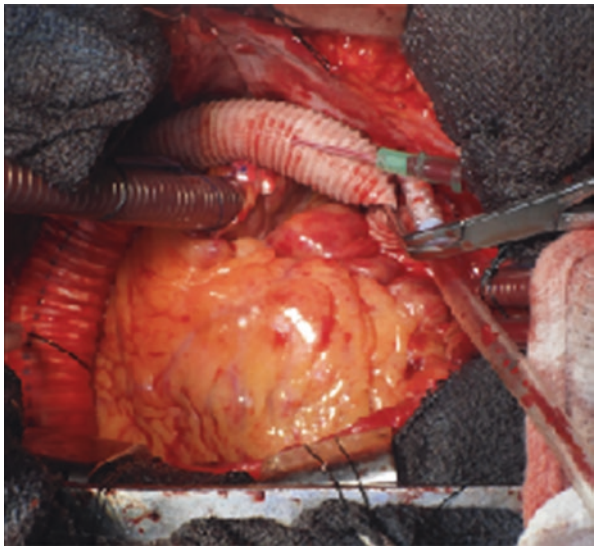

Fig. 10 Pump de-airing; vent in outflow graft and clamp above as LVAD is turned on

general teams will wait 15–30 min prior to administering protamine. Close attention is paid to the CVP and PAPI. CVP of greater than 18 mmHg is concerning in this period.

It is important to note weaning from bypass should be done slowly and in stepwise fashion; slowly leaving volume in the heart and dropping CPB flows as elevating the LVAD RPMs. This can be case-specific and surgeon-specific. Attention is paid to LVAD RPMs, LVAD pulsatility index, and LVAD flows. Great care is also given to the echo and the intraventricular septum. As the LVAD RPMs are titrated up it is important to note that the septum remains midline. Ramping of the LVAD RPMs too high will cause septal shifting into the LV and thus compromise RV function.

Once safely off cardiopulmonary bypass and when there is good assurance RV function is adequate, protamine can be administered and cannulas removed. The chest is drained with multiple Blake drains and temporary pacing wires secured if need be. Meticulous hemostasis is achieved to avoid large transfusions of blood products in the postoperative period which also may compromise RV function. As mentioned before right-sided pressures are monitored closely and treated accordingly. Figure 11 demonstrates the completed VAD inserted. The chest is closed in the standard fashion, anti-adhesive barriers can be utilized especially if chest reentry is considered in the future for cardiac transplantation. Finally with chest closed and prior to removing TEE probe, LVAD flows/pulsatility index are optimized ensuring the septum is still midline.

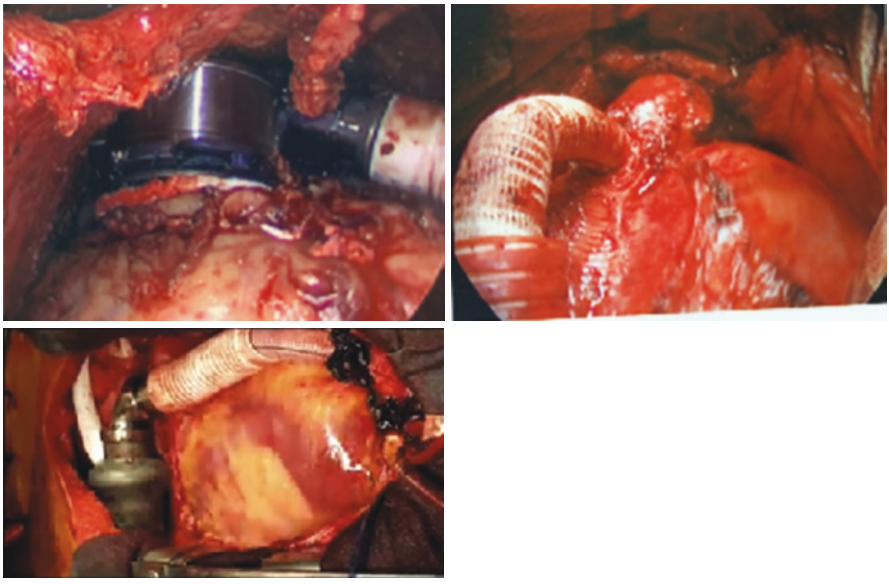

Fig. 11 Completed installation. (**a**) HeartMate 3. (**b**) Outflow graft. (**c**) HeartMate 2

Intra-op TEE

1. Prior to start of procedure, it is important to evaluate for aortic insufficiency, intracardiac thrombus (especially in the LV apex and LAA), tricuspid regurgitation (if significant can lead to RV failure), right ventricular function and shunts (PFO). Aortic insufficiency: if moderate or severe, then surgical intervention may be indicated via repair or replacement of the valve.
2. Intra-op, after coring make sure margins of the core are clean and smooth (heartware instruction handbook).
3. Post-implant VAD, it is important to use the TEE to monitor for bubbles during de-airing of the heart and observe the ventricle and septum during initiation of VAD therapy. It is important to note the flows and position of the LVAD.
4. As the VAD speed is increased, it is important to use TEE to monitor valvular function and septal positioning. Specifically, you want the septum midline (not bowing in either direction). Note any regurgitation, most of the time, MR lessens as LV is unloaded. Look for AI. Undiagnosed AI leads to improper output from the VAD and can lead to volume overload and worsening heart failure.

Anesthesia Pearls

1. Make sure no PFO
2. Central access/lines
3. Make sure no catheter is too far in, causing damage to potential structures such as valves
4. Pulmonary hypertension—minimize with milrinone, inhaled nitric oxide
5. Provide RV support
6. Likelihood of vasoplegia and treatment plan (inotropes, methylene blue)
7. Maintain adequate preload to avoid suction events (causing sucking in of tissue and/or ectopy)
8. Likelihood of bleeding, treatment planning. Have multiple units of packed red blood cells, fresh frozen plasma, and platelets in the OR

Intraoperative Management

In OR, prior to start of procedure:

1. Call electrophysiology to adjust settings on the patient's internal cardiac defibrillator, if the patient has this device. It is recommended to turn off all tachycardia therapies (ATP & shock) however there should be a back up rate so the RV maintains support.
2. All patients should have central venous access, preferably two sites of access. A multi-lumen catheter is necessary as is central venous introducer for pulmonary artery catheter monitoring, an arterial line, and TEE monitoring.

3. Remove any previous lines the patient may have to reduce infection.
4. Check echo with bubble study to make sure there is no PFO. If a PFO is missed, the patient will have a right to left shunt which will lead to hypoxemia and paradoxical embolization. If a PFO is found, this must be closed during the procedure.
5. Consider if a patient needs a TV annuloplasty: If the mean pressure gradient across the valve is >5 mmHg then a repair is recommended.
6. Prophylactic antibiotics given prior to skin incision.

During Procedure

While on bypass, it is very important to montor blood pressure and MAPs. It is important to keep MAPs above 60 in order to protect the kidneys. Patients may require pressors if MAPs drop below 60.

Perioperatively, monitor CVP. It will give you an idea of volume status. Generally, if their CVP is >15, they are hypervolemic. If <10, they are considered hypovolemic and may require IVFs or blood products.

When pump is first initiated:

Make sure LV full prior to initiating LVAD

- **HVAD**: Start at 1800, de-air, go up by 100 RPM intervals, slowly increase RPMs to 2300. Go up slowly to avoid suction events. This could lead to ingestion of tissue or ectopy. If at anytime you lose pulse variability on the monitor, tell the OR team and go back down by 100.
- **HM2**: Start at 7000 RPM. Watch PIs. Normal range is 2.5–6.5.
- **HM3**: Start at 3800, go up to at least 4800. Watch PIs. Normal range is 2.5–6.5.

Pearl: If the patient is on inotropes and has low pulsatility, not okay to leave this, must be addressed.

- Watch for low or no pulsatility, hypotension, and arrhythmias. Watch for low flow alarms and increased PI alarms (too low preload or too high speed).
- Prior to coming off bypass and starting ventilation, make sure inhaled nitric oxide (iNO) has been initiated to lower PAPs to support the RV. iNO 12 ppm is generally recommended.

Most important to protect and support the RV while initiating LVAD therapy and for the first week after initiation. The right ventricle is used to being "lazy" in response to the failing left ventricle. Once the LVAD has been initiated, the CO dramatically increases, therefore, the right ventricle needs time to get used to the increased work from the left ventricle. The right ventricle is supported with inotropes (dobutamine), inhaled nitric oxide, and increased heart rate (remember HR × SV = CO) via pacing. Start low on speed and slowly increase speed over the next days to weeks.

Pearl: Make sure you keep track of what happens throughout the procedure. If the patient had VT, blood loss, difficulty coming off bypass, etc., any other issues. Knowing what happened in the operating room will help with post-operative management.

Concomitant procedures:

1. LAA ligation
2. LAA clip
3. AV closure
4. MV ring
5. TV annuloplasty

Postoperative Management of the VAD Patient

Sarah E. Schroeder and Sarah Schettle

Immediate Postoperative Care

Return to the Intensive Care Unit

Following surgery, VAD patients oftentimes recover in the intensive care unit (ICU). Upon the return to the ICU, a flurry of information is discussed between the ICU nurses, anesthesia, and respiratory teams, including the operating room staff. There are multiple things to think about based upon the role of the VAD clinician in individual implanting centers such as hemodynamic instability, arrhythmias, device-related complications, coagulopathy, and right ventricular failure [1]. Some VAD clinicians attend the surgical implant in the operating room, and stay through the immediate recovery in the ICU room to ensure stability of the VAD patient.

Necessity of the Implantable Cardio-Defibrillator

Implantable cardio-defibrillators are important to have in place following VAD implantation due to the high incidence of ventricular arrhythmias [2]. An excised core of the left ventricular apex is removed at the time of surgery to make room for the left ventricular cannula. This is one potential substrate for ventricular arrhythmias, along with another substrate potential from incisions in the anterior atrial wall from repair of either the mitral or tricuspid valves [3]. Reversible causes should be investigated for ventricular arrhythmias in the immediate postoperative period. This

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may include hypovolemia, electrolyte abnormalities, tamponade and right ventricular failure, and suction events. Arrhythmias occurring within a week post VAD implantation are associated with higher risks of morbidity and mortality [3]. The most significant risk of ventricular arrhythmias post VAD implantation is the stress to the unprotected right ventricle.

There is inconsistency in the literature for recommendations regarding the benefit of implantable cardio-defibrillators in VAD patients [4–6]. There is also minimal literature on settings of the implantable cardio-defibrillators following VAD implantation [6], the importance of maintaining the function of the left ventricular lead for biventricular pacing effects [7], and the significance of the use of antitachycardic pacing prior to defibrillation [6]. Therefore, settings of implantable cardio-defibrillators will be unique to individual centers and guided based on each individual VAD patient.

Inotrope Use

Perioperative cardiac dysfunction occurs in upwards of 20% of cardiac surgeries. This dysfunction can manifest itself by hypotension and cardiogenic shock, or cardiac stunning [8]. Inotropes are often used to gain vasodilatory effects in treating cardiogenic shock, increase cardiac output and end-organ perfusion, and assist in resolving vasoplegia that is quite commonly found following cardiac surgery [9]. Decreased cardiac output secondary to cardiogenic shock or post-cardiac surgery leads to hypoperfusion of the tissue, resulting in hypoxia, and lactic acid build up. Inotropes are helpful to increase cardiac output in these situations to prevent multiorgan failure and mortality [10]. Regardless, the use of inotropes post VAD implantation is not well described in the VAD literature, and will be subjective to individual programmatic decisions. See Table 1 for a more thorough description of medications used in the postoperative VAD setting [11, 12].

Chest Tube Output

Following VAD implantation, chest tubes are placed to assist in clearance of post-surgical bleeding and retained blood. The more clot the chest tubes get in the immediate postoperative period, the higher chance of cardiac tamponade, leading to potential for re-operation and wash out. Bleeding is a common complication post VAD implantation, and may be identified by having more than 200 mL/h [13]. Taking individuals back to the operating room increases risk of complications, including mortality and increased blood transfusions [14]. Literature suggests benefits to active tube clearing of the chest tubes for reduction of reoperation due to bleeding [14]. Coagulopathy should be corrected if abnormalities are found to decrease chest tube output. The number of chest tubes placed, locations, and chest tube sizes will be made at the discretion of the implanting surgeon.

Table 1 Medications used in the post-VAD setting [11, 12, 40]

Medication name/ classification	Mechanism of action	Dosing	Potential side effects
Dobutamine (inotrope)	– Stimulates beta-1 adrenergic receptors – Raises blood pressure and decreases left ventricular end diastolic pressure by increasing cardiac output	2–20 mcg/kg/min	– Arrhythmias – Increased heart rate – Increases myocardial oxygen demand – Refractory hypotension
Dopamine (inotrope)	– Vasodilation of coronary and renal arteries (low doses) – Increases blood pressure – Increases pulmonary capillary wedge pressure (mid doses) – Increased afterload due to potent vasoconstriction (high doses)	1–20 mcg/kg/min[a]	– Arrhythmias – Increased heart rate – Palpitations – Hypertension
Epinephrine (vasopressor/ inotrope)	– Acts on beta-1 adrenergic receptors (low doses) causing vasodilation – Acts on both beta-1 and beta-2 adrenergic receptors causing vasoconstriction (high doses)	0.01–0.2 mcg/kg/min[a]	– Decreased peripheral perfusion – Increased lactic acidosis – Tachyarrhythmias – Gastric mucosal hypoperfusion – Hyperglycemia
Milrinone (inotrope)	– Potent pulmonary vasodilator – Increases cardiac output by enhancing contractility – Decreases heart rate	0.125–0.750 mcg/kg/min	– Hypotension – Arrhythmias
Norepinephrine (vasopressor)	– Acts on alpha-1 adrenergic receptors producing vasoconstriction – Increases systolic pressure and decreases diastolic pressure	0.01–0.04 mcg/kg/min	– Arrhythmias – Increased myocardial demand – Hypertension
Sildenafil (phosphodiesterase III inhibitors)	– Inhibits phospho-diesterease type 5 (PDE-5) function in smooth muscle of the lungs – Resulting in vasculature relaxation of the lungs and vasodilation (decreasing blood pressure in the lungs and decreasing right ventricular afterload)	20 mg three times daily	– Flushing – Headaches – Hypotension – Hearing loss

mcg/kg/min (microgram per kilogram per minute)

Nitric Oxide Use

Pulmonary hypertension secondary to left ventricular heart disease is the most common cause and generally defined by a resting mean pulmonary artery pressure of greater than or equal to 25 mmHg. This raises the mortality risk post VAD implantation and often excludes an individual for consideration of orthotopic heart transplantation, should the pulmonary vascular resistance be greater than 5 woods units or having a transpulmonary gradient of higher than 16 mmHg [15]. The overall pathophysiology of this type of pulmonary hypertension is thought to be from remodeling caused from a poor functioning left ventricle, causing decreased availability of nitric oxide leading to further arterial remodeling, yet still not well described in the literature [15]. Inhaled nitric oxide has been used post VAD implantation to assist in pulmonary vasodilation. The function of inhaled nitric oxide is not well described in the VAD literature either, however is frequently being used. This form of nitric oxide has been found to function as a potent vasodilator, and in turn decreases the pressure of the afterload of the right ventricle. Once inhaled, it crosses the alveolar-capillary membrane, is rapidly diffused and assists in the anti-inflammatory process as well as bronchodilation. Nitric oxide is responsible for activation of certain solubles on the cellular level, which in turn is responsible for conversion of intracellular components, leading to physiologic pulmonary vasodilation [16]. Sometimes pulmonary hypertension secondary to left heart disease is simply improved or resolved by off-loading the left ventricular pressures with the VAD itself. Right ventricular dysfunction is more prominent when the left ventricular is not sufficiently off-loaded [17].

Ventilator Management

Ventilator management is crucial to an individual's success following VAD implantation as there is noted increased morbidity and mortality for those with prolonged ventilatory support. There are many factors that feed into successful ventilator weaning, including the patient's individual pulmonary disease history and right ventricular function following implantation. Avoiding respiratory complications and acidosis will minimize right ventricular failure [18]. While there are many different types of ventilator settings to use postoperatively, pressure control allows for titration of settings based upon inspiratory effort instead of utilizing a set tidal volume, protecting individual patients from barotrauma. The pressure control setting allows for consistent airway pressure, leading to generalized alveolar distention and decreased dead space [19].

Ventilator weaning parameters will be based upon individual program policies. There are many things to consider when determining a patient's readiness to wean from the ventilator:

- Stable hemodynamics while on minimal inotropic support
- Adequate right ventricular function

- Normalized arterial blood gases with a pH ≥7.25, arterial blood oxygen levels ≥60 mmHg, minimal oxygen support with fraction of inspired oxygen level of ≤0.4
- Patient's ability to trigger the respiratory cycle without prompts [18]

Echocardiography Guidance with Speed Optimization

In the immediate postoperative period following VAD implantation, despite which pump is being implanted, echocardiography will assist in maximizing the function of the new pump in relation to the native heart function [18]. Many centers utilize echocardiography as early as the first postoperative day to evaluate five key characteristics: left ventricular end-diastolic dimensions (LVIDD), septal position, mitral valve regurgitation, right ventricular function, and status of the aortic valve opening or closing [20]. Beyond these dimensional assessments, another key purpose of echocardiography post VAD implantation is to optimize the speed of the individual devices. Each VAD team should have individual protocols for speed optimization in accordance with instructions for individual devices. For example, single-speed adjustments with the HeartMate II device will cause internal dimensional changes almost immediately, while speed adjustments with the Heart Mate 3 device, internal dimensional changes may not be seen for 24 h. Regardless, the initial speed is important to note on imaging prior to starting speed adjustments. Appropriate left ventricular offloading is determined by a normalized LVIDD. When adjusting speeds, the opening status of the aortic valve is important to note as to not subject the patient to further risk of aortic insufficiency development [20], as well as maintaining hemodynamic parameters with a mean arterial pressure ≥65 mmHg, and an interventricular septum that is located midline [21]. Interval echocardiography is important among the life of a VAD and should be incorporated into routine follow-ups [20].

Management of Surgical Lines

Surgical line needs are dependent on programmatic practices. Common surgical lines placed in preparation for VAD implantation may include (but not limited to) a central venous access line with multiple ports for high potency medication delivery and measurement of central venous pressure, a pulmonary artery catheter line for measurement of cardiac output and pulmonary pressures, and an arterial line for accurate blood pressure monitoring. Due to risk of infection from colonization of germs on the individual ports of each line, strict aseptic technique and protocols should be followed at each VAD implanting site. This will combat the prevention of central line-associated infections [22].

Antiplatelet and Anticoagulation Use in LVAD

LVAD patients require anticoagulation to mitigate risks of hemolysis and thrombosis, though these risks are reduced with the use of a fully magnetic levitation centrifugal flow device compared to axial flow devices and hybrid levitation centrifugal flow pumps [23]. Typically, anticoagulation consists of combination therapy with Aspirin and Warfarin as the gold standard approach. Limited reports exist for replacement of warfarin with novel oral anticoagulants [24] and larger studies to validate the use of such approaches and ensure safety and non-inferiority would need to be undertaken before such a change could occur on a larger scale. In some patients with a history of gastrointestinal bleeding, de-escalation of anticoagulation can be considered, either with reduction of aspirin dosing, or reduction of INR goal range. In patients with pro-thrombotic history or underlying conditions such as factor V Leiden, increases to INR goal ranges may be considered, and addition of alternative antiplatelet drugs such as P2Y12 receptor blockers have been utilized.

Heparin

Prior to LVAD, patients may or may not require warfarin due to comorbid conditions. However, it is not advised to proceed to LVAD implantation actively on warfarin, and instead, bridging with heparin is typically recommended. Dosage of heparin may be at low, medium, or high-intensity nomograms, and can be monitored via activated partial thromboplastin time (aPTT) or antifactor Xa monitoring. Heparin is a glycosaminoglycan that combines with antithrombin to inhibit activated coagulation factors [25]. Specifically, heparin inactivates thrombin to stop the process of thrombus formation with fibrin. Heparin cannot break up a thrombus that has already formed, but it can be used to stop the development of new thrombus or to stop the progression of an already existing thrombus.

Warfarin

Warfarin, which is metabolized in the liver and renally excreted, has its effect through the inhibition of the vitamin K epoxide reductase complex 1 (VKORC1) [26]. The effects of Warfarin are seen after 1–3 days, but several days of dosing are needed to achieve peak therapeutic effect. INR goal ranges for LVAD patients typically target 2.0–3.0, with patient-specific adjustments made at clinician discretion for cases of bleeding or clotting concerns. Frequently heparin bridging post-LVAD implant occurs concomitantly with warfarin initiation and titration until a therapeutic INR is achieved, facilitating the discontinuation of heparin bridging.

Aspirin

Aspirin is used in LVAD patients for its antiplatelet effect. It blocks the cyclooxygenase (COX-1) enzyme which ultimately stops platelets from aggregating [27].

Dosing typically ranges from 81 mg daily to 325 mg daily. It is metabolized in the liver and starts to inhibit platelets within 60 min of administration [28].

Generalities Due to Pump-Specific and Program-Specific Guidelines

LVAD devices of different generations do have slight differences in anticoagulation and antiplatelet recommendations. Manufacturer-specific instructions for use (IFU) guide timing and recommendations for antiplatelet and anticoagulation. Fully magnetic levitation centrifugal flow devices typically target Aspirin dosing of 81–100 mg daily, though some centers still utilize 325 mg daily, along with Warfarin. Hybrid levitation centrifugal flow pumps typically target Aspirin dosing of 325 mg daily along with Warfarin. Axial flow devices are now rarely done as primary implants and comprise less than 2% of implants in 2019 [23].

Timing of Extubation

Pulmonary Hygiene and Lung Volume Expansion

Any cardiac surgery involving a sternal incision affects the integrity of the chest wall musculature responsible for respiratory function. This can lead to increased atelectasis and postoperative pain. Other causes of pulmonary dysfunction include blood transfusions, surgical trauma, inflammation caused from the use of cardiopulmonary bypass, and increased ischemia with reperfusion [29]. Providing pulmonary hygiene and lung volume expansion early on in the postoperative phase is important in maximizing pulmonary function and promoting early extubation. Pulmonary hygiene consists of airway secretion clearance through suction catheter use, deep breathing exercises through the use of incentive spirometry, use of nebulizing medications (such as bronchodilators) to open up airways and loosen secretions, and use of other assistive devices designed to loosen secretions such as a Flutter valve or intermittent positive pressure breathing (IPPB) devices [30]. Chest X-rays may be useful in monitoring daily volume expansion and for evaluation of atelectasis and pleural effusions.

Spirometry

Incentive spirometry is important following VAD surgery as the main purpose is to mimic slow deep breathing that is performed with sighing. Proper technique is key in performing incentive spirometry in order to benefit respiratory function. Patients should be sitting as upright as possible. The individual performing incentive spirometry needs to use nose plugs to inhibit air escaping from the nose, and then slow deep inhalation over a minimum of 2–3 s followed by breath holding for 5 s. The inhalation goal should be individualized per patient based upon height and weight. Incentive spirometry when used frequently and appropriately, can prevent or reverse atelectasis and increase lung volumes [31].

Nutrition in a VAD Patient

LVAD patients can be frail [32] and may not have optimal nutrition prior to LVAD implantation. Such factors portend worsened outcomes post-LVAD regardless of the underlying cardiac disease, and optimization should be undertaken to improve patient outcomes post-implant. Engagement of nutrition services prior to and while hospitalized is an important first step. Some patients may require tube feedings for nutritional support before transitioning to a normal diet. Other patients may require high-calorie nutrient-dense liquid shakes to meet their nutritional requirements until they are able to consume the necessary calories. Still other patients may need guidance on reallocating their caloric choices. These choices may be complicated by underlying medical conditions such as diabetes [33] which may require additional effort for patients to make appropriate choices. Patients may return to a home environment with meal options that may be inadequate to meet their nutritional requirements. Addition of a multivitamin to the patient medication regimen should be considered. Time should be spent to educate the patient on the importance of nutrition targeted specifically to their individual needs and understanding of other dietary components such sodium and fluid intake, and their impact on underlying heart failure.

Labs and Imaging of the Hospitalized VAD Patient

Laboratory Checks

Daily laboratory checks are performed on LVAD patients to monitor patient progress while hospitalized. Complete blood count (CBC) can help guide the clinician to determine hemodynamic stability and warn of concerns for bleeding, infection, or thrombocytopenia. Both fully magnetic levitation centrifugal flow devices and hybrid levitation centrifugal flow pumps also allow for entry of the most recent hematocrit value to calculate a more accurate flow reading from the LVAD. Metabolic panels can demonstrate renal function, hepatic congestion, nutritional status, and electrolyte balances and can guide appropriate diuresis and electrolyte repletion. Laboratory checks to measure anticoagulation and antiplatelet therapy can help guide dosing of these agents. Additional labs that are often utilized regularly may include, but are not limited to, lactate dehydrogenase and plasma hemoglobin to rule out concerns of hemolysis or thrombosis, B-type natriuretic peptide (BNP) to assess for fluid overload and worsened heart failure, and anti-HLA antibody testing for LVAD patients that are transplant candidates, and others.

Blood cultures and driveline cultures may be drawn with suspicion of infection. When possible, cultures should be obtained prior to antimicrobial commencement to ensure that culprit organism(s) are identified prior to treatment. Early engagement of infectious diseases teams to help guide infection treatment can be instrumental in timely treatment of these patients, along with pharmacy support to mitigate concerns with other medications taken concomitantly, as well as dose reduction based on organ function.

Imaging Studies and Procedures

In the postoperative setting, chest X-rays may be performed daily to assess for stability, fluid, positioning, and other concerns. Other imaging studies and procedures that may be obtained in LVAD patients in the postoperative include, but are not limited to, invasive line placement for infusions and blood draws, transfusions to maintain hemodynamic stability, electrocardiograms (ECG) or ICD interrogations to monitor rhythm status, echocardiograms (echo) to guide speed and medication adjustments, and right heart catheterization to determine pressure tracings. When patients leave their room for such studies, it is important to have a plan in place for a VAD-trained individual to be present and able to assist with device concerns, particularly when a study or procedure requires sedation.

Frequency

Early in the postoperative setting, the frequency of laboratory checks and imaging should be more frequent, and often will occur daily. As patients stabilize and day-to-day perturbations decrease, a de-escalation in the frequency may be considered. Such de-escalations may be considered when patients transition from the intensive care setting to a progressive care unit, or from a progressive care unit to an inpatient rehabilitation setting. Frequency of checks should be guided by patient progress and clinical necessity.

Importance of Right Ventricular Function Following Implantation

Right Ventricular Strain

Right ventricular failure occurs in upwards of 40% of individuals undergoing VAD implantation. Much literature exists describing the causal effects of right ventricular failure and different ways to predict right ventricular failure. One measurement in recent literature includes the measurement of right ventricular free wall strain, which when found prior to surgery is predictive for right ventricular failure [34, 35]. Overall, individual implanting centers should have a systematic way for assessing for right ventricular strain predisposing individuals to right ventricular failure.

Early Right Ventricular Failure

Increased workload of the right ventricle is needed following VAD implantation, in order to keep up, causing the right ventricular preload to increase and right ventricular afterload to decrease. Right ventricular failure can occur immediately following

VAD implantation due to this increased workload, potentially leading to increased right ventricular strain and dilation, affecting contractility and leading to the need of a temporary right ventricular assist device (RVAD) to allow for the right ventricle to rest. The stress of right ventricular failure can be resultant from the reduced cardiac output of the right ventricle, affecting the functionality of the left-sided VAD, leading to worsening dysfunction and failure [36]. Echocardiographic assessment of the right ventricle and the tricuspid valve would identify a reduced tricuspid annular plane systolic excursion (TAPSE) measurement. Other echocardiographic findings may include increased right ventricular end-diastolic dimension and intraventricular septal bowing to the left ventricle, along with hemodynamic changes including increasing pulmonary artery pressures, increasing central venous pressure and hypotension [36]. Right ventricular failure post VAD implantation carries a higher morbidity and mortality risk.

Consideration of Right Ventricular Assist Device

Temporary right ventricular assist device support is necessary until the right ventricular function has been restored. Echocardiography will be used oftentimes following VAD implantation to evaluate the function of the VAD, but more importantly assess the right ventricular function. While there is no one consensus on the most appropriate ways to evaluate right ventricular function, there are multiple assessment tools that may be useful. The ratio of right ventricular end-diastolic dimension to left ventricular end-diastolic dimension of >0.72 is associated with higher incidence of right ventricular failure post VAD implantation. Tricuspid regurgitation and TAPSE measurements should also be evaluated post VAD implantation as these can be additional assessment measurements to indicate right ventricular failure. Interventricular septal position in right ventricular failure oftentimes bows toward the direction of the left ventricle. When considering the use of a temporary RVAD, the evaluation of pulmonary artery pressures will be important [36, 37].

Use of Phosphodiesterase-5 Inhibitors

As mentioned previously, pulmonary hypertension secondary to left heart dysfunction is the most common type and can be problematic after VAD implantation. Immediately in the postoperative setting, inhaled nitric oxide is often used to assist in pulmonary hypertension seen following surgery. A similar oral version of inhaled nitric oxide, known as Sildenafil, has been described in single studies, and found somewhat useful in combating right heart failure caused from pulmonary hypertension when initiated in the post-surgical setting. It is typically well tolerated with minimal side effects [38]. Classified as a pulmonary vasodilator at specific doses, Sildenafil has been found to decrease pulmonary vascular resistance and pulmonary artery pressures, which in turn contributed to the

prevention of right ventricular failure in the immediate post VAD implantation setting [39, 40]. One caution to remember in the discharge process is that often times insurances will not cover Sildenafil outside the hospital due to concerns of "off-label" use.

Pain Mitigation and Bowel Regimen

Postoperatively, it is important to manage surgical pain with an increasing emphasis toward limiting the use of opioids due to the risk of misuse and addiction as well as association with morbidities [41]. Some centers have implemented opioid-sparing approaches to pain to reduce the risk of opioid dependence [42]. If opioids are used, slowing of gut motility can also result known as opioid-induced constipation (OIC) [43], necessitating the implementation of a bowel regimen. First steps toward treatment of OIC begin with prevention and prophylaxis by ensuring adequate fluid, increasing fiber ingestion, and encouraging the patient to move [43] followed by addition of bowel regimen to the prophylactic measures. For patients with underlying chronic pain concerns, early engagement of pain management teams to ensure appropriate use and management of pain strategies is important. Over time, pain tends to decrease for most LVAD patients. One reason for pain improvement post-VAD may be attributable to the pro-inflammatory cytokines associated with advancing heart failure that are attributable in other pain pathways. Post-VAD, normalization of flow could cause a decrease in pro-inflammatory cytokines and subsequent improvement to pain [44].

Consideration of Blood Products

LVADs may be implanted as bridge to transplant (BTT) depending on candidacy for cardiac transplant. The need for transfusion in the operative period exists for the majority of the patients, and may recur with comorbid conditions such as gastrointestinal bleeding. For BTT patients awaiting a heart, regular measurements to assess sensitization toward donor organs are obtained to ensure appropriate matching when an organ becomes available. Some centers exercise greater caution in transfusing blood for BTT patients to avoid further sensitization or transfuse leukoreduced, irradiated, ABO identical blood products to mitigate sensitization risks [45].

Activity Post VAD

Sternal Precautions

The majority of patients proceed with LVAD implantation via median sternotomy, though lateral thoracotomy approach [46, 47] can be considered in selected patients.

For patients who undergo a sternotomy for pump placement, precautions or restrictions are typically initiated postoperatively to facilitate sternal healing. These precautions may entail weight limits while lifting items, range of motion limitations typically to include over the head movement, driving restrictions, and others [48]. Such restrictions or precautions may be center-specific regarding lifting and movement guidelines. Sternal wound healing complications range from infection to sternal instability [48]. These may require debridement or return to the operating room for further intervention.

Multidisciplinary Team Engagement

When possible, patients proceeding with LVAD implantation should be assessed by physical therapy, occupational therapy, and/or physical medicine and rehabilitation teams to appreciate baseline limitations and level of activity prior to surgery. These teams may also be able to assist in assessment of frailty preimplant. Determination of a baseline is useful to help guide treatment postoperatively and assist patients to returning to prior or improved level of functioning. Simple tasks and activities of daily living (ADLs) are more complicated and require more time following LVAD implantation due to the requirement to carry around the weight of the equipment and batteries during activities, the need to balance the weight of this equipment, and the need to maintain a waterproof environment while performing activities such as showering. Practicing activities to be performed in the home environment while hospitalized can help to facilitate a smoother transition to home and empower the patient and caregiver in this process. It is also important to highlight education surrounding the need for driveline securement. As patients increase their activity level and mobility, ensuring the driveline is appropriately secured through the use of an abdominal binder, Foley anchor [49], or other mechanisms can mitigate infection risk from a tugged driveline.

Engagement of Inpatient/Outpatient Rehab Options

Some implanting centers may have inpatient rehabilitation facilities within their center where LVAD patients may be admitted for further strengthening and conditioning, and others may contract with rehabilitation facilities. Strengthening and conditioning of patients postoperatively is not limited only to the inpatient setting. Frequently, patients are encouraged to engage in outpatient cardiac rehabilitation to continue the exercising and strengthening process initiated while hospitalized. These facilities may benefit from education about LVAD, alarms, and common alterations to typical patient vital signs such as lack of pulses and blood pressures in LVAD patients to increase comfort and familiarity with this patient population. Providing contact information should concerns arise can be helpful in mitigating additional concerns if they arise.

Patient and Caregiver Education Preparation

Multiple topic discussions are required to assist in discharge preparation of both the patient and the available caregivers. There are a multitude of resources available to patients and caregivers, yet research is lacking to date on how to deliver this education. Ventricular assist device programs should develop protocols of what needs to be covered regarding preparation education. Many VAD programs are beginning discussions prior to implantation to assist in memory recall. First and foremost, all recommendations need to be tailored to individual patients based upon instructions from the companies of the devices.

How to Carry the LVAD

When mobile, VAD patients need to determine what is best for them in order to carry their external equipment. One option may include a vest-type holster to place the batteries on each side of the VAD patient with securement options of the controller. Other options include concealed carry shirts, fishing vests, and other consolidation bags, both offered through the individual companies or offered commercially for a fee. Whichever way the patient chooses to carry their external equipment, the effects of carrying should be comfortable to limit pain or discomfort while providing stability of driveline during movement.

How to Shower with the LVAD

Each patient should follow the recommendations from their implanting center regarding the opportunity to shower. For those individuals who have been cleared for shower, there are a few things to consider. With each shower, the company's shower bag should be used every time in order to limit water exposure to the external equipment. Patients should be on their portable power sources to limit electrical discharges and potential damage to the external equipment or other adverse events to the patient. Lastly, the driveline dressing should be covered with some form of occlusive covering to limit direct water exposure, fully knowing that there is potential for moisture to get on the dressing itself. Some centers will require dressing changes following every shower, regardless of passive water exposure.

Alarms

Each device has its own alarms that need to be reviewed with patients and their available caregivers. Ventricular assist device coordinators should ensure that all alarms have been reviewed, discussed, and demonstrated with patients and caregivers. Hazard and advisory alarms should be shown to the patients and caregivers in order to troubleshoot these potential alarms in the outpatient setting.

Excursions (Where Applicable)

While excursions at one point were mandatory prior to a patient's discharge and return to the community, many sites are no longer mandating excursions and in turn are providing closer outpatient care. The functionality of an excursion was to prepare the patients and their caregivers for life on the outside of the hospital, without any medical professionals there to hold their hands. This was usually performed within a few days prior to the scheduled discharge, was a minimum of 3 h outside the hospital, and could have been anything from a lunch to running errands to going to a park.

Calling the LVAD Team

On multiple occasions, the VAD team needs to review with the patient and their available caregivers on reasons to call the VAD team. The reasons may include (but are not limited to): alarms, symptom management, medication questions, lab inquiries, or traveling issues. The patient and their available caregivers should have available to them the 24/7 call number in order to address their questions and concerns.

Inpatient Driveline Dressing Management

There is no consensus on driveline management globally making best practice guidelines difficult to develop. Many centers have moved to combining dressing items in a singular kit to ease the amount of risk for break in sterility. The first dressing change has occurred within 48 h post implantation for many centers [50]. Frequency of dressing changes in the hospital is protocol specific for each implanting site, however daily dressing changes have been reported in many institutions [50]. There are no guidelines on teaching caregivers clean or sterile technique as neither technique has been validated in the literature, although many companies recommend aseptic technique. There is a consensus report available as a member-only benefit developed by individuals of the International Consortium of Circulatory Assist Clinicians (ICCAC), discussing driveline exit site management and the steps needed for education. These steps include handwashing and preparation of the area, dressing removal and cleansing and disinfecting the driveline exit site, protection of the skin, antiseptic site covering, overall exit site coverage and lastly, utilizing the anchoring device.

Equipment and Dressing Supply Distribution

Ventricular assist device coordinators need to ensure the preparation of all discharge equipment and dressing supply distribution prior to discharge. Each VAD program has individualized protocols based upon the makeup of the program itself. This may

include the use of biomedical engineers to ready the equipment. Upon discharge, it is recommended to discharge the patient with all equipment needed for VAD function at home. This may include external power sources (A/C power source and external batteries), battery charger, shower bag, extra controller, battery clips, and back up bag. Again, this will need to be individualized based upon the device chosen by the patient. Dressing kits and sterile gloves are also important to send with the patient at discharge to bridge the time it will take for outside companies to supply the dressing supplies to the patient. Each center will have a plan in place for dressing kit distribution based upon the contracted companies for supply distribution.

Discharge Preparation

Rehabilitation Center Needs

Most LVAD patients will benefit from spending time in a formalized cardiac rehabilitation setting, either as in inpatient, outpatient, or both. Exercise in this format is beneficial for patients [51] and can reduce hospitalization and mortality [52, 53] as well as improve functional capacity and patient-reported health status [54]. Collaboration or contracting with a rehabilitation center to assist LVAD patients in strengthening and rehabilitation post-LVAD should be considered when such options are not offered at the implanting hospital. Offering training and educational sessions on LVAD patients, device management, and other guidance for cardiac rehabilitation staff members can aid in comfort and familiarity with LVAD patients and can help build a successful partnership.

Local Laboratory

Patients undergoing LVAD implantation may discharge to a community separate from the implant center where return to the implanting center may not always be feasible. Providing standing order labs to be drawn upon request can be a prophylactic step that is quite useful when patients present locally with concern for gastrointestinal bleeding, electrolyte disturbances, or other concerns where laboratory draws can prove useful in diagnosis and management of the condition.

Community Contacts

Encouraging patients to re-establish care with their local providers when they are discharged from their implant hospitalization can be helpful to allow their primary care provider or cardiologist to familiarize themselves with the LVAD prior to the patient presenting with new concerns coupled with the device in place. It is important to maintain these relationships as patients will require ongoing care for

preventative visits and for non-LVAD concerns. Ensuring good communication between the LVAD team and the patient's local medical providers is critical to maintaining this partnership for the patient. It can be helpful to send out letters prior to the patient's discharge delineating information about LVADs as well as the teams contact information for device-specific questions to begin this dialogue early. Centers will frequently collect a list of key contacts and their addresses from the patient or caregiver prior to LVAD implant or while the patient is convalescing in the hospital after device implant to comprise letters to the patient's local community. Addresses typically requested may include the primary care provider, cardiologist, electric company, EMS teams, fire department, and emergency departments, among others. Additional letters are frequently written for patients to provide to airport security or for events where security systems are in place that would require patients to be scanned. Such letters typically provide a general overview of the LVAD, explanations about why patients should not pass through high-powered scanners, and other relevant information specific to security personnel.

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Ventricular Assist Device Complications

Angela Washenko, Jami Bennett, and Justin Hamm

Introduction

One of the primary goals of LVAD therapy is to restore an adequate quality of life back to the patient, one who has been robbed by advanced heart failure. While in many cases this is achieved, adverse events experienced while on LVAD support can quickly diminish any gains that have occurred. Some adverse events might lead to frequent hospital readmissions which can lead to psychological and/or financial strains on the patient and their loved ones. For patients looking toward transplantation, these adverse events can also have a negative impact on transplant candidacy and may disqualify a patient altogether.

Bleeding

Bleeding is the most common adverse event in patients with LVADs and can be categorized into two groups, early and late. Early bleeding is usually associated with the intraoperative and immediate postoperative phases. Prevention of surgical bleeding involves normalizing anticoagulation preoperatively, optimizing nutrition, and optimizing volume status [1]. During the perioperative phase, it is important to maintain hemostasis by using antifibrinolytics, reversing heparin at the end of

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cardiopulmonary bypass, and transfusing whole blood collected from the cardiopulmonary bypass machine via Cell Saver. The surgeon should also ensure hemostasis using surgical techniques by reinforcement with sutures, pledgets, and electrocautery [1]. Intraoperatively and postoperatively, blood products can be utilized to decrease bleeding and should be focused on correction of the deficient product. Fresh frozen plasma can be given for an elevated prothrombin time (PT) or partial thromboplastin time (PTT) [1, 2]. Platelets can be given if the patient is thrombocytopenic (generally a platelet count of 50,000 or less). Cryoprecipitate can be given for patients that are fibrinogen deficient. Factor VII and prothrombin complex can be given to patients with life-threatening hemorrhage [2].

Late bleeding is manifested in several different ways, including gastrointestinal bleeding (GIB), epistaxis, and hemorrhagic stroke. Both GIB and epistaxis may be related to shear stress-induced acquired von Willebrand factor deficiency (AvWF) [3]. In this condition, due to the force of blood entering the device the proteins of von Willebrand factor, known as high-molecular-weight (HMW) multimers, are cleaved off thus destabilizing the clotting factor and creating an overall net body deficiency [4]. GIB may also be attributable to arteriovenous malformation (AVM) due to angiodysplasia of the gastrointestinal vasculature suggested in studies to be related to decreased pulsatility in continuous flow LVADs (cf-LVAD) [5–10]. Platelet dysfunction is also a risk for GIB [11]. Anticoagulation with vitamin K antagonists, such as warfarin, increases the risk of bleeding in LVAD patients.

Gastrointestinal Bleeding

Gastrointestinal bleeding can occur throughout the GI tract from the esophagus to the rectum. LVAD patients can experience GIB at a rate of 20–40% [8]. The risk of GIB is similar in current era devices: 15.2% for HeartMate II™ (Abbott), 15.9% in patients with HeartMate 3™ (Abbott), and 14.4% for HVAD™ (Medtronic) [9]. Signs and symptoms of GIB include melena, hematochezia, and/or hematemesis. Patients may also present with complaints of fatigue, shortness of breath, and lightheadedness. Exam findings would reveal tachycardia and hypotension as well as pallor and decreased capillary refill. Intravascular volume depletion leads to decreasing pump flow, potentially causing low flow alarms on the LVAD and the potential for suction events. Patients should be taught signs and symptoms of GIB and how to report them promptly to their LVAD team. If GIB is suspected, anticipate orders for complete blood count, comprehensive metabolic panel, international normalized ratio, fecal occult blood testing as well as orders to hold anticoagulation and antiplatelet medications. The patient should withhold oral intake and gastroenterology consultation should be obtained. Transfuse blood products as needed based on lab results. The benefit of blood transfusion should be weighed against the risk of developing Panel Reactive Antibodies (PRAs) if the patient is a bridge to transplant (BTT) candidate. Additional diagnostic tests include esophagogastroduodenoscopy (EGD), colonoscopy, capsule endoscopy, push enteroscopy, and if unable to locate suspected bleed, double-balloon endoscopy [7]. LVAD patients should be prescribed

a proton pump inhibitor for GIB prevention. Consider doxycycline 100 mg by mouth twice a day [12, 13] and octreotide 10 mg intramuscularly once a month [9, 12] for prevention of repeat GIB. Angiotensin-converting enzyme inhibitor (ACEI) and angiotensin receptor blocker (ARB) therapies have been shown to reduce the risk of GIB in LVAD patients [9, 14]. Thalidomide has been used in refractory cases of GIB [9, 15, 16] when the patient met defined criteria due to the high-risk side effect profile.

Patient education includes reiterating signs and symptoms of GIB and the importance of timely recognition, fall precautions, INR goal management, and taking proton pump inhibitors as prescribed. Consideration of removal of antiplatelet therapy and lowering the target INR goal for patients with recurrent GIBs may be recommended based on severity.

Epistaxis

Epistaxis is another common bleeding risk for LVAD patients with an incidence of 10–17% [17]. Causes of epistaxis are related to mucosal trauma, and possibly AvWF deficiency, although 80–90% of epistaxis is spontaneous [17]. There is no clear link to increased epistaxis with supratherapeutic INR. Treatment of epistaxis includes manual pressure, oxymetazoline spray, cautery with silver nitrate, packing with hemostatic material, and in severe cases, angiography with embolization.

Patient education is centered around prevention. Instruct patients to avoid nasal mucosal trauma and keep the mucous membranes moist by using saline nasal spray and humidification as needed. In the event the patient has a nasal bleeding, they should be instructed to hold manual pressure for 20 min, keeping the head in neutral position to avoid swallowing blood. If manual pressure does not stop the bleeding, using oxymetazoline spray and holding manual pressure again may resolve the bleeding. If a patient needs further medical attention, consider a referral to an otolaryngologist, or treatment in the emergency department.

Hemorrhagic Stroke

Common symptoms may be headache, impairment of consciousness, muscle weakness, or vision impairment. In considering the treatment for hemorrhagic stroke it must be determined whether the hemorrhage is primary or a conversion from an ischemic stroke. The goals of treatment of primary hemorrhagic stroke include control of blood pressure, control of intracranial pressure, reversal of anticoagulation, and prevention of expansion of the bleed [18, 19]. LVAD patients on Warfarin therapy and who have acquired von Willebrand syndrome are at significantly higher risk of having an extended bleed [18]. Reversal of anticoagulation must be considered noting that there are risks involved, including pump thrombus. Prothrombin complex concentrates or fresh frozen plasma (FFP) can be used to help reverse anticoagulation if the INR is elevated [18, 20]. Other treatments to

consider are platelet infusions, desmopressin, and protamine as a reversal agent to warfarin [18, 20]. Surgical intervention may be necessary, including craniotomy to relieve the pressure on the brain, evacuation of the hematoma or bleed, and/or repair or clipping of the aneurysm. The decision when to resume anticoagulation will depend on a variety of factors including type of stroke, size of the bleed if hemorrhagic, the presence of hemorrhagic conversion, and the stability of the hematoma. In general, any evidence of device thrombus will prompt earlier re-initiation of aspirin and warfarin [18].

Right Ventricular Failure

Right ventricular failure (RVF) is a constant consideration during the pre- and post-implant life of the VAD patient and requires constant ongoing assessment by the LVAD clinician throughout the duration of support. Increased attentiveness in the immediate postoperative implant phase is critical. Once LVAD support is initiated, the LV is now being supported with the LVAD as it starts to decompress the LV. This increases dependence on the RV's ability to provide adequate preload to the pump in order to deliver the necessary blood volume. RVF is estimated to occur in 9–42% of patients post-LVAD implantation [21, 22].

While there is no universal definition accepted for RVF, multiple journals and centers have created descriptions and predictor scores for RVF [21]. INTERMACS defines RVF by specific guidelines of clinical symptoms, hemodynamic measurements, continued use of inhaled nitric oxide, and prolonged need for inotropic support. In addition, laboratory values including total bilirubin and creatinine are also incorporated. INTERMACS has a grading score from mild, moderate, to severe, and severe-acute [23]. The LVAD clinician should assess these indicators regularly to optimize LVAD speed and evaluate overall performance in relation to the right ventricular functional capability in order for the LVAD to optimally support the patient's cardiac demand [22, 24]. The clinical assessment of the acute RVF will exhibit lower extremity edema with elevated jugular vein pressure (JVP). Prior to LVAD implantation, it is important to optimize the patient medically to a euvolemic state to promote favorable postoperative outcomes and minimize RV strain. Post-operatively, guideline-directed medical therapy (GDMT) is recommended primarily to support the vulnerable RV. GDMT should gradually be prescribed once intravenous inotropes are discontinued after LVAD implantation [23].

Biochemical and hemodynamic considerations related to the right ventricle include early post-op hemodynamic goals to optimize preload and afterload. This includes maintaining CVP goal <15 and keeping the pulmonary artery pressure (PAP) and pulmonary capillary wedge pressure (PCWP) close to normal limits as possible. Biochemical markers such as arterial blood gases and liver function tests (LFT) also represent RV congestion when elevated along with rising creatinine and low hemoglobin. It is important to avoid hypoxia, hypercarbia, and acidosis as much as possible as these clinical scenarios will also increase RV strain and workload. In order to protect the RV, the LVAD clinician should be monitoring for signs

of RV weakness vigilantly while optimizing preload volume, right heart function, heart rate, and rhythm. Concurrently treating reduction of afterload work of the RV by maintaining a normotensive state of PAP and MAP is advised [21, 25].

Even though there still remains a need to create a universal definition of RHF, the consensus among INTERMACS and the European Registry for patients with Mechanical Circulatory support (EUROMACS) both observe severe RVF as a need for RV assist device (RVAD) support, central venous pressure (CVP) or right atrial pressure (RAP) >16 mmHg, continued need for inhaled nitric oxide or intravenous vasodilators beyond 48 hours, and use of inotropes ≥14 days from the initial implant [23, 26, 27]. Current research has shown that early identification and intervention with right-sided mechanical unloading may improve patient mortality.

The structural-functional characteristic of the RV starts once the LVAD is turned on. The LVAD clinician assesses this via TEE monitoring in the operating room focusing on these three key factors:

1. Maintain a midline interventricular septum (IVS). The goal is to prevent leftward shift and LV suck-down as well as to minimize RV affliction and geometrical alteration. If the IVS shifts leftward this can acutely put strain on the RV, potentially causing the RV to fail, which may necessitate going back on cardiopulmonary bypass (CBP) or even require RVAD placement. In order to avoid IVS leftward shift the LVAD clinician adjusts LVAD speed down while pre-load and afterload are being optimized. Good communication with the anesthesia and surgeon helps avoid LV suck-down and IVS bowing. LV suck-down should be avoided as it can lead to arrhythmias and weakens the RV [21, 22, 26, 28].
2. Evaluation of mitral regurgitation to ensuring it remains minimal. Higher volume of mitral regurgitation will create backflow to the pulmonary system and thus increase RV workload.
3. Aortic valve (AV) assessment. Aortic valve opening intermittently helps to wash-out the aortic valve and prevent thrombus formation. Additionally, research has shown that a consistently closed AV leads to aortic insufficiency (AI) after LVAD implantation [26, 28]. If AI worsens, a closed loop physiology will develop with blood pumping from the device to the aorta and falling back thru to the LV via the incompetent AV. This subsequently creates a backup of forward flow and thus can lead to RV strain.

Of these three structural-functional characteristics, the interventricular septum (IVS) remaining at midline is most critical. As the LVAD is turned on there can be leftward shift of the septum leading to RV bowing increasing right-sided burden [26, 28, 29]. The ongoing assessment of these three vital structural-functional aspects of LVAD optimization is done with TTE at various monthly intervals. Assessment of tricuspid regurgitation, measurement of right ventricular end-diastolic function and longitudinal strain are all guides for the continuing RV assessment in relation to the LVAD and the new demand on the RV to keep up with increased preload [26, 28, 29]. Low flow alarms can also be a

signal of RVF and the need for reducing pump speed or considering additional intravenous inotropic support may be the clinical pathway when RVF becomes severe [26, 28, 29].

Arrhythmia

Cardiac arrhythmias as defined by INTERMACS, "any documented arrhythmia that results in the clinical compromise… also separated in two categories of sustained ventricular arrhythmias or sustained supraventricular arrhythmias" [23]. This would include any patient who received a shock from an ICD or required hospitalization. When considering arrhythmias in patients with LVADs it is important to remember preload; the VAD relies on an optimal cardiac rhythm to send adequate filling volume to the LV for the pump to circulate blood. The ideal rhythm is a normal sinus rhythm to sinus tachycardia with a heart rate around 110. Additional increases in heart rate and irregularity in rhythm minimize ventricular filling to the pump therefore compromising preload and subsequently afterload delivery. Arrhythmias with accelerated rate and irregularity can also result in low flow alarms. The clinical intervention to resolve the alarm condition would be to treat the rhythm and evaluation of the VAD speed; it may be indicated to lower the speed of the LVAD to avoid LV suction events which can further exacerbate the ventricular arrhythmias (VAs) if the speed is thought to be causative [30].

Atrial and ventricular arrhythmias continue to be treated with the standard antiarrhythmic medical and surgical treatment options. Atrial arrhythmias (AAs) are mostly concerning for embolic strokes however the research has not shown that this risk increases post LVAD. VAs are the more frequently associated arrhythmia in LVADs. Depending on the etiology of the heart failure and pre-existing arrhythmia, previous heart surgery, ischemic, non-ischemic cardiomyopathy, dilated and non-dilated cardiomyopathy have all correlated with VAs while smaller LV size and pre-existing VT storm have been the highest predetermining risks for later VA development post LVAD implant [30–32]. Treatment with the appropriate antiarrhythmic medications and procedures for correcting these arrhythmias continues to be essential in the acute heart failure patient after LVAD implantation [23, 26, 30–32].

VAs in LVADs can first be explained by the anatomical location of the inflow cannula which sits directly in the apex of the left ventricle. The surgical process of coring the apex and inserting the inflow cannula can interfere with the electrical conduction. Moreover, if there is fibrous or scar tissue this can be a precursor and require intraoperative ablation with LVAD implantation. Pumps sewn to the outside of the ventricle (Medtronic HVAD and Abbott HeartMate 3) also causes ventricular irritability. Pumps such as the Abbott HeartMate II do not have this issue as the device motor sits below the heart avoiding direct motor vibration irritation. If the pump speed is too high this can lead to LV suction of the myocardium over the inflow cannula causing VAs in addition to RV stress and dilation [28]. The IVS has

its own electrical conduction anatomy and avoiding drastic geometrical strain with excessive LVAD speed is important in considering the heart's electrical pathways and exacerbating or inducing arrhythmias. Keeping the IVS at midline will minimize LV suction events, arrhythmias, and RV strain [26, 27, 30–32]. For these reasons, the LVAD clinician needs to always consider the IVS position in determining pump speed. This will preserve RV function and protect septum integrity for rhythm conduction [28, 30, 31].

Arrhythmias in cf LVADs can indicate LV suction events related to high pump speed, RVF, and/or electrolyte imbalances. RV vulnerability after LVAD implant is directly correlated to arrhythmias. The goal of the pump speed is to deliver enough blood to achieve a cardiac index of 2.2 L/min/m^2 multiplied by the patients body surface area (BSA). This should be achieved while keeping the interventricular septum (IVS) at midline, minimizing mitral regurgitation (MR), and allowing the AV to open intermittently.

VAs that occur later are primarily correlated with the native ventricular scars. The inflow cannula can also change over time as the ventricle remodels with mechanical unloading this can also contribute to arrhythmias. It is more common now for LVAD patients to already have cardiac resynchronization therapy (CRT) or CRT with Defibrillation (CRT-D). CRT-D provides more preload assistance and RV support in optimizing the LVADs ability to deliver adequate circulating blood volume in the form of rhythm support. It should be noted that LVAD patients have shown less hemodynamic instability with VAs as compared to those without VAD support. The continuous flow circulation sustains perfusion even in a lethal rhythms such as ventricular fibrillation or ventricular tachycardia as perfusion is still provided via the continuous flow of blood with the pump. Although arrhythmias generally tolerated, prolonged periods of VAs can become fatal as the RV will eventually fail [31, 32]. ICD shocks may also enhance RV stunning and induce failure. Regular CRT interrogation is recommended to optimize CRT benefits related to the LVAD assessing the need for increased threshold and ATP to prevent shocks along with the need for LV lead to preserve battery life to avoid lead revisions [30–33].

Infection for Length, Consider Removing this Completely

Infection remains a significant complication for patients living with an LVAD. Further details regarding these postoperative infection complications can be found in the chapter "Infectious Concerns and Prevention for Patients with Ventricular Assist Devices."

Stroke

Neurologic dysfunction is a major contributor to mortality in LVAD patients. In the most recent INTERMACS annual report at the time of this publication, neurologic

dysfunction was listed as the second highest cause of death, 15.6%, behind withdrawal of care [34] . Although, historically, it has been the leading cause of death [34]. This mortality risk, along with an increased risk of stroke after LVAD implant [35], has remained a barrier to the continued growth of LVAD therapy and hinders access to earlier stage patients for implant.

During the destination-therapy (DT) trials for HeartMate II and HVAD, stroke rates for these devices ranged from 12.1% to 29.7% at 2 years [36, 37]. However, results from the MOMENTUM 3 trial showed HeartMate 3 to have the lowest ever published stroke rate for a continuous flow LVAD. The pivotal cohort of 515 patients had a stroke rate at 2 years of only 9.9% [38]. This was followed by an even lower rate of 9.1% for the continuous access protocol (CAP) cohort, which included 1685 patients [39]. As a comparison, during the Momentum 3 trial, the HeartMate II arm of the pivotal cohort ($n = 505$) experienced a 2-year stroke rate of 19.4% [39].

Despite the positive results surrounding HeartMate 3 and stroke, this still continues to be a challenging complication post VAD. Patients in the MOMENTUM 3 trial who experienced a stroke had significantly greater mortality at 2 years, regardless of stroke type or severity [40]. This finding was in line with other analysis of stroke from the INTERMACS registry which showed poor survival after a stroke event [41, 42].

Even with a marked improvement in stroke shown in MOMENTUM 3, patients with LVADs still experience a higher risk of stroke post implantation compared to other patients with significant cardiovascular disease. During the ROADMAP trial, which compared the effectiveness of LVAD versus optimal medical management (OMM) in non-inotrope-dependent patients, OMM patients experienced a stroke rate of only 3.9% at 2 years [35]. However, eliminating all strokes is not obtainable given the current risk of stroke in advanced heart failure patients [35] and patients undergoing cardiac surgical procedures [43–45].

Multiple risk factors for stroke have been described in LVAD patients such as female sex, infection, increase blood pressure, pump thrombosis, intra-aortic balloon pump, and antithrombotics [42, 46–48]. Willey et al. [18] concluded after a literature search that systemic infection was the most consistent risk factor for ischemic stroke in LVAD patients, even leading to an almost doubling of stroke at their institution. Bloodstream infections have also been shown to increase the risk of hemorrhagic stroke [49–52].

With infection, likely causes include septic emboli [18] or mycotic aneurysms [53, 54]. With bloodstream infections, the LVAD can become seeded with a bacterial or fungal organism; this would effectively lead to a persistent state of “LVAD endocarditis” and the need for chronic suppressive antibiotic therapy. Heart failure patients, in general, have a degree of peripheral vascular dysfunction due to their low-output syndrome. The low pulsatility state that heart failure patients experience is compounded by the presence of an LVAD, creating an environment of increased peripheral vascular dysfunction that can lead to microvascular injury and therefore neurologic events [55]. In a study completed by Fan et al. [56], autopsies were completed on 21 LVAD patients and all 21 had evidence of varying cerebral injuries, including 19 which had cerebral microvascular injuries. In another study, Yoshioka

et al. [51] analyzed brain MRI results of former LVAD patients who had been transplanted or had their LVADs explanted for recovery. They found a similar high incidence of cerebral microvascular injuries, specifically cerebral microvascular bleed. LVAD patients are known to have acquired Von Willebrand syndrome which can also predispose patients to bleeding [57] and the risk of neurologic events.

Diagnosis of neurological events in the LVAD patient can be challenging because magnetic resonance imaging (MRI) cannot be completed. Reliance for diagnosis must be on signs and symptoms, history and assessment, CT scan, and vascular imaging studies [18]. Access to a consulting neurologist to assist in the diagnosis, assessment, and intervention of patients suffering from an acute neurological event is important.

All stroke patients should undergo assessment with a standardized examination tool, such as the National Institutes of Health Stroke Scale (NIH), and a measurement of consciousness, such as the Glasgow Coma Scale, for monitoring of progress with reproducible, objective measurement devices [18]. Emergent neuroimaging with a head CT is necessary to differentiate between ischemic or hemorrhagic origin. The head CT is often repeated at least once within the first 24 h of the initial scan to monitor the status of the insult or to assess for hemorrhagic conversion of an ischemic event; it is also repeated in the following days to assess for further complication and to aid in determining when anti-thrombotic therapy can be resumed [18]. Vascular imaging might also be useful in patients with neurologic injury of ischemic origin in need of endovascular therapy. Last, digital subtraction angiography (DSA) provides the most detailed information on pathology and the formation of collateral vessels, but because DSA is invasive it should be reserved for acute stroke therapy or detection of aneurysms [18].

Treatment of acute ischemic stroke can include the administration of tissue plasminogen activator (tPA) or endovascular therapy such as thrombectomy. Several reports exist that show continuous-flow LVAD patients are likely to have limited benefit and a high risk of hemorrhagic complications from treatment with tPA [18, 58]. The risk of conversion from ischemic stroke to hemorrhagic stroke cannot be ignored. Factors that elevate the risk of hemorrhage in LVAD patients are an infectious process as the source of the thrombus, the presence of warfarin and antiplatelet agents in the patient's system, and the von Willebrand factor deficiency [18, 20, 50, 58]. A focus on endovascular intervention and the resumption of antithrombotic agents for secondary prevention is key. Endovascular stroke therapy may provide specific clinical benefits due to eliminating the use of systemic fibrinolytic therapy and the ability to focus on and visualize the vessel affected [18, 58]. The risk of hemorrhagic transformation with endovascular stroke therapy appears similar to that of systemic thrombolysis [18], therefore discussion in a multidisciplinary forum of risks versus benefits, if time allows, might be beneficial.

Stroke, as a complication in the LVAD population, continues to be a leading cause of mortality and poor quality of life. Little is known about the true cause and risk factors of stroke and it can be said that a significant proportion of the stroke risk for LVAD patients has more to do with the type of pump and the mechanics of the pump and not patient-related factors [42]. The only variable that has shown a

reduction in stroke risk has been the evolution to the HM3 pump which has shown enhanced hemocompatibility [40]. Questions still exist surrounding the increased risk of stroke with a history of atrial fibrillation, so data is not clear on whether an intervention such a left atrial appendage clipping is warranted [42]. The few risk factors that are modifiable and controllable are strict blood pressure control and anticoagulation monitoring and prevention of infection [40, 42].

Pump Thrombosis

During the modern era of continuous-flow LVADs, pump thrombosis (PT) has been a vexing issue plaguing clinicians. After DT HeartMate II approval, concern arose around the apparent increase in thrombosis rates with the HeartMate II device. A large retrospective multicenter study showed increased confirmed pump thrombosis at 3 months after implant [59]. The PT rate increased from 2.2% to 8.4% during the timeframe of the study [59]. A task force was assigned and concluded that the risk of early pump thrombus with HeartMate II could be mitigated through conforming to surgical and medical management standardization [60]. Results from this showed a reduction in PT rates down to 2.9% at 3 months and 4.8% at 6 months [60].

With the introduction of the newest generation LVAD, HeartMate 3, came what seemed like a reduction in most all PT. While certainly not immune to PT, rates from the Momentum 3 trial showed a reduction in PT with a freedom from PT at 2 years to 1.4% [38].

Causes

There are two main causes of PT. The first is de novo, meaning thrombus that is formed inside of the device itself. This type of PT usually results in a slower onset of symptoms since the thrombus builds over time. The second type is caused by thrombus being ingested into the device. PT of this nature can either result in sudden onset of symptoms or mimic de novo PT with symptoms worsening over time. If the ingested thrombus is large enough to block off a portion of the LVAD's blood flow pathway or interferes with the movement of the rotor then the output of blood delivered to the patient will be immediately reduced. However, if the ingested thrombus becomes lodged in the pump but fails to cause either obstruction or restriction of the rotor movement then the patient may experience limited to no symptoms. This type of PT can then mimic de novo thrombosis, with the thrombus growing over time leading to a later onset of symptoms. On occasion, ingested thrombus that passes through the pump can then lead to a neurologic event.

The cause of PT can be singular or a combination of events. Anticoagulation therapy is a gold standard in patients with LVAD devices and helps to prevent de novo thrombus formation as well as other potential sources of thrombus which are likely to be cardioembolic in nature. Suboptimal anticoagulation therapy can increase the risk of pump thrombosis in patients implanted with an LVAD. Atrial

fibrillation and the presence of a mechanical valve are conditions that increase the risk of thrombotic events in all patients, not just those with LVADs. These patients will already be on an anticoagulation regimen and will continue to be so post LVAD implant, for both the preexisting condition(s) as well as protection of the LVAD.

Device position can also play a role in PT. Should the inflow cannula of the LVAD become misaligned, either by suboptimal surgical placement or resulting from left ventricle remodeling after implant, the risk of a thrombotic event is higher. If the inflow cannula contacts the endocardium of left ventricle there is a potential for thrombus to form. Also, malalignment of the inflow cannula will likely lead to flow changes in the left ventricle apex region. These flow changes could result in a stagnation of blood in that area which could lead to apical thrombus formation. With either of these scenarios, any thrombus that forms could potentially become mobile and be ingested into the pump.

Low flow states also pose a risk for potential thrombus formation inside of the LVAD. With a decrease in flow through the pump there is a higher likelihood for blood to become stagnant inside the device. Also, LVADs with mechanical bearings that rely on adequate blood flow through the pump to dissipate any heat which might be generated are at more risk for PT when encountering low flow states.

In addition to device-related causes of PT there are also patient risk factors. Some of these risk factors include younger age, female gender, high BMI, severe right heart failure, mean arterial pressure >90 mm Hg, aspirin dose ≤81 mg, international normalized ratio (INR) ≤2, and INTERMACS profile ≥3 at implant [61, 62].

Diagnosis

Diagnosis of PT is usually done by a combination of patient assessment, device assessment, clinical imaging studies, and laboratory interpretation. The initial presentation of PT might be a new onset of heart failure symptoms, device parameter fluctuations, dark rust-colored urine, or it might simply be seen on routine laboratory monitoring.

LVAD patients usually have routine or standard of care labs that are drawn at certain intervals. Part of these labs are to assess for potential PT. The hemolytic markers lactate dehydrogenase (LDH) and plasma-free hemoglobin (pfHb) are the two most common labs that are drawn on LVAD patients. Typically, a LDH greater than 3 times the upper normal value or a pfHb greater than 40 are considered suspect for potential PT [63]. Hemolysis is a result of blood cell damage caused by turbulent blood flow from thrombus within the LVAD. Other laboratory values, when associated with elevated hemolytic markers, can also point to potential PT. These are an elevated creatinine, elevated bilirubin, transaminitis, decrease in hemoglobin, and hematuria on a urinalysis. Patients might also report dark, tea-colored urine if the hemolysis is significant enough.

Changes in pump parameters can also help detect PT. If the thrombus contacts the device rotor, this can impart drag, leading to an increase in pump powers. Depending on the level of involvement, the power elevations can be in the form of

power spikes or persistent elevations in power. However, if the thrombus does not contact the rotor, power elevations will not be seen. In this case, should the thrombus be large enough, or grows large enough over time, it will create an obstruction and may lead to lower powers and flows on the device. It was shown that a focused analysis on pump power characteristics obtained from log files of Medtronic HVAD patients was an important factor in successfully diagnosing PT in its early stages [64].

Should the thrombus negatively affect the amount of support that is provided to the patient, heart failure symptoms will arise. This is a result of more demand being placed on the weakened left ventricle to support the patient. These symptoms can range from increasing shortness of breath to volume overload.

Echocardiograms are a useful tool to aid in the diagnosis of PT. Ramped ECHO studies can help determine if the pump is properly offloading the left ventricle and flow is effectively moving through the pump. This specialty echocardiogram incrementally increases the VAD speed while evaluating left ventricular end-diastolic dimension to evaluate if there is a linear decrease with higher speed as expected. CT or CTA can also be used to evaluate for the presence of thrombus within the left ventricle or portions of the pump.

Treatment

Depending on the severity of PT, treatment options can vary from escalating anticoagulation up to and including device exchange. Escalation of anticoagulation with either heparin, glycoprotein IIb/IIIa antagonists, tissue plasminogen activator (tPA), or a combination can be used in an attempt at medically managing PT [64]. However, success of medical treatment alone is highly dependent on the nature of the thrombus and of the device type. Escalation with high levels of anticoagulation, including thrombolytics, is more acceptable and has shown the highest rates of success with a centrifugal flow device, although only about half of these treatments were successful [62, 65, 66]. This medical therapy does significantly increase the patient's risk for bleeding events, most importantly hemorrhagic stroke [65].

Pump exchange, while invasive, does provide the best likelihood of completely resolving PT. Despite the risk of pump exchange, the procedure itself has been shown to have acceptable outcomes and mortality [66–68]. Techniques for pump exchange can range from complete device exchange to removal of only the main pump body, leaving the existing outflow graft and inflow cannula (if separate from the pump body) in place. When performing the later technique, it is important to ensure there is no thrombus present, or remains, in either the retained portions of the pump or within the left ventricle.

Prevention

Prevention of PT begins during the evaluation phase for advanced therapies with risk stratification. Preexisting conditions which can predispose a patient for pump

thrombosis include atrial fibrillation, existing left ventricle thrombus, and prothrombotic conditions. Intraoperatively, it must be ensured that any left ventricle thrombus is removed, and no remnants from the apical core site or surgically excised tissue are loose with the potential of being ingested into the pump. The inflow cannula must be directed toward the mitral valve and have no contact with the myocardium. Another strategy to mitigate risk with the patient who has a history of atrial fibrillation is ligation or clipping of the left atrial appendage, however this is still being debated in the literature.

Flow optimization with pump speed and blood pressure control is also an important factor in preventing thrombus formation. Low flow states can be a risk factor for the formation of thrombus, therefore running the pump at an adequate speed to maintain appropriate flow is paramount. Avoiding high blood pressure is important as the increased afterload can reduce flow through the pump and can contribute to the formation of PT.

Anticoagulation plays a significant role in the prevention of thrombus formation within the device. Patients should be maintained on Warfarin therapy with a target INR goal that is consistently maintained. Any planned or unexpected interruptions to anticoagulation therapy or drop in INR below goal should trigger a bridge with low molecular weight heparin or unfractionated heparin. Antiplatelet therapy is also utilized to prevent PT, with the most common therapy being aspirin.

Pump Obstruction

While the most common cause of device obstruction within the inflow cannula or outflow graft can be attributed primarily to thrombosis, other factors should be considered. A common cause of inflow cannula obstruction is a malaligned cannula. In this instance, the inflow cannula is positioned close to the left ventricular wall and blood flow into the pump will be impeded.

Most outflow graft obstruction will be mechanical in nature. One common cause is outflow graft kinking related to an outflow graft that is too long, either due to surgical measurement error or heart remodeling post implant. Another cause is external compression of the outflow graft which can be caused by "biodebris" collected in between the outflow graft and bend relief [69, 70] or from a hematoma or pericardial effusion. Twisting of the outflow graft has also been seen and can lead to obstruction [71, 72]. Causes related to this complication can be unexplained, surgical error at implant, or even potentially a device-related complication [69].

If inflow or outflow obstruction presents acutely, device flows and power will suddenly decrease. However, should the obstruction manifest itself over time, then device flows and powers will trend down slowly over time. Some patients may experience a return of heart failure symptoms or have hemolysis related to the obstruction. Advanced imaging studies with TTE and CT should be performed, as together, they can provide a more accurate picture of the nature of the obstruction [73].

Treatment option for patients with outflow graft obstruction vary. If the patient has no related complications, then a conservative surveillance approach can be taken. Another option might be an endovascular intervention. Depending on the cause of the obstruction balloon "graftoplasty" or stenting could be considered [70]. Other options are surgical in nature and range from mechanically relieving the obstruction, graft repair/replacement, or device replacement. Inflow cannula obstruction can sometimes be amendable to thrombolytic therapy should the culprit be thrombus, but device exchange is usually the preferred treatment [69]. However, if the obstruction is related to inflow cannula malalignment an attempt can be made surgically to realign the cannula. This realignment of the inflow cannula can be difficult though, as the angle of the cannula is mostly dependent on the apical core site made during the implant surgery.

Short-to-Shield

Short-to-Shield is a malfunction that can happen in the HeartMate II percutaneous lead also referred to as the driveline. There are six-wires in the percutaneous drive line that are wrapped in a silver-plated copper braided shield. The shield is grounded when connected to alternating current or power base from a direct battery current. Its purpose is to prevent electrical interference [74]. Each wire also has an additional protective insulation [74, 75].

Over time, as the patient becomes active with frequent manipulation of the line, this shield can become fatigued and fray, leaving the wires exposed. This exposure can in turn cause the energy in the wires to drop the signal. As the patient comes off direct-energy current, the current that is usually grounded with the shield stops at the area of break-down which can cause the pump to stop. The signal is dropped from the damaged shield-shorting the connection hence the term "short-to-shield" [74, 75]. Often this is found when the LVAD clinician interrogates the patient's device.

Pump interrogation can show power fluctuations as well as alarms, including the most lethal, pump stop. It may be helpful for the MCS clinician to ask about any unusual events or alarms prior to connecting the HMII patient to the monitor as this can result in pump stoppage and subsequent syncope. A short can occur anywhere along the driveline from internal to external area. Pending the location on the external portion, there is an FDA-approved method for engineers to repair the area of the line without having to go back to the OR. A series of X-rays are taken to assess for break down and then engineers can splice in new wires with a protective shield preventing further episodes. MCS coordinators should place a small radiographic item such as a paperclip on the exit area to indicate where the driveline exits the body as to be seen on the films. In cases where the break-down occurs on the percutaneous driveline internally, or closer to the pump, a pump exchange is required [74, 75].

Conclusion

Preservation in quality of life experienced after implant is heavily dependent on decreasing the number, and severity, of adverse events experienced by LVAD patients. To ensure that this therapy continues to grow and thrive, the adverse event burden experienced by patients supported with these devices must continue to decline as new technology emerges and management techniques further improve. Device manufacturers must ensure that future generation devices are even more hemocompatible, as adverse events often precede one another. Clinicians must continue to improve how both devices and patients are managed and do so in a multidisciplinary approach. Prevention of complications should always be the primary goal, but when these events do happen, quick identification and treatment should occur.

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Infectious Concerns and Prevention for Patients with Ventricular Assist Devices

Marcia Stahovich, Krista Marz, and Jennifer Nowaczyk

Wise and humane management of the patient is the best safeguard against infection. (Florence Nightingale)

Infection Definitions

The International Society for Heart and Lung Transplantation (ISHLT) in 2011 proposed consensus guidelines for standardized pump-related infection definitions. The multidisciplinary workgroup defined three categories: VAD-specific, VAD-related, and non-VAD-related [1]. VAD-specific infection involved a device component: the pump, inflow and outflow cannulas, pump pocket, and driveline site. These infections may be further categorized as superficial and/or deep. VAD-related infections may occur as a result of VAD placement and also be a consequence of bloodstream infections, endocarditis, mediastinitis, and sternal wound infections. These types of infections occur in both VAD and non-VAD patients, but require special attention in the VAD patient. Attention will be needed to distinguish correct diagnosis and the etiology. Non-VAD infections are independent from VAD implantation and include pneumonia, cholecystitis, and urinary tract infections [1]. Non-VAD-related infections often occur in the first 3 months following implant and are commonly related to sources such as central venous catheters, urinary catheters,

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Table 1 Classification of infections in patients using ventricular assist devices

VAD-specific infections
• Pump and/or cannula infections
• Pocket Infections
• Percutaneous driveline infections
– Superficial infection
– Deep infection
VAD-related infections
• Infective enclocardilis
• Bloodstream infections (including CVC-associated BSIs)
CVC present
– Bloodstream infection presumed VAD-related
– Bloodstream infection presumed CVC-related
No CVC present
– Bloodstream infection VAD-reLated
– Bloodstream infection non VAD-related
• Mediastinitis
– VAD-related
• Sternal wound infection SSI-organ space
• Pocket infection (continuous with mediastinum or already situated in the mediastin urn depending on the device used)
– Non-VAD related
• Other causes of mediastinitis, perforation of the esophagus
Non-VAD infections
• Lower respiratory tract infection
• Cholecystitis
• *Clostridium difficile infection*
• Urinary tract infection

BSI blood stream infection; *CVC* central venous catheter, *VAD* ventricular assist device

Hannan, M.M. et al. (2011) Working formulation for the standardization of definitions of infections in patients using ventricular assist devices. The Journal of Heart Lung Transplant. 30 (4) 375–384

post-operative pneumonia (PNA), and clostridium difficile infections [2]. These definitions assist in guiding clinicians with further evaluation, diagnosis, and treatment, in addition to standardizing how infections are discussed in research and across institutions. Table 1 lists the three classifications of infection and examples of each.

Preoperative and Intraoperative Planning

There is a wide range of preop antibiotic prophylaxis studies. Selection of an antimicrobial agent that covers staphylococcal activity, such as vancomycin or cefazolin, in both the preoperative and postoperative phases are highly recommended, according to a recent ISHLT consensus [3]. Careful consideration for antibiotic administration related to surgery cut time should also be considered. Antibiotics should be started within 1 h of cut time, no later than 15 min, with the exception of

vancomycin, which should be started within 2 h of cut time, no later than 15 min [1]. Drug doses should be chosen that are appropriate for the patient's renal function and allergies.

Nasal decolonization for staph aureus is a widely used approach for most implanting centers [1]. Preoperative chlorhexidine baths have also been shown to reduce surgical site infections [1, 4]. Antibiotics could be re-dosed during the operation to ensure adequate blood and tissue concentrations if the duration exceeds two half-lives of the drug or excessive bleeding and the patient's renal function per hospital policy. Postoperatively, antibiotics should be continued for up to 48 h postop. Many centers will extend this to 48 h after chest closure [3, 4]. If the chest is closed the same day as the implant, antibiotics may be discontinued after 48 h. If the chest closure is delayed for 24–48 h, antibiotics should be discontinued 48 h after chest closure. Close monitoring is important, paying attention to renal function and drug therapeutic levels. Be cautious to include the preoperative vancomycin dose as dose number one when considering when to obtain peak and trough levels. It may be beneficial to obtain random vancomycin levels daily until the vancomycin is discontinued. Creating order sets that include these different drug and/or dose options and therapeutic monitoring labs could be beneficial to prevent errors.

Fungal infections are associated with up to a 90% mortality rate but are not as common as bacterial organisms such as staphylococcus [3, 5]. Prophylactic coverage for fungal infections was universally used in the early days of durable VAD implantation and is still administered at some centers in the current era. However, consulting with the organization's infectious disease team (ID) for patient-specific recommendations or local epidemiologic data is strongly recommended [3].

Once the pump is prepared for implant, it should be kept wrapped in a sterile towel within the sterile field. ID experts may recommend using a sterile towel soaked in an antibiotic solution or a biofilm prophylaxis such as rifampin. It is important to consult your ID team for guidance [3].

Driveline Exit Site Infection

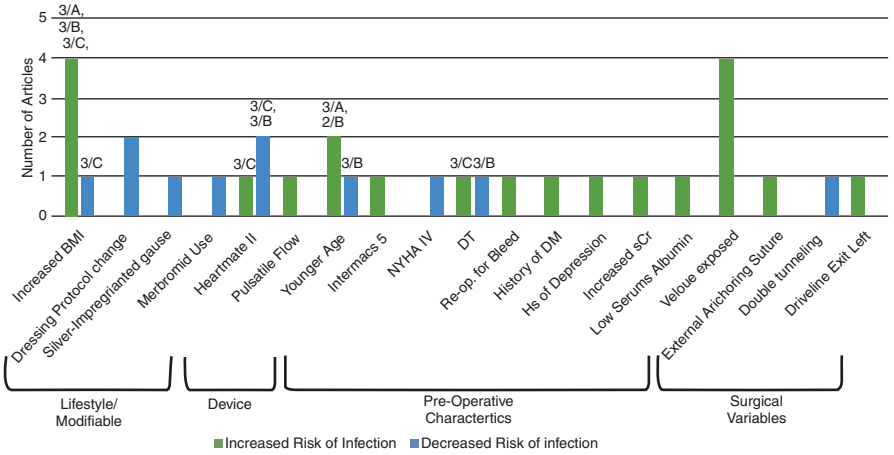
Background and Prevalence

Overall infection rates in the LVAD patient population range from 19% to 39% with driveline exit site infections (DLES) being the most frequent occurring in 12–35% of implanted patients [6–12]. LVAD infections usually occur >30 days after implantation. DLES are noted in >10% LVAD deaths demonstrating the important morbidity and mortality associated with an infection in this population [7, 13, 14]. A higher incidence of DLES infection-related deaths in the destination therapy population suggests time on support increases the incidence of driveline infection [13]. Pump pocket infections, discussed later in this chapter, occur in 2–10% of patients and are usually an extension of a DLES infection [6, 9, 11].

The design of current continuous-flow pumps including HeartMate II (HM2, Abbott), HeartWare HVAD (HVAD, Medtronic), and HeartMate 3 (HM3, Abbott) have shown to evolve with improvement in design and decreased size, however infection remains as a high adverse event. These drivelines are anti-abdominal wall, not tunneled in the intra-abdominal space. Studies have shown the more the rigid a driveline is, the greater risk for infection due to increased torque at the exit site [15]. The newer pumps have less rigid and thinner drivelines, as well as no pump pocket, contributing to a reduce rate of infection [13, 16, 17]. A DLES infection rate of 0.25 events per patient year for HeartWare HVAD was shown in a recent study and attributed to the thinner driveline [18]. The MOMENTUM 3 randomized controlled trial compared the HeartMate 3 with the Heartmate II and did not demonstrate a statistically significant difference in the rate of driveline site infection [19–21]. Studies show that the more rigid a driveline is, the greater risk for infection due to increased torque at the exit site. This is thought to disrupt the integrity of the barrier formed at the skin [15]. Stiffness is thought to be a significant factor when discussing DLES infections.

The vexing problem of DLES infections is the association with obesity and younger age. LVAD patients with higher body mass index and continued post-implantation weight gain have also been at higher risk for driveline site infections [22]. Younger age has been associated with DLES infections due to higher activity rates and resulting in increased risk of local site trauma [7, 13]. Infection risk increased by 20% for every 10 years decrease in age. Table 2 illustrates risk factors associated with VAD related infections.

Table 2 Statistically significant variables associated with risk of LVAD-related infection



Pavlovic et al. (2018), Risk of left ventricular assist device driveline infection: A systematic literature review

DLES Pathogens

As devices evolved over many years, introduction of microorganisms remains the same. The driveline is tunneled via skin, which contains normal skin flora. Driveline trauma provides a portal of entry for microorganisms. Common pathogens colonize and adhere to implanted material and create biofilm [1].

The most common cause of DLES infections is staphylococcus, followed by gram-negative *Pseudomonas aeruginosa* such as *E. coli* and *Klebsiella* followed by *Enterococcus* species [1, 3, 23, 24]. Fungal LVAD infections, such as *Candida*, are less common in the continuous flow pumps affecting 2–8% [7, 15, 25]. The most common pathogens evaluated by Nienaber et al. were reported as gram-positive cocci (44.8%) and gram-negative rod (24.1%) [9].

DLES Infection Staging

Any site change observed during routine dressing changes or during special evaluation following warrants a call to the mechanical circulatory support (MCS) team for further evaluation. A staging chart may be used by patients to identify the exit site stage. Current technology allows patients to send photos of changes to the MCS Team for evaluation, adjustments to site care, and to determine the need for urgency of visit.

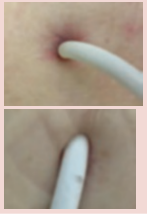
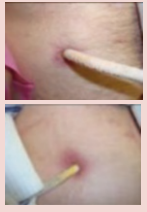
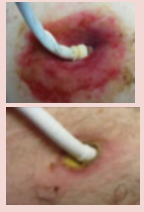
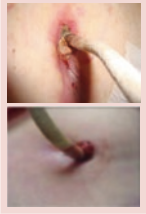
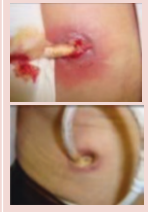
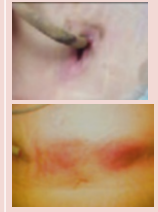
Sharp Memorial Hospital (San Diego, CA) developed a site classification tool that standardizes the condition and approach to treatment for patients who develop a change in driveline site (Table 3). The recent DESTINE staging proposal introduced an additional stage for a normal, asymptomatic driveline site [26] (Table 4).

Superficial infections involve the tissue around the DLES that have erythema, warmth, and drainage without signs of sepsis or systemic illness. It is important not to culture normal-appearing sites. Sites should be rinsed with saline prior to culture to prevent contamination of normal skin flora causing false results [27]. Gram stain can identify inflammatory cells consistent with infection rather than bacterial colonization [1].

DLES Diagnosis and Treatment

Superficial driveline exit site infections spare the fascia and muscle layers and are generally not associated with fevers or systemic signs of infection [5]. The stage one diagnosis usually occurs when the provider, patient, or caregiver note a change at the driveline site including warmth, redness, or drainage. A review of site care with the patient is important including stabilization measures. Infection may be difficult to differentiate from irritation due to common features to both situations. An increase in dressing changes usually begins with the noted site change as well as

Table 3 Sharp memoral hosptial driveline infection staging table

Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
					
Appearance: – Approximated, healing, no redness or drainage.	**Appearance:** – Pink, healthy tissue incorporating into the driveline – Little or no erythema – No Tenderness – No drainage	**Appearance:** – Persistent disruption of skin at exit site – Some erythema – Mild tenderness – Possible local cellulitis – Excoriated – Small amount of drainage (note color, odor, and amount) may be culture negative	**Appearance:** – Systemic symptoms of infection, persistent skin disruption, granulation tissue may be forming, pulled away from the driveline, gap present – Erythema – Severe tenderness – Moderate to copious amounts of drainage, culture positive	**Appearance:** – Systemic symptoms of infection, severe skin disruption, bleeding from granulation tissue, pulled away from the driveline, possible cellulitis or bleeding – Erythema – Severe tenderness with infection tracking along driveline tract – Copious amounts of purulent drainage, culture positive	**Appearance:** – Systemic symptoms of infection, severe skin disruption, bleeding from granulation tissue, pulled away from the driveline, cellulitis or bleeding – Erythema, severe tenderness – Infection tracking along driveline may involve pump pocket – Copious purulent drainage, site and blood cultures positive
Treatment: Call if changes and send photo to MCS email	**Treatment:** Call if changes and send photo to MCS email.	**Treatment:** Must be seen in MCS office.	**Treatment:** Must be seen in MCS office or hospitalize	**Treatment:** Hospitalize	**Treatment:** Hospitalize possible OR pump replacement

Chinn R, Dembitsky W, Eaton L, Chillcott S, Stahovich M, Rasmusson B, Pagani F. Multicenter experience: prevention and management of left ventricular assist device infections. ASAIO J. 2005 Jul–Aug;51(4):461–70. https://doi.org/10.1097/01.mat.0000170620.65279.aa. PMID: 16156314. Sharp Memorial Hospital Driveline Site Infection Staging Table

Table 4 DESTINE wound staging and recommended actions in the prevention and management of DLI

STATE	State 0 - asymptomatic		State 1 - local wound healing disorder		State 2 - local infection		State 3 - systemic infection	State 4 - systemic infection with increased severity	State 5 - progressive systemic infection with deep DLI and/or signs for ascending infection
	0 a	0 b	1 a	1 b	2 a	2 b			
DEFINTION	• Bland, unswollen, dry DLES • No erythema • No microbial detection at DLES • No infection	• Clinically and visually unremarkable dry DLES • No erythema • Microbiologically positive smear of the DLES	• Dry DLES with localized erythema • Microbiological smear of the DLES may be positive	• Wet DLES without erythema • Microbiological smear of the DLES may be positive	• Local infection of DLES • Expanded erythema, pruritus and/or swelling • No pyrexia • No positive blood cultures • Microbiological smear of the DLES may be positive	• Local infection of DLES • Expanded erythema, pruritus and/or swelling • Pus retention or discharge • No pyrexia • No positive blood cultures • Microbial detection at DLES	• Signs of systemic infection • Erythema/pruritus • Skin disruption and tenderness • Significant amount of discharge (Pus) • Pyrexia • Positive blood cultures • Microbial detection at DLES	• Signs of systemic infection • Potential phlegmone • Severe skin disruption and tenderness • Significant amount of discharge (Pus) • Bleeding from granulation site • Positive blood cultures	• Signs of systemic infection • Potential phlegmone • Severe skin disruption and tenderness • Significant amount of discharge (Pus) • Bleeding from granulation site • Positive blood cultures
DIAGNOSTICS & THERAPIES	**1. Dressing schedule:** Dressing change 1-2x weekly **2. Dressing procedure:** Standard Operating Procedure (SOP) of the implanting center **3. Diagnostics:** Photo documentation during dressing change **4. Smear:** on routine examination at VAD outpatient clinic **5. Therapy:** not required	**1. Dressing schedule:** see state 0a **2. Dressing procedure:** see state 0a **3. Diagnostics:** see state 0a, additional information to VAD outpatient clinic and affected patient **4. Smear:** additional smear in VAD outpatient clinic upon DLES state change **5. Therapy:** increase awareness	**1. Dressing schedule:** see state 0a **2. Dressing procedure:** SOP, additional application of bacteriostatic silver- or polyhexanid-containing material **3. Diagnostics:** see state 0a, additional information to VAD outpatient clinic and affected patient **4. Smear:** additional smear in VAD outpatient clinic upon DLES state change **5. Therapy:** see state 0b, additionally consider adjuvant therapy (e.g. cold plasma)	**1. Dressing schedule:** Dressing change adjusted to degree of wetness (aim: dry exit site) **2. Dressing procedure:** see state 1a **3. Diagnostics:** see state 0a, additional laboratory diagnostics for systemic signs of infection, immediate presentation at a physician with VAD experience and timely outpatient follow-up after 1-2 weeks at a physician with VAD experience **4. Smear:** additional smear timely (after 1-2 weeks) at a physician with VAD experience **5. Therapy:** see state 0b	**1. Dressing schedule:** see state 1b (aim: dry exit site) **2. Dressing procedure:** see state 1a **3. Diagnostics:** see state 0a, additional laboratory diagnostics for systemic signs of infection and coagulation status, immediate presentation at VAD outpatient clinic and timely outpatient follow-up after 1-2 weeks at VAD outpatient clinic **4. Smear:** additional smear timely (after 1-2 weeks) at VAD outpatient clinic **5. Therapy:** see state 0b Consider initiation of calculated antibiotic therapy	**1. Dressing schedule:** see state 1b (aim: dry exit site) **2. Dressing procedure:** see state 1a **3. Diagnostics:** see state 0a, additional laboratory diagnostics for systemic signs of infection and coagulation status, immediate presentation at VAD outpatient clinic and timely outpatient follow-up after 1-2 weeks at VAD outpatient clinic **4. Smear:** additional smear timely (after 1-2 weeks) at VAD outpatient clinic **5. Therapy:** initiation of calculated followed by targeted antibiotic therapy Consider risk / benefit adjusted surgical debridement or vacuum-assisted closure therapy	**1. Dressing schedule:** increase frequency **2. Dressing procedure:** see state 1a, optional coverage by abdominal binder **3. Diagnostics:** contact VAD outpatient clinic, hospitalization most likely required, laboratory diagnostics on dynamics of systemic signs of infection and coagulation status **4. Smear:** blood and deep wound cultures **5. Therapy:** initiation of calculated/ targeted antibiotic therapy, consider silver nitrate for granulation tissue Consider risk/benefit adjusted surgical debridement or vacuum-assisted closure therapy	**1. Dressing schedule:** increase frequency **2. Dressing procedure:** see state 1a, optional coverage by abdominal binder **3. Diagnostics:** contact VAD outpatient clinic, hospitalization mandatory, laboratory diagnostics on dynamics of systemic signs of infection and coagulation status, consider PET-CT and TEE for evaluation of invasiveness of infection **4. Smear:** blood and deep wound cultures **5. Therapy:** initiation of intravenous calculated/targeted antibiotic therapy, surgical debridement and potential vacuum-assisted closure therapy	**1. Dressing schedule:** increase frequency **2. Dressing procedure:** see state 1a, optional coverage by abdominal binder **3. Diagnostics:** contact VAD outpatient clinic, hospitalization mandatory, laboratory diagnostics on dynamics of systemic signs of infection and coagulation status, consider PET-CT and TEE for evaluation of invasiveness of infection, consider device-associated endocarditis if blood cultures remain constantly positive **4. Smear:** blood and deep wound cultures **5. Therapy:** initiation of intravenous calculated/targeted antibiotic therapy, consider implantation of antibiotic beads, perform surgical debridement and vacuum-assisted closure therapy, consider pump replacement

Bernhardt AM, Schlöglhofer T, Lauenroth V, Mueller F, Mueller M, Schoede A, Klopsch C; Driveline Expert Staging and Care DESTINE study group, a Ventricular Assist Device Driveline Infection Study Group. Prevention and early treatment of driveline infections in ventricular assist device patients—The DESTINE staging proposal and the first standard of care protocol. J Crit Care. 2020 Apr;56:106–112. https://doi.org/10.1016/j.jcrc.2019.12.014. Epub 2019 Dec 17. PMID: 31896443

scrubbing the site and driveline with an antiseptic. The goal of disrupting the source of the infection is the best way to eliminate the biofilm and allow the tissue to reincorporate into the velour [28].

If the patient is asymptomatic, empiric oral antibiotics may be started once a culture is taken of the site, subsequently adjusted to the specific pathogen. In the stable patient, some centers will delay the start of antibiotics until the culture result is known [24, 29, 30]. If cultures are negative, but there remains concerns for infection, empiric antibiotic therapy should be initiated and evaluated by the infectious disease team based on clinical response [1].

Deep driveline infections involve the fascia, muscle layers, and into the deeper tissues, where incorporation with the driveline is disrupted and needs immediate diagnosis and treatment. Signs of infection are temperature ≥38°, local pain and tenderness at site with erythema, induration, and swelling. An abscess may present as a deep incision dehiscence or as a deep unincorporated area around the DLES. Superficial driveline cultures of drainage or fluid collection should be obtained. Culture results should be used for targeted therapy. Laboratory and imaging studies to diagnose deep DLES infections are discussed in depth later in this chapter, but may include CT abdomen and/or ultrasound to determine if a fluid collection is present as they image differently. Blood cultures are necessary to rule out a bloodstream infection. A complete blood count to check white blood cells with an increase in neutrophils and immature leukocytes (i.e., left shift). Debridement may be necessary if unincorporated, but unlikely if caught early, surgical debridement is also discussed in depth later.

Therapeutic drug monitoring should be performed for specific antibiotic therapies (including vancomycin, aminoglycosides, voriconazole, and posaconazole). Antibiotic therapy may affect the international normalized ratio (INR), initial monitoring with the initiation of antibiotic therapy is imperative to maintain the INR goals for the patient [1].

DLES Prevention Techniques

Prevention of DLES is extremely important. DLES infections still occur despite the most compliant patient care. Nurses, patients, and caregiver education is a staple to prevent LVAD DLES infection. Coordinators must take into consideration nursing turn over, patient/caregiver health care literacy, and annual re-education [22].

A multidimensional strategy is needed to prevent DLES infections and it begins during the operative procedure. It is important to prevent a surgical hematoma [7, 31]. The tunneling technique requires special attention through muscle. The cutaneous exit site must be selected to provide for easy recipient usability by avoiding belt lines, dominant hand side considerations, or oddities of patient anatomy that might subject site to trauma. The course of the driveline from peritoneal or intrathoracic cavity seems best suited through the rectus muscle since it is the most vascular obstacle to exit. This muscle layer is well vascularized, and therefore a source of nutrition substrates and antimicrobial elements. The rectus sparing technique locates the driveline above the posterior fascia and leaves the preperitoneal fat layer intact [32].

Attention to the exit site and the location of the velour to the cutaneous surface has been pivotal. Velour used on the driveline allows tissue growth for stabilization of the device intra-abdominally. Studies have found the velour has micro gaps which allows microorganisms to migrate and allows for biofilm formation [33]. Biofilms are communities of microorganisms that attach to a surface and have a protective extracellular matrix, leading to resistance. When microorganisms adhere to external portions of the driveline, they colonize, and Biofilms are formed [33]. Biofilms have an altered metabolic rate and can spread, leading to more invasive infections [33]. Biofilms are difficult to treat/clear with antibiotic therapy. Surgical techniques leaving the velour exposed have significantly higher risks associated with LVAD DLES infection [22]. One must also take into account the material used to make the smooth portion of the driveline and the glue used to connect these two parts. The smooth portion of the drivelines are made from polyurethane, Teflon, or silicone-based biomaterials. A HeartMate II (HMII) study revealed that keeping the velour-covered portion of the driveline in the subcutaneous tissue creates a silicone skin interface that can immobilize and lessen the trauma to the deeper portion of the velour cover where tissue ensues. The Silicone Skin Interface Registry was formed in 2012 and registered 400 HM II patients. It collected data on driveline velour being fully percutaneous, resulting in the silicone portion of the driveline interfacing with the skin at the exit site. This data registry showed a 50% reduction in DLES infection when velour was completely buried compared to when a portion of velour was exposed externally [34].

The driveline is generally surgically fixed externally with an anchoring suture to stabilize the tract and allow for healing. Some centers go further and attach a piece of a red rubber catheter to protect the area of the DLES that is being anchored down. The length of time that the suture is left in place varies by center with a range of 1–4 weeks or until the site is incorporated and stable [35].

DLES Care

Driveline exit site care is center-specific, and currently superiority studies have not been done. The driveline site is cleaned using strict aseptic technique using solutions such as chlorhexidine gluconate (CHG), hydrogen peroxide, or povidone-iodine. CHG intolerance has occurred and varies from anaphylaxis to skin irritation from repeated exposure [29, 36]. Approaches currently used to decrease irritation from CHG include a more dilute solution, solution without alcohol, and adequate drying time before applying dressing. Povidone-Iodine (PVP-I) has been used as an antiseptic and was thought to have cytotoxic effects decreasing wound healing, but human clinical trials have suggested that impaired wound healing is not as impaired as previously thought [37]. PVI-P can be used as an alternative to CHG as antisepsis; however, the site may need increased observation [36]. In addition, newer products on the market with broad antimicrobial coverage containing, 0.1% Polyhexanide (PHMB) and 0.1% Betaine (Surfactant) or sodium hypochlorite (which offer beneficial cleansing power) have been used and will need further research.

Alternative therapies include topical silver-impregnated gauze that has decreased the DLSI rates during the first 6 months after surgery [38, 39]. Silver has been used

for its antimicrobial properties that are effective against *Staphyloccus aureus*, *Staphyloccus epidermis*, *Pseudomonas aeruginosa*, and *Enterobacter faecium*, the most common pathogens seen in driveline site infections [40]. Antimicrobial CHG patches at the driveline site have been used like those made for central venous catheters, and are shown to inhibit bacterial growth at site for up to 7 days [28, 41, 42]. Ultraviolet B (UVB) radiation has been used with the HeartMate 2 patients needing further investigation [14, 43].

Driveline immobilization begins in the operating room and becomes a critical part of the dressing changes to help prevent infections. Immobilization at the exit site can prevent pulling at the site, which causes shearing of the tissue and an opening for infection. Using a device such as the Centurion Foley Anchor Device (Centurion Medical Products, Williamston, MI) or the CathGrip (BioDerm, Largo, FL) secure the driveline to the skin to minimize movement at the exit site. These devices are smooth and prevent damage to the driveline silicone. An abdominal binder may also be used for securement, though patients reported more freedom and comfort from the securement devices [40].

A consistent dressing change protocol using aseptic technique is determined by institutional policies. In general, handwashing, sterile gloves, and masks are the minimum required [1]. A "Driveline Management System" kit can be used for consistency of supplies and to simplify the procedure, increasing patient and caregiver compliance [40, 44, 45]. Exit site care may be altered on patient's hypersensitivity profile. Kits generally include sterile masks for patient and provider, two pairs of sterile gloves, CHG for antisepsis, skin protectant, antimicrobial covering for site, exit site cover, and driveline anchor. The frequency of the dressing change is determined by institutional policy and site drainage. A small retrospective study on patients after they left the critical care unit compared different frequencies of dressing changes: daily, three times per week, and weekly. This study found that weekly dressing changes may be safer in certain groups [46].

Patients need to be taught the importance of daily hygiene. They may need to wash at a basin initially until the exit site becomes incorporated, usually between 1 and 8 weeks [1, 47, 48]. There is no evidence in the literature that is available to indicate that showering with water on a surgical wound increases infection [49]. Decisions regarding showering are made on an individual basis and are center-specific. DLES infections from *Pseudomonas* may be reduced when showering is stopped in some patients [50]. Patient and caregiver instruction using the manufacturer's instruction for use (IFU) on the protective covers supplied for the safety of the equipment must be reviewed. The consensus among many centers is that showering with the driveline site covered should be enough to prevent water infiltration. As such, some sites have their patients cover the dressing with an additional waterproof covering to keep the exit site dry while showering [40]. The driveline site dressing should be changed immediately after showering.

Management of a DLES infection is costly and impacts quality of life due to medication changes, hospitalizations, and imposition on caregivers. DLES infection prevention is most important prior to patient discharge. Training patients and their caregivers to strictly adhere to the dressing change protocol is most important to

infection prevention. They must know when to report site changes, when to send a photo of site changes, and when to call the coordinators to report when trauma occurs. Handouts can be used for dressing change procedure, site staging, and hygiene to help decrease infection (Table 3).

Pump Pocket Infection

Creating a pump pocket is part of the surgical technique used with some devices and can be pericardial, sub-diaphragm, or close to the abdominal wall. Pump pocket infection was reported to be as nearly as common as DLES infection, but usually the second most common VAD-specific infection [15]. Pocket infection should be considered when there are persistently positive blood cultures for gram-positive cocci. ISHLT created major and minor clinical criteria to diagnose VAD-specific pocket infection and is listed in Table 5 [51].

Using these major and minor clinical criteria, a pocket infection can then be further classified as proven, probable, possible, or rejected [51]. A proven pump infection requires both major criteria are being met, while probable is one major with three minor or four minor criteria.

Pump Pocket Infection Treatment

Treatment plans for VAD-specific infections are dependent on transplant eligibility and stability of the patient. For transplant-eligible patients, proceeding with urgent heart transplantation may be the best option, while some may need to stabilize the infection before moving toward transplant. Device explant to recovery and device exchange are other options. For patients who cannot get a transplant, survive explant, or exchange, more conservative approaches should be pursued. All these options are discussed in further detail.

Table 5 ISHLT pump pocket infection criteria

Major clinical criteria:
• Microbiological: aspirated fluid culture positive or fluid/pus diagnostics of infection
• Radiologic: new fluid collection by radiologic criteria
Minor clinical criteria:
• Fever ≥38 °C with no other recognized cause
• New local erythema over pocket site
• Local pain and tenderness
• Induration or swelling
• Radiologic: lymphangitis seen radiographically, or
• New fluid collection without major criteria and without diagnostic culture but not explained by other clinical conditions

Adapted from Kusne S, Mooney M, Danziger-Isakov L, et al. An ISHLT consensus document for prevention and management strategies for mechanical circulatory support infection. J Heart Lung Transplant 2017,36(10):1147–8; with permission

Intravenous antibiotics are started empirically and then narrowed once the causative pathogen is identified. This may stabilize the infection, but a pocket infection will still need surgical management. One treatment strategy is surgical drainage and debridement of infectious tissue, bacterial and fungal cultures obtained, followed by thorough lavage of the wound. The debridement and washout is repeated until cultures return negative and then closure can occur. This strategy has been successful in clearing 65% of patients in one study [52]. Notably, it was less successful when *Pseudomonas* was the causative pathogen compared to *Staphylococcus aureus*, *Candida* species, and other gram-negative organisms [52]. Several papers report using antibiotic bead placement at the location of the debridement. These are replaced at each repeat washout and then removed prior to final closure [52, 53]. Both vancomycin and tobramycin-impregnated polymethylmethacrylate (PMMA) beads have been reported in the VAD-specific infection literature. However, the optimal bead material, volume, and size are not defined [54]. Both negative pressure wound therapy (NPWT) and omental flap transposition without removal of the device are closure options supported in the literature [55, 56]. Closure techniques are discussed in further detail below. Oral antibiotics for pocket infection are typically continued chronically as suppressive therapy.

Achieving eradication of the infection is unlikely unless the VAD can be completely explanted to recovery or the patient can undergo heart transplant. Urgent heart transplant should be pursued when appropriate. Surgical pump exchange has a low peri-op mortality [57]. However, there can be high rates of infection recurrence, as high as 38% at 6 months post exchange [58]. One comparison of pump exchange versus debridement and antibiotic beads showed the former effective at eliminating persistent infections, while the latter was not [54]. Pump exchange can be risky, and the risks must be weighed appropriately. Postoperative survival with pump exchange is better when the exchange is performed early, after medical management has failed. It is important to note that indication for device exchange impacts outcomes. Those who are exchanged due to LVAD-specific infection have higher mortality compared to those exchanged for device malfunction [59]. Table 6 provides a summary of treatment recommendations for different level of VAD-specific infections.

Table 6 Management of bacterial ventricular assist device-specific and -related infections

Infection types	Medical management	Surgical management
Superficial DLI	Treat with IV or oral antibiotics for a minimum of 2 weeks or until infection has resolved (drainage, redness, tenderness, and so forth). Reinforce patient and caretaker education about DL immobilization techniques.	Not applicable
Deep DLI (or unclear depth)/ pocket infection	Treat with IV antibiotics until clinical stabilization and improvement of infection (usually 6–8 weeks), followed by long-term oral suppression therapy.	Surgical debridement with or without wound VAC may be needed. Recommend abscess drainage. New DL exit site away from previous infection may be required.

Table 6 (continued)

Infection types	Medical management	Surgical management
VAD pump and/or cannula	Treat with IV antibiotics for at least 6–8 weeks. If bacteremia resolves, recommend oral suppression (if possible) until transplantation in BTT patients. If intraoperative cultures are positive, recommend 4–6 weeks of IV antibiotics following transplantation; if they are negative, recommend 2 weeks of oral antibiotics following transplant. In DT, IV antibiotic treatment is followed by long-term oral antibiotic suppression.	Surgical drainage and debridement may be required to control infection. Source control is as follows: in BTT, explant of the device for HT; in DT, explant/exchange of the device for control of infection.
Persistent bacteremia/ relapsing infection, despite adequate antimicrobial and surgical therapy	In BTT, IV antibiotics should continue until after HT, with continuation of antibiotics following HT as previously mentioned based on intraoperative cultures. In DT, IV antibiotic treatment is followed by long-term oral antibiotic suppression, though at times oral options are not available and IV therapy is continued beyond 8 weeks duration of antibiotics treatment after device exchange depends on the clinical course and pathogen. Longer course (4–6 weeks) may be offered in positive intraoperative cultures or recent preoperative bacteremia, and a shorter course (14 days) may be offered in the absence of such conditions.	Strong consideration should be made for device explant/ exchange. One could consider bridging patients with a percutaneous device so that infection control is achieved before new VAD placement.
VAD-related bacteremia	Duration of antibiotics depends on the source, organism, and clearing of bacteremia. CRBSI secondary to *Staphylococcus aureus* is treated for 4–6 weeks, and the catheter is removed. If not *S. aureus*, blood cultures become negative within 24–48 h and there are no signs of metastatic infection; 2 weeks from the first negative blood culture may be adequate (e.g., urinary tract source). If no source is identified, treatment may be considered as with VAD pump and cannula infection.	
Bacterial mediastinitis	Duration of antibacterial therapy is at least 6–8 weeks after last surgical debridement.	Surgical debridement is often indicated. Open chest and VAC wound closure may be needed.
Infective endocarditis	Duration of antibacterial therapy is the same as for VAD pump and cannula infection.	Surgical intervention may be required.

BTT bridge to transplant, *CRBSI* catheter-related bloodstream infection, *DL* driveline, *DT* destination therapy, *HT* heart transplant, *IV* intravenous, *VAC* vacuum-assisted closure

Adapted from Kusne S, Mooney M, Danziger-Isakov L, et al. An ISHLT consensus document for prevention and management strategies for mechanical circulatory support infection. J Heart Lung Transplant 2017,36(10):1147–8; with permission.

Aslam, S. (2018) Ventricular Assist Device Infections. Cardiology Clinics. 36; 507–517

Pump/Cannula Infection

VAD pump and cannula infections are the least common yet among the most serious of VAD-specific infections. These infections can lead to dehiscence of pump anastomoses and pump failure due to obstruction of flow and septic emboli. Like pump pocket infections, ISHLT published major and minor clinical criteria to diagnose VAD-specific pump and/or cannula infection and are listed in Table 7 [51]. The definition is partially based on modified Duke's criteria which is predictive of infective endocarditis. Proven pump and/or cannula infection must have microbiology, histologic features of infection from tissue samples, and two major clinical criteria. Probably infection is one major plus three minor criteria, or four minor criteria. Also possible is one major plus one minor, or three minor [51].

Treatment regimens typically follow the same path as pump pocket infections and are summarized in Table 6. Intravenous antibiotics are started empirically and then narrowed once the causative pathogen is identified. If possible, patient proceeds with urgent heart transplantation or VAD explant. In cases where that is not quickly possible, patient undergoes surgical debridement, antibiotics, and possible pump exchange. Device exchange should be prompted by relapsing or persistent infection, septic emboli, or sepsis despite adequate antibiotic. If post-debridement the device remains exposed, then coverage with well-vascularized healthy tissue is needed for infection management. Rectus abdominis muscle flap is a viable option given proximity to the VAD and generous length, and this is the most reported flap option [60]. Vascularized omental flaps are reported as a viable alternative [60]. Case reports suggest after surgical debridement, negative pressure wound therapy (NPWT) or vacuum-assisted closure with instillation (VACi) should be utilized. This is followed by eventual closure of the defect with a rectus abdominis flap and lifelong antibiotics [61]. There are reports of successful eradication of infection with retention of hardware by using this technique [62, 63].

Table 7 ISHLT pump/cannula infection criteria

Major clinical criteria:
• Indistinguishable organisms recovered from two or more peripheral blood culture >12 h apart with no other focus of infection
• When two or more positive blood cultures are taken from the CVC and peripherally at the same time and defined as a BSI-VAD related or presumed VAD-related
• Echocardiogram positive for VAD-related infectious endocarditis
Minor clinical criteria:
• Fever ≥38 °C
• Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracerebral or visceral, conjunctival hemorrhage, and Janeway's lesions
• Immunologic phenomena: glomerulonephritis. Osler's nodes, Roth spot
• Microbiologic evidence: positive blood cultures that does not meet criteria as noted above

Adapted from Hannan MM, et al. Working formulation for the standardization of definition of infections in patients using ventricular assist devices. J Heart Lung Transplant. 2011;30(4):375–84; with permission

Approach to the Patient with a Suspected VAD Infection

Infection may present with generalized symptoms like malaise, lethargy, and fatigue. These symptoms have a wide differential diagnosis and can make initial diagnosis difficult. Patients should be educated to record their temperature, among other vital signs, every day at home and report abnormal values to their clinical team. Low-grade fever, mild to severe pain at DLES site, or purulent discharge should all prompt suspicion. Workup and evaluation start with a thorough history and review of systems. A physical examination should include device interrogation, evaluation of the driveline exit site, and inspection of surgical wounds [51]. If superficial DLES infection is suspected, this may be evaluated and treated in the outpatient setting. If a deep DLES infection, pocket infection, pump infection, or sepsis is suspected, the patient should be admitted for inpatient evaluation. Laboratory evaluation may include white blood cell count, two sets of blood cultures, procalcitonin, inflammatory markers including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), bacterial and fungal cultures, and gram stain of fluids. Initial imaging of driveline and device components may include abdominal ultrasound (US) and computed tomography (CT). Imaging techniques for infection in VAD patients are further discussed in the next section. Further evaluation will likely be warranted for more severe and complex infections. Given the most common pathogens are *Staphylococcus* species and *Pseudomonas*, empiric antibiotic therapy should be targeted for these pathogens and informed by institutional epidemiologic patterns.

Imaging

There are clear definitions categorizing VAD infections, but there are not clear diagnostic standards. There is not a single, perfect imaging modality for diagnosing deep tissue space infections and VAD infections. CT and US have been long utilized and recommended to identify deep drive line, pocket, pump, and cannula infections [1]. Traditionally, a CT scan is first performed looking for induration, fluid collection, or an abscess around an infected peripheral driveline, centra pump pocket, or cannula for LVAD-specific infections. However, a criticism of both CT and US is that they lack specificity and require that an infection to be advanced in causing morphological changes that can be picked up by these modalities [8, 64]. Another limitation to CT imaging is the metal-hardening artifact making interpretation of images difficult. Magnetic resonance imaging (MRI) is contraindicated in LVAD patients. Transesophageal echocardiogram (TEE) may be able to detect fluid collection or abscess formations, as well as vegetations, in LVAD endocarditis or concomitant cardiac implantable electrical device lead-endocarditis. Like CT, TEE is better at imaging advanced infections [8]. Metal-hardening artifact may also affect TEE.

Nuclear imaging techniques are unique in that they target intracellular metabolic processes and cell expression. This can allow for earlier detection of infection before

morphological changes would show on other methods like CT or US. Several different nuclear imaging techniques have been evaluated as it relates to VAD infections. With leukocyte scintigraphy, white blood cells are removed from the patient, tagged with an indium-labeled radioisotope, and then introduced intravenously back into the patient. The tagged leukocytes then localize to the areas of acute infection. It has been described as a "gold standard" used to identify deep infection, but can lack specificity due to lack of anatomic landmarks that would allow for localization. Single-photon emission computed tomography (SPECT) enables for more precise localization and interpretation of images [55]. Combining SPECT/CT with radiolabeled leukocytes increases sensitivity for infection detection and anatomic location. It can also be potentially used to identify distal infectious emboli [65–67]. Widely reported in more recent literature is using fluorodeoxyglucose (FDG)-positron emission tomography (PET) imaging in VADs. This type of test was widely used in clinical settings to identify cardiac device infections and prosthetic valve endocarditis. It can facilitate an earlier diagnosis with high accuracy [68, 69]. It can also guide therapy by accurately describing the severity and extent of the infection [68]. Kim and colleagues showed that FDG PET/CT identified 80% of LVAD patients scanned to show metabolic evidence of LVAD infection, confirmed by microbiology and clinical follow-up, compared to CT scan only identifying 11% as infected [70]. FDG PET/CT use has been further studied in LVAD infection cases and found to have high sensitivity 92–95%, and specificity reported anywhere from 83% to 91% [71, 72]. When looked at specifically regarding driveline infection, the sensitivity and specificity were reported as high as 96% and 99% respectively [72]. Early image-guided surgical intervention may allow a less complicated subsequent course [73].

Bacteremia

Bloodstream infections (BSI), mediastinitis, and infective endocarditis are all considered VAD-related infections as shown in Table 1 [51]. Each of these infections requires careful evaluation to assess if they involve the VAD device or not.

BSI in a VAD patient is a very serious complication and unfortunately has an incidence rate reported anywhere from 12% to 54% incidence rate [2, 65, 74]. BSI are associated with poor outcomes and can account for 20% of mortality within 6 months of implant [65]. DLI may account for 43% of BSI in VAD patients [75]. In a MOMENTUM 3 trial analysis, 80% of sepsis events were due to bacterial pathogens; the others were 3% fungal, 1% viral, and 14% unknown [21]. Though ISHLT definitions call all BSI in VAD patients as a VAD-related infection, it is important to investigate the etiology of the BSI further. Esquer Garrigos and colleagues grouped BSI into three subcategories:

- Non-VAD-related. There is a confirmed etiology other than the VAD or VAD components. Examples are UTI, PNA, and central venous catheter [76].
- VAD-related. The BSI is caused by an infection from VAD components.
- VAD-associated is then used for all other cases where etiology remains unknown or indeterminate [76].

Initial treatment for BSI should be empiric antibiotics aimed at *Staphylococcus* species and *Pseudomonas aeruginosa*, followed by targeted therapy. The antibiotic therapy needs to address the specific organism, should be bactericidal/fungicidal, biofilm penetration, dose, and duration. A high dose should be recommended when treating a biofilm-based infection. For transplant candidates, antibiotics should continue until after the heart transplant is performed, with longer courses considered for patient with positive cultures intraoperatively. For VAD patients not undergoing transplant, IV antibiotics are typically prescribed for 6–8 weeks, and then followed by long-term antibiotics suppression. If the BSI is VAD-related, or persistent, then source control may be needed with explant or pump exchange as discussed in previous sections.

Mediastinitis/Infective Endocarditis

Mediastinitis is a VAD-related infection when it is due to the VAD device. It is possible for it to be non-VAD-related, if it is clearly from another source such as esophageal perforation [51]. Mediastinitis can be very difficult to manage, and surgical debridement is often indicated, followed by at least 6–8 weeks of antibiotics [1]. The use of lifelong suppressive antibiotics is reported [61]. Leaving the chest open may be necessary, and there are case reports of using alternative closure techniques such as negative pressure wound therapy, and muscle flaps that were previously discussed. Antibiotics should be continued for at least 6–8 weeks after last surgical debridement. Debridement often indicated, open chest VAD wound closure may be necessary [1]. Infective endocarditis should be treated with antibiotics with the same duration as infected for pump and cannula VAD-specific infections. ID consultation and surgical intervention may be required. For both mediastinitis and infective endocarditis, mortality is as high as 70% in VAD patients [77].

Stroke

Infection in VAD patients is well known to increase the patients' risk for stroke. This is due to the underlying prothrombotic, or hyper-coagulable state an infection creates. The inflammatory states caused increasing atherosclerosis and acute phase reactants cause the pro-thrombotic state [74]. Device infection is associated with higher pump thrombosis rates, which can trigger neurological events. Of VAD patients experiencing an ischemic stroke, 51% had an active infection at the time, and 20% have a BSI [78]. Systemic fungal infections also cause severe inflammation, and can be associated with higher risk of stroke [78]. Table 8 describes treatment approaches for patients with fungal infections. BSI in VAD patients is specifically associated with both hemorrhagic and ischemic stroke at higher rates than LVAD patients without BSI [2, 74, 79]. Both *Pseudomonas* and *Staphylococcus aureus* BSI have been specifically associated with a higher stroke rate [15, 74].

Table 8 Management of fungal ventricular assist device-specific and -related infections

Infection Type	Medical Management	Surgical Management
Candida sp superficial DLI	Routine blood cultures shouldbe perfomed to dianose/rule out concomitant fungemia. Superfical infection in clinically stable patients with negative blood cultures should be treated with an azole for a minimum of 2 wk.	Not applicable
Candida sp deep (or unclear depth) DLI/pocket infection	Routine blood cultures shouldbe perfomed to dianose/rule out concomitant fungemia. It should be treated with an echinocandin or L-AmB for 6–8 wk, followed by long-term oral suppressive theraphy thereafter. If device is replaced surgically or after HT, antifungal agents should be continued for a minimum of 6 wk and possibly longer if surgical cultures are positive.	Surgical drainage may be required for control of extensive infection with or without a wound VAC. Routine device replacement in the setting of an FI is not recommended. If the device requires replacement, then the new driveline needs to be placed in a different site.
Candida sp pump/cannula infection	Recommend treatment withh an echinocandin or L-AmB for 8–12 wk, from the first negative blood culture, followed by long-term suppression with an oral agent. Flucytosine can be added to L-AnB in select patients. If device exchange or HT occurs, then antifungal agents should be continued for a minimum of 6 wk and possibly longer if surgical cultures are positive following surgery.	Routine device replacement in the setting of an FI is not recommended. Device exchange or placement on the cardiac transplant list is recommended if patients have a relapse despite appropriate treatment (antifungal agent, dose, and duration).
Candidemia	Investigations are recommended to determine the precise source, including microbiologic cultures (driveline, pocket, and CVC) and imaging. Empirical therapy with an echinocandin or L-AmB is recommended. Once identification and sensitivity testing has occured, patients are clinically stable, and blood cultures are negatice, antifungal agents should be de-escalated to the narrowest spectrum agent possible. If the source of the candidemia is a CVC, it has been removed, blood cultures become negative within 24–48 h, and there is no obvious metastatic infection. then 2–4 wk of antifungal therapy is recommended from the date of first negative blood culture. A complete ophthalmologic examination for endophthamitis bbefore discontinuation of theapy is recommended.	Not applicable
Candida sp mediastinitis/ infective endocarditis	The type and duration of antifungal therapy for mediastinitis and infective endocarditis is the same as for a VAD pump/cannula infection.	Through surgical debridement of mediatinitis with an open chest a ± VAC wound closure is recommended

Abbreviations: CVC, central catheter; FI, fungal infection; L-AmB, liposomal amphotericin B; VAC, vacum-assisted closure.

Adapted from Husain S, Sole A, Alexander BD, et al. The 2015 International Society for Heart and Lung Transplantation guidelines for th management of fungal infections in mechanical circulatory support and cardiothoraric organ transplant recipients: executive summary. J Heart Lung Transplant 2016;35(3):276–7; with permission.

Transplant Outcomes

Heart transplant is suggested as the most definitive treatment for many LVAD-related infections, therefore it is important to look at the impact of infection on transplant outcomes. The reported data has variable outcomes, but overall has been supportive of continuing to list and transplant these patients. Some papers demonstrate patients with LVAD-related infections may have an increased risk of post-heart transplant infectious complications [80] though others have demonstrated no relapse in VAD-specific infection post-transplant [76]. A small study suggested that by treating VAD-specific infections for 2 weeks with pathogen-directed therapy post-heart transplant, and treating patients with non-VAD infection or uncomplicated VAD-related infections with standard surgical prophylaxis, infection relapse can be prevented [76]. There are studies showing similar post-heart transplant survival outcomes between LVAD-related infection and non-LVAD-infected groups [81–83]. However, a large meta-analysis of 6067 LVAD patients shows a decrease in post-heart transplant survival for patients with an LVAD-related infection, and this was consistent across pulsatile and continuous-flow pumps [84].

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Anticoagulation for Ventricular Assist Devices

Colleen Labuhn and Lisa Peters

Anticoagulation and Antiplatelet Agents

Both anticoagulants and antiplatelet agents are used for prevention of thrombosis in patients with LVADs. Typical therapies include heparin in the immediate postoperative period and aspirin and warfarin for long-term prevention of LVAD thrombosis. Characteristics of these agents are noted in Table 1.

Table 1 Antiplatelet and anticoagulation drug therapy

	Mechanism	Duration of effect	Elimination
Antiplatelet agent			
Aspirin	Inhibits cyclo-oxygenase I, causing loss of thromboxane A2 synthesis → results in decreased platelet aggregation	7–10 days	Renal
Anticoagulants			
Heparin	Binds to antithrombin III, enhancing inhibition of thrombin and factor X	3–4 h	Clearance by the reticuloendothelial system
Warfarin	Inhibition of vitamin K epoxide reductase, causing inhibition of activation of clotting factors II, VII, IX, and X	2–5 days	Liver

Reference: Cheng-Ching E, Samaniego EA, Naravetla BR, Zaidat OO, Hussain MS. Update on pharmacology of antiplatelets, anticoagulants, and thrombolytics. Neurology. 2012 Sep 25;79(13 Suppl 1):S68–76 [1]

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Perioperative Management of Anticoagulation

Cardiopulmonary bypass (CPB) is typically utilized during LVAD implantation, necessitating the use of heparin, adjusted based on activated clotting time (ACT). The Society of Thoracic Surgeons recommends maintaining the ACT above 480 s during CPB. Viscoelastic tests, such as thromboelastography (TEG), have also been recommended by various organizations to assist in the management of cardiac surgery-related bleeding; these can be used to determine when transfusion is necessary [2]. At the end of the surgery, protamine is used to reverse heparin. In the immediate postoperative period after LVAD implantation, the patient is at risk of post-surgical bleeding. The Instructions for Use (IFU) for the HeartMate II, HeartWare HVAD, and HeartMate 3 recommend starting heparin between 12 and 48 h after the LVAD implantation surgery if the patient has no persistent bleeding, chest tube output has decreased to 40–50 mL/h, and hemoglobin is stable [3]. After heparin is initiated, the IFUs recommend initially targeting a partial thromboplastin time (PTT) of 40–50 s for 24–48 h and then increasing to a target PTT of 50–60 s, with an additional recommendation for the HeartMate 3 LVAD to increase the target PTT to 55–65 s after another 24 h. Implanting centers vary in their approach to use of heparin in the postoperative period, with some centers using no heparin at all and others starting it later than 48 h after surgery [3, 4].

Implanting centers also vary in the heparin protocols utilized in LVAD patients. Rather than using PTT for heparin monitoring, some centers use anti-factor Xa heparin assay (anti-Xa) monitoring during continuous intravenous heparin therapy due to its reported superiority for achieving therapeutic anticoagulation more quickly and with fewer dosing adjustments when compared to PTT monitoring [5]. However, the IFUs for the various continuous-flow LVADs provide no recommendation for a target range for anti-Xa values when administering heparin infusion therapy to patients with LVADs. Prior analyses of anti-Xa versus aPTT monitoring in patients implanted with the HeartMate II LVAD have shown dramatic variation between anti-Xa and aPTT levels which appear to be driven by the presence of hemolysis or device obstruction and by the use of concomitant warfarin therapy [6]. One implanting center reported their single-center experience with good outcomes utilizing a heparin protocol targeting anti-Xa values of 0.1–0.3 IU/mL [7].

Long-Term Anticoagulation and Antiplatelet Therapies

The Instructions for Use (IFU) for the HeartMate II, HeartWare HVAD, and Heartmate 3 LVADs all recommend use of aspirin as long-term antiplatelet therapy for patients implanted with these devices. The IFUs recommend starting aspirin within 5 days of implantation for the HeartMate II, within 24 h for the HeartWare HVAD, and within 3 days for the HeartMate 3 [3]. The dose of aspirin varies in trials of these devices from 81 mg daily to 325 mg daily [8–10]. Use of the higher dose of aspirin 325 mg daily was found to reduce thrombosis risk in patients implanted with the HeartWare HVAD [11]. However, the European Trace trial found that

eliminating aspirin therapy entirely in patients implanted with the HeartMate II decreased the risk of bleeding and did not increase the risk of thrombosis or ischemic stroke [12]. One analysis of the MOMENTUM 3 study of the HeartMate 3 device indicated that bleeding and thrombosis events were similar between patients who received aspirin 81 mg daily and 325 mg daily, provoking the question of whether aspirin use provides any benefit in patients implanted with the HeartMate 3 [13]. The ongoing ARIES trial will randomize HeartMate 3 patients to aspirin 100 mg daily or placebo with a primary endpoint of survival free of any non-surgical major hemocompatibility-related adverse event at 1-year post implant [14]. This trial will help to guide future use (or nonuse) of antiplatelet therapy for HeartMate 3 patients. Clopidogrel 75–150 mg daily is recommended in the IFU for the HeartWare HVAD in patients who are intolerant of aspirin, after a loading dose of 300 mg. The IFU for the HeartWare HVAD also recommends consideration of the use of enhanced antiplatelet therapy in patients who cannot take more than 81 mg daily of aspirin, i.e., clopidogrel plus aspirin or dipyridamole plus aspirin [3]. However, the use of other antiplatelet agents in LVAD patients has not been well-studied [15].

The use of warfarin in patients with LVADs has also varied. The IFUs recommend starting warfarin within 48 h of implantation for the HeartMate II, within 4 days for the HeartWare HVAD, and within 3–5 days for the HeartMate 3 [3]. The IFU for HeartMate II recommends targeting an International Normalized Ratio (INR) of 2–2.5, while the IFUs for the HeartWare HVAD and HeartMate 3 recommend targeting an INR of 2–3. One report analyzing outpatient anticoagulation in the HeartMate II LVAD suggested a target INR of 1.5–2.5 due to a noted higher risk of ischemic stroke in patients with INR <1.5 and higher risk of bleeding in patients with INR >2.5 [16]. Due to the lower risk of thrombosis with the HM3, the MAGENTUM pilot study reviewed outcomes in 15 HM3 patients after decreasing the target INR to 1.5–1.9 at 6 weeks after implantation of the HM3 LVAD [17]. Results found one patient had a gastrointestinal bleed and no patients had thrombotic events. Larger studies will be needed to further assess lower INR goals for HM3 patients. Some patients may require alterations to the goal INR range due to risk factors for bleeding (i.e., prior bleeding events) or thrombosis (atrial fibrillation, presence of mechanical valve, and/or history of stroke or pump thrombosis).

Maintenance of INR in the therapeutic range is key for optimal outcomes; one analysis found that in the 30 days before a bleeding event, LVAD patients spent 41.2% of time above the INR goal range [18]. Another analysis found that time in the therapeutic INR range was 11.8% lower in the time period prior to a confirmed pump thrombus or ischemic stroke [19]. Unfortunately, a meta-analysis found that LVAD patients had a mean time in the therapeutic INR range of only 46.6% [20]. Patient education about the impact of dietary vitamin K intake, alcohol use, and use of over-the-counter medications and herbal supplements on INR is critical to assist in maintaining a stable INR. Careful management of fluid intake and avoidance of fluid overload is also very important, as liver congestion can also increase the INR [21].

Management of drug-drug interactions is key to maintaining a stable INR in patients taking warfarin. Most LVAD patients take many medications and require changes to their medication regimens on a regular basis. When new medications are added, their potential interaction with warfarin must be considered. Medications that strongly inhibit the metabolism of warfarin via the cytochrome 450 (CYP450) system in the liver include amiodarone, −azole antifungals such as fluconazole, sulfamethoxazole-trimethoprim, and metronidazole. When these medications are initiated, a 20 to 50% reduction in warfarin dose may be necessary. It is recommended to draw an INR 3–5 days after initiating any of these medications in combination with warfarin to monitor for increased INR. Due to the long half-life of amiodarone, weekly INR monitoring after initiation, adjustment, or discontinuation of amiodarone is recommended until the INR is stable. Other medications may also increase INR when co-administered with warfarin, including various antibiotics and prednisone. More frequent INR monitoring may be required during the use of these medications, depending on the length of therapy. Medications that induce the metabolism of warfarin include rifampin, carbamazepine, and nafcillin. The induction of CYP450 enzymes can have a more delayed onset and offset, so INR monitoring 1–2 times per week until a stable INR is reached may be required when an inducer medication is initiated or discontinued. The interaction with rifampin is especially strong, sometimes requiring warfarin doses of greater than 20 mg daily to achieve a therapeutic INR. Achieving the target INR during the use of inducer medications can be very challenging, so alternatives to these medications should be considered. Patients should also be educated to avoid the use of nonsteroidal anti-inflammatory drugs; these do not generally increase INR but they do increase the risk of gastrointestinal bleeding while on warfarin [22]. Patients should also be educated regarding the potential interaction of cannabis enhancing INR levels [23].

Warfarin management protocols typically recommend changes in the weekly warfarin dose of 10–20% when the INR is out of range [22]. While this can be a helpful rule of thumb, consideration of patient-specific changes in clinical status, diet, and medication therapies may warrant deviations from such protocols to maintain INR in the goal range. This is especially true for LVAD patients, as they tend to have more variation in INR compared to non-LVAD patients.

Direct oral anticoagulants have become preferred therapies in some disease states due to superior outcomes when compared to warfarin, the elimination of the need for INR monitoring, fewer drug-drug interactions, and lack of interaction with foods containing vitamin K. However, these therapies are not well-studied in patients with LVADs. One small study comparing dabigatran to warfarin in HeartWare HVAD patients was stopped prematurely after thromboembolic events occurred in 4 out of 8 patients receiving dabigatran [24]. In contrast, a case report described a patient implanted with a HeartMate II LVAD with recurrent GI bleeding on warfarin who experienced no further bleeding episodes after stopping warfarin therapy and switching to apixaban 2.5 mg twice daily [25]. Further study of the use of direct oral anticoagulants in LVAD patients is needed before they can be recommended for wider use in this patient population.

Monitoring INR

A crucial component of LVAD therapy is the monitoring of INR to assure that INR remains in the goal range [26]. As discussed above, many adverse events are associated with INR values outside the goal range; the goal of close INR monitoring is to decrease the incidence of these events. The majority of INR checks will occur through venipuncture or plasma INR (P-INR) either at a lab, anticoagulation clinic, or through home health point of care therapy with results being reported to the LVAD team for management of the INR level and adjustment of the warfarin dose [26]. Timing of INR checks will vary based upon the changes to the warfarin dose. Many patients will have INR checks weekly to biweekly and sometimes more frequent if dose changes have occurred or if there is a narrower goal INR range due to a previous adverse event [26]. Due to the delicate balance of warfarin dosing and testing, point of care (POC) testing with home INR machines is becoming increasingly common and studies have evaluated the correlation between venipuncture results and POC results. One study out of Columbia University showed that there was moderate correlation between the two different tests, specifically the Alere home INR machine. The Alere machine showed that 44/50 patients recorded higher results on the home POC machine [26]. Self-testing has been shown to increase patient satisfaction and simplifies the process of frequent monitoring while also increasing the amount of time spent within the desired therapeutic range [26]. Another international multicenter study investigated the correlation of INR via venipuncture versus POC-INR. The findings indicated that while the POC-INR may have tended to be higher at times, there was no statistically significant difference between the two methods, particularly when they were measured within 4 h of each other [27]. This multicenter study concluded that the use of POC-INR likely would not alter warfarin dosage or patient management significantly when compared to the use of INR via venipuncture [27]. There is currently a debate within the literature for use of lovenox to bridge subtherapeutic INR results as an outpatient to avoid readmission. Studies have shown little or no complication of bleeding rates while others have cited an increase in major bleeding events [28, 29].

Modification of Anticoagulation for Adverse Events

Adverse events (AE) associated with LVAD therapy include gastrointestinal (GI) bleeding, stroke, and pump thrombosis, all of which are described in chapter "Ventricular Assist Device Complications." Each of these adverse events may have a direct correlation to anticoagulation either pre- or post-AE and will require manipulation of anticoagulation medication. GI bleed is one of the most common AEs that patients with LVADs will experience, although incidence will vary depending upon type of device and management at each institution. In the MOMENTUM 3 study 27% of HM 3 patients experienced a GI bleed, and in the HeartWare HVAD ENDURANCE study 35.1% of patients experienced GI bleeding at 2 years post-implant [30]. There are multiple factors associated with high GI bleed rates and

LVAD, including development of acquired Von Willebrand disease, anticoagulation with antiplatelet therapy, and narrowed pulse pressure [30]. The most common strategy for management of GI bleeding in an LVAD patient is discontinuation of anticoagulation and antiplatelet medications, particularly if the INR is supratherapeutic. In some cases, administration of vitamin K or fresh frozen plasma may be required to reverse anticoagulation and to control bleeding [30]. It is critical to consider patient- and pump-specific risks for thrombosis before administering reversal agents, as pump thrombosis can be an unwarranted consequence of the manipulation of anticoagulation. Patients will typically undergo diagnostic testing to find the source of GI bleeding prior to resumption of anticoagulation and may require heparin bridge to a therapeutic warfarin dose as well as close monitoring for any additional GI bleeding.

Pump thrombosis can be a significant complication associated with LVAD therapy and anticoagulation management. Not all pump thrombosis is associated with a subtherapeutic INR and can occur from non-physiological flow patterns that result in shear stress and formation of thrombus within the pump [31]. Pump thrombosis can cause stroke, failure of the pump itself, and systemic embolism; therefore, patients should be monitored for thrombus development closely throughout the duration of LVAD support [32]. Pump thrombosis may be suspected based on LVAD parameters, hemolysis lab values, or patient symptoms. The target INR range is typically 2.0–3.0 and there is a direct correlation to a period of time with an INR less than 2.0 and pump thrombosis [33]. Clinical symptoms associated with pump thrombosis may vary because a thrombus can occur in the inflow cannula, the rotor, or the outflow graft; each of these thromboses may present different signs and symptoms [34]. Achievement of early therapeutic INR, bridging with heparin for subtherapeutic INR, and maintaining warfarin within an INR goal range of 2.0–3.0 are crucial to limiting the development of thrombus formation.

Once a thrombosis has been identified, medical management of the thrombosis is crucial. Treatment protocols for thrombosis will vary based upon the patient's clinical presentation and center-specific protocols. Many centers will start with an unfractionated heparin infusion potentially followed by tissue plasminogen activator (tPA) treatment (i.e., a 10-min intravenous infusion of 10 mg tPA followed by an infusion of 10 mg tPA per hour) if no resolution of thrombosis is identified with intravenous heparin alone [31]. VAD clinicians should monitor patients closely for risk of hemorrhagic stroke when given tPA. Pump exchange may be warranted in patients that do not have resolution with the above therapies or for patients that are deemed unstable hemodynamically with unstable pump parameters [31]. Heparin-induced thrombocytopenia can be a potential cause of thrombosis in patients with LVADs; this condition has been managed in LVAD patients with the use of argatroban, bivalirudin, and/or use of plasmapheresis [35, 36].

Neurological adverse events are a frequent and devastating complication of LVAD therapy; these events include hemorrhagic stroke and embolic stroke. Anticoagulation management can be difficult in patients with neurological events [37]. While embolic stroke is often associated with pump thrombosis as discussed previously, hemorrhagic stroke can be more difficult to manage and can be

associated with factors such as mechanical fall, traumatic injury, hypertension, supratherapeutic INR, additional antiplatelet therapy, and conversion from a previous ischemic injury [25, 38]. There has been as an associated increase in hemorrhagic events in patients taking triple therapy with aspirin, warfarin, and clopidogrel [38]. These patients should be monitored very closely to maintain INR in the therapeutic range. Discontinuation of anticoagulation and antiplatelet therapies is often necessary after hemorrhagic events. Decisions regarding resumption of anticoagulation should be made in conjunction with a multidisciplinary team including neurology and neurosurgeon when indicated, keeping in mind patient characteristics and clinical history.

A comparison of HVAD and HeartMate II pumps during the ENDURANCE trial indicated that there was a higher percentage of disabling strokes in the HVAD group (16.9% vs 14.6%) but this difference was not statistically significant [39]. One analysis of 200 LVAD patients found a 13% stroke rate (26/200); 13 strokes were ischemic and 13 were hemorrhagic [40]. Review of anticoagulation strategies in this cohort showed that 9/13 patients with hemorrhagic stroke had all anticoagulation discontinued, 2/13 were started on aspirin only, and 1/13 resumed aspirin as well as warfarin (with a lower goal of 1.5–2.0). Anticoagulation strategies for the 13 ischemic stroke patients included increase of ASA from 81 mg to 325 mg daily and target INR goal of 2.5 for 11/13 patients and 2 patients remained on aspirin 81 mg daily with an INR goal of 2.0–3.0 [40]. This analysis highlights that patient-specific changes in anticoagulation and antiplatelet therapies are important after a stroke event.

Reversal of Anticoagulation

Reversal of anticoagulation in LVAD patients should only occur in the event of a life-threatening adverse event that will require a lower INR goal for treatment and management. Examples of emergencies that may require reversal are hemorrhagic stroke, life-threatening GI bleed requiring immediate upper or lower GI scope, or trauma such as a fall with evidence of intracranial bleed [38]. Warfarin has routinely been reversed with Vitamin K with a recommended dose of 10 mg given intravenously, fresh frozen plasma (FFP), or prothrombin complex concentrates (PCC) which are dosed based on weight and INR result [38]. In 2013, the Food and Drug Administration (FDA) approved PCC and recommended them as the first-line reversal agents for patients with coagulopathy [38]. PCC reversal agents have recommended guidelines for dosing based on INR ranges; for example, dosing recommendations for four-factor PCC are as follows: INR 2.0–3.9: 25 units/kg, INR 4.0–6.0: 25 units/kg, and for INR greater than 6.0: 50 units/kg [38]. INR rechecks should be done within 2–12 h to evaluate for the success of the therapy. Guidelines suggest giving FFP if an INR <1.4 is not achieved after PCC is given. Reinitiating anticoagulation will be variant based upon the reason for reversal and the outcome achieved after the reversal. It will be crucial for the VAD team to aggressively monitor patients for the development of device thrombosis when warfarin is reversed.

Management of Anticoagulation in Patients Who Refuse Blood Products

Patients that refuse blood products will require a different approach to the management of anticoagulation and may require closer monitoring for adverse events so interventions can occur sooner. There is little literature on bloodless LVAD management because few centers are willing to implant LVADs in patients that refuse blood products. There have been reports of minimally invasive LVAD implants but no publications exist providing guidance for management of adverse events in bloodless LVAD patients or anticoagulation management in this patient population. University of Chicago Medical Center in Chicago (UCMC), Illinois is a high-volume bloodless center that has implanted approximately 20 LVADs without the use of blood products (both HVAD and HM 3) between the years of 2014–2021 [41]. While the surgical implant requires a skilled surgeon, the postoperative care and the management of anticoagulation also need a skilled team that is able to identify and handle issues quickly and proactively. University of Chicago Medical Center follows the recommended protocols from each company (81–325 mg ASA and Warfarin with INR goal 2.0–3.0) for routine anticoagulation [41]. For preoperative patients, UCMC gives patients epoetin alfa 20,000 units every 48 h and a total of 1000 mg IV iron sucrose over 10 days, either 100 mg every 24 h or 200 mg every 48 h. The goal hemoglobin level is 12 g/dL for all preoperative patients. Post LVAD, patients remain on epoetin alfa and iron until a hemoglobin of 12 g/dL is achieved and until INR is therapeutic. Due to the thrombogenic potential of epoetin alfa, these patients are monitored carefully for signs of pump thrombosis. All labs within the hospital setting are drawn twice per week in pediatric tubes. Anticoagulation is adjusted based on weekly lab draws once the patient is discharged and the team may be more aggressive with lowering the anticoagulation goal in the event of a GI bleed [41]. If a patient is admitted with a GI bleed, anticoagulation will be stopped and diagnostic tests such as colonoscopy, double-balloon endoscopy, etc. will be completed quickly to find the source of bleeding. When anticoagulation is resumed, it is likely that heparin will be avoided, and the INR will slowly trend up to avoid recurrent bleeding. For neurological complications, the same protocols are followed for patients that do accept blood [42].

Anticoagulation in Pediatric Patients with LVADs

Pediatric patients with advanced heart failure can benefit from left ventricular assist device implantation to achieve improved bridge to transplant or wean rates when compared to pediatric patients managed on extracorporeal membrane oxygenation (ECMO). Research on optimal anticoagulation strategies in this patient population is sparse. However, in the Berlin Heart EXCOR Pediatric VAD (EXCOR) IDE study, the Edmonton Anticoagulation and Platelet Inhibition Protocol was created and utilized to reduce the risks of bleeding and thrombosis [43]. This protocol is a guideline for anticoagulation and antiplatelet therapy using standard management

of anticoagulants (heparin, enoxaparin, and/or warfarin) and thromboelastography results to modify therapy. Enoxaparin rather than warfarin was utilized in patients less than 12 months old due to difficulty with management of warfarin in this age group. The incidence of stroke (28%) and major bleeding (43%) was significant in this study, demonstrating the complexity of managing pediatric patients with LVADs [43]. Further research is indicated to determine the optimal anticoagulation strategy for this patient population.

Conclusion

Patients implanted with LVADs are at risk both for bleeding and thrombotic events; therefore careful management of antiplatelet and antithrombotic medications is critical to the clinical success of these patients. Involvement of clinicians who are experts in anticoagulation management, extensive patient education, and awareness of the importance of antiplatelet and anticoagulation therapies among all professional and personal caregivers of patients with LVADs is key to ensuring optimal outcomes for these patients.

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Exercise and Physical Therapy with Ventricular Assist Devices

Louise M. Fuller

Cardiac Rehabilitation in Literature

It is known that cardiac rehabilitation programs are safe and improve VO_2 max, functional capacity, quality of life (QOL), and reduce both heart failure (HF) symptoms and hospitalizations in patients with HF [1–3]. However, there is limited data to support the effect of cardiac rehabilitation programs on HF patients with a VAD. Haddad et al. [4] completed a systematic review and meta-analysis on outcomes of cardiac rehabilitation (CR) on patients with an LVAD. A total of six studies were included involving 183 patients with 125 of these undergoing cardiac rehabilitation programs and 58 receiving standard treatment (ST) (no formal exercise prescription other than walking daily). Cardiac rehabilitation was associated with improved VO_2 max compared to ST in all but two trials and showed improved QOL in all but one trial. Duration of follow-up varied from 1 to 18 months post LVAD implantation with initiation of CR ranging from hospitalization time to 10 months post LVAD implantation. Median CR session frequency ranged from 3 to 5 sessions weekly. Quantitative analysis was performed on 3 randomized control studies that included 39 having CR and 22 receiving ST [5–7]. CR was associated with significantly greater VO_2 max (MD = 3.00 mL/kg/min; 95% CI, 0.64–5.35, $p = 0.001$) and 6MWD improved in CR compared to ST group (MD = 60 m; 95% CI, 22.61–97.5, $p = 0.002$). Analysis on QOL was unable to be completed due to a variety of differing tools [4]. This demonstrates evidence for improvements in functional capacity and VO_2 max for patients with LVAD who undergo CR.

Another systematic review was undertaken by Scheiderer et al. in 2013 examining exercise parameters for rehabilitation of LVAD patients in the early postoperative stage [8]. Six retrospective studies were included with 102 patients and 3 case

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studies. Definitive guidelines could not be concluded from this review other than that it is safe to exercise VAD patients in the early phase.

Ben Gal et al. (2015) surveyed 77 LVAD implanting centers from the European Society of Cardiology and 58% had a functional exercise training program that began early post discharge and 24% offered long-term maintenance programs [9]. The majority of programs (84%) included aerobic training at low-intensity levels, resistance training (47%), respiratory muscle training (55%), and balance training (44%) [9].

However, there is still a paucity of evidence about the format of the rehabilitation programs including time to initiation, frequency, duration of sessions, content, and follow-up. Further large, multicenter studies assessing clinical benefits of CR in LVAD and biventricular assist device recipients are urgently needed.

Clinical Assessment

Prior to commencing early postoperative mobilization, consideration needs to be given to the expertise and skills of the health care professional providing the mobility exercise. The physiotherapist should be familiar with exercise physiology, VAD device function including alarms in addition to the institutional emergency practices (Table 1). A full medical history and functional status must be known prior to the commencement of any mobility or exercise training. Vital signs including mean arterial pressure (MAP), self-reported pain/symptom scores, and VAD functions must be monitored. The VAD team should be consulted if there are any alarms during the exercise. The patient should be informed about the exercise plan and give their consent.

Factors That Can Limit Functional Exercise Training

Heart failure myopathy from pre-existing immobility needs to be assessed with functional exercise capacity measures such as the six-minute walk test (6MWT), short physical performance test (SPPB), and strength testing on a dynamometer or with isokinetic dynamometry.

Table 1 Key staff competencies

1.	Identification of VAD hardware and understanding of basic function
2.	Key components of VAD: speed, pressure, flow, power
3.	Complete battery check and change
4.	Complete cables and controller change
5.	Identification of signs and symptoms of suckdown, low flow and thrombus
6.	Action to be taken in event of No.5
7.	Identification of all equipment to travel with the patient
8.	Identification of care plan
9.	Identification of goals of rehabilitation

Modified from Wells et al. [30]

In the LVAD patient, right ventricular (RV) function needs to be monitored and the multi-disciplinary team (MDT) can inform the physiotherapist of any changes to ensure appropriate exercise prescription. Additionally, any residual left ventricular (LV) function or recovery will also alter exercise prescription.

Both vascular and respiratory function may also alter exercise prescription. Consultation with the dietician to ensure that body mass index (BMI) is optimized as some patients may be required to lose weight prior to heart transplantation (HTx). The physiotherapist and dietician can work closely to balance the nutritional needs and exercise participation. Dietary counseling has been shown to prevent obesity in this population [10].

Anemia should be corrected as 6MWD has been shown to be improved following infusion [11].

Pump speeds must be optimized by the medical team and once programmed to the best setting for the patient have been shown to improve functional exercise capacity [12]. The VAD speed is set for each individual patient to obtain normal cardiac index and balanced ventricular function.

Monitoring Exercise Training

Cardiopulmonary exercise testing (CPET) measures peak oxygen consumption (VO_2 peak) with progressive ramp protocols. These protocols vary institutionally and aim for volitional exhaustion on a bike or a treadmill. Most VAD rehabilitation outpatient programs use moderate rating of aerobic exercise prescription that is 50–60% of VO_2 maximum [13].

Six-minute walk test (6MWT) is a submaximal exercise capacity test that is commonly used in VAD patients according to a standardized protocol [14]. VAD patients with a low 6 MW distance (6MWD) of less than 300 m have an increased mortality and a 21% overall risk for mortality for every 10 m less than 300 m [15]. Six MWD can be associated with VO_2 max results [16].

VAD patients are difficult to monitor during aerobic exercise performance. The Borg scale of shortness of breath (SOB) and perceived exertion (RPE) are commonly employed [17] to ensure adequate training and exercise progression. Aiming for a Borg SOB of 3 (scale 0–8) and RPE of 13 (scale 6–20) will ensure that aerobic training is maximized for each individual patient.

Mean arterial pressure (MAP) can be monitored at the commencement of the programs in the outpatient setting to ensure hemodynamic stability and can be used pre and post 6MWTs.

Figure 1 summarizes the exercise prescription for each phase. At each phase monitoring and re-assessment is needed to ensure that exercise modification and progression are tailored to each patient.

	ICU/acute phase	Sub-acute	Long term
Functional training	-Bed mobility -Sitting balance training -Sit to stand (repetition) -Marching on the spot -Mobility with/without aid -Independence in self-care	-Mobility with aid/ without aid -Stair negotiation -Sit to stand (timed) -Squats	-Running training -Work specific activities -Sport activities(non contact) -Leisure activities
Muscle strength	-Low repetition, low weight for both ULand LL -Elastic resistance bands	-Increasing both repetition and weight for UL and LL, 10RM -Cable resistance machines – for quads, hamstrings and UL	-High weight, low repetition for UL and LL -Cable resistance machines -Free weights
Aerobic training	-Marching on the spot -Seatedpedal training -Bike training–interval, no resistance	-Treadmill training (increasing duration, speed and incline) -Bike training increasing wattage or MET and duration Moderate intensity 50%-60% continuous for 15 minutes each modality	HIIT(if stable) Running training Skipping training
Pulmonary	-ACT -Diaphragmatic breathing exercises -Cough/Huff control	-ACT -Breathing pattern on exertion	
Education	-Role of physiotherapy -Sternal guidelines -Exercise limitations/progression -Rehabilitation/discharge plan	-UL /sternal guidelines -Safe and effective exercise guidelines	-Pathway and rehabilitation requirements for HTX -Identify any barriers and motivators to exercise
Postural re-education	-Balance re training	-Management of cervical or thoracic spine pain due to VAD bag weight and positioning -Core stabilizer exercises in sitting	
Outcome measures	-Mobility distance and independence -Clinical stability during mobility training -No changes in MAP (<60mmHg>100mmHg)	-CPET (if available) -6MWT (aim >300m) -STS –timed -dynamometry strength testing (if available) -Increasing independence in mobility, ADLs	-6MWT

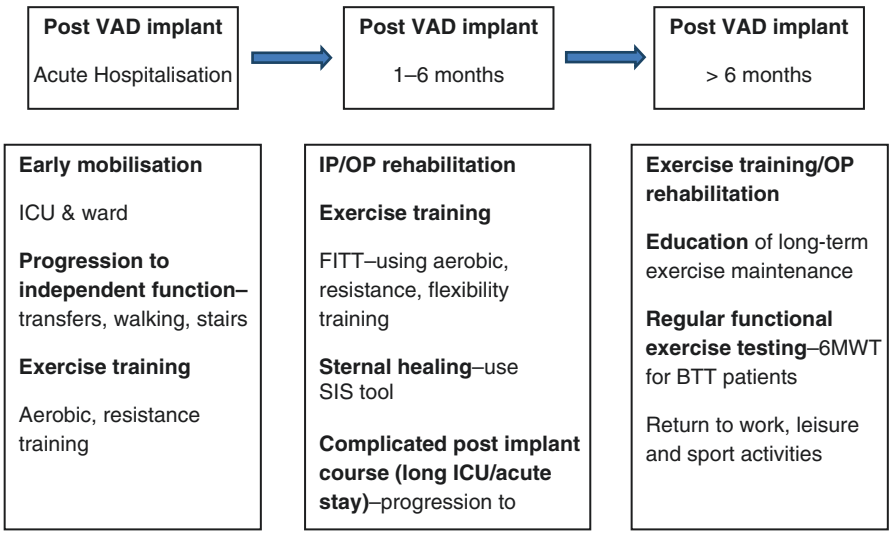
Fig. 1 Rehabilitation progression for VAD recipients. *UL* upper limb, *LL* lower limb, *RM* repetition maximum, *MET* metabolic equivalence of task, *HIIT* high-intensity interval training, *ACT* airway clearance techniques, *VAD* ventricular assist device, *MAP* mean arterial pressure, *6MWT* 6 minute walk test, *m* meters, *CPET* cardiopulmonary exercise test, *ADLs* activities of daily living

Implementation of Exercise Training

Based on available evidence, the following recommendations are generalized. Prior to commencing exercise training, consideration should be given to local expertise, available national recommendations and facilities, and a clinical assessment of each individual patient.

The VAD patient's journey can be divided into three phases post implantation. The acute hospitalization phase is when the patient remains in ICU and the acute

Table 2 Overview of exercise training for VAD patients



inpatient (IP) ward setting, followed by the second phase of sub-acute rehabilitation and the third phase is the long-term stage from 6 months after the VAD implantation (Table 2).

Acute Hospitalization

Early Mobilization

The frequency, intensity, timing, and type (FITT) [13] of the exercise sessions must be given consideration once the patient is clinically and hemodynamically stable.

The trained therapist/nurse should be responsible for securing all lines including the drive line and external VAD device components. A battery check should be made before commencing to avoid interruption. A driveline stabilization belt or securement device must be worn during mobilization and exercise training to secure the line from trauma and pulling. The VAD patient will be able to complete transfers from the bed with the assistance of gait aid if required and after training for usage of gait aid undertaken. Marching on the spot should be mastered prior to commencing mobility training.

Muscle strength training at this early stage should be centered around functional activities including bed mobility, utilizing a gait aid, rising from sitting, and increasing mobility distances. Light weights or light elastic resistance bands can be used. Balance training should be included as the VAD equipment can weigh 2–3 kg and the patient needs to become accustomed to this weight and managing any gait aid. Airway clearance techniques and respiratory care must be maintained. The physiotherapist has an education role to inform the patient about the rehabilitation program and assist the patient to plan future goals.

Sternal Complications and Precautions

VAD insertion is typically via midline sternal incision and is closed with stainless steel or titanium wires. The number, size, and type of these wires varies according to the patient characteristics and the surgeon's discretion. The sternum forms a keystone of the thoracic cage around which motion of the upper limbs and trunk takes place [18] and thus upper limb (UL) activities may have a marked impact on sternal movement, pain, and healing. Sternal instability refers to abnormal or excessive motion of the sternal edges due to disruption of the sternal closure [19]. Reports of sternal complications are low, ranging from 0.4% to 8%, but if left undetected it is associated with a higher mortality rate ranging from 14% to 47% [19–21]. Impaired sternal healing may lead to an increase in postoperative pain, delayed functional recovery, and increased patient morbidity [20, 22]. Preoperative factors for sternal complications may include obesity, chronic obstructive pulmonary disease, diabetes mellitus, and/or peripheral vascular disease, female gender, macromastia, and an increased disability classification. Peri-operative factors such as repeated sternal incisions, coronary artery bypass grafts, prolonged cardiopulmonary bypass procedures, and/or surgery time can contribute to the development of sternal complications.

Sternal complications are usually diagnosed by the presentation of subjective or objective findings of sternal infection and/or instability. Signs of erythema, fluid collection, wound dehiscence or discharge and sternal instability can be present. Patients may report increasing pain, clicking or crepitus, abnormal/unstable feelings during rest or movements of the upper limbs [19, 21].

It is important that that the sternum is assessed and re-assessed at all stages to ensure safe and adequate prescription of UL exercises and instructions on loading limits during daily activities. Prior to increases in loading, the sternal instability scale (SIS) tool should be used. This manual examination tool is a four-point manual scale that reliably rates sternal separation from 0 (stable sternum with no detectable motion) to 3 (completely separated sternum with marked increase in motion) [22]. This test establishes a difference between post-surgical pain and detectable sternal movement. Inter-therapist and intra-therapist reliability for this scale were estimated at 0.97 and 0.98 (ICC) respectively for median sternotomies [23].

Postoperative sternal precautions to prevent complications are routinely applied [22–24]. These precautions include significant limitations on the use of the UL and trunk [24]. However, these time points are historical and based on arbitrary figures drawn from the orthopedic literature on the fracture healing of long limb bones such as the radius, rather than studies on breastbone healing following a median sternotomy [24].

UL exercise progression must be interwoven with assessment of sternal stability. One practice may use two-dimensional ultrasound (2DUS) to further measure any sternal separation in both the sagittal and coronal planes. This provides an additional quantitative measure to ensure safe and effective UL exercise prescription [25].

Sub-acute Phase

Many formats for rehabilitation programs for VAD patients on discharge from hospital are currently utilized, but due to a paucity of studies, the optimal duration and timing of rehabilitation programs is still unknown. Many outpatient programs are based on cardiac rehabilitation formats with aerobic, walking, muscle strength training, or a combination of these modalities [26].

Clinical stability is required before undertaking any exercise program and prior to each session, VAD parameters and MAP should be recorded. Any variations should be reported to the VAD team.

Centers typically recommend thrice weekly 1 hour sessions comprising of 30 min of aerobic training and 30 min of muscle strengthening and functional exercises. Typical programs should be staffed by physiotherapists and Allied Health Assistants (AHA) with a staff to patient ratio of 1:5 to ensure adequate safety and supervision. All patients should undergo a 1 hour assessment session prior to commencement of the program. This assessment consists of a 6MWT, sit to stand test in 1 min, and full musculoskeletal assessment of both UL and LLs. A sternal stability assessment is completed to ensure safe UL exercise prescription. Aerobic training is aimed at 50 to 60% from 6MWD and the training is aimed to Borg scale of SOB of 3 and RPE of 13 [17]. Lower limb (LL) strength training is aimed to increase quadriceps and hamstrings muscles. UL strength training is dependent on sternal stability and pain and aimed at restoring all large UL muscle groups to near normal strength. Additionally, at this session explanations about infection control policies in the gym environment, goal setting, and exercise progression are discussed. FITT principles of exercise prescription apply to all modalities [13].

Aerobic training outpatient is often completed on a stationary bike and treadmill with 15 min training on each modality. Borg scale of SOB and RPE is taken at the half-way point and adjustment to workload can be made for the remainder of the training time. Short interval training can be used for de-conditioned patients until they are able to complete training continuously.

Muscle strength training targets quadriceps and hamstring muscle groups using both functional and resisted exercises. Leg strength improvements have been shown to improve significantly in LVAD patients undergoing rehabilitation programs compared to those who completed walking-only programs [7]. Squats, timed step ups, and gait training are included. Cable resistance machines, leg press, and quadricep extension machines are used and exercises progressed in both repetition and load.

UL Strength Training

Once the sternum has been assessed, UL training can commence with range of movement exercises and low resistance elastic bands. This will progress increasing both repetition and load for the large shoulder and arm muscle groups. Cable resistance machines can provide resistance once the sternum is stable. Lateral

pull downs, incline bench press machines, and seated free weights can all provide graded resistance. The physiotherapist must provide education and guidelines for loading limits for functional activities at home. In the longer term phase, the physiotherapist can also advise on load limits for suitable leisure activities and a planned return to low-level non-contact sports if medically cleared.

Core stabilizing exercises in upright sitting and postural muscle training should also be added to the program for deconditioned patients. Pilates© reformer work in supine particularly for leg resistance work can be added.

Long-Term Phase

Maintaining exercise training and muscle mass is essential for VAD patients. Continued physical therapy is key for patients awaiting transplantation to ensure the optimal outcomes from another major operation. Continual monitoring of the program with a 6MWT is advised. The exercise program should be revised, and any changes implemented to meet the patient's changing needs. Guidelines recommend to continue exercising and testing patients using the 6MWT at monthly intervals until 6 months post VAD implantation. High-intensity interval training (HIIT) (80–90% VO_2 max) can be safely introduced as this has been shown to well tolerated and can increase aerobic capacity more than moderate training [27]. Encouragement to participate in leisure, community or return to employment (if possible) activities is recommended. Running training can be commenced in clinically stable patients and with approval of the VAD provider team using intervals of running on the treadmill. Patients must wear the driveline support belt or stabilization device whilst undertaking running training. Running training has been shown to not be associated with increased driveline infections [28].

Contraindications and Precautions to Exercise

Exercise in all three phases should be ceased if there are any signs and symptoms of light headedness, severe dyspnea (Borg SOB >4), chest discomfort or alteration to MAP or evidence of hemodynamic instability that is unusual for that patient.

Malfunction of the VAD, suction events, pump thrombosis, arrhythmias or rapidly altering VAD parameters require urgent medical attention and institutional emergency procedures should be initiated.

During exercise sessions, advice to ensure that VAD patients do not Valsalva or breath hold during resistance work should be given. If prone position is necessary padding can be placed around the driveline. Table 3 summarizes the contraindications to exercise for VAD patients.

Table 3 Contraindications to exercise for VAD patients

1. Signs and symptoms of light headedness, dyspnea (Borg SOB score >4), chest pain, tachycardia, dizziness or de novo neurological signs
2. MAP <60 mmHg or alteration to hemodynamic stability
3. Weight increase >2 kg in last 2 days (check patients' fluid balance restriction)
4. Cardioverter-defibrillator intervention
5. VAD complications during or after exercise
(a) Alarm activation that is unusual for the patient, suction or alteration in flow
(b) Ventricular tachycardias—maybe asymptomatic
(c) Evidence of bleeding, hematomas, epistaxis
(d) Thrombus on impeller associated with marked increase in wattage
6. Joint pain or other musculo-skeletal injuries

Adapted from Adamopoulos et al. [31]
SOB shortness of breath, *MAP* mean arterial pressure, *kg* kilogram, *VAD* ventricular assist device

Infection Control

Infection control procedures are essential for ensuring the prevention of infectious diseases. Institutional guidelines will vary from center to center and need to be strictly adhered to, particularly those on equipment cleaning, hand washing and isolation practices. VAD patients are susceptible to drive line infections and an increased risk can be attributed to increasing BMI, younger age and exposed driveline velour [29]. Continued wearing of driveline support belt or stabilization device during exercise is required particularly in long-term patients who are completing more intensive exercise sessions. Any reports of ongoing abdominal discomfort should be escalated to the MDT.

Multidisciplinary Team (MDT)

For the successful management of these patients, an integrated MDT approach is recommended with access to the dietician, psychologist, social worker in addition to the physiotherapist. This would be arranged by the VAD coordinator.

Recommendations for Research

As there will be increasing advances in VAD development and demands for implantation, it is vital that large, quality, multicenter trials are undertaken to provide evidence for CR programs at all stages of the VAD patients' journey. The long-term benefits of rehabilitation, home-based versus center-based programs, specific programs for biventricular assist device patients versus sole LVAD patients are areas for research attention. Investigating exercise modality guidelines and appropriate monitoring should also be topics for further investigation.

To allay fears physiotherapists may have about commencing a rehabilitation program with VAD patients, it is important that they are trained in VAD management and view the VAD as an aid to improve the rehabilitation of the patient. Rehabilitation programs following VAD implantation should be an important part of the management for this unique group of patients.

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Nutrition for the Advanced Heart Failure and VAD Patient

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Importance of Nutrition and the Role of the Registered Dietitian Nutritionist in Patient Care

Nutrition intervention is low-risk and cost-effective for improving the quality of care of hospitalized patients, and the registered dietitian nutritionist (RDN) should be included in the multidisciplinary healthcare team for specialized focused attention to the nutrition assessment and progress for all patients [1]. The RDN is educated and credentialed in dietetics practice, food and nutrition science, and uses clinical judgment and evidence-based practice to promote health and wellness. The intent of these interventions is to prevent, delay, and manage acute or chronic conditions [2]. For patients with heart failure (HF), nutrition status is of vital importance to success in all phases of care. Nutrition screening, monitoring, and malnutrition prevention has been shown to improve patient outcomes [1, 2]. Malnourished patients are more likely to have complications, including an increased risk of pressure ulcer and decreased wound healing, with subsequent need for higher level of nursing care; immune suppression and increased infection rate; muscle wasting and functional loss, resulting in less independence and increasing risk of falls; more medication requirements; longer length of stay, higher readmission rates, higher treatment costs, and increased mortality [1, 3]. These findings are consistent across various patient populations and geographic location, reinforcing the potential detrimental effects that malnutrition can have on clinical outcomes [3].

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The registered dietitian nutritionist is uniquely qualified to provide medical nutrition therapy (MNT), and based on the Academy of Nutrition and Dietetics (AND) scope of practice for RDNs, they can implement MNT for numerous medical conditions, including cardiovascular disease, diabetes, metabolic syndrome, pulmonary disorders, critical illness or conditions, malnutrition, organ transplant, and weight management [2]. The AND's evidence-based Heart Failure 2017 Guideline highlights the importance of the RDN in caring for adults with all stages of HF, and recommends MNT for treating HF and the conditions that may contribute to it, including hypertension, hyperlipidemia, and obesity [4].

Malnutrition in Heart Failure and the Nutritional Implications of Cardiac Cachexia

Due to the many complications and consequences of malnutrition, both medical and financial, it is challenging to accurately define this complex issue. Malnutrition, or undernutrition, is described as "a continuum of inadequate intake and/or increased requirements, impaired absorption, altered transport, and altered nutrition utilization" per the 2012 consensus statement by the AND and the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.), with weight loss frequently seen in this process [5]. It is estimated that 15–60% of adults are malnourished, but this estimate varies based on patient population and also on the wide variety of tools used to assess malnutrition [2]. Inflammation in the setting of hypercatabolic conditions can increase the risk for malnutrition, but the AND and A.S.P.E.N. do not recommend using inflammatory markers or lab values, including serum albumin and prealbumin, for diagnosing malnutrition [5, 6], as they are not consistent or predictable in reflecting weight loss or inadequate energy and protein intake, especially in the setting of inflammation [5].

The intricacies of malnutrition mean there is no single parameter for diagnosing it, so the AND and A.S.P.E.N. recommend identifying two or more of the following six characteristics to qualify for malnutrition: insufficient energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, localized or generalized fluid accumulation that may sometimes mask weight loss, and diminished functional status as measured by hand grip strength [5]. Because nutrition status can shift over time along this continuum, these criteria differentiate between severe and non-severe malnutrition in the context of acute illness or injury, chronic illness, and social or environmental circumstances. These criteria are summarized in Table 1, and should be reassessed frequently as a patient's clinical status evolves or progresses [5].

The effects of malnutrition are closely associated and often overlap with the complex physiological impairments resulting from advanced HF. Examples of this overlap can include gut edema causing malabsorption, cytokine production leading to anorexia, increased work of breathing and fatigue further perpetuating decreased food intake, functional impairment due to loss of skeletal muscle and insufficient protein and energy delivery, immune dysfunction, anabolic and catabolic

Table 1 Malnutrition criteria [5]

	Malnutrition in the context of acute illness or injury		Malnutrition in the context of chronic illness		Malnutrition in the context of social or environmental circumstances	
Clinical characteristic	Non-severe (moderate) malnutrition	Severe malnutrition	Non-severe (moderate) malnutrition	Severe malnutrition	Non-severe (moderate) malnutrition	Severe malnutrition
Energy intake	<75% of estimated energy requirement for >7 days	≤50% of estimated energy requirement for ≥5 days	<75% of estimated energy requirement for ≥1 month	<75% of estimated energy requirement for ≥1 month	<75% of estimated energy requirement for ≥3 months	≤50% of estimated energy requirement for ≥1 month
Weight loss	1–2% in 1 week 5% in 1 month 7.5% in 3 months	>2% in 1 week >5% in 1 month >7.5% in 3 months	5% in 1 month 7.5% in 3 months 10% in 6 months 10% in 1 year	>5% in 1 month >7.5% in 3 months >10% in 6 months >10% in 1 year	5% in 1 month 7.5% in 3 months 10% in 6 months 10% in 1 year	>5% in 1 month >7.5% in 3 months >10% in 6 months >10% in 1 year
Loss of subcutaneous fat	Mild	Moderate	Mild	Severe	Mild	Severe
Loss of Muscle mass	Mild	Moderate	Mild	Severe	Mild	Severe
Fluid accumulation	Mild	Moderate to severe	Mild	Severe	Mild	Severe
Reduced grip strength	N/A	Measurably reduced	N/A	Measurably reduced	N/A	Measurably reduced

imbalance, neuroendocrine abnormalities, inflammatory system activation, and increased lipolysis [7–10]. Micronutrient deficiencies are often seen as a result of these metabolic alterations, including calcium, magnesium, selenium, zinc, iron, thiamine, folate, and fat-soluble vitamins [7, 9, 11–13]. These various complications can also cause laboratory anomalies including low total cholesterol, anemia, and lymphopenia, along with low serum albumin and prealbumin [7, 9, 12–14].

Body mass index (BMI) as a measure of nutrition status for advanced HF patients has been studied, with low BMI indicating higher mortality [7–9, 14], but BMI can be skewed when edema is present and often does not indicate a patient's true nutrition status [14]. Similarly, loss of lean body mass can be hidden by peripheral edema, and weight loss related to malnutrition can only be diagnosed when peripheral edema is stable [7, 8]. There is a known "obesity paradox" in patients with established HF, in which patients with higher BMIs may have better nutrition status and decreased mortality than patients with low or normal BMI [7, 9, 12–14]. Muscle wasting, or sarcopenia, is also a consequence of HF causing loss of muscle strength, decreased functional capacity, and overall weight loss [7–9, 14].

These many comorbidities related to weight and loss of function can progress to cardiac cachexia, which is a metabolic wasting syndrome characterized by unintentional edema-free weight loss of muscle, fat, and bone tissue, peripheral edema, and functional status decline related to the inflammatory process of HF [7–9, 15]. It is the presence of chronic inflammation that differentiates cachexia from starvation-related malnutrition, although anorexia and nutrient deficiencies are seen in both cases, making them all the more difficult to accurately discern [7, 8, 16, 17]. All of these factors contribute to increased mortality rate in the HF population [9, 10, 17], and consequently increase the risk for complications when surgical intervention with a ventricular assist device (VAD) is considered [7, 12].

Nutrition Screening and Assessment Parameters

Nutrition screening can help the RDN and other healthcare providers identify the patients who may be at high risk for malnutrition, and such screening should be done for all advanced HF patients [4, 6] or potential VAD candidates. The nutrition-related parameters for screening and assessment should include the patient's clinical history and diagnosis, subjective diet intake and weight history, anthropometrics, review of pertinent laboratory values and medications, and functional assessment [4, 5, 9, 12]. The AND's Heart Failure 2017 Guideline recommends the RDN also take into account the severity of the patient's HF using the New York Heart Association (NYHA) functional classification in order to adequately develop a nutrition care plan [4].

Biochemical data, including inflammatory markers such as serum albumin, prealbumin, transferrin, and retinol-binding protein still frequently used in nutrition assessment for HF patients undergoing evaluation for ventricular assist device (VAD), despite the well-known problems with their accuracy in indicating nutrition status [12, 14]. As with malnutrition versus cachexia, the inflammatory state of HF

is the key factor when using visceral protein stores as nutrition markers. In the setting of acute inflammation and critical illness, liver synthesis of albumin and prealbumin is reprioritized to generate acute-phase reactants, and these markers may not return to normal in a state of chronic inflammation, and therefore are poor markers of nutrition status and protein stores [12, 13, 18]. However, serum albumin has been shown to be a predictor of morbidity and mortality in cardiac surgery patients [19]. This leads to the importance of clinical history and physical examination as part of nutrition assessment in addition to the review of laboratory data.

A nutrition-focused physical examination is another parameter recommended for nutrition assessment; the RDN can perform a head-to-toe, system-based assessment of the patient to further identify micronutrient deficiencies [20]. Handgrip strength (HGS) assessment is a reliable measurement of muscle function and marker for muscle wasting, with lower HGS indicating increased length of hospitalization and thus may help in preoperative VAD evaluation [21]. Computed tomography (CT) and ultrasonography are also emerging tools for assessment of lean body mass and skeletal muscle, especially in critically-ill HF patient who may be unable to provide adequate history or participate in handgrip strength assessment [13, 22].

Due to the vast array of nutrition-related factors that must be accounted for, there are varying estimates on the prevalence of malnutrition in patients with HF (8–62%) depending on the definition and criteria used for assessment [7, 9, 23]. Many screening tools have been developed to streamline the process for identifying patients at nutrition risk, but hospitalized patients are often unscreened and consequently do not receive any formal evaluation of nutrition status [24]. The tools in Table 2 have been reviewed for accuracy in determining malnutrition particular to the HF, VAD, and cardiac surgery populations.

Multiple studies have compared the validity of many of these tools. The Subjective Global Assessment (SGA) is widely used across all populations including HF, VAD, and cardiac surgery [3, 7, 9, 12, 28, 31]. The Malnutrition Universal Screening Tool (MUST) and the Mini Nutritional Assessment-Short Form (MNA-SF) have been shown as the most accurate in a hospital setting [30]. These two tools, along with the Mini Nutritional Assessment (MNA), have demonstrated the best predictive ability for mortality risk for HF and VAD patients [14, 27, 29] as well as accurate prediction of postoperative complications for cardiac surgery patients [28]. Also in VAD patients, the Nutritional Risk Index (NRI) and the Prognostic Nutritional Indicator (PNI) have also been associated with survival outcomes and complication risks [16, 18]. The Cardiac Surgery-Specific Undernutrition Screening Tool (CSSUST) was shown to identify 90% of undernourished patients awaiting cardiac surgery [25]. However, the use of these tools does not eliminate the need for extensive and in-depth nutrition assessment by the RDN.

Another important and challenging aspect of the RDN's assessment of the HF patient is estimating energy and protein needs. The catabolic state of HF can contribute to increased metabolic rate and increased resting energy expenditure (REE) [8, 12, 16]. Indirect calorimetry (IC) measures oxygen consumption (VO_2, mL/min) and carbon dioxide production (VCO_2, mL/min). The REE is calculated using these

Table 2 Malnutrition screening tools

Tool	Criteria	Population studied	References
Cardiac Surgery-Specific MUST (CSSM)	MUST score + age, sex	Cardiac surgery	[25]
Cardiac Surgery-Specific Undernutrition Screening Tool (CSSUST)	BMI, weight loss, appetite, preop hospitalization	Cardiac surgery	[25]
Controlling Nutrition Status (CONUT)	Serum albumin, total cholesterol, lymphocytes	HF	[9, 23, 26]
Mini Nutritional Assessment (MNA)	BMI, weight loss, food intake, mobility, psychological stress or acute disease, neuropsychological problem	HF, cardiac surgery, VAD	[3, 9, 14, 27–29]
Mini Nutritional Assessment-Short Form (MNA-SF)	BMI, weight loss, food intake, mobility, psychological stress or acute disease, neuropsychological problem	HF, VAD	[3, 8, 29, 30]
Malnutrition Screening Tool (MST)	Weight loss, appetite	Cardiac surgery	[3, 28, 30]
Malnutrition Universal Screening Tool (MUST)	BMI, unintentional weight loss, acute disease	HF, cardiac surgery	[3, 7–9, 28]
Nutritional Risk Index (NRI)	Weight, serum albumin	VAD	[16]
Nutritional Risk Screening 2002 (NRS-2002)	Age, BMI or weight loss, food intake, severity of disease	HF	[3, 8]
Nutrition Risk in the Critically Ill (NUTRIC)	Age, APACHE II, SOFA, comorbidities, ICU LOS, IL-6	Critically ill, HF	[9]
Prognostic Nutritional Indicator (PNI)	Serum albumin, serum lymphocytes	HF, VAD	[9, 18, 26]
Subjective Global Assessment (SGA)	Patient history, physical examination	HF, cardiac surgery, VAD	[3, 7, 9, 12, 28, 31]
Short Nutritional Assessment Questionnaire (SNAQ)	Weight change, appetite, supplementation (does not incorporate medical diagnoses or inpatient status)	HF, cardiac surgery	[3, 9, 28]

pulmonary gas exchanges, and "represents the energy expended by the body during a 24 h non-active period to maintain involuntary functions such as substrate turnover, respiration, cardiac output, and body temperature regulation [32]." IC also determines the patient's respiratory quotient (RQ) and current substrate utilization of carbohydrates, fat, or protein [32]. This allows nutrition support to be individualized based on the patient's specific metabolic needs [32], and therefore it is the gold standard for energy needs estimation [4, 12, 31–35]. IC is usually performed by the respiratory therapist in the intensive care unit using a metabolic cart, which completes REE calculations automatically [32], but online calculators are also available [36].

IC has been used reliably for estimated energy needs in HF patients and both before and after VAD implantation, but it can be contraindicated with critically ill patients requiring high levels of ventilation and sedation, as well as when there may be moisture or leaks present [33]. When IC is not available, predictive equations are

frequently used for estimating nutrition needs, and it has been shown that the equations developed for critically ill patients predicted REE better in HF patients compared with IC results than the equations designed for healthy individuals [33, 34]. Every equation, however, predicted REE larger than IC, further suggesting the use of IC in HF patients when able [34].

Protein requirements are also higher in the HF population due to the increased muscle protein breakdown and malabsorption, and if this breakdown is not compensated for by increased protein intake, the risk of sarcopenia, muscle wasting, and protein-losing enteropathy increases [8, 16]. The AND's Heart Failure 2017 Guideline recommends protein provision to maintain positive nitrogen balance [4], and protein needs increase further with the addition renal replacement therapy [31]. The RDN must individualize these estimations for each patient, taking into account the specific clinical history, and frequently reassess the patient's status and adjust estimated needs accordingly in the setting of an advanced disease process such as HF [33]. Table 3 provides a summary of guidelines for estimating nutrition needs for the HF and VAD patient [4, 12, 13].

Table 3 Estimating nutrient needs [4, 12, 13]

Nutrient	AND Heart Failure 2017 Guideline	Banerjee et al. (2017)	Montgomery et al. (2012)
Energy	• Indirect calorimetry • NYHA Classes I–IV/AHA Stages B and C – 22 kcal/kg actual body weight (for normally nourished patients) – 24 kcal/kg actual body weight (for malnourished patients) • NYHA Class IV/AHA Stage D – 18 kcal/kg actual body weight • Activity factors for estimating total energy needs (NYHA Classes I–IV/AHA Stages B, C, and D): – *Sedentary*: 1.0 or more to less than 1.4 – *Low active*: 1.4 or more to less than 1.6 – *Active*: 1.6 or more to less than 1.9 – *Very active*: 1.9 or more to less than 2.5	• Indirect calorimetry • Brandi equation • 25–30 kcal/kg dry weight • 11–14 kcal/kg actual dry weight (BMI >30)	• 30–35 kcal/kg or RMR + 15–25% minimal physical activity and additional 10–20% for hypermetabolism • Metabolic cart or 21 kcal/kg actual weight (BMI >30)
Protein	• 1.1–1.4 g/kg actual weight	• 1.2–2.0 g/kg actual dry weight • ≥2.0 g/kg ideal weight (BMI >30)	• 1.0–1.5 g/kg • 1.5–2.0 g/kg ideal weight (BMI >30)

Nutritional and Surgical Interventions

Nutritional intervention for hospitalized HF patients with malnutrition has been shown to lower risk for complications, optimize protein intake, improve prognosis, and decrease risk of hospital readmissions [35]. The most common diet intervention for HF is sodium restriction, although this recommendation has been debated, with recommendations varying from 2000 to 4000 mg restriction per day [37]. Fluid restriction of 1.5–2 L/day is frequently recommended alongside the reduced sodium diet [12, 13]. Diet composition in patients with HF can be inadequate in both macro- and micronutrients, including greater than recommended carbohydrate, trans-fatty acids, and sodium intake, and lower than recommended intake of omega-3 and omega-6 fatty acids, calcium, potassium, and vitamin D [11, 38], which also adds to the importance of education on balanced dietary intake as well as to the possible need for nutrient supplementation as appropriate. Micronutrient supplementation of many of the above nutrients has been studied, but there are limited data to recommend the efficacy on HF outcomes, and the AND's Heart Failure 2017 Guideline recommends an interdisciplinary approach to micronutrient supplementation [4, 39–41].

A diet higher in plant-based foods (fruits, vegetables, nuts, seeds) and lower in animal products seem to have beneficial and preventive effects regarding both HF and atherosclerosis; the Dietary Approaches to Stop Hypertension (DASH) diet and the Mediterranean diet are two diet patterns often followed [9, 37, 42]. The RDN should educate on the appropriate eating plan based on the stage and class of heart failure and any other comorbidities, including energy and protein intake, sodium and fluid intake, physical activity, and the monitoring of weight and symptoms [4].

Many nutrition benefits have also been seen from surgical intervention with VAD placement, including metabolic recovery, reversal of low albumin, improved perfusion to gut and skeletal muscle, and increased physical activity and functional capacity [9]. However, VAD implantation surgery can also bring challenges related to optimizing and maintaining adequate nutrition status. Patients with HF have high surgical risks related to underlying and often undetected malnutrition, low BMI, as well as potential delayed surgical treatment [7, 15]. The extensive physical operation further exacerbates inflammatory response; therefore, cachectic patients who already have decreased organ reserve will be more likely to develop complications [28].

Nutrition Support for Perioperative and Postoperative Critical Care

With these risks and potential postoperative critical illness in mind, adequate nutrient delivery and intake by mouth is often not possible. Nutrition support is traditionally regarded as adjunctive care designed to provide exogenous fuels to preserve lean body mass and to support the patient throughout the stress response [22], and has been deemed safe in patients with cardiac cachexia [15]. High protein oral

Table 4 Signs of inappropriate nutrition provision [13]

Underfeeding	Overfeeding
Increased presence of nosocomial infections (due to immunosuppression)	Hyperglycemia
Loss of lean body mass	Hyperlipidemia
Impaired immune function (seen with lower immunoglobulin concentrations)	Hepatic steatosis
Depressed ventilator drive (seen in prolonged mechanical ventilation duration due to decreased diaphragmatic strength)	Failure to wean from mechanical ventilation (due to hypercapnia)
Delayed wound healing	Azotemia

nutrition supplements (ONS) are typically the first form of nutrition support. ONS can help prevent underfeeding and worsening malnutrition in the immediate postoperative phase of care, and also have been shown to significantly reduce the risk of development of pressure ulcers [43, 44]. Despite the relative simplicity of using ONS, they appear to be underused in the hospital setting and in surgery patients [44].

For the critically ill patient requiring prolonged mechanical ventilation and other forms of intensive care, enteral or parenteral nutrition support is often needed for adequate provision of energy and protein. The A.S.P.E.N./Society of Critical Care Medicine (SCCM) guidelines for the adult critically ill patient provide direction on the best practices for initiation, administration, and monitoring of nutrition support [22]. Patients should be assessed for nutrition risk on admission to the intensive care unit (ICU) and nutrition goals should be developed based on the patient's calculated energy and protein requirements. Enteral nutrition (EN) should be initiated within 24–48 h following the onset of critical illness and increased to goal over the first week of ICU stay; aspiration precautions and enteral feeding protocols are recommended to optimize EN delivery [22].

Enteral nutrition support is recommended over parenteral nutrition due to lower infection risk, lower cost, improved gut perfusion and renal function, and greater ability to meet estimated nutrition needs, even in the setting of hemodynamic instability [12, 13, 19, 22, 28]. The RDN provides specialized input and individualized recommendations for nutrition support based on each patient's individual clinical status, including disease-specific formulas with differing macronutrient, micronutrient, and electrolyte content, as well as close monitoring of tolerance. Table 4 includes possible signs of inappropriate nutrition provision in VAD patients [13].

Postoperative Education, Discharge Process, and Role of Interdisciplinary Care Team

Postoperative diet education is an integral part of the discharge planning process in order to strengthen the patient's understanding and chances for compliance and success with recommended diet restrictions and recovery goals [12]. Programs with organizational strategies to incorporate the management of cardiac cachexia, dietary quality, micronutrient supplementation, and management of obesity may have less

morbidity and mortality after VAD implantation [9]. The discharge process should include protocol-driven policies for HF and VAD-specific education including, but not limited to, sodium and fluid restriction, multivitamin and mineral supplementation for those on diuretic therapy and restricted diets, and iron and vitamin D for those deficient [9]. In addition, it is crucial to provide instruction on the importance of glycemic control in promoting wound healing and preventing infection [43], as well as drug-nutrient interactions with anticoagulation.

Although diet recommendations and nutrition goals for the advanced HF and VAD patients are likely to be addressed by the RDN throughout hospitalization, the utilization of an interdisciplinary approach from implantation through discharge is essential to achieve optimal long-term outcomes. From the intensive care unit to the rehabilitation department, a collaborative approach is required to improve the short- and long-term recovery of the VAD patient, and this team should include a pharmacist for medication reconciliation and discharge education, and often a diabetes educator for additional guidance for hyperglycemia. The RDN's assessment of energy expenditure and nutrition goals for caloric and protein supplementation should be taken into consideration during daily multidisciplinary rounds. Physical, occupational, and speech therapists also play a vital role. This team approach will allow healthcare providers to collaborate for the most appropriate diet and nutrition recommendations based on the patient's medical condition, increasing functional status, and exercise tolerance from the time of implant until discharge. All members of the healthcare team should provide documentation of multidisciplinary discussion, collaboration, education, and discharge readiness for each patient, as it is a universal expectation for a VAD program undergoing program certification.

While the role of the VAD coordinator varies among implanting centers on a global scale, all institutions include persons who perform standardized VAD education in a class-like format prior to discharge. In conjunction with multidisciplinary team members, this educational platform should reinforce the role of diet adherence and exercise compliance in decreasing readmissions, increasing survival, and improving a patient's quality of life [4, 12, 35], and it is recommended that each center creates and utilizes a VAD binder with printed materials detailing each patient's specific goals and recommendations for diet, medications, weight, and glycemic control. This binder should include logs for recording daily weights, blood sugars, time spent in exercise, and other relevant values.

Outpatient Follow-Up

Throughout the spectrum of care, it is important to ensure that the multidisciplinary approach on the inpatient setting is equally comprehensive and accessible in the outpatient setting. This includes access to a registered dietitian nutritionist, pharmacist, diabetes educator, endocrinologist, physical and occupational therapists, cardiac rehabilitation, psychologist, psychiatrist, heart failure clinic, and social worker. Adherence to the above diet restrictions and other medical regimens after discharge can be difficult without ongoing counseling and support provided by the

multidisciplinary team members [9, 40], and noncompliance with their prescribed diet may amplify the adverse event profile in VAD patients [45]. Therefore, nutrition and diet should be a key component in the discharge process and upheld at each follow-up clinic visit.

The newly implanted VAD patient is routinely discharged with a VAD-trained home care agency providing registered nurses as well as physical and occupational therapists to clinically monitor and assist with medical management in the home. Involving these home care providers is invaluable for further monitoring and managing knowledge deficits with regard to diet, exercise, laboratory, and medication compliance, as well as for providing ongoing alimentary education to patients and caregivers on the interactive role these factors have on the patient's clinical progress. There are numerous remote monitoring programs, industry-driven educational toolkits, and third-party vendors to aid in these efforts.

As the patient's functional status improves, home care services will be adjusted. Upon completion of home physical and occupational therapy regimens, a referral to outpatient cardiac rehabilitation (CR) should be instituted for continued behavioral counseling and exercise. Physical activity and training with CR can improve functional and exercise capacity, quality of life, and may reduce the risk of hospitalization and 1-year mortality [46–50]. Because current contemporary VADs require anticoagulation with, warfarin, this may be managed by the home care nurse in conjunction with the VAD team initially, but pharmacy-driven anticoagulation clinics should be considered as they provide an additional opportunity to educate patients regarding diet, medication reconciliation, and VAD management. The healthcare provider (most often a VAD coordinator) will typically discuss the ongoing need for these services upon discharge from home care during follow-up clinic visits. Addressing transportation, psychosocial environment, and financial concerns upon referral will also assist with program compliance.

Close monitoring of the patient's prescribed diet composition and nutrition goals should be reviewed during routine clinic visits with VAD clinicians. VAD parameters and vital signs, physical assessment, laboratory and diagnostic data, blood glucose, and daily weights should be reviewed in order to monitoring patient adherence and make necessary modifications to dietary and fluid restrictions, diuretic regimens, and electrolyte and vitamin supplementation in order to avoid precipitation of adverse related events. The patient's goals should be reinforced at each clinic visit, and as program staffing allows, the RDN should be involved in the outpatient monitoring and management of the patient's diet compliance and nutrition progress [9]. Additional recommendations to endocrinology or pertinent consulting providers should transpire when necessary during these visits. Follow-up education regarding nutrition interventions in VAD patients with obesity [45] should occur on a regular basis.

With the rates of obesity steadily increasing [49], there are more HF patients with morbid obesity (BMI $\geq$35 kg/m^2), which is a barrier to candidacy for heart transplantation [51]. Therefore, more of these patients are undergoing VAD implant as a bridge to weight loss in order to eventually qualify for heart transplantation, or as destination therapy. Despite the aforementioned obesity paradox, current data suggests that obese

patients actually have a higher risk of complications, including infection, pump thrombosis, and right ventricular failure after VAD implantation [45, 52, 53]. Although obese patients receiving a VAD may have improved short-term mortality, there's no difference in mortality observed in long-term survival [52]. In addition, it has been recognized that most patients with obesity actually gain weight after VAD implantation resulting in ineligibility for heart transplantation, increased complications, and a poorer quality of life [52–54]. Therefore, long-term weight loss must be a goal for these patients, which should be done with a multidisciplinary approach.

According to the AND's Heart Failure 2017 Guideline, the RDN may consider intentional weight loss interventions once the patient is stable and euvolemic [4], but often there is a need for adjunctive therapies to help VAD patients who lack dietary conformities and cannot lose weight to improve health or become a transplant candidate with lifestyle interventions alone. In addition to diet and exercise, behavioral interventions for weight loss in VAD patients with obesity may help. This may involve counseling on diet, exercise, self-monitoring, identifying and solving barriers to weight loss, and facilitating a support system and relapse prevention [45]. There is a paucity of evidence regarding different pharmacological weight loss intervention in VAD patients, therefore this therapy is not currently recommended. The safety and feasibility of bariatric surgery after VAD implantation has been demonstrated in a small number of VAD patients [45, 55–58]. Collaborating with a bariatric weight loss center should be considered and implemented in coordination with the implantation center. Referrals should occur in patient selection meetings when the obese heart failure patient is undergoing consideration for advanced surgical intervention and in obese VAD patients.

Hospital Readmissions and Other Barriers to Nutrition Progress

Recognizing barriers to nutritional progress is imperative in order to appropriately modify the plan of care. Short-term and long-term barriers may differ and range from an immediate postoperative complication or diet tolerance to an adverse event and subsequent rehabilitation standpoint. It may be as simple as a dislike in menu offerings to a behavioral modification or gastrointestinal failure. Financial disparities must also be taken into consideration when considering compliance with dietary recommendations.

It is important for the clinician to comprehend when dietary nonconformities or knowledge deficits contribute to hospital readmissions. A consult to the RDN should occur with each readmission directly or indirectly related to a nutritional lapse or noncompliance. The implication and role of the social worker in evaluating and identifying psychosocial and financial barriers should also be reestablished. Often continued follow-up with a psychologist or psychiatrist is essential to encourage behavioral modifications when applicable and the level of rehabilitation with physical and occupational therapy or inpatient cardiac rehabilitation should be reinstated. Involving a substance abuse counselor may also be indicated in some cases.

Ensuring all members of the multidisciplinary team remain involved throughout the continuum of care will support a reduction in adverse events related to diet or nutrition idiosyncrasies from the inpatient to the outpatient setting. Readmissions due to failure to thrive may require pharmacological assistance, nutritional modifications and supplementation, along with a more aggressive inpatient or outpatient rehabilitation program. Admissions as a result of stroke or bleeding should readdress the interaction of the nutritional regimen and medication reconciliation with regard to blood pressure management, anticoagulation and its impact on compliance with time spent in therapeutic range, and gastrointestinal prophylaxis. The interaction between diet, fluid intake, and medication timing can be an integral part in preventing electrolyte and fluid imbalances which may precipitate suction events or arrhythmias as well as prevent anemia, infection, or heart failure exacerbations. Including a thorough review of systems and laboratory work up, in addition to the physical examination will benefit the provider in appropriate diagnosis and treatment referrals.

Overall, nutrition is vitally important for the success of HF and VAD patients. VAD programs should incorporate nutrition screening tools into admission protocols for identifying risk for malnutrition in patients with HF being evaluated for VAD candidacy. The registered dietitian nutritionist should be utilized for specialized patient assessment and malnutrition diagnosis. Nutrition support interventions can assist in optimizing nutrition status prior to VAD implantation, perioperative and postoperative recovery, and in long-term weight management. These interventions will be more successful with an interdisciplinary approach, and the RDN should be included in all phases of care, both inpatient and outpatient, to promote nutrition progress and favorable clinical outcomes.

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Outpatient Management for the VAD Patient

Lori Edwards and Thomas Berg

Thorough outpatient management for the ventricular assist device patient population is essential in preventing re-admissions and diagnosing early complications [1]. In this chapter, we will cover timing of clinic visits, blood pressure management, diagnostic testing, important multi-disciplinary team members, benefits of telemonitoring, and safely traveling with a VAD. The necessary elements of an outpatient visit, assessment, and follow care will also be described [2, 3].

Upon Discharge

Before the LVAD patient has been discharged from the hospital, it is important for the patient to have the first clinic visit already scheduled. Three components to lowering readmission rates are:

1. Early assessment via a telephone call the day after discharge to reassess and reinforce compliance with medications.
2. Review of LVAD emergency management education to EMS agencies.
3. Weekly labs and phone calls to assess the patient's volume status, bleeding risk, anticoagulation dose adjustments, and signs of early decompensation while also evaluating the LVAD equipment to ensure safe operating function [4].

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Table 1 Example from INOVA Fairfax Hospital's CPG

Comprehensive VAD visit schedule																	
Weeks post-implant							Months post-implant										
	3	4	5	6	8	10	3	4	5	6	7	8	9	10	11	12	Thereafter
Office visit	X	X	X	X	X	X	X	X	X	X			X			X	q3 months, monthly if status 3
Routine laboratories																	
PT/INR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	q1 months
LDH							X			X			X			X	q3 months
CBC	X	X	X	X	X	X	X	X	X	X			X			X	q3 months
BMP, Mag	X	X	X	X	X	X	X	X	X	X			X			X	q3 months
LFTs	X	X	X	X	X	X	X	X	X	X			X			X	q3 months
NT-proBNP							X			X						X	Annually
PRA							L			L						L	q6 months or upgrade in status
Iron studies							X										
Drug monitoring																	
Digoxin							X									X	Annually
Other testing																	
ECHO/ECG							X			X			X			X	Annually
Quality of life							X			X						X	q6 months, yearly after 2 years
Frailty testing										X						X	
Right heart cath				X													Listed yearly, other patients PRN
Non-con chest CT							L										PRN
Referral to cardiac rehab							X										

X = all VAD patients, L = listed patients only
For patients who did not receive testing prior to hospital discharge

Alam et al. demonstrated that implementation of the above strategies resulted in no readmissions or deaths within 30 days after discharge in 16 patients implanted with the Heartmate 3 LVAD (Abbott, Pleasanton) [4].

Every center should have clinical practice guidelines (CPG) which help navigate patient care. Having established guidelines for the institution can help with consistent care for the LVAD patient population. An example of a comprehensive outpatient VAD schedule is featured in Table 1.

Clinic Visits

A comprehensive cardiac exam, discussion of heart failure symptoms, and functional status are basic evaluations that should occur at each visit [5]. VAD-specific assessment components include a review of pump parameters and alarms history along with obtaining a mean arterial blood pressure (MAP) and assessing laboratory results and driveline status [5]. Utilizing an electronic medical record (EMR) to trend all the above parameters will facilitate proper and timely patient care.

Regardless of the type of VAD device, all parameters on the pump need to be evaluated during a clinic visit. Assessment of history logs and looking for variations in settings may be early indicators for trouble ahead. If any area of concern is noted, download log files have to be sent to the manufacturer for a deep assessment based on the manufacturer's protocols. Upon sending these files, a review can be performed by the device manufacturer engineers to interpret information beyond what a controller interrogation will show. This can be used for diagnosis of pump or driveline dysfunction, battery clip or cable malfunctions, power consumption trends, and patient practices related to power usage.

A goal mean arterial pressure (MAP) less than or equal to 80 mmHg is the 2013 International Society of Heart and lung Transplantation (ISHLT) MCS Guidelines recommendation [6]. Some centers have the capability of supplying each patient with a blood pressure cuff and Doppler for home monitoring. This will enable patients to monitor their readings at home and call in results to the VAD center. The use of automatic blood pressure cuff vs Doppler assessment should be based on the center-specific guideline.

Driveline assessment is completed by removing the existing dressing and assessing for any signs of infection at the exit site. A mild degree of erythema at the percutaneous exit site is expected with normal healing; however, marked erythema, pain, induration, or purulent drainage indicate exit site infection [7]. See chapter "Infectious Concerns and Prevention for Patients with Ventricular Assist Devices" for a specific review of driveline infection assessment. The dressing should be reapplied in the same clinic visit following the VAD center's driveline exit site care guideline.

Routine Parameters to Be Monitored in Clinic

- Weight
- Mean arterial blood pressure
- International normalized ratio (INR) value and oral anticoagulation
- Symptoms (dyspnea, edemas, nausea, fatigue, dark urine, nosebleeds, and black stool)
- Driveline status and review with caregiver of any changes being noted at home
- VAD values (flow, power, speed, possibly PI value)Deviations from these values should be highlighted in previously defined areas and prompt a response/intervention that is also defined
- Furthermore, tools for recording mental health and QoL questions can be embedded
- Studies from Europe [8] and the USA [9] show that if these requirements are met, there are acceptance and (economic and health) benefits
- 6-Minute walk test to evaluate functional capacity
- Expiration of equipment and integrity checks of all peripheral equipment including backup controller, backup batteries, and battery cables/clips
- Backup battery information for the Heatmate II and Heartmate III primary and backup controllers. Coordinators should routinely be assessing when the battery is reaching expiration and intervening prior to this time

Labwork Monitoring

Monitoring certain labwork can give important information on the efficacy of the VAD therapy; specifically to assess for any infection, bleeding, electrolyte imbalance, hemolysis, kidney, and liver dysfunction. Labwork to assess includes:

- CBC (Complete blood count)—assessing hemoglobin, hematocrit as well as white blood count
- CMP (Complete metabolic panel)—assessing kidney and liver function
- PT/INR (Prothrombin time)—assessing for Coumadin dosing
- LDH (Lactate Dehydrogenase) is the stand measure of hemolysis and thus surveillance for device thrombosis in patients on a VAD [10]
- Urinalysis (if LDH is elevated)—assess for hemoglobinuria

Pump Speed Optimization

Echocardiogram and right heart catheterization (RHC) are two procedures to help ensure the VAD settings are benefitting your patient. The 2013 International Society of Heart and Lung Transplantation (ISHLT) guidelines for MCS recommend an echo every 6 months for the first 2 years after LVAD implant and then annually [6]. In reviewing the echocardiogram, it is important to note the size of the LV (left ventricle) to assess appropriate decompression while avoiding over-decompression, which puts strain on the RV and may result in suction events [5]. It is also helpful to note the position of the septum, as a rightward shift indicated suboptimal LV decompression or fluid overload and leftward shift suggests LV over depression or RV failure [5].

A right heart catheterization is a quick, low-risk procedure that can be completed in the patients with an LVAD using a 5–7-F venous sheath and balloon-tipped catheter without the need to interrupt anticoagulation often without fluoroscopy [11]. This procedure should be strongly considered in patients with persistent HF symptomatology (New York Heart Association III–IV symptoms), <300 m achieved on a 6-minute walk test distance due to dyspnea) and/or high diuretic needs at 3–6 months or more postoperative regardless of echo findings [11].

Telemonitoring

As part of successful VAD therapy, the use and support of patient resources is important in order to reduce the need for hospitalization as much as possible. Telemedical options play an important role in making this possible. Studies show that remote telemonitoring such as frequent phone calls, video telehealth visits, or remote monitoring applications demonstrate the potential for improved follow-up care for VAD patients and may reduce costs at the same time [12]. It is of great importance that acceptance and user-friendliness and safety are taken into account when employing these strategies.

Types of Remote Monitoring

Structured telephone contacts can be used here as a basis. Studies by Schlögelhofer et al., for example, show a significant increase in the 24-month survival—(89% vs 57%) in a control group [13].

The use of smartphone-based applications (assuming the appropriate device availability) has further potential for improved management of VAD patients. The independence from the local support of the "VAD clinic" increases with the possibilities of using corresponding applications to monitor the VAD-relevant functions [14]. There are multiple applications that have been developed by various providers with a wide range of options for adapting to specific needs; advantages for patients and clinicians of VAD patients at all levels can be realized with these apps [15].

The future step in monitoring VAD patients would be the ability to remotely monitor the VAD parameters, which, similar to defibrillators, uses permanent data transmission via tele-monitoring in order to record the VAD functions in real time and without active data entry by the patient. While the potential for this capability is available, it has not been put into clinical practice at the time of publication [16].

Multidisciplinary Team Involvement

A patient with a VAD requires a multidisciplinary team to manage co-morbidities and should be included when appropriate for the outpatient visits. Other than the heart failure cardiologist, cardiac surgeon, and VAD coordinator, below is a list of other providers who may be part of the team:

- Primary Care Physician
- General Cardiologist
- Electrophysiologist
- Infection Disease Specialist
- Nephrologist
- Nutritionist
- Wound Care Specialist
- Palliative Care and Social Work

Leaving the Home and Traveling

The goal for all VAD patients is to resume all their activities of daily living which may include traveling. All patients are issued a backup controller and spare batteries to carry with them at all times [17]. Allowing MCS patients to drive is determined by the VAD center or governing state. If traveling by air, the patient will need a Transportation Security Administration (TSA) or international equivalent agency letter stating the patient must carry all equipment on board the plane to avoid losing by checking baggage. This letter will also inform the security agency that patients

cannot pass through the normal metal detectors and must use other means for a security assessment.

Once the VAD team is aware of the location the patient will be traveling, it is a courtesy to call the closest VAD center to let the center know there will be a patient traveling in their area. Some centers want to have the patient's insurance information along with last clinic visit assessment faxed or scanned to their center in case the patient needs help.

Conclusion

In conclusion, outpatient management of this patient population requires the dedication of many team members. It is important for your patient to know a schedule for follow-up visits and what is entailed in taking care of themselves in order for this journey to be a success.

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Regulatory Agencies Impacting Mechanical Circulatory Support Programs

Peggy Blood, Roxanne Siemeck, and Linda Staley

Introduction

The use of ventricular assist devices, whether as bridge to transplantation or as destination therapy, carries a high burden of risk for harm and is an expensive service to provide. Thus, national agencies became interested in understanding the utility of the therapy and to determine reimbursement criteria for services provided. VAD programs worldwide have regulatory obligations that must be followed to establish and maintain a safe and financially sustainable service to VAD patients. Oversight from national agencies responsible for payment of services should be anticipated in each country. Regulations regarding the development, manufacturing, and distribution of the VAD device is required for the safety of the public. The intent of this chapter is to introduce several key regulations for consideration in provision of care for the VAD patient.

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Industry and Clinical Investigation Oversight

There has been a rapid development of mechanical circulatory support devices in the last two to three decades both in the United States of America (US) and internationally [1]. Each country has a designated agency to provide oversight of medical equipment and clinical trial for both feasibility and efficacy. It is important to have these regulatory agencies to provide guidance and regulations for the safe manufacturing and deployment of medical devices and the development of improvements in technology. Clinical trials are critical to ensure safety for the patient while developing newer mechanical devices to be smaller, more biocompatible and more durable to function normally for longer periods of support [2]. There have been significant enhancements to the peripheral pieces of equipment that support MCS devices over the same time period. The clinical trials to test new devices and equipment are typically performed in the United States and Internationally.

The regulatory agencies ensure that the device manufacturers follow established guidelines and requirements are place to ensure the safety of the patients. These agencies have strict inclusion and exclusion criteria to implant a mechanical circulatory support device on the target population it is intending to investigate. The goal of the regulatory agencies is to assure safety and efficacy while allowing access to innovative therapies [3]. This balance is difficult to achieve because of the complexities of the new devices, with high adverse event profiles, and the severity of illness of the end-stage heart failure targeted population [4]. Being able to balance the regulations and innovations so that the safest devices are placed into the community while allowing the right patients to benefit from the implantation of mechanical devices is crucial. Regulatory bodies have the onus of evaluating the risk each device imparts with the benefit it hopes to achieve. The expectation is that safety and effectiveness is vetted during the clinical trials before they are available to the end-stage heart failure patients outside of the clinical trials [5].

The concept of mechanical circulatory assistance came after cardiac operations which date back to the 1960s with the development of mechanical circulatory support devices such as intra-aortic balloon pumps (IABP), ventricular assist devices (VADs), and total artificial hearts (TAH) [6, 7]. Individual academic medical center review groups that evolved into the institutional review boards regulated the development of initial clinical evaluations of devices. The Food and Drug Administration (FDA) in the United States entered into the arena in 1976 with the advent of the FDA section for device regulation based on passage of the 1976 Medical Device Amendments. The FDA is committed to monitoring total product life cycle of medical devices including early development preclinical development, clinical study, marketing approval, post-approval evaluation, and the development of subsequent medical device generations [8].

A VAD program that is interested in performing research should investigate their institutional research requirements by contacting their Investigational Review Board (IRB). This department within organizations functions as an independent ethics committee composed of scientists and non-scientists to review

potential research studies and serve as the resource to monitor and protect the rights of patients who are enrolled in a research study. The field of ventricular assist devices continues to grow, and it is not unlikely that an industry partner could sponsor a new device trial. Having the infrastructure in place, prior to a sponsor reaching out, would be ideal. A program interested in participating in research would benefit from a dedicated research coordinator who closely monitors the study participants and completes required study follow-up at proper intervals. VAD programs may choose instead to utilize their VAD coordinator/Clinician to function in the research coordinator role. Depending on program size, this may be sufficient, but as the VAD patient population grows, it would be beneficial to have a dedicated research coordinator, who is not distracted by clinical demands, to improve the integrity and timeliness of all research submissions. The organization should identify who will act as the Principle Investigator (PI) for research studies. The PI has the responsibility of oversight and management to ensure study requirements are carried out in ethical manner. The PI is usually a Cardiovascular Surgeon or Advanced Heart Failure Cardiologist, but may also be a VAD coordinator or clinician. The IRB will monitor the research team to ensure they disclose any conflict of interest and are properly trained prior to initiating research. An IRB may choose to utilize an agency partner such as the Collaborative Institutional Training Initiative (CITI) to ensure that research education occurs in a clear and concise manner. The use of an organization, such as CITI for research education, assures that systematic and uniform training occurs within the organization. The IRB maintains close contact with the principle investigator and research coordinator until the study concludes, and all necessary documentation is provided to the study sponsor [9].

Registry Participation

Though not a regulatory agency per se, MCS registries are mentioned here due to the requirement of participation in a national registry as a standard of certification in the United States and for reimbursement in Japan. At this time, there is only one national registry in North America. INTERMACS, now known as STS/INTERMACS, is a North American registry and was established in 2005 for patients who are receiving FDA-approved mechanical circulatory support device (MCSD) therapy to treat advanced heart failure. Intermacs became part of the Society of Thoracic Surgeons National databases January 1, 2018. The initial INTERMACS registry was established as a joint effort of the National Heart, Lung, and Blood Institute (NHLBI); the Food and Drug Administration (FDA); the Centers for Medicare and Medicaid Services (CMS); clinicians, scientists, and industry representatives in conjunction with Dr. James K. Kirklin and the University of Alabama at Birmingham [7]. The intent of the registry was to refine patient selection and improve outcomes, identify predictors of good outcomes, develop consensus best practices, assist industry with design and improvements in device technology and guide clinical testing and approval of new devices [10]. The Pediatric Interagency

Registry for Mechanical Circulatory Support (PediMACS) designed for patients less than 18 years of age mirrors INTERMACS and was launched in September 2012 [11]. The STS/INTERMACS and STS/PediMACS collect clinical data relevant to MCS devices from Pre-MCS implant through follow-up evaluations and any rehospitalizations or adverse events [12]. At designated intervals, the time of adverse events or re-hospitalization and end of VAD life, multiple variables are collected and entered into this web-based secure database. INTERMACS is the first MCS registry to standardize definitions of adverse events and create a subclassification of clinical profiles to better describe the time course and acuity of decompensation at the time of implantation of the VAD [7, 10, 13]. The INTERMACS Profiles have become standard nomenclature for describing advanced heart failure symptoms at the time of VAD implantation. Also unique to this registry is the adjudication process and periodic audits for data validation. This longitudinal registry has become the benchmark for durable device performance measures and process improvement metrics in many centers.

To participate in the STS/INTERMACS or STS/PediMACS registry, the VAD center must apply and remit payment for participation. In turn, INTERMACS provides quarterly standardized reports and provides the VAD Center access to their data in real time. Both registries have acquired a waiver for patient consent to participate, however some organization's IRB do not honor this waiver. It is important to confirm the waiver status with your organization's leadership.

There are parallel registries throughout the world. The European Registry for Patient with Mechanical Circulatory Support (EUROMAX) is a voluntary registry supported by the European Association for Cardio-thoracic Surgery (EACTS). Hospitals located in various nations across Europe participate including the United Kingdom, Switzerland, Germany, Denmark, France, Belgium, Czech Republic, Netherlands, Spain, and Italy. Data has been entered into this secure database since 2011 [14].

The Japanese registry for Mechanically Assisted Circulatory Support (J-MACS) was established in 2009. Participation in this registry is required for hospitals to receive reimbursement for care of VAD patients as well as for manufacturers to receive approval. The J-MACs was initially funded by the Pharmaceuticals and Medical Devices Agency (PMDA) of Japan and comprised of seven different academic societies, participating hospitals, and VAD device manufacturers. Since 2018, the council for clinical use of VAD-related societies has run the registry. The registry has a separate oversight process and a designated committee adjudicates adverse events [15]. All centers in the United Kingdom are required to submit clinical data to the VAD Database hosted by the National Health Services Blood and Transplant agency. This database is commonly referred to as the UK Registry [16].

These registries have now partnered with the International Society for Heart and Lung Transplantation (ISHLT) Mechanically Assisted Circulatory Support (IMACS) (Kinugawa second report 2020). IMACS, which opened enrollment in January 2013, is a global registry comprised of all countries and hospitals that choose to voluntarily participate [17].

Centers for Medicare and Medicaid Services

In October 2003, the Centers for Medicare and Medicaid (CMS) approved reimbursement coverage for use of FDA-approved ventricular assist devices for destination therapy. At this time, VAD center criteria consisted of an attestation from the VAD center confirming adequate staff, clinically trained surgeons and processes in place to fully inform the patient of the risks and benefits of VAD therapy. Over the years, these criteria have expanded to include specific criteria for appropriate candidate selection. In the United States, CMS determines "medical coverage is limited to items and services that are reasonable and necessary for the diagnosis and treatment of an illness or injury" [18]. National coverage determinations (NCDs) are made through an evidence-based process with opportunities for public participation. The most current NCD version for ventricular assist devices (VAD) has an effective date of 10/30/2013. The National Covered Indications were revised in October 2020 which removed the current therapeutic intent-to-treat criteria of bridge-to transplant (BTT) and destination therapy (DT). This removed the BTT requirements that a patient is active on the waitlist maintained by the Organ Procurement and Transplantation Network (OPTN). It also removed that the implanting center needed written permission from the Medicare-approved transplant center prior to implantation of the VAD (retrieved 03/29/2021 from https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=298&type=Closed&bc=AIgAAAAACAAA).

The patient selection for VADs were also updated that had previously been applied to only the DT patient population now extends to all LVAD procedures for short-term (e.g., bridge-to-recovery and bridge-to-transplant) or the long-term (e.g., destination therapy). The patient selection criteria are covered for patients who have chronic end-stage heart failure and meet the following conditions:

- Have New York Heart Association (NYHA) Class IV heart failure; **and**
- Are inotrope dependent
  OR
- Have a cardiac index (CI) <2.2 L/min/m^2 while not on inotropes and also meet one of the following:
  - Have been on optimal medical therapy for at least 45 out of the last 60 days and are failing to respond
    OR
  - Have advanced heart failure for at least 14 days and are dependent on an intra-aortic balloon pump or similar temporary mechanical circulatory support device
- Have a left ventricular ejection fraction (LVEF) <25% [18]

Mechanical Support has evolved over the years from the short-term use to bridge a patient to recovery or to heart transplantation (BTT). Later came the mechanical support devices that remained in patients for the rest of their life to manage their end-stage heart failure symptoms and to improve the patient's quality of life (QOL)

[5]. This therapy was termed destination therapy (DT). The indications for mechanical support have also evolved over the years. Today the indication to receive the mechanical support devices are no longer viewed as bridge to transplantation or destination therapy but rather short-term or long-term mechanical support. CMS adopted this vernacular in December 2020, thus removing the requirement for distinguishing DT versus BTT at the time of implantation. Patients over the years have moved fluently from being actively listed for heart transplantation to becoming a destination therapy patient and vice versa. There are patients that have been listed for years with a mechanical support device and never received a transplant, and there are destination therapy patients that overcome their barriers to transplant candidacy and become actively listed for transplant.

The CMS NCD also states that the facility must be credentialed by a credentialing organization which is approved by the centers for Medicare and Medicaid services. Those credentialing organizations are the Joint Commission or Det Norske Veritas (DNV).

Program Certification

VAD program certification has its roots in hospital accreditation though hospitals have not always been required to meet standards in delivering care to patients. Ernest Codman, MD first proposed the idea of "end result system" of hospital standardization in 1910, and the American College of Surgeons was then founded and made the end result system an objective for this newly formed society. In 1917–1918, the American College of Surgeons developed a one-page document titled "Minimum Standard for Hospitals" and was expanded to 18 pages in length in 1926. The Joint Commission on Accreditation of Hospitals, founded in 1951, was formed by the joint efforts of the American College of Physicians, the American Hospital Association, the American Medical Association, and the Canadian Medical Association whose purpose was to provide voluntary accreditation. The Social Security Amendments of 1965 passed with a provision that hospitals accredited by the then called JCAH was "deemed" to be in compliance with conditions for participation (CoP) for hospitals, and thus able to participate in the Medicare and Medicaid programs. Over the next 25 years, JCAH expanded its accreditation to other healthcare organization and changed its name to Joint Commission on Accreditation for Healthcare Organizations (JCAHO) to reflect this expansion. Subsequently, in 2007, JCAHO rebranded itself as The Joint Commission (TJC). TJC was the first agency to certify population-based programs with VAD programs added in 2007 [19].

Becoming a sustainable VAD center in the United States includes the need to obtain certification by an accreditation organization, according to CMS guidelines. The center can choose to obtain certification from The Joint Commission (TJC) or DNV, which stands for Det Norske Veritas. CMS approval is required in order for the organization to receive CMS reimbursement for VAD implant operations and associated care along the continuum, thus is considered "deemed."

DNV was founded in Oslo, Norway, in 1864. It began as a regulatory body for the shipping industry and expanded to the healthcare industry. Today, DNV is a global corporation leading risk management and quality assurance across multiple industries. DNV has been approved by CMS to credential programs implanting VADs since 2015. The DNV reviews a program for compliance with a Quality Management system that tracks performance improvement indicators and most importantly takes corrective action when measures are not at goal. DNV evaluates program management, staffing models, and an ability to deliver safe VAD care, with an emphasis on alignment to program-specific VAD education directives. DNV surveyors investigate the program's dedication to infection prevention and control as a part of the overall ability to care for VAD patients safely and effectively. DNV certification includes an overview of the multidisciplinary approach to care from initial evaluation through discharge of newly implanted patients. This includes utilization of support staff such as social work, financial coordinators, therapist, palliative and home health care. New or existing programs looking to have DNV certification can expect some similarities with their surveys. One such similarity is that all surveys, whether for new or existing programs, include two surveyors, one that is a NIAHO and ISO 9001 standards expert (Lead Surveyor) and the second surveyor is a clinician with experience specific to the VAD patient population and program delivery (Technical Expert). All surveys with DNV are announced and scheduled in collaboration with the program leadership. An agenda, along with required and requested documents, is provided prior to the survey, to allow time for preparation. DNV allows an open line of communication between the program leadership and lead surveyor via the DNV Healthcare Client Drop Box at any time prior to the survey [20].

A new VAD program wishing to obtain certification from DNV will find their process streamlined into a pathway that can be initiated prior to their first implant. After initial survey, if the infrastructure is deemed acceptable, DNV submits verification of the findings to CMS deeming the program suitable for certification. DNV would return 6 months after the initial survey to evaluate the remaining aspects of the program, including medical record review of VAD recipients as well as multidisciplinary team training, tracer activity, and quality measures. A new program that met the requirements at 6-month review would again be surveyed 6 months later, and annually thereafter. DNV credentials programs for 3 years [20]. The initial surveys are 2 days, with annual surveys of 1 day. Outside of a pandemic, these are all on site surveys. There are no necessary data submissions outside of the survey, with the exception of a response to findings that occur during the survey.

DNV findings can include the following Immediate Jeopardy (IJ), Nonconformity 1 Condition Level (CL), Nonconformity 1 (NC1), and Nonconformity 2 (NC2) [20]. Immediate Jeopardy is an active process, found by the survey team in which there may be serious patient, staff, or visitor harm. This finding must be mitigated during survey activities, and the survey team must stay on site until mitigated. Once the process is mitigated sufficiently, it is reduced to a CL finding. If it cannot be mitigated, it can result in inactivation of a program. An example of this would be, if a program received a field corrective action (FCA) from industry partner,

related to a particular device component that is deemed unsafe, or in need of replacement, and there is no proof by the program that chain of command was followed and/or device components were quarantined from supply. CL findings indicate that there is a process that could result in serious patient, staff, or visitor harm. NC1 finding is a systemic issue, where there may not be a process in place, or if there is, many of the elements are not occurring as designed. An NC2 finding is when the process is in place, but it is not occurring every time, or there are a few missing elements. DNV is unique, in that they report "Opportunity for Improvement" or OFI's and "Noteworthy efforts." An OFI is a finding that identifies an issue with a process that could become a nonconformity if left unattended or unimproved. A noteworthy effort is a process identified by surveyors as something the program does exceptionally well and could be considered a model to other centers looking to improve their management of said process. If a nonconformity is found, the program must complete a survey report and corrective action plan (CAP). In this form, they will need to identify the root cause of the nonconformity, the CAP, staff education or training plan, the person responsible for the CAP and the date it will be implemented and completed. The program must also identify their method of follow-up (i.e., audit, chart review), how often they will follow-up, what constitutes a measure of success, and how to achieve sustained compliance with the CAP. Further details can be found here: https://brandcentral.dnvgl.com/original/gallery/10651/files/original/c9752e54dd51424e8f8b58208ef082e7.pdf.

Another option for VAD program certification in the United States is the Joint Commission Disease-Specific Certification (DSC), VAD. In 2007, CMS announced that Medicare-approved hospitals performing VAD surgery as long-term therapy (DT) will be required to be certified by TJC by March 27, 2009 [16]. (Six years later, DNV was also approved as a certifying agency.) A panel of representatives of well-known healthcare associations, VAD clinical experts comprised of surgeons, cardiologists, and VAD coordinators convened to provide expert content to the first standards published by TJC in 2007. Prior to publication, these standards were approved by CMS. Not until 2013 were the standards first revised, then again in 2021 to be effective from January 1, 2022. Disease-specific certification is awarded after an on-site review demonstrates compliance within these three categories: (1) compliance with consensus-based national standards, (2) effective integration of evidence-based clinical practice guidelines, and (3) an organized approach to performance measures and performance improvement including data collection and analysis. Certification is awarded for a 2-year period [21].

A new program seeking certification from TJC should first contact the TJC to obtain access to the standards and identify the account executive designated for your organization for clarification and inquiries. A 90-day free access to the standards can be obtained here: https://www.jointcommission.org/accreditation-and-certification/certification/certifications-by-setting/hospital-certifications/disease-specific-care-certification/apply-now-for-disease-specific-care-certification/ eligibility requirements include having implanted at least one durable VAD into one patient in order to demonstrate the application of your programs' established

processes. The implanting surgeon must have implanted at least 10 durable VADs in the last 36 months with activity within the past year [21, 22]. This may be accomplished during their surgical fellowship, at another VAD center or at your own center. Additionally, the program will need to have a minimum of 4 months of performance measure data at the time of the onsite review.

The organization will receive a 30 business day notice of the initial review which will be conducted by one DSC VAD reviewer over 1½ days. Prior to this onsite review, the organization will be notified of the documents to have available for the reviewer. In general, the request will include clinical practice guidelines and policies, lists of active patients, minutes of VAD team meetings, and performance improvement data and analysis. The VAD Center should be prepared to provide a brief presentation of their VAD program and a comprehensive presentation of their performance improvement initiatives. The reviewer will utilize the tracer methodology: following the experience of care for the patients through the VAD program's continuum of care and Individual Tracer Activity designed to "trace" the experiences of the specific patient will be identified. This will allow the reviewer to assess the application of the VAD program's processes and validate compliance with the standards through interviews and observations. At the close of the on-site review, the organization will have a verbal report of the reviewer's observations and access to the on-site review via the Joint Commission Connect, a secure internet site specific for communications between TJC and the organization [21].

The VAD program will be assessed for compliance with standards defined in six chapters. The Certification Participation Requirements (CPR) chapter differs from eligibility requirements. This chapter surrounds standards and EPs that apply to the certification process. Program Management (DSPR) defines the infrastructure that supports the patient and practitioner activities, leadership engagement and support for the program, and scope of services provided. Delivering or Facilitating Clinical Care (DSDF) focuses on the delivering, facilitating, or improving high-quality clinical care and ensuring practitioners are appropriately licensed and prepared to care for this specific population. Supporting Self-management (DSSE) addresses the program's ability to engage the patent and family in participating in their care, preparing them to care for themselves both in the hospital and in their home community. Clinical Information Management (DSCT) is designed to assess the communication processes to ensure all healthcare providers for the patient across the continuum of care throughout their VAD care. The final chapter Performance Measurement (DSPM) assesses the VAD program's process improvement initiatives are clearly defined, measured, analyzed, and utilized to improve care [21].

Deficiencies will be communicated during the review to the VAD team member present at the time of the observation. An Immediate Threat to Life (ITL) is the most critical and is defined as any condition that the reviewer believes poses a threat to public or patient health or safety. The reviewer will immediately notify the Joint Commission Central Office and the review could be stopped and certification denied. The organization is expected to take immediate corrective action. After this

corrective action is validated, a follow-up review will assess ongoing implementation of this corrective action. An ITL could trigger a for-cause accreditation survey if the organization is accredited by TJC.

If an element of performance (EP) is considered to be out of compliance, then it will be cited as a Requirement for Improvement (RFI). Each RFI is placed on the Survey Analysis for Evaluating Risk (Safer®) Matrix according to its likelihood to cause harm to patients, staff, or visitors (low, medium, high) and the scope or prevalence of the finding (limited, pattern, widespread). In response to these findings, the VAD program will address all RFIs with an Evidence of Standards Compliance (ESC) submission within 60 days from the review. As the finding is assessed as higher risk or more widespread, the greater engagement from the senior leadership will be required in the action plan. A final determination of certification will follow submission of an acceptable ESC report [21].

Outside of a pandemic, all bi-annual reviews are conducted on-site, and an intracycle conference call at 1-year post certification is conducted. The intracycle conference call is conducted to review updated clinical practice guidelines, analysis of data on the four performance measures, and an attestation of continuing compliance with TJC standards. The intracycle conference call is scheduled at mutually agreeable time and lasts approximately 1 h. The VAD Center will receive a 7-day business notice of the planned biennial on-site recertification review.

Non-U.S. Programs

Globally, reimbursement is variable and accreditation even more so. The Asian Pacific (APAC) region generally refers to East Asia, South Asia, Southeast Asia, and Oceania. The APAC countries with local accreditation requirements for their LVAD programs are Australia, Singapore, Japan, Korea, Taiwan. Other countries that have LVAD programs but do not have official government accreditation are India, Malaysia, Brunei, Thailand, Vietnam, Philippines. European VAD programs are typically funded through their respective national health plan with defined terms for eligibility. Lack of funding can severely limit utilization of MCS device therapy.

Summary

VAD therapy is effective for supporting patients short- or long-term periods. For VAD centers to provide this niche service, the leaders must be informed of the requirements. Before beginning a program, the leaders of the organization or program should investigate and identify the specific requirements for the region where the program resides. These resources can typically be found via an internet search or through discussions with the respective regulatory agency. Remaining continuously compliant with regulatory conditions of participation provides for uninterrupted care for the patients with advanced heart failure needing MCS support or already supported with a VAD.

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Reimbursement in Ventricular Assist Device Implant and Care

Erin Davis and Michelle McCardell

Defining Reimbursement and Terminology

VAD reimbursement is comprised of coverage, coding, and payment. Each aspect interacts with the other and can be influenced to yield a monetary positive result returned to the program. The FDA, under the guidance of Health and Human Services (HHS), reviews and approves all medical devices and medications used in the United States. Each insurance provider, government or private, must then decide which services, procedures, devices, and supplies to financially reimburse. Coverage is the first aspect of reimbursement, communicated to providers and hospitals in the form of medical policies or coverage determinations, and acts as a guidance to the appropriate treatment of the patients. Hospitals and providers then verify the coverage for each patient prior to delivering services and billing the patient's insurance. If the patient's insurance company does not cover VAD implantation and subsequent related services in their medical policies, there are often other pathways to obtain coverage such as Compassionate Use or Emergency Use.

Coding is the second driver of reimbursement. It is a pre-defined language describing services rendered based on documentation in the patient's medical record and submitted to the insurance company in the form of claims. Three types of coding commonly used when working with VAD reimbursement are International Classification of Diseases, Tenth Revision (ICD-10), Current Procedural Terminology (CPT), and Healthcare Common Procedure Coding System (HCPCS).

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1. ICD-10: The World Health Organization (WHO) developed a code set called International Classification of Diseases, 10th Edition, known as ICD-10. This code set provides consistent and reliable communication to describe diagnoses and procedures for inpatient billing purposes. ICD-10 CM relates to diagnostic coding, and ICD-10 Procedural Coding System (PCS) relates to procedural coding.
   (a) Common ICD-10-PCS code for durable LVAD services:
      - 02HA0QZ—Insertion of implantable heart assist system into heart, open approach.
2. CPT: The American Medical Association (AMA) developed Current Procedural Terminology (CPT) codes for provider and other clinician billing professional services. Most payers use and recognize CPT coding to identify which provided services they will cover.
   (a) Common CPT codes for durable LVAD services:
      - Implant: 33979—Insertion of ventricular assist device, implantable, intracorporeal, single ventricle.
      - Removal: 33980—Removal of ventricular assist device, implantable, intracorporeal, single ventricle.
      - Interrogation: 93750—Interrogation of ventricular assist device (VAD), in person, with physician analysis of device parameters (e.g., drivelines, alarms, power surges), review of device function (e.g., flow and volume status, septum status, recovery), with programming, if performed, and report.
3. HCPCS: The Healthcare Common Procedural Coding System (HCPCS, often pronounced "hics-pics") is a uniform coding system created by CMS to report professional services, procedures, and supplies for payment.
   (a) Common HCPCS codes for durable LVAD external components:
      - Q0477–Q0506: batteries, controllers, chargers, cables, adapters, modules, monitors, bags, belts, vests, clips.
      - Q0508: miscellaneous code mainly used to bill for driveline management systems and other equipment not already assigned a code.
      - Q0509: to report any VAD equipment provided to a Medicare patient who was not a Medicare patient at time of LVAD implant.

Payment is the third factor in reimbursement and shows the value assigned to a service or procedure. Depending on the insurance's contract with a hospital or provider, payment for VAD services is most commonly provided using either a Diagnosis Related Group (DRG) system, a type of bundled payment, or a fee-for-service payment in which services are assigned a specific amount of money and not bundled together. Other payment types such as capitation, a fixed amount paid in advance, is less common for VAD services. The most common DRG system is the Medicare Severity Diagnosis Related Group (MS-DRG). This system classifies inpatient medical cases into one capped payment amount based on the patient's condition and level of services provided as described by the ICD-10 CM and PCS codes. This payment amount is set each year by Medicare based on claims data

obtained from hospitals across the United States. Many private or commercial insurance companies also follow a DRG-based payment system of one capped payment for services. There are over 740 DRGs recognized by CMS that patients are categorized into based on their similar hospital resource use, diagnoses, and procedures. An outlier payment can be added to the capped amount if certain conditions and documentation exist during the specific patient's hospitalization to justify a higher level of payment over the base DRG amount. For outpatient procedures or supplies, fee-for-service payment is most common where payers have fee schedule with predetermined amounts of payment assigned to specific codes.

Demystifying Insurance Payers: Government vs. Private

In the United States, there are four main government insurance payers: Medicare, Medicaid, Indian Health Services (IHS), and the military system known as Veteran's Affairs (VA).

Medicare is the federal health insurance program in the United States and is administered by CMS. Medicare provides health insurance for Americans that have paid into Social Security and meet one of the Medicare entitlement requirements: age 65 and older, people that are determined to be disabled under the Social Security Act (SSA), and people with End-Stage Renal Disease (permanent kidney failure requiring dialysis or a kidney transplant).

- Part A (Hospital Insurance) covers inpatient hospital stays, care in a skilled nursing facility, hospice care, and some home health care.
- Part B (Medical Insurance) covers certain doctors' services, outpatient care, medical supplies, preventive services, and most professionally administered prescription drugs.
- Part C plans are often called Medicare Advantage plans or Medicare Replacement plans. Medicare Advantage is an all-in-one alternative to traditional Medicare. These "bundled" plans include Part A, Part B, and usually Part D, and are delivered through commercial payers. Most plans offer extra benefits that traditional Medicare does not cover—like vision, hearing, dental, and more. Medicare Advantage Plans have yearly contracts with Medicare and must follow Medicare's coverage rules. The plan must notify beneficiaries about any changes before the start of the next enrollment year.
- Part D (Prescription Drug Coverage) covers the cost of prescription drugs (including many recommended shots or vaccines).

VAD therapy has been covered by Medicare through a National Coverage Determination (NCD) since 2002 and was most recently revised in 2020. NCD 20.9.1 describes the indications and limitations for patients with Medicare to receive left VAD implant. If the Medicare patient needs a right ventricular assist device (RVAD), biventricular assist devices (biVAD), is less than 18 years old, has acute heart failure without chronic heart failure, or has complex congenital heart disease

without meeting NCD criteria, coverage for these cases will be made by the local Medicare Administrative Contractor (MAC) who determines regional medical policy or local coverage determinations (LCDs). The current MACs can be found at https://www.cms.gov/Medicare/Medicare-Contracting/Medicare-Administrative-Contractors/Who-are-the-MACs#MapsandLists.

Medicaid provides health coverage to millions of Americans, including eligible low-income adults, children, pregnant women, elderly adults, and people with disabilities. Medicaid is administered by each state, according to federal requirements. The program is funded jointly by states and the federal government. Most state Medicaid covers VAD therapy, but there are a handful of state Medicaid that have strict criteria or rules excluding VAD therapy coverage. Some state Medicaid can be managed plans or Medicaid plans provided through commercial payers. Traditional Medicaid is usually the lowest paying insurance provider.

Military health coverage in the United States is offered to military service members, reservists, guardsman, their dependents, and some retirees, through TriCare, TriWest, or the Veteran's Administration. TriCare is the main insurance option for military personnel and family, whereas TriWest covers Community Care network, and service-connected conditions are covered directly by the VA benefits. The military health coverage usually follows Medicare coverage and benefits including VAD therapy. However, depending on the type of military coverage, VAD candidates sometimes have to be referred to specific hospitals to receive treatment or be eligible and utilize the community care network through the Mission Act.

Indian Health Services (IHS) is the healthcare system for members of federally recognized Native American Tribes and Alaska Native people in the United States. VAD therapy for patients with IHS is reviewed on a case-by-case basis.

Private or commercial health insurance is available for a cost to citizens of the United States through private, for-profit companies. The majority of these plans are provided by an employer or other organization that the policyholder has an affiliation. Private health insurance can be purchased on a group basis or by individual consumers. The other main opportunity for individuals or families to obtain private health insurance is through the Affordable Care Act (ACA). Some people elect to purchase an individual plan through health insurance companies or insurers. Common examples include Aetna, Anthem, Blue Cross Blue Shield, Cigna, Humana, United Healthcare, etc. The majority of private and commercial insurance plans cover VAD therapy and will have medical policies in place to define their coverage benefits and criteria patients must meet to be eligible.

Prior Authorizations and Medical Necessity

A prior authorization or preauthorization is a process used by health insurance companies that determines if a medical treatment is deemed medically appropriate to be performed. Despite an insurance payer covering VAD therapy as in their medical policies, it does not mean that patients will be able to automatically receive VAD implant. Most payers, other than traditional Medicare, require prior authorization

before services are rendered. Prior authorization for VAD implant involves submitting specific clinical data, progress notes, and written requests demonstrating the patient meets the payer's policies so the procedure can be financially covered by the insurance. Most insurances involve case management, or a gatekeeper, for the prior authorization process to approve or deny the request for services. Traditional Medicare and some Medicaid do not require a prior authorization and do not have mechanisms to request review for special cases that do not meet the NCD or the Medicaid VAD policy. At times, medical necessity for VAD implant is more urgent and there is no time for a prior authorization process to take place.

Medical necessity is the rationale for a procedure or service based on the patient's condition, diagnosis, and acceptable standard of care for that diagnosis. The best way to demonstrate medical necessity is to document thoroughly in the medical record using evidence-based medical practice and national standards of care, such as peer reviewed journals and studies. This documentation is required before the prior authorization can be obtained and especially when developing an appeal of a denial of coverage from an insurance payer.

Patient Impact

There are often times in which payers and providers do not agree on a treatment plan or meet criteria for implant. Prior authorization and medical necessity determinations can be extremely stressful for a patient in these instances. Ultimately, the patient or patient guarantor is financially responsible for any billed service that the health insurance plan does not cover. Therefore, the outcome of this prior authorization falls on the responsibility of the patient. Whenever possible, the patient should contact their health insurance plan and make certain that the requested treatment is prior authorized before the treatment begins. If the requested service is denied, the patient should contact their provider to see what steps can be taken to appeal the denial from their health insurance.

Financial coordinators in a VAD program have a very important role to review the potential costs to the patient when undergoing VAD therapy. They can confirm if a patient will be in-network or out-of-network with the hospital and with the physicians. Patients will often have a deductible amount of money they must pay before the insurance covers the hospital or physician bills. Financial coordinators should also review the patient's copayments, set rates paid for visits or prescriptions, and coinsurance, a percentage of the costs the patient will owe after meeting their deductible, before a patient receives VAD therapy.

Program Impact

Failure to obtain prior authorization, when required, for VAD implant and services may result in a significant loss of revenue for a very high-cost service. On average, durable VAD systems can range in cost anywhere from $90,000 to $140,000. This

amount does not include the costs for the hospitalization, operation, or any physician fees. Programs should have processes in place with designated financial coordinators or program management personnel that know the specific circumstances for obtaining VAD therapy coverage. Often VAD services are not included in the normal hospital authorization for services. Coverage may fall under transplant-related services within the payers' policies or other special considerations. Successful programs build in safety nets for ensuring financial authorization is in place prior to implanting VADs. These safeguards may include designated financial coordinators, electronic medical record work queues, billing and coding experts who have been educated on VAD therapy, and routine financial review of coding, billing, and payment.

Coding

As briefly described above, coding is language that identifies the types of patients and services delivered so that payment can be assigned appropriately. The VAD should be added to the inpatient bill under Revenue Code 278 as it is an implantable device. At the time of implant, all external equipment should be given to the patient to support them for at least 1 year post implant. All external equipment associated with the VAD such as controllers, batteries, cables, monitors, power supplies, chargers, bags, holsters, etc. should be added to the inpatient bill under revenue code 274 as they are considered to be prosthetic/orthotic devices and not durable medical equipment (DME). This means that all VAD equipment will fall under the patient's major medical benefits and not DME benefit categories which often have co-insurance or payment caps. All VAD supplies are paid under the MS-DRG payment for Medicare patients or under the patient's private/commercial insurance's major medical benefit for non-Medicare patients. As with all medical devices, the VAD program should work within their hospital's policies to determine the appropriate charge rates for the VAD device and external equipment to appropriately cover the costs and expected payments.

Professional coders, through a thorough review of the medical record documentation, complete coding for VAD implant. They look for comorbidities and complications (CCs) and major comorbidities and complications (MCC) to determine which DRG the hospitalization will map to. When a patient has a comorbid condition or complication in addition to and above their admitting diagnosis, they generally require more hospital resources, and therefore additional payment is warranted. In VAD therapy it is extremely important to capture any and all MCCs. The difference in payment for a VAD implant without MCCs (MS-DRG 002) and a VAD implant with MCCs (MS-DRG 001) can be as much as $100,000. There are over 3000 MCC codes but some of the common ones for VAD therapy include cardiogenic shock, hypovolemic shock, types of sepsis, acute myocardial infarction, ventricular fibrillation, acute heart failure, stroke, influenzas, pneumonias, respiratory failure, and acute kidney failure. It is important to note that the MCC must be secondary to the initial diagnosis and cannot be the same as the admitting diagnosis in order to be captured as an MCC.

It is important for VAD programs who also have heart transplant programs to follow their coding and billing closely, especially when implanting a durable VAD for bridge to transplant (BTT). Medicare, and many payers, will only reimburse the hospital one MS-DRG payment for the entire inpatient stay. This means that in order to receive one payment for the VAD implant and one payment for the heart transplant, the patient must be discharged between VAD implant and the transplant and not have them performed on the same admission. Also, note that VAD implantation does not have a global period. This means that providers can bill for all additional services, such as VAD interrogation (CPT 93750) starting on post-operative day one through the entire implant stay and after discharge. Other cardiac surgeries, including heart transplantation, usually have global periods such as 90 days where the surgeon cannot bill any additional charges in addition to the surgery during this time.

Outpatient Supplies

Durable VAD implant is one of the highest paid surgeries and is reimbursed on the inpatient side similar to heart transplantation. However, unlike transplant, these LVAD patients require a large amount of external equipment to control and support their device's function. As mentioned above, this external equipment is considered prosthetic and orthotic devices, and not DME. After initial implant and during all outpatient follow-up visits, one of the largest reimbursement dilemmas revolves around the durable LVAD equipment and supplies. Some centers choose to develop equipment monitoring and replacement plans within their own program to track and replace patient VAD supplies as a source of revenue for their program. Other centers choose to relinquish the responsibility of replacing and billing for these outpatient supplies to VAD-specific DME providers. The nomenclature of DME provider overseeing the LVAD outpatient supplies even though these supplies are not considered DME can be confusing.

Table 1 is an excerpt of a Durable Medical Equipment, Prosthetics, Orthotics, and Supplies (DMEPOS) fee schedule from CMS as of 2022. Each insurance payer has a similar fee schedule for these HCPCS codes. It is important to know if the payer will cover these codes prior to implanting the device. These fee schedules are updated on a regular basis, usually quarterly, and can be accessed for each U.S. State at https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/DMEPOSFeeSched/DMEPOS-Fee-Schedule.

If a VAD program plans to manage their VAD patients' equipment, it is essential that the program is knowledgeable about each insurance payer's guidelines for replacing expensive VAD items.

- The hospital or clinic replacing these supplies does not have to hold a DME license since these items are billed to the patient's prosthetic benefit category. For Medicare patients, the hospital or clinic should bill Medicare Part B contractor (MAC) under revenue code 274.
- Durable VAD equipment should only be replaced when medically necessary for the safety of the patient, using the device manufacturer's lifetime use recommendations as a guide.

Table 1 Device-specific codes and average reimbursement

HCPCS	Description	# Billed for/ MUE[a]	Frequency of replacement[b] if known	National payment average
Q0477	Pwr module pt cable lvad rpl	1		$855
Q0478	Power adapter, combo vad	1	12 months	$203
Q0479	Power module combo vad, rep	1	12 months	$13,206
Q0480	Driver pneumatic vad, rep	N/A		$99,249
Q0481	Microprcsr cu elec vad, rep	1		$16,013
Q0482	Microprcsr cu combo vad, rep	N/A		$5,015
Q0483	Monitor elec vad, rep	1		$20,662
Q0484	Monitor elec or comb vad rep	N/A		$4,012
Q0485	Monitor cable elec vad, rep	1		$387
Q0486	Mon cable elec/pneum vad rep	N/A		$322
Q0487	Leads any type vad, rep only	N/A		$376
Q0489	Pwr pck base combo vad, rep	N/A		$17,912
Q0490	Emr pwr source elec vad, rep	N/A		$775
Q0491	Emr pwr source combo vad rep	N/A		$1,218
Q0492	Emr pwr cbl elec vad, rep	N/A		$98
Q0493	Emr pwr cbl combo vad, rep	N/A		$279
Q0494	Emr hd pmp elec/ combo, rep	N/A		$236
Q0495	Charger elec/combo vad, rep	1		$4,603
Q0496	Battery elec/combo vad, rep	1	6 months	$1,652
Q0497	Bat clps elec/comb vad, rep	2		$516
Q0498	Holster elec/combo vad, rep	1		$566
Q0499	Belt/vest elec/combo vad rep	1		$184
Q0500	Filters elec/combo vad, rep	N/A		$34
Q0501	Shwr cov elec/combo vad, rep	1		$563
Q0502	Mobility cart pneum vad, rep	N/A		$716

Table 1 (continued)

HCPCS	Description	# Billed for/ MUE[a]	Frequency of replacement[b] if known	National payment average
Q0503	Battery pneum vad replacemnt	N/A		$1,433
Q0504	Pwr adpt pneum vad, rep veh	N/A		$756
Q0506	Lith-ion batt elec/ pneum vad	8	12 months	$941

[a]Medically Unlikely Edits (MUEs), defined by MACs, identify the maximum units of service that a provider should report under most circumstances for a single patient. If more than the identified number of items are billed, a manual audit may trigger

[b]Medicare has only published "reasonable useful lifetime" recommendations for a few types of equipment identified above

- Medicare has the most published information on how frequently some VAD-specific HCPCS code can be reimbursed. See column 4 in Table 1.
- Majority of VAD equipment can be replaced and covered 12 months post discharge.
- If the patient has private/commercial insurance, it is highly recommended to have prior authorization in place before replacing the equipment. Most private payers follow the HCPCS codes and lifetime use recommendations from the manufacturers. The patient may have copays and deductibles related to the replaced equipment, and thus it is important to educate VAD patients on this financial responsibility.
- It is financially better for a program to replace durable VAD equipment in the outpatient setting. If VAD supplies are replaced during an inpatient readmission, there is a chance that payment for this expensive equipment may be rolled into the inpatient bill. If the payer has a bundled or DRG payment cap for that readmission based on the patient's readmission diagnosis, there is a chance the inpatient stay is reimbursed at a much lower rate than what the equipment costs.
- If a patient needs medically necessary VAD equipment replaced sooner than the expected lifetime use, such as stolen or damaged items, the modifier "RA" must be added to the HCPCS code.
- VAD program leadership should work closely with their institution's contracting department to review and determine if additional payments, or carve outs, are warranted for private/commercial payers to cover VAD equipment and supplies.
- Medical necessity should be clearly documented in the patient's medical record every time VAD equipment or supplies are replaced.
- Always include ICD-10-CM Diagnosis code of Z95.811, presence of heart assist device, with all claims.

VAD Driveline Management Supplies or VAD Stabilization Systems (avoid the term "dressing change supplies") are similar to supplies needed for ostomies. These are also considered Prosthetic and Orthotic Supplies and not just dressing supplies. They have been assigned HCPCS code Q0508 which is a miscellaneous code. They

are submitted via a CMS 1500 form, for physician offices or DME providers, or on a UB04 claim form for hospitals and must include an invoice for these supplies. For Medicare patients, these claims are reviewed manually by the local MAC and assigned coverage and payment. There have been many updates to how these critical driveline supplies are covered. Again, medical necessity for these must be documented in the patient record with the correct number of kits or systems documented for each patient.

Program Financial Success

VAD program financial success is more than just coding, coverage, and payment. It involves oversight at all levels of the program. Financially successful programs should recognize and review their payer mix at all phases of care; from outreach and referred patients to implant and post discharge care. Consider holding regular meetings with hospital and physician contracting in order to lobby for new payer contracts or rates and complete all eligible applications for Centers of Excellence (COEs) with each of the payers. At time of referral, the patient's insurance should be reviewed immediately to make sure the hospital and physicians are in network and VAD therapy is a listed benefit for that patient. This is the point where single case agreements (SCAs) can be initiated by the contracting department and the insurance company if they are not a recognized payer at the institution. During evaluation for VAD therapy, the program should provide a financial coordinator or resource to the patient to review what the patient's financial impact might be if they choose to receive a VAD.

Successful programs review their coding and payments from cases at least quarterly to ensure correct documentation and coding practices are optimized. If a program chooses to manage all outpatient equipment, they might consider a monthly review of all equipment given and charged to patients to make sure they have not missed billing opportunities. During this review of VAD equipment replacement practices, it will be important to note which insurance payers require prior authorization and make plans to request these prior to the patient's clinic visits.

At some point in the life of a VAD program, additional staffing will be needed for program growth. The request for additional employees is more easily made with a solid financial plan including revenue and case margins and is additionally strengthened when downstream revenue is presented in addition to revenue from VAD implants. Downstream revenue should include clinic visits, imaging such as echocardiograms, catheterizations, non-VAD operations, and any additional hospitalizations. Program quality initiatives should include fiscally responsible improvements such as decreasing length of stay which can decrease costs, increasing contribution margin for the one DRG payment.

Additional Resources

1. CMS Program Transmittal R1159OTN5 and CMS MLN Matters MM7888.
2. https://www.cms.gov/.
3. https://www.medtronic.com/us-en/healthcare-professionals/reimbursement/cardiac-rhythm-heart-failure/resources-device-type/mechanical-circulatory-support.html.
4. https://www.cardiovascular.abbott/us/en/hcp/reimbursement/hf/acute-mechanical-circulatory-support.html.
5. https://www.medicaid.gov/medicaid/index.html.
6. https://www.ihs.gov/aboutihs/eligibility/.
7. https://www.medicare.gov.
8. https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/MM6945.pdf.
9. https://www.cms.gov/Medicare/Coding/NationalCorrectCodInitEd/MUE.

Ventricular Assist Devices for the Pediatric Population

Mary Mehegan and Jenna Murray

Introduction

There is great diversity among pediatric patients with advanced heart failure. The underlying diseases leading to heart failure range from simple to complex congenital heart disease (CHD) to various forms of cardiomyopathies. Patients can present anytime from infancy to adolescence, and these size differences have important implications for support options.

General Pediatric Indications and Contraindications

In general, VAD therapy should be offered if its potential benefit outweighs the expected risks. The risk benefit profiles, however, vary across different age groups and cardiac diagnosis, as does the institutional experience in pediatric VAD therapy. Although there is no uniform criteria for instituting pediatric VAD support, there are some learned basic tenets [1]. Pediatric Cardiologists can easily appreciate when their patients meet the criteria of heart failure although there is challenge to determining reversibility and further difficulty in deciding when the appropriate time is to suggest MCS to a child and parent.

There have been great advances in VAD treatment for children. VAD support augments cardiac output which improves heart failure symptoms, end organ function and general condition, and consequently provides beneficial effects on

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post-transplant outcomes. Patient selection, timing of implantation, and selection of device for each patient are critical for optimal clinical outcomes [2].

Generally, children with advanced heart failure whom medical therapy is failing may be evaluated for VAD support [3]. Typically, infants can show signs of respiratory failure more commonly than older children who show signs of compromised end-organ perfusion. While no one should wait until severe end-organ damage is established, instituting VAD therapy too early is also counterproductive due to the inherent risk profiles associated with it [1]. The single most important predictor of patient mortality is the degree of end-organ dysfunction, specifically renal and hepatic dysfunction, at the time of VAD implantation [3]. Careful monitoring of serial changes in end-organ function, as well as nutritional status, is thus essential, and, if seen, VAD therapy should be considered.

The contraindications to mechanical circulatory support in pediatric patients are similar to those in adults. When the indication for a VAD serves as a bridge to transplantation, any contraindication to transplant constitutes a contraindication to use of mechanical support.

Generally, active systemic infection, extreme prematurity, very low body weight (<2.0 kg), severe significant neurologic damage, a constellation of congenital anomalies with poor prognosis, and chromosomal aberrations are considered contraindications for mechanical circulatory support [4, 5]. Chronic graft dysfunction (primarily diastolic dysfunction), due to the setting of coronary ischemia may also be difficult to support. Multisystem organ failure is a relative contraindication, however, special consideration needs to be given as hemodynamic improvement may reverse end-organ dysfunction in some cases. Both hepatic and renal dysfunction have been shown to improve with VAD-related improved hemodynamics [6]. Likewise, among the described contraindications, several of these are relative contraindications and need to be evaluated on an individual patient basis [2].

Pulmonary hypertension and elevated pulmonary vascular resistance are commonly encountered complications of chronic heart failure. VAD support may improve pulmonary hypertension by unloading the left ventricle (LV) and decreasing the left atrial pressures [7]. The presence of irreversible pulmonary hypertension is considered a contraindication for VAD support; however, these patients should be evaluated for candidacy for biventricular support rather than left ventricular support alone prior to excluding from the mechanical circulatory support [2].

Pre-implant Considerations

Prior to VAD implantation, all patients should be evaluated for valvar insufficiency. Competence of the native aortic valve is important in left ventricular assist device (LVAD) setting. Aortic valvar regurgitate flow can make the device ineffective for hemodynamic support. Aortic valve regurgitation should be addressed prior to implantation of the device. In patients with severe aortic regurgitation with structural abnormality, the aortic valve needs to be replaced, repaired or potentially a modified closure.

Device selection is an important aspect of pediatric VAD therapy which is influenced by several factors: patient size, type of support, left ventricular assist device (LVAD) or biventricular assist device (BiVAD), anticipated duration of support, the ultimate goal of support, and device availability. In patients with heart failure of acute etiology, consideration of using a temporary mechanical support device may be contemplated. Patients with relatively short-lived etiologies, such as viral myocarditis and acute rejection of cardiac grafts, may experience a recovery of cardiac function when the inflammatory/immune storm subsides; thus, VAD therapy simply supports the circulation as the underlying process runs its course. In such circumstances, temporary devices are a preferred mode of support [8, 9]. Temporary VAD support is also helpful when presented with a patient who requires circulatory support but whose etiology of heart failure, neurological status, or candidacy for transplantation is unknown. Historically, and even now in many pediatric heart centers worldwide, extracorporeal membrane oxygenation (ECMO) has been used for this particular purpose [10, 11]. One of the major advantages of ECMO over short-term VAD support is the option of peripheral cannulation, thereby avoiding the need for sternotomy. That being said, in a critically ill child, avoidance of a sternotomy should not be the primary determinant of treatment strategy. Permanent damage or loss of cervical vessels is also not without consequence. Conversely, the failing left ventricle is decompressed to a lesser degree with peripheral ECMO than VAD.

An example of a circuit configuration of short-term VAD support is a rotary or centrifugal pump, such as CentriMag/PediMag (Thoratec Corp.; Pleasanton, CA) and Jostra Rotaflow (MAQUET Cardiovascular; Wayne, NJ). Centers have also used these same devices for longer support.

There also has been growing interest in the use of percutaneous VADs in children such as the Impella axial VAD catheter. The Impella family has several different sizes, with the smallest (Impella 2.5, Abiomed Inc., MA) being 12 Fr in size at its pump motor delivering a max flow of 2.5 L/min. Greater experience is warranted to identify the lower margin of size limitations with this device. Despite there being limited experience in the pediatric population [5, 6], these percutaneous VAD technologies may play an important role in management of pediatric heart failure in select situations (e.g., unstable hemodynamics during or after catheter procedures).

When the etiology of heart failure is chronic in nature, hence less prone to recovery, the patient will most likely need durable support in the form of a long-term VAD. The EXCOR (Berlin Heart, Inc.; The Woodlands, TX) is the only pediatric-specific device that enjoys global acceptance. This system contains several different pump sizes (10, 15, 25, 30, 50, and 60 mL) and cannula sizes (5, 6, 9, and 12 mm). Choosing an appropriately sized pump and cannula is of utmost importance to avoid patient–device size mismatch, which is known to be a significant risk factor for poor outcome in long-term VAD therapy in children [7].

Adult continuous-flow devices are being increasingly used in children. The use of implantable continuous-flow VADs such as HeartMate 3 (Abbott) has recently received pediatric indication. This is a dramatic paradigm change not only for healthcare professionals but also for the society at large.

Single Ventricle VAD Support

This subdivision of pediatric MCS continues to baffle the community for the past decade. It is the art of trying to fit a square peg into a round hole. There are no VADs that are designed to support patients with this physiology but as pediatric VAD clinicians, it is our job to make it so. A 2018 Pedimacs report on pediatric VAD support showed a 60% survival at 6 months for patients with single ventricle disease compared to 80% survival for non-congenital heart disease patients. The Berlin Heart Database suggests that survival is based on the stage of the palliation, with 26% survival for stage 1 patients, 39% for stage 2, and 67% for stage 3 [12]. Though centers have been improving over the years, overall even large implanting centers still struggle with managing this population safely and successfully to transplant.

Because of this data, it is hard to determine appropriate timing to implant vs allowing the disease process to unfold and continuously observe. Because pediatric programs average at most 20–30 VADs a year and less than half are single ventricles, it is hard to gain expertise in these cases. Additionally, only a few sites will accept this challenging population. Collaboration among Pediatric VAD programs is needed to focus on this challenging patient population as to create a standardized evidenced based approach to investing in this cohort of patients.

Table 1 highlights one site's implant criteria for single ventricle VADs and Fig. 1 subsequently outlines the patients surgical plan based on the stage of palliation of the patient's weight. This serves only as a guideline which may not be effective at every center based on the culture and resources of each implanting center. Devices available, comfort with single ventricle VADs, and referral bases, are some of the factors that influence the treatment strategies a pediatric VAD program will chose for this challenging population.

Table 1 One example of a centers approach

Indications for VAD: In general, patients requiring VAD support meet at least one of the following clinical criteria.
• Inability to wean from ECMO
• Two or more vasoactive infusions (inotropes, vasodilators, etc.)
• On one vasoactive infusion (or unable to tolerate any vasoactive infusion) and with at least one of the following findings due to heart failure:
– Feeding intolerance
– Renal dysfunction
– Hepatic dysfunction
– Positive pressure ventilation
– Unmanageable arrhythmia or severe incessant sinus tachycardia
– Change in neurologic status (i.e., profound irritability or lethargy)
– Significantly reduced age-appropriate activity level
Exclusion criteria:
• SVAD support is generally not indicated for patients with isolated PLE or PB with normal systolic function, normal AV valve function, and normal hemodynamics.
• SVAD support is also not indicated for any patient who is not able to tolerate any anti-thrombotic therapy.

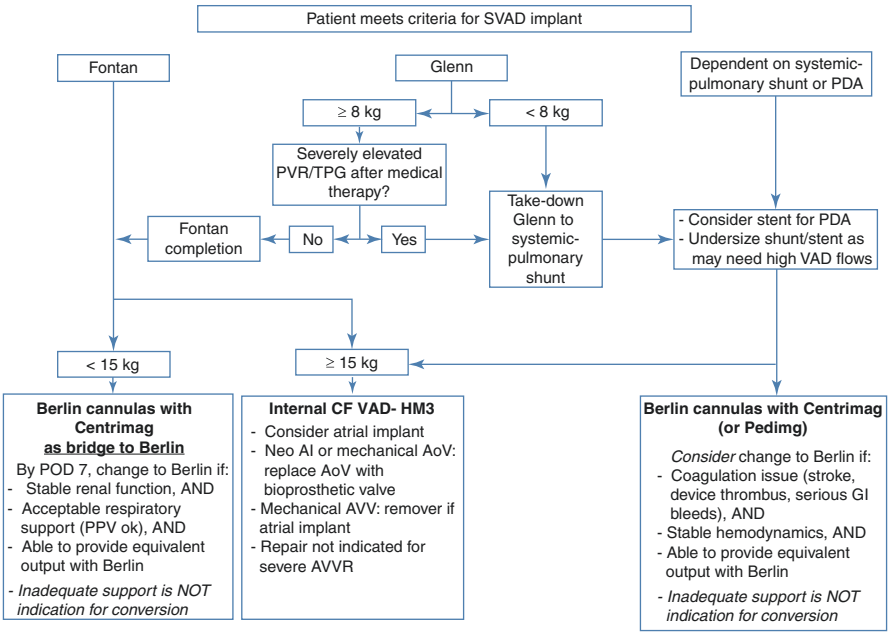

Fig. 1 One example of a centers approach

Paracorporeal Pumps in Pediatric VAD Support

Many times, paracorporeal pumps can be ideal in the pediatric population. As children are small and growing, these devices offer flexibility with space in the chest and the ability to grow into other sizes that may be externally changed while on support in the inpatient setting. The two pump brands that pediatric centers gravitate toward most are the Berlin Heart Excor and the Centrimag/Pedimag (Abbott). The challenge to paracorporeal support is thrombogenicity. These devices are mostly plastic lending themselves to a much higher stroke rate (12–30%) than the intracorporeal devices that are made of titanium. To combat this high stroke rate, the pediatric VAD community has evaluated utilization of other drugs such as bivalirudin instead of heparin and warfarin as well as dual antiplatelet therapy (aspirin and Plavix or Persantine) and even at times steroid use to dissolve clots and prevent stroke. One major limitation to paracorporeal pumps is the inability to discharge from the acute care environment. Though it is a goal, we as a community are striving for discharge to be possible for any child on a Berlin heart. Pedimag/Centrimag (Abbott) are not dischargeable other than for hospice that we know of at this time but Berlin heart is working to create a freedom driver that can be used for all size pump outside of the hospital. There have been a few reports of larger adult size patients on this device being able to be discharged but it is not the standard of care here in the United States.

Nutrition

Malnutrition is common in pediatric heart failure due to many factors [13]. Decreased intake secondary to fatigue, abdominal pain and anorexia coupled with increased nutrient requirements resulting from gastrointestinal losses, inflammation, hypermetabolism and malabsorption all lead to a deficit of available energy to meet increased metabolic needs [13–18]. The importance of nutrition in both pediatric and adult heart failure cannot be overstated, as malnutrition has been associated with both poor wait list outcomes and reduced post-transplant survival [19].

Malnutrition is highly prevalent in pediatric heart failure. According to the Pediatric Cardiomyopathy Registry, 23.7% of children with dilated cardiomyopathy are malnourished, and several studies have shown that between 14% and 18% of children on the heart transplant wait list have a BMI below the 5th percentile [18, 19]. Furthermore, the importance of nutritional status on outcomes is well established. In children, Godown et al. reported that a BMI greater than the 95th or below the 1st percentile was a risk factor for both waitlist and post-transplant mortality in cardiomyopathy patients [19]. In a separate analysis, Godown et al. reported that 12% of waitlisted children less than 2 years of age were moderately or severely wasted and that wasting was a risk factor for wait list mortality [19]. After transplant, Rossano et al. reported that 21% of children had a BMI below the 5th percentile at transplant and that being underweight was an independent predictor of reduced graft survival [20].

Use of VAD support can facilitate nutritional rehabilitation; patients with VAD have been shown to have significant improvements in weight-for-age and/or BMI for age during the listing period as compared to medically managed patients who tend to worsen. This result is likely due to reduction of heart failure symptoms and improved hemodynamics, allowing for a concomitant increase dietary intake while reducing metabolic demand and nutrient losses.

While cachexia (body mass index <22) has consistently been identified as a risk factor for perioperative death, published reports provide conflicting evidence as to whether obesity is associated with adverse outcomes after LVAD. Current devices provide adequate support for obese patients, and although issues regarding infection are a consideration, outcomes more likely depend on accompanying comorbidities rather than the obesity itself. Because durable LVAD implantation is generally applied in the setting of acute decompensation, and in light of the tenuous hemodynamic status of these patients, strategies to address obesity first with bariatric surgery are not practical.

Some centers report that children with paracorporeal devices struggle with adequate PO intake. Most photos one will see of these children will reveal a nasogastric tube. There is no evidence that the tunneled cannula has a negative impact on a child's will to eat by mouth but there is data to suggest it is a common problem. Although adequate calories are easily achieved through nasogastric feeds, continued encouragement to have this child eat by mouth will go a long way in their post-transplant nutritional needs.

Unique Psychosocial Needs for the Pediatric VAD Patient: Top Five Differences and Considerations

1. For smaller children and babies that are unable to be implanted with a dischargeable VAD to go home or leave the acute care environment, this is a huge lifestyle change for even the most well-adjusted families. Pediatric heart transplantation wait times are much longer for this population, and there is limited respite for those dedicated caregivers that want to be at the bedside. This unpredictability in wait times can place challenges on the already stressful experience. VAD programs may consider establishing a normal routine such as training trustworthy families to go for independent walks with their children in the hospital or providing bath time. Creating schedules driven by the caregivers can provide feelings on inclusion with caring for their child while the medical care is addressed by the hospital staff.
2. When embarking on implanting a VAD in a child, the entire family needs to be committed and educated. Primary and secondary caregivers are essential to the success and stamina to this endeavor. At baseline, children require care and VAD patients elevate this need with the addition of anticoagulation, heart failure medication, and the mechanics/equipment of the VAD. This creates a high burden for a primary caregiver, and thus it not recommended to be a solo responsibility.
3. Body image is seen in both male and female patients and even at younger ages than would be anticipated. School age children do not want to look different than their peers and VAD equipment may set them apart in a poor mindset. Backpacks and other smaller more child-friendly ways to have their VADs carried has been shown to help make the pediatric patient feel more confident with their VADs. Efforts should be made to show the patient from other children with VAD either thru photos or meeting other children that current have a device or have since gone on successfully to transplant as this has been proven to be helpful. Since pediatric programs have small numbers of patients of varying ages compared to large adult VAD programs, support groups have not been successful, however, utilization of social media can connect children of similar ages to create these relationships.
4. Teenagers need to be empowered to participate in their care as early as possible and need to be able to be part of the decisions surrounding their health. It can be difficult for the patient to feel "fine" one day and then in the cardiac ICU the next. Approaching teens about their health care is requires special care and time. It is useful to talk to the caregivers about how they feel the child best processes information and which approach may be beneficial such as visual, verbal, or written information. Child Life and Child Psychology as well as social work are vital in this journey. Though hard in the beginning, the investment is worth making so they feel in control and know who they can approach with questions. This allows the teen to communicate effectively to those that can help them rather than acting out and not taking medications or not caring for their VADs which could have dire consequences. Examples of involvement can include completion

of their healthcare proxies or goals of care packets so they feel heard and in charge of their outcome. This approach should be considered for older children with higher maturity.

5. One of the hardest things about pediatric VAD support is the acuity of the presentation; children usually come to care in a crisis and there is no "elective" VADs. This results in minimal time for digestion of the huge life changes. They require multiple inotropes, are massively fluid overloaded, develop arrhythmias and sometimes even respiratory compromise. Patients have severe symptoms and often unable to retain anything other than the need for have surgery. If the patient requires ECMO, the possibility exists the VAD team will not have opportunity to meet the child prior to undergoing implant as caregivers will provide consent. This creates a distressing situation in which the patient awakens after surgery to a completely new life that they may never have chosen. SSRIs have been shown to help in this massive adjustment disorder and anxiety. This population requires a lot of patience and explanation on their own time frame to help them prepare for possibly another procedure such as heart transplant.

Rehabilitation

Children who require VAD support are subject to prolonged hospital stays, which exposes them to significant morbidity, including physical deconditioning, deficits in activities of daily living, delays in cognitive and social development, and depression.

Physical therapy rehabilitation program for VAD children should incorporate much diversity to meet the goals of a wide population of ages with ranges in cognitive and physical ability level. Inpatient rehabilitation focuses on conditioning as well as supporting normal development. Therapy should start early in postoperative recovery and have a structured regiment of care outlined and adjusted as tolerated.

Daily physical and occupational therapy schedules are a must and should always be posted in the room for a guide to promote adherence. Bedside caregivers are encouraged to always promote the routine scheduled therapy sessions and try to avoid foregoing sessions that are critical to the patient's recovery.

Centers should clearly define and discuss what activities are safe and what personnel are required to be present during certain activities. For example, having the VAD trained RN available for all patient transfers in and out of bed that are on paracorporeal pumps. Discussions on safe handling of the cannula and how to manage VAD alarms are crucial to success. Activities as easy as putting a child in a high chair need to be done with close observation of the cannula, making sure nothing is pushing on cannula or causing the cannula to bend thus potentially impeding blood flow through the cannula.

Older children sometimes want to push the boundaries of physical activity, especially when they are feeling strong. Reminding the patient that activity restrictions are temporary and are in place for their safety may enhance

adherence to activity limitations. For example, using a tread mill is a great exercise, but running fast on one is dangerous and could cause a catastrophic accident to occur.

Incorporating routine VAD education specific for the therapy teams can be very beneficial and help facilitate rehabilitation. Physical therapy strengthens the body but it also can help the child's mood and overall happiness.

Discharge and Community Reintegration

Historically, children requiring VAD support as a bridge to transplant were supported in hospital, with waitlist times varying from months to years. In the last decade, the advancement of pediatric VAD's has enabled pediatric centers to now discharge intracorporeal VAD patients home and integrate them back into their communities. Creating standard work flow processes to ensure the educational needs of the patient, family, and community are met will enable programs to successfully manage VAD patients at home [10].

Training and education in preparation for the discharge of a pediatric VAD patient is crucial to the success and comfort of the patient and caregivers and comes with many considerations. Discharge planning needs to start early on in the hospitalization. Using language like "when you are home" or "when children like this go home" will help reinforce the goals. Utilizing or creating a VAD journey map will help everyone stay on track of achieving the necessary educational and medical goals to be successfully discharged. Such milestones could include postoperative goals, device learning, medication education, and even independent excursions around the hospital to encourage confidence in caring for the VAD patient.

Each center should develop their own medical readiness for discharge [10]. Generally, recovery from cardiac surgery, tolerance of nutrition, safe activities of daily living, and then stable medication and anticoagulation regimen are indicators for readiness. With regard to VAD education, families need to demonstrate the ability to correctly manage VAD alarms and VAD equipment. Centers should have a guideline or checklist of VAD equipment education for the patient and family to assist in tracking VAD education. Repeated sessions with caregivers using educational VAD equipment labeled as "not for clinical use" is essential in creating a good knowledge base and help them feel capable in caring for the VAD. VAD driveline dressing changes are included in the education. Having parents demonstrate and change the VAD driveline dressings while still inpatient is ideal, along with sharing the signs and symptoms of infection prevention and how to assess the driveline for any possible infection. Additionally, showering with the VAD is another skill to practice that is useful to do while inpatient. Talking through all possible scenarios that may occur at home while the patient is still hospitalized will help them prepare for life outside the hospital.

Having a child with a VAD at home also means having an electrically dependent person at home. Having discussions about action plans in the event the home loses

power is another discharge preparation that should occur. Although VAD manufacturers do not require a generator as part of safe discharge planning, many families are distressed with potential power loss, and thus the VAD team should assist in creating action plans should an electrical outage occur.

Providing a VAD discharge binder will prove a useful resource for families at home. Items to consider including are the manufacturer patient manual on the device, all equipment that was provided for home, dressing change information, contact numbers of who to call and when, medication list, nutritional and physical rehabilitation goals, activity guidance, and finally discharge instructions with expected follow-up appointments.

Making sure that families know they have support from the implanting center with a provider, either a MD or NP and assistance from the VAD coordinator, to help with any questions they have at home. Families need to know when to call for help and when notification of providers is necessary and helpful.

The model for the outpatient VAD clinic is catered to the medical needs of the patient. Generally, centers may want to schedule a visit a few days to a week after hospital discharge to make sure the family feels supported, then evolve to a monthly visit schedule. This visit schedule may need to be altered if the patient lives far away from the implanting center. Consideration could be to see the local cardiologist in between times seen at the implanting center.

VAD clinic visits include a full physical assessment, including blood pressure measurements, routine lab checks including anticoagulation levels, electrolytes, complete blood counts, and hemolysis markers. The center may want to obtain routine echocardiograms to assess septal position, valves, and wall function. Finally, clinic visits need to include obtaining log files from the VAD, assessing any VAD alarms, inspecting the driveline exit site, and continuing to answer any questions relating to the VAD and equipment.

Each child with a VAD will have their own unique needs for successful reintegration back into the community. Pediatric VAD patients living in the community is relatively new and most local services will not have had previous experience with VAD patients. Consider first the groups that will come in contact with this child. This list typically includes schools, first responders, local emergency departments, local pediatrician and cardiologist, and even local hospitals. Additionally, rehabilitation centers and psychological support may be necessary to continue a child's convalesce at home. Education for these services should focus on what their needs may be combined with the knowledge of collaboration with the implanting center.

For school integration, the focus of education should be for personnel that are routinely available at school and ones that will likely have the most contact with the child. Examples include the school nurse, teachers, and administrators [10]. Congratulate the school for welcoming the return of the student and fulfilling their need to return to some normalcy of life. While the VAD team will offer VAD education to focus on emergency equipment management for the school, a child's parents should remain as the primary contact when illness or other medical needs arise. Reinforce with school representatives during VAD education that this child is well and if the child is not feeling well, call the parents; if there is a medical emergency,

call emergency services like one would for any medical emergency. It is also beneficial to have a written action plan for the school so they have a document that informs them of VAD equipment management, alarm information, potential adverse events of the device, and anticoagulation along with contact numbers. Participation in physical education at school is a thought-out choice of the VAD team and parents. Physical activity is always encouraged but risking injury that could occur with children running around a gym is something to avoid. This is true for home activity as well, skateboards and bikes should carry caution as device malfunction with a fall and personal injury under anticoagulation is a real danger and should be avoided.

Destination Therapy (DT)

Pediatric DT programs are now developing throughout the world. These programs need a large multidisciplinary approach in order to support a patient at home, in absence of the plan for heart transplantation. One of the early pediatric DT patients had Duchenne Muscular Dystrophy, which excluded them for heart transplant. The use of VADs for DT in children will continue to evolve as device technology improves, narrowing the gap between quality of life and survival outcomes for VADs compared to heart transplant. Ethical implications related to VAD use to alter the natural history of life limiting conditions need to be balanced by the family and the implanting center.

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Temporary Mechanical Circulatory Support

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Introduction

Temporary Mechanical Circulatory Support (MCS) plays a vital role in the management of patients with acute cardiogenic shock. Cardiogenic shock is defined by hemodynamic parameters, including systolic blood pressure less than 80 mmHg or mean arterial pressure 30 mmHg less than baseline; severe reduction of the cardiac index (CI) to less than 1.8 L/min/m^2 without support or less than 2.0–2.2 L/min/m^2 with support with LV end diastolic pressure greater than or equal to 18 mmHg or RV end-diastolic pressure greater than or equal to 10–15 mmHg [1]. Clinical signs of cardiogenic shock include signs of hypoperfusion and end-organ dysfunction such as cool extremities, decreased urine output, renal failure, liver dysfunction, and altered mental status. With widespread availability of temporary MCS, these devices can be utilized to stabilize these patients during an acute decompensation in an attempt to recover end-organ function while determining the next steps of care.

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Table 1 Common temporary MCS devices

	Left heart support	Right heart support	Oxygenation
IABP	Yes	No	No
Impella	Yes	Yes	No
Tandem	Yes	Yes	No
ECMO	Yes	Yes	Yes

Temporary MCS devices span from minimally invasive, percutaneous devices that can be placed at bedside or in the catheterization lab to more robust devices that require surgical implantation. With proper timing and appropriate patient selection, the use of temporary MCS can improve survival of this very sick patient population. Here, we will discuss the most commonly used temporary MCS devices, outlining indications, management techniques, and potential complications. Table 1 describes characteristics of the most common devices used.

Intra-Aortic Balloon Pump (IABP)

The intra-aortic balloon pump (IABP) is a commonly utilized method for acute support given its ease of implantation and widespread availability in smaller community hospitals. Since its initial implant in the 1960s, it has been the main form of temporary MCS for patients with cardiogenic shock. The IABP augments hemodynamics by allowing for left ventricular unloading and increased coronary perfusion.

Configuration and Mechanism of Action

The IABP catheter is comprised of a long 20–50 mL closed polyurethane balloon distally mounted on a flexible catheter with dual lumens. One lumen allows for aspiration and flushing of the distal tip, as well as pressure monitoring, ultimately impacting the timing of the device, while the other lumen shuttles gas to and from the balloon. The therapeutic cycle of the balloon is controlled by a mobile console containing helium which allows computer control of the synchronized inflation/deflation circuit (Fig. 1).

The IABP catheter is placed percutaneously under fluoroscopy guidance most commonly in the common femoral artery, though the axillary or subclavian artery can also be used for placement. The catheter is advanced over a guidewire with the distal tip positioned in the proximal descending aorta, 1–2 cm below the left subclavian artery, and the proximal end of the balloon above the renal arteries so as to not impair renal blood flow.

The hemodynamic effects of IABP counter-pulsation are increased coronary artery blood flow and decreased left ventricular end-diastolic pressure (LVEDP) which in turn result in left ventricular (LV) afterload reduction, decreased preload, and a modest increase in cardiac output.

The inflation of the balloon should coincide with the onset of diastole, which is when the aortic valve closes. The inflated balloon then displaces blood back to the

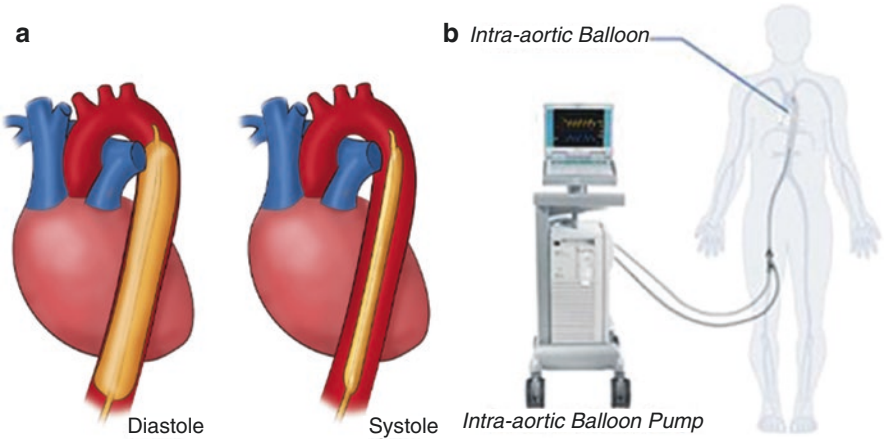

Fig. 1 (**a**) Inflation/deflation of the IABP and (**b**) exterior components

aortic root which increases the diastolic pressure. The coronary arteries also fill during diastole, so this displaced blood results in increased coronary blood flow to the myocardial tissue. With proper timing of the inflation/deflation cycle, an increase in cardiac output of 10–20% may be noted [2]. The rapid deflation of the balloon should occur just ahead of the aortic valve opening, which identifies systole causing a suction effect within the aorta, propelling the blood volume forward, thus decreasing afterload, preload, and myocardial workload. Augmentation can be set to change as the patient has recovery of their native heart function. Most patients are placed on a 1:1 augmentation as the starting setting, meaning the balloon inflates and deflates with every valve opening. As there is recovery of native heart function, and contributing underlying cardiac output improves the augmentation on the pump may be changed to either 2:1 (inflating and deflating with every other opening) or 3:1 (inflating of deflating with every third opening) before removal of the pump 3.

Indications and Contraindications

IABP therapy is considered beneficial for a multitude of cardiac indications and common uses in practice. Indications for placement include cardiogenic shock, intractable angina, or myocardial ischemia. This is especially useful in severe left main coronary artery disease awaiting further therapy or surgical bypass. An IABP can be placed as precautionary therapy during high-risk percutaneous coronary intervention or as temporary treatment of refractory ventricular arrhythmias and acute mitral valve regurgitation. Often an IABP can be used for low cardiac output patients while weaning from cardiopulmonary bypass or as a bridge to advanced heart failure therapies such as durable VAD or transplant. It is considered the simplest and most cost-effective therapy to implement in the treatment of cardiogenic shock, and therefore it is still one of the most commonly used, especially in many

smaller hospital settings [3]. An IABP can also be used in conjunction with VA ECMO to serve as an "vent" to allow for left ventricular unloading while receiving ECMO support.

The IABP should not be used in cases of aortic dissection, abdominal aortic aneurysm, complex aortic valve stenosis, or aortic insufficiency. Caution should be used in cases of severe vasodilatory or septic shock and severe peripheral artery disease as the risks may outweigh any benefits of support. The balloon's counterpulsation will worsen an incompetent aortic valve by displacing blood volume through the valve during diastole increasing the preload of the left ventricle and minimizing the potential additional blood flow to the coronaries.

Complications

Potential adverse events related to insertion include bleeding, hematoma, infection, thrombocytopenia, limb ischemia, vascular injury, or arterial perforation and should be vigilantly monitored for occurrence. Observe for any excessive bleeding and drainage at cannulation site and frequently assess limb perfusion by checking relevant pulses, appropriate capillary refill, temperature, and color.

In respect of the mechanical action of the balloon, potential complications may include aortic dissection or an embolic event related to helium, plaque, or thrombus. Of note, errors in timing of the balloon inflations and deflations may also cause complications subtherapeutic effects of the IABP therapy. Monitoring timing of the balloon inflation with waveforms is imperative to avoid complications. Early balloon inflations can cause an increase in afterload, an increase in myocardial oxygen consumption, and a decrease in stroke volume. Both early inflations and late deflations can be a very dangerous error due to the acute increase in afterload, resulting in a potential range of complications from a marked decrease of cardiac output to cardiac arrest. If the balloon deflates too early, there will be minimal or no decrease in the afterload. Early balloon deflations and/or late inflations will result in less time for the diastolic filling of the coronaries thus minimizing additional coronary flow [4].

Impella (Abiomed)

Engineering and Function

The Impella pump (Amiomed, Danvers MA) is the culmination of a series of innovations which has revolutionized temporary ventricular assist devices. Its design is largely based on the Archimedes' screw in using rotational force to generate the power necessary to eject blood forward (Fig. 2).

The Impella is a micro axial blood pump that supports circulation and provides between 2.5 and 6 L/min of flow, depending on the cannula being used. The Impella motor spins creating a negative pressure that pulls blood from the inflow area through the cannula and unloads into the outflow area. The impella is controlled by the Automated Impella Controller (AIC) which provides the interface for

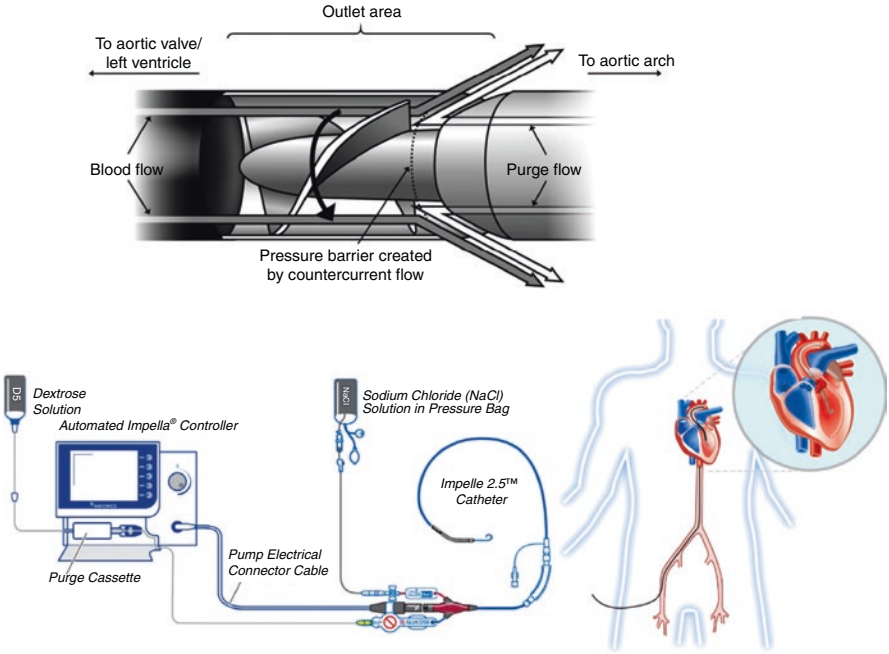

Fig. 2 Impella pump design. (Used with permission from [5])

monitoring and controlling the speed. The speed of the impeller rotation is adjusted by Performance Level, or commonly referred to as P-Level. P-Levels 0–9 correlate to expected flow ranges on a scale of RPMs, with P9 being the highest speed or RPMs (Impella 2.5 only goes as high as P8). The amount of mechanical ventricular unloading can directly be controlled by titrating P-level, as long as the impella positioning is adequate.

A correctly positioned cannula places the inflow area in the middle of the left ventricle and the center of the cannula sits across the aortic valve, while the outflow is in the ascending aorta. Cannulas come equipped with sensors in the distal tips that provide waveforms on the console. These waveforms help determine how the cannula is positioned in relation to the aortic valve. The Ao Placement Signal indicates if the outlet area of the cannula is in the ventricle or aorta by a sensor reading current pressures. In cases where there is little cardiac function, a flat Ao or placement signal may be present. Pulsatility on the waveform may return as cardiac function improves. The motor current measures the energy intake and fluctuates with speed and pressure changes throughout the cardiac cycle. When the cannula is positioned correctly across the aortic valve, the motor current will produce a pulsatile waveform. Since the inlet and outlet areas are on opposing sides of the aortic valve, the device detects the different pressure readings from either end of the cannula as the valve opens and closes. This produces the pulsatile motor current waveform. If the cannula slides out of correct position and the inlet and outlet are both in the ventricle or aorta, the motor current will become flat, as there is no longer change in the

pressure between the two ends. In cannulas equipped with SmartAssist, an additional LV waveform is present when set P-4 or higher. The LV placement signal is calculated from the Ao Placement signal and the gradient of the motor current.

Waveforms should be monitored on the placement screen which displays real-time operating data for the impella. Questionable waveforms should be evaluated by echo to view the positioning across the aortic valve, to ensure the cannula is appropriately positioned or make necessary adjustments. Abiomed also offers a remote monitoring option, Impella Connect, in which one can log into the AIC and view the device status, waveforms, and alarms. Table 2 reviews potential waveform expectations.

In addition to close monitoring of waveforms for proper placement, frequent assessment of external cannula length and exit site should be evaluated for marking changes, bleeding, or signs of infection. It is also important to monitor volume status to prevent suction or hemolysis. If suction occurs, the P-level should be reduced and the cause of suction evaluated and treated.

The catheter uses a purge system which both cools the motor and prevents clot formation. The solution is a combination of heparin and 5% dextrose. The console automatically adjusts the purge flow and provides a purge pressure value to monitor. Attention should be paid to the purge flow and purge pressure as raising values can be an indicator of clot formation and/or impending pump dysfunction.

While the heparin within the purge solution has a systemic effect, it may be necessary to start a heparin drip in order to maintain adequate anticoagulation. Most studies report a target aPTT range from 55 to 80 s. Abiomed recommends use of ACT goal during patient support of 160–180 s. Table 3 represents all the available impella devices currently approved.

Table 2 Expected impella waveforms by cannula type

	2.5	CP with SA	LD	5.0	5.5 with SA	RP
Sensor type	Open pressure port	Fiber optic sensor	Differential pressure sensor	Differential pressure sensor	Fiber optic sensor	Differential pressure sensor
Placement waveform	Aortic (ventricular indicates in the wrong position)	Aortic (ventricular indicates in the wrong position)	Pulsitile (may look like ventricular waveform, but incorrect position would produce a flat waveform)	Pulsitile (may look like ventricular waveform, but incorrect position would produce a flat waveform)	Aortic (ventricular indicates in the wrong position)	Pulsitile (may look like PA waveform, but incorrect position would produce a flat waveform)
LV waveform	Not available	Present P4 or higher	Not available	Not available	Present P4 or higher	Not available
Motor current	Pulsitile (if flat, indicates in the wrong position)	Pulsitile (if flat, indicates in the wrong position)	Pulsitile (if flat, indicates in the wrong position)	Pulsitile (if flat, indicates in the wrong position)	Pulsitile (if flat, indicates in the wrong position)	Pulsitile (if flat, indicates in the wrong position)

Table 3 Current impella devices available for use

	Impella 2.5	Impella CP with SmartAssist	Impella LD	Impella 5.0	Impella 5.5 with SmartAssist	Impella RP
Flow	2.1–2.5 L/min	3.1–4.3 L/min	4.2–5.2 L/min	4.2–5.2 L/min	~6.0 L/min	3.9–4.4 L/min
Insertion	Percutaneous 12 Fr sheath	Percutaneous 14 Fr sheath	Surgical-open	Surgical-axillary cut down	Surgical-axillary cut down or open	Percutaneous
Length of time	<1 week	<1 week	<2 weeks	<2 weeks	<1 month	<2 weeks
Pros	– Speed – Accessibility	– Speed – Accessibility	– Shorter catheter – Ease of direct insertion	– Pt can ambulate	– Maximal support – Pt can ambulate – Smart assist	– Percutaneous insertion vs. central cannulation for surgical RVAD
Cons	– Pt immobility – Catheter migration – Less support than a surgical impella	– Pt immobility – Catheter migration – Less support than a surgical impella	– Open chest insertion and explant	– No smart assist – Less flow than 5.5	– Surgical implant	– Need for fluoroscopy – Pt immobility
						

Indications/Contraindications

The impella line of devices have several indications. The left-sided percutaneous impella, namely the impella CP, is currently used for hemodynamic support during high-risk percutaneous coronary intervention (PCI) and may be the first line of support in the management of acute coronary syndrome complicated by shock. The surgical impellas are often used to manage progressive cardiogenic shock from pre-existing advanced heart failure and may also be used in cases of post cardiotomy shock. Impella is more frequency being used as a vent for VA ECMO patients to unload the left ventricle and help lower mortality rates. The impella RP can be used to provide right-sided support in complicated right ventricular infarction as well as in the support of right ventricular failure post durable left ventricular device implantation. The impella CP is currently being investigated for offloading prior to PCI in Anterior wall MI and high-risk cardiac surgery.

The use of the impella in AMI complicated by cardiogenic shock increased after the SHOCK II trial failed to show mortality benefit with the use of intra-aortic balloon pump [6]. While there have been many trials to investigate the mortality benefit of impella, most have been either poorly randomized or underpowered. With advancements in both catheter engineering and operator experience, more recent trials have demonstrated a decrease in hospital length of stay and 30-day mortality with early impella support [7].

Contraindications to impella support include known iliofemoral arterial occlusion (percutaneous catheters), severe aortic stenosis, LV thrombus, mechanical aortic valve, and contraindication to systemic anticoagulation.

Complications

Percutaneous impella support can be complicated by issues related to insertion, vessel occlusion leading to limb ischemia, and bleeding. The PROTECT I trial sited an insertion site hematoma in 8 out of 20 patients, although none necessitated transfusion or vascular intervention [8]. The risk of retroperitoneal hemorrhage is 0–2.2% when extrapolated from TAVR data [9]. The risk of pseudoaneurysm as extrapolated from cardiac catheterization is 0.4% and up to 3.4% in large bore access [10]. The rate of acute limb ischemia has been reported as high as 12% and often results in increase morbidity and mortality [11].

Hemolysis remains a challenging complication of Impella catheters. Hemolysis is breakdown of the red blood cell caused by sheering forces which disrupt membrane integrity. VAD hemolysis is discussed in a similar context in chapter "Ventricular Assist Device Complications."

Hemolysis is evidenced by hemoglobinuria either occult (laboratory analysis) or apparent (tea-colored urine, as in Fig. 3), anemia, indirect hyperglobinemia, and/or abnormal pump function. Rates of hemolysis have been reported to be approximately (or as high as) 10.3% [12]. Failure to recognize and treat hemolysis can lead to acute renal failure, platelet aggregation, and thrombosis with increased morbidity and mortality. Investigation in impella-related hemolysis begins with a transthoracic

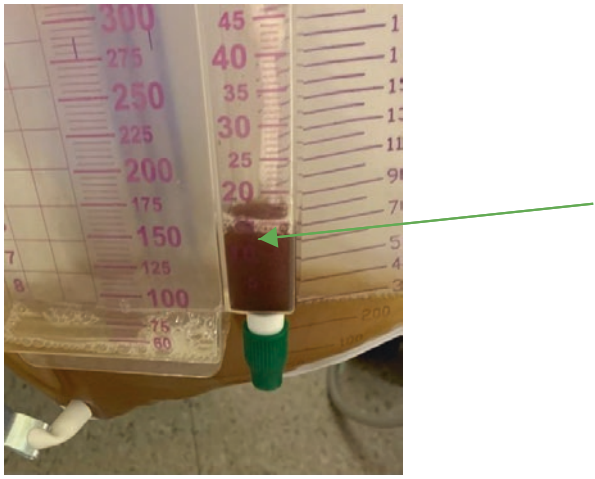

Fig. 3 Urine color during episodes of hemolysis

echocardiogram evaluating appropriate positioning of the catheter and ventricular volume status. Treatment should be directed toward the inciting cause and include catheter repositioning, adequate anticoagulation, administration of volume, or augmentation of RV function.

Indications for Surgical Impella/Escalation

In the setting of cardiogenic shock with or without existing MCS, the presence of persistent shock symptoms should prompt consideration of escalation of support. Hemodynamic and serologic findings consistent with shock include:

- Need for vasopressor support to keep the SBP >90
- Cardiac index <2.2 L/m^2
- PCWP greater than 15 mmHg
- Lactate level >2.0
- Urine output <0.5 mL/kg/h

The surgically implanted impella (5.0 or 5.5) allows for increased support, increased patient mobility including ambulation due to its axillary artery approach, and the ability to provide longer duration of temporary support. In a study of 58 surgically implanted impellas implanted at three centers, 33% expired on support and 67% were bridged to other therapy. Of those bridged to other therapy, 51% were bridged to LVAD, 39% received transplant, and 10% were weaned off support [13].

Weaning

Proper weaning of the impella device is key in determining the next step of care for the supported patients. Failure to wean off the impella may result in the need for

bridging to durable LVAD or heart transplantation. Weaning should be considered once there is evidence of end-organ recovery, minimal rhythm disturbances, particularly ventricular arrhythmias, minimal need for vasoactive drugs, and signs of native left ventricular recovery, including echo evidence of improved function, minimal mitral regurgitation, increase arterial line pulsatility, and improved invasive hemodynamics (low CVP and wedge pressure, stable cardiac index greater than 2.2). The impella can be weaned by gradual reduction of the P-level, resulting in more native contribution of the heart. SmartAssist technology on the CP and 5.5 catheters allows for monitoring specific to weaning with the LVEDP trends screen. Information displayed should verified with patient's hemodynamics, but as the P-levels are being reduced, you can view MAP, native cardiac output, Impella flow, and LVEDP trends over specific time frames. As percutaneous support is reduced, cardiac output and native heart function should remain stable. If the patient has adequate hemodynamics (i.e., CVP <12, CI >2, no escalation in vasopressor agents) at P2, the catheter can be removed. If the patient cannot tolerate weaning, long-term support options, such as durable VAD, heart transplantation, or inotropic infusion, should be explored.

Left Atrial to Femoral Arterial Bypass

Left atrial to femoral arterial bypass (LA to FA bypass), more commonly known by its typical trade name of Tandem Heart (LivaNova LifeSPARC, London, UK), is a method of mechanical cardiopulmonary support which allows oxygenated blood to be delivered from the left atrium to the femoral artery, bypassing the ailing left ventricle. This device may be considered as an acute form of support in the rapidly deteriorating patient as a bridge to another form of support, such as a durable left ventricular assist device (LVAD) or a heart transplant, or when the cause may be reversible. The advantage of LA to FA bypass is that it can be rapidly deployed anywhere fluoroscopy or echocardiography is available.

Highly specialized care is needed for these patients once they are supported with this device and should only be undertaken by staff who have been trained extensively. Cannula securement is of utmost importance. When cannulated with transsepetal approach, even very small movements can dislodge the catheter so anchoring the cannulas with additional external holders and monitoring cm markings on cannulas help ensure cannulas remain in the appropriate place. Due to the size of the cannulas and their placement in the groin, frequent neurovascular checks are required to ensure adequate blood flow continues to circulate to extremities. Distal perfusion catheters can also be used to prevent limb ischemia.

Configuration

An LA to FA bypass device circuit is typically comprised of a long cannula (21 Fr 62 cm or 72 cm) that is placed via the right femoral vein and introduced into the left atrium using a transseptal puncture from the right atrial side of the heart (Fig. 4).

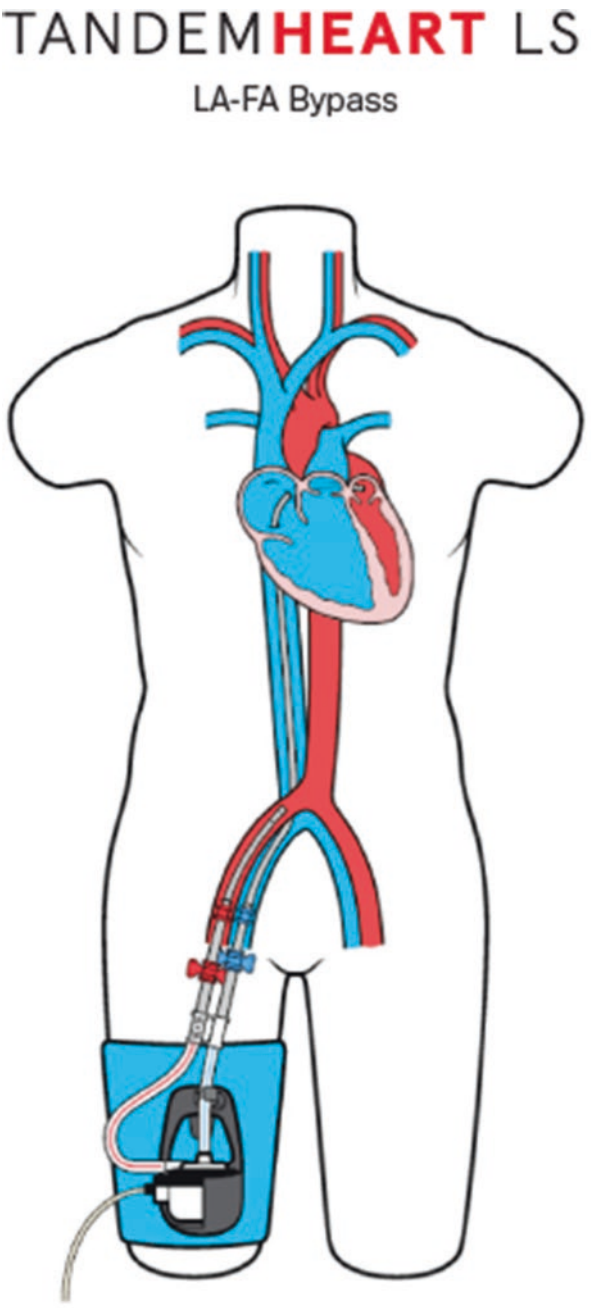

Fig. 4 Tandem configuration

The blood is pulled from the left atrium of the heart, sent through a centrifugal pump, and then placed back into the body via a short cannula (typically a 15 or 17 Fr) in an artery, usually femoral.

Indications and Contraindications

Indications for use include any form of left ventricular failure including but not limited to acute, chronic or acute-on-chronic heart failure, myocarditis, and acute myocardial infarction. This device may also be paired with a right ventricular support device to provide biventricular support to the patient. This support can be continued until a determination is made of myocardial recovery, until the patient can be bridged to durable support device or heart transplantation or terminal wean for palliative care [14].

Support is contraindicated for those patients with irreversible pre-existing conditions limiting survival such as those who are not candidates for transplant or durable VAD or non-recoverable disease such as advanced malignancy, unwitnessed cardiac arrest or prolonged CPR due to likelihood of severe anoxic brain injury, severe end organ dysfunction, severe coagulopathies, or recent or expanding hemorrhage, especially in the brain. Patients with a left atrial thrombus or very small peripheral vasculature are considered borderline candidates for therapy and must be considered carefully prior to selection.

Weaning of the device is done by slowly turning down the flow on the pump while monitoring the patient. If the patient cannot be weaned to recovery, advanced therapies such as durable VAD or transplant, or a terminal palliative wean would need to be considered.

Complications

Potential complications related to the insertion of LA to FA bypass include bleeding from cannulation sites, peripheral vessel perforation, distal ischemia, complications with the transseptal puncture such as puncture of the wall of the left atrium, or complications due to the cannula falling back into the right side of the atrium causing shunting of deoxygenated blood to the body. Other more generalized complications such as bleeding due to anticoagulation, thromboembolism, infection, neurological injury, and kidney failure can also occur [15].

Right Atrial to Pulmonary Artery Bypass

Right atrial to pulmonary artery bypass (RA to PA bypass), more commonly known by its typical trade name of Protek Duo (LivaNova, London, UK), is a method of mechanical cardiopulmonary support which was introduced in 2014. When a patient

has severe right ventricular failure that may rapidly progress to another form of support, such as a heart transplant, or when the cause may be reversible, this device may be considered for use. RA to PA bypass typically must be deployed with the availability of both fluoroscopy and pulmonary pressure monitoring capability by the trained physician.

Highly specialized care is needed for these patients once they are on this device and should only be undertaken by staff who have trained extensively for their management. Close attention needs to be paid to the fluid volume status as these pumps are preload-dependent. Frequent assessment of cannula kinks, chatter present, arrhythmias, intravascular volume, and filling pressures need to be evaluated. Similar to LA-FA bypass, cannula securement is very important with the Protek Duo. Because there is only one cannula site in neck, ambulation with this device is much easier. Tandem provides a vest to help secure the pump, but extra precaution should be taken whenever moving the patient.

Configuration

An RA to PA bypass device circuit is typically comprised of a long dual-stage cannula (29 or 31 Fr). Typical access site is the right jugular vein due to ease of placement via this approach, though other cannulation styles are possible. The cannula is positioned with one opening in the pulmonary artery and one opening in the right atrium. The blood is pulled from the right atrium, sent through a centrifugal pump, and then placed back into the pulmonary artery (Fig. 5).

Indications/Contraindications

Indications for use include any form of right ventricular failure including acute myocarditis, myocardial infarction, pulmonary embolism, etc. This device may also be paired with a left ventricular support device to provide biventricular support to the patient, including those with right ventricular failure following acute or durable LVAD placement, as well as other progressive myopathies. This support can be continued until evidence of recovery or as a bridge to heart transplantation, or palliation. Typically patient's requiring biventricular support without evidence of right ventricular recovery would not be considered for durable VAD, though there may be exceptions in rare cases.

Support is contraindicated for those patients with irreversible pre-existing conditions limiting survival such as those who are not candidates for transplant or non-recoverable disease such as advanced malignancy, unwitnessed cardiac arrest or prolonged CPR due to likelihood of severe anoxic brain injury, severe end-organ dysfunction, severe coagulopathies, or recent or expanding hemorrhage, especially in the brain.

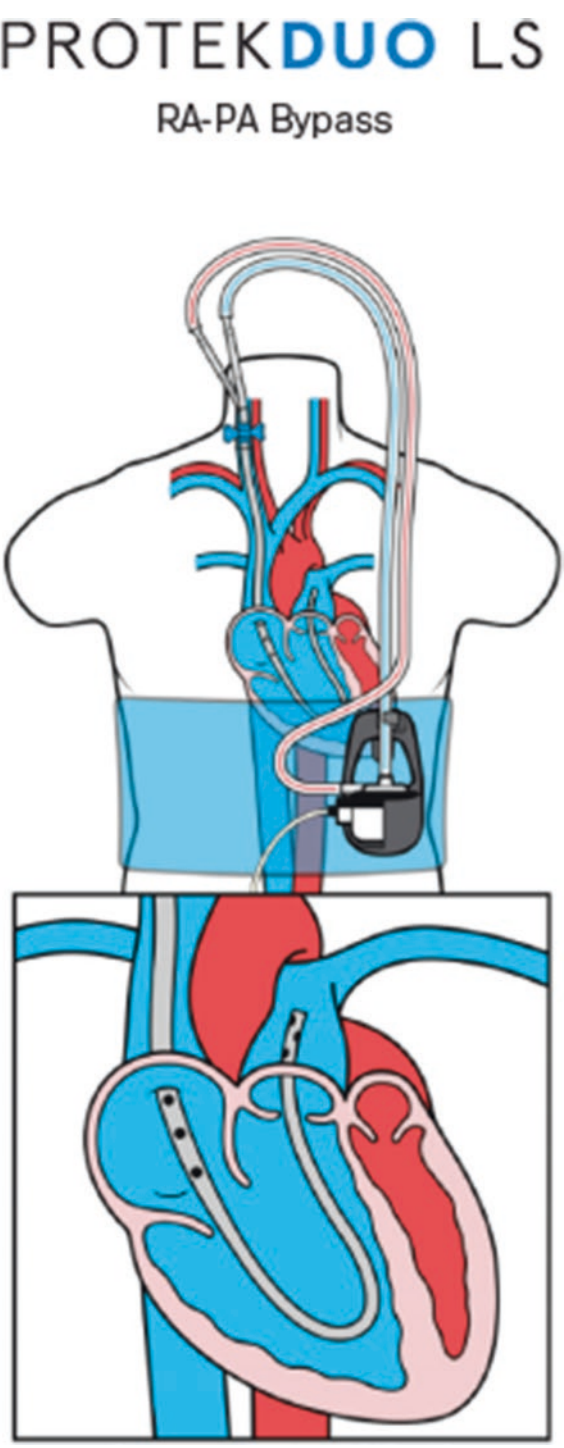

Fig. 5 Protek Duo cannulation

Complications

Potential complications of RA to PA bypass include procedure-related complications such as bleeding from the venous site or peripheral vessel perforation. Other more generalized complications such as bleeding due to anticoagulation, thromboembolism, infection, neurological injury, and kidney failure can also occur [16].

Extracorporeal Membrane Oxygenation (ECMO)

Extracorporeal membrane oxygenation, more commonly referred to as ECMO, is a method of mechanical cardiopulmonary support which was introduced in the 1970s but has become more frequently used over the past decade. ECMO may be utilized to manage severe biventricular failure (VA ECMO) or severe respiratory disease (VV ECMO) which is refractory to conventional treatment. ECMO deployment and management should only be performed by trained clinicians within prepared medical centers, and therefore transfer to an ECMO capable facility may be necessary for evaluation and care. Frequent blood draws from the ECMO machine are expected to monitor its function. Most programs require a perfusionist or ECMO Specialist to be at the bedside at all times to respond to emergent circuit issues like pump malfunctions, air in circuit, or clots in the circuit. In case of these emergencies, they are specially trained to exchange circuit and restore ECMO flow.

Configuration

An ECMO circuit is comprised of the following components

- an oxygenator, which oxygenates blood and removes carbon dioxide,
- the blender, which provides a mixture of nitrogen and oxygen to the oxygenator,
- centrifugal pump to continuously move the blood,
- large bore cannulas for blood drainage and return,
- the controller to allow the operator to adjust the settings (typically RPMs and sweep speed).

There are two types of ECMO: venovenous (VV) and venoarterial (VA), both of which provide pulmonary support by oxygenating blood but only VA ECMO provides hemodynamic support. ECMO can be used in the acute setting with bedside peripheral cannulation of the femoral venous/arterial circulation or can be placed surgically with central cannulation of the great vessels or cardiac structures. The surgeon can alter inflow and outflow cannulation sites based on the need for support and the patient's clinical scenario.

In VV ECMO, deoxygenated blood is extracted from the right atrium or vena cava by direct cannulation or via a cannula in the femoral vein or right internal jugular vein. The blood is passed through an extracorporeal circuit to be oxygenated and

filtered of carbon dioxide, then returned to the right atrium by direct cannulation or via a second cannula accessed in either the femoral vein or right internal jugular. Typically the femoral vein access is used for drainage at the junction of the IVC/right atrium and the right internal jugular for return to SVC/right atrium to minimize recirculation. In the VV method, blood does not bypass the heart and tissue perfusion is dependent upon the patient's own cardiac output and pulsatility.

In VA ECMO, deoxygenated blood is extracted via the venous system and then after being cycled through the oxygenator it is recirculated to the systemic circulation via the aorta either by direct cannulation or via a cannula in the femoral or axillary artery, bypassing the heart and lungs. By flowing directly into the systemic circulation, VA ECMO results in an increase in afterload, which needs to be considered when managing acute cardiogenic shock, as this may result in increased LVEDP and worsen LV strain, ischemic and ventricular arrhythmias. Commonly, an LV vent is placed to actively reduce the LVEDP while relying on VA ECMO to provide sufficient hemodynamic support. The LV vent may be a surgical catheter placed via the pulmonary vein, LA or LV in the centrally cannulated patients or a percutaneous MCS device such as an Impella CP, TandemHeart, or IABP.

Indications/Contraindications

Indications for ECMO initiation include hypoxemic respiratory failure despite optimal ventilator settings, hypercapnic respiratory failure, massive pulmonary embolism, failure to wean from intraoperative cardiopulmonary bypass, scenarios of severe biventricular heart failure requiring support and may be needed as a bridge to lung or heart transplant or surgical ventricular assist device (VAD).

ECMO support is unsuitable, and therefore contraindicated, for irreversible preexisting conditions limiting survival such as those who are not candidates for transplant or durable VAD, non-recoverable respiratory disease, advanced malignancy, unwitnessed cardiac arrest or prolonged CPR due to likelihood of severe anoxic brain injury, severe organ dysfunction, coagulopathies, or recent or expanding hemorrhage.

Complications

Potential complications of ECMO include bleeding due to continuous anticoagulation and platelet dysfunction, thromboembolism since thrombus may form within the circuit, infection, neurological injury, kidney failure, heparin-induced thrombocytopenia (HIT). There are also cannula-related complications including distal ischemia, vessel perforation, and arterial dissection. Complications specific to venoarterial (VA) ECMO include cardiac thrombosis, pulmonary hemorrhage or edema, and cerebral hypoxia due to North-South (Harlequin) Syndrome (reference). North-South Syndrome may occur in cases of femoral cannulation of VA ECMO due to poorly oxygenated blood being distributed from the impaired lungs

to the ascending aorta to perfuse the upper body and brain while the ECMO circuit supplies well-oxygenated blood to the lower body. This causes a cyanosis of the upper body and hyperoxia of the lower body. A hybrid VVA ECMO configuration, i.e. the addition of a right internal jugular cannula integrated into the circuit, may improve this uneven perfusion issue.

As mentioned earlier, VA ECMO does not unload the left ventricle so due to stagnant LV blood and increased filling pressures, ECMO places the patient at risk for cardiac thrombosis, pulmonary edema, or pulmonary hemorrhage. In this instance, LV decompression via a surgical vent, IABP, or percutaneous left ventricular assist device (Impella) may be warranted.

Conclusion

Temporary MCS devices have been gaining in popularity and becoming more widely used as a means to bridge patients to transplant and to stabilize end-organ dysfunction prior to VAD implant. The various devices discussed in this chapter highlight their ability to support very complex hemodynamic needs. These pumps require skilled monitoring and in-depth understanding of device mechanism of action, placement of catheters, and potential complications to be successful in use. Each device is tailored for a specific purpose and is chosen based on the appropriate need for the patient's condition. With design changes over the years, it will be interesting to see what the future holds for temporary MCS use.

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Administrative Aspects of the Ventricular Assist Device Program

Peggy Blood, Kathleen Davidson, and Anne Luke

Development

First and foremost, identifying the need for a VAD program is essential. Many variables are evaluated to determine if a VAD program is necessary and is an appropriate business strategy for an institution. One of the first steps is to undergo a market analysis and estimate the number of prospective LVAD implants that may take place annually within the institutional catchment area. The financial and business leadership of the institution should be able to guide this determination by assessing the center's heart failure referral data, readmission rates and length of stay for patients with advanced heart failure. Some organizations welcome the input of VAD manufacturer partner representatives who can assist with accessing regional data.

Upfront Costs

It is important to anticipate that initially a VAD program may not be cost effective due to the amount of capital expenditures needed to establish the infrastructure. Conversely, not only will the VAD program provide direct revenue for the institution, it will also produce an increase in returns for the medical center via the

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downstream revenue associated when evaluating a patient for candidacy. During the evaluation phase for a VAD, the candidate may undergo many procedures, surgeries, electrophysiology procedures, and tests, which are all associated with revenue for the institution. Many of the potential candidates will not meet the criteria for advanced therapies but the clinical evaluation for candidacy will be profitable for the health system. This is an important factor to present clearly to hospital leadership to garner full support of this expensive endeavor [1, p. 932].

Leadership and Team Structure

To ensure a successful program having capable, motivated, and effective VAD program, leadership is vital [2]. The core VAD program leadership should include the following:

- Qualified cardiothoracic surgeon with training and experience in mechanical circulatory support (MCS) implantation and management.
- Qualified advanced heart failure cardiologist.
- Either or both surgeon and cardiologist mentioned above will serve as Medical or Surgical Director with responsibility to oversee the program clinical practices, assess, and manage patient selection, quality outcomes, regulatory compliance, and financial contributions to the organization.
- VAD Coordinator will assist with creating and evaluating policies, initial and ongoing MCS education, and periodic competency assessments. Clinical responsibilities include troubleshooting device malfunctions, monitoring during procedures, facilitate treatment of complications, outpatient clinic management, as well as manage data management systems, i.e., INTERMACS registry. Physician Assistant, Nurse Practitioner, Registered Nurse, Biomedical Engineer, and Perfusionist are the common roles to fulfill this position. It is common in Europe for a surgeon or engineer to fill this role. It is critical to protect the scope of practice within the law.

  Additional team personnel to identify include:

- Additional VAD Coordinators: Establish triggers to recruit and hire additional staff members when programmatic growth begins to rise.
- Data personnel: Programs may choose to partner with an existing quality department in the initial stages of development. It is important to have a dedicated team member that is specific to the VAD program to evaluate metrics.
- MCS Educators: Typically these responsibilities are yielded to the VAD Coordinator initially however as the program grows, leadership should consider partnering with unit educators or establishing a dedicated role within the VAD program.
- Equipment management personnel: Typically new programs designate the VAD Coordinator for this role and identifies alternate non-licensed personnel later as the program increases in size.

- Social worker: In the United States, it is a regulatory requirement to have a social worker as a member of the core team who is knowledgeable in the unique needs of the VAD patient and caregiver.
- Palliative care services: In the United States, it is a regulatory requirement to have access to palliative care as needed and there be representation within the core team. Palliative care is specifically addressed in chapter "Psychosocial and Palliative Aspects of VAD Care."
- Psychologist: Should be knowledgeable of the unique needs of the VAD patient and caregiver. Many programs consider clearance from psychiatry vital to ensure the patient and family can handle the device and the mental health strains that accompany VAD therapy.
- Physical therapist and occupational therapists: It is crucial for patients recovery to ensure increased physical activity. This is addressed in detail in chapter "Exercise and Physical Therapy with Ventricular Assist Devices."
- Nutritionist/dietician: Nutrition before and after LVAD implantation are vital to successful outcomes for wound healing and ensuring appropriate caloric intake. This is described in further detail in chapter "Exercise and Physical Therapy with Ventricular Assist Devices."
- Financial team representatives: As discussed in chapter "Reimbursement in Ventricular Assist Device Implant and Care," ensuring appropriate and accurate billing and coding is crucial to ensuring financial integrity. This is also a key factor in discussing with the facility administration when increased resources are needed.
- Anesthesiologist: It is important to collaborate with the provider team for safe anesthesia during the implant operation and subsequent procedures requiring anesthesia.
- Specialty service partners: Gastroenterology, Infectious Diseases, Nephrology, Neurology, and Neurosurgery should preemptively be included.

Cost Analysis

Once the core team is established and in agreement, a presentation to the hospital leadership should be developed with the intention of securing their support. A great deal of attention will be centered around the costs and revenue associated with the program. Prepare a thorough financial analysis which includes community need, patient benefits, marketing strategies, program infrastructure, in addition to capital and operating expenditures. This should encompass items such as salaries and benefits, hospital owned equipment, single use equipment items, and operating items, such as office supplies. It will be vital to demonstrate all anticipated revenue; this includes not only the surgical implant but the evaluation period as well as the longer term revenue for the length the patient is on support. Items to consider discussed here include echocardiograms and right heart catheterizations.

When presenting to hospital, leadership create a clear and large scale vision that will be encouraging while including the possible short-term positives. Successful programs need to be built on evidence-based practice and expert recommendations

to gain administrative support. An essential factor to ensure support is aligning the initiatives with national priorities, especially those that are avant-garde and specific to the institution. Once funded by the institution, it is important to provide frequent program updates to help transition from being helpful to a becoming fully committed in the support of the successes of the LVAD program [1, p. 933]. Remember that this is not a one-time venture. It is crucial to keep the administration on board for long-term support.

Preparing for Implantation

Once the core team is established, an educational roll out is needed for the team and facility. Education is critical, and it is important to start with a structured competency model. An education model to consider is one that has tiers that range from VAD awareness to VAD expert. Staff resistance to this change should be anticipated. It is important to recognize that culture change is fundamental to program success [3, p. 509]. Having unit-specific VAD Champions is a helpful way to decrease the staff resistance. Education will be a big endeavor for the VAD Coordinator in the beginning of the program and ensuring early success is key. Utilization of the unit champions and staff educators can assist with the long-term education that will be needed periodically. Various units such as the operating room (OR), emergency room (ED), interventional radiology (IR), gastroenterology lab (GI) have different educational needs and it will be easier on the VAD team if staff in these departments are empowered to do the ongoing education that is required within their own department.

If this is a destination therapy (DT) program, identifying a nearby heart transplant program is essential. Having a good rapport with the personnel at this transplant center is important, especially for patients who have LVADs as a bridge to decision or who later become bridge to transplant (BTT) [1, p. 934]. Having this relationship will help build the infrastructure for the new program and it would be helpful to align some of your policies regarding patient selection and long-term care of the patient.

Programmatic Guidelines

In the early years of the program, it is advantageous to develop guidelines as opposed to hospital policies so that changes can be made easily and quickly. Changes to administrative policies can take time to get on agendas for review. As the program grows and the “kinks” are worked out, then these guidelines can be converted to hospital policy as appropriate. Keep in mind policies are hard and fast rules for the organization, whereas guidelines are evidence-based practices established to reduce variation but may be modified in practice based on individual patient needs. Consider meeting with your department with oversight responsibilities for organizational policies to provide guidance within your hospital structure. Bear in mind, programs should not reinvent the wheel and should rely on team member exposure and prior

experience when starting the program. Networking with other established programs and utilizing guidelines shared from others will direct the program initially, then fine-tune them over time as your institution culture and practices are better defined.

Once these guidelines/policies are in place and staff is educated, the program is now ready to implant the first case. Multiple aspects happen simultaneously and while this is certainly very exciting, it is also an extremely busy time. Recognize this will become easier as the program becomes more comfortable, especially if there is a solid foundation within the team and education plan.

Certification

Hospital administration will need to determine which certifying agency should be evaluating the program; the Joint Commission (TJC) and Det Norske Veritas (DNV) are two US regulatory bodies that certify VAD programs. Depending on which certificating agency the hospital selects the VAD program will need to participate in a nationally audited implant registry. At the time of this writing, STS/INTERMACS is the only one of this sort. The VAD program will need to apply for participation in order to enter this first implant in a timely manner.

In the United States, the Centers for Medicare and Medicaid services (CMS) has determined certification is required for reimbursement of VAD medical care. CMS has granted DNV or TJC the privilege of being a certifying agency on their behalf. It will be necessary to implant one VAD into a patient prior to being eligible for certification, and thus reimbursement by CMS.

Generally, hospital administration will choose to cover all costs instead of delaying the start of the program [1, p. 934]. Further details on these certifying agencies can be found in chapter "Regulatory Agencies Impacting Mechanical Circulatory Support Programs."

Equipment

Equipment that supports the VAD patient should be considered within the administrative and organizational aspects of the program. Peripheral equipment requires tracking, long-term follow-up and replacing when appropriate. This is labor-intensive and should be considered from a financial mindset not solely for the equipment but also the personnel that are responsible for the maintenance. Having a relationship with a durable medical equipment DME company can be beneficial to take on this management. It may be financially advantageous to bill, track, dispense, and re-order equipment solely within the organization structure as discussed in chapter "Reimbursement in Ventricular Assist Device Implant and Care." Should this be the decision, advocate for an equipment manager or establish processes that limit the equipment management time requirements for the VAD Coordinator as this task can become very time consuming with a large number of patients. This activity is critical to revenue integrity, Food and Drug Administration (FDA) requirements, CMS

compliance regulations, and designated certifying agency standards. Mistakes can be costly for the organization and should not be taken lightly. As the program population grows, the equipment management tasks increase seemingly and exponentially.

Growth and Evolution

Long-term success of the program occurs with continued growth and good outcomes. These are both achieved when the team continues to work together. Long-term goals need to be established collectively as well as how to grow the program and when to add new team members. The program can grow quickly and if triggers for adding personnel are not set at the beginning, the program may suffer from VAD Coordinator burn out due to increased responsibilities. Reminding the administration that it takes at least 6 months to develop a VAD Coordinator to the competent level may be beneficial.

Continued Coverage

Often forgotten about for VAD program development is on call coverage during off hours. Programs must set up a system whereby the VAD patients can be in contact with a team member 24/7 in emergency settings. As this device is considered life supporting and mechanical, it does not always fall into the 9–5 timeframe when typical medical offices are open for patient care. The other area for administrator education is the variation from traditional cardiothoracic surgery patients. VAD patients are longitudinally, clinically managed by the VAD team unlike a patient with a CABG or a valve intervention which are transitioned back to their primary teams after a short time. The program population continues to grow which is a positive as the only loss of the patient is due to transplantation or eventual mortality.

Outreach

Outreach is critical in the beginning of a program. Educating the community and colleagues in health care about the new services provided by the VAD program is vital for growth. Referrals typically come from the cardiologist or primary care physician in the community setting and teaching them about VADs is part of the program's responsibility. Helping providers know when to refer a patient is vital to continuing successful referrals. Maintaining open lines of communication whether the patient is accepted as a VAD recipient or not helps gain more knowledge, and by extension, helps the program. Communicating program outcomes to the referring providers will maintain the relationship so they continue to refer patients. When a patient that is referred receives an LVAD, it is a good practice to request the patient to visit the referring provider. It is a great way to reinforce the timely referral: that the therapy is effective and the patient can do very well post-operatively. The patient will also be able to share their experience and thus market the program.

Lastly, developing a plan to align and prepare community resources to care for LVAD patients is critical to successful living away from the VAD center. Resources such as local first responders, often affiliated with fire departments and police stations but may include ambulance companies, need to be trained in emergency responses for a patient with a VAD. In urban areas with multiple VAD centers, it is possible these first responders have already been educated and simply notifying them of the program's initiating VAD services may be all that is needed. Collaborating with those other centers to share the burden of emergency management systems (EMS) training may be prudent. However, if the program is rural or isolated, the burden is solely on the implanting facility to prepare the EMS for responding to and transporting the VAD patient to the nearest appropriate resource. Additional community resources to consider are subacute and acute rehabilitation facilities, dialysis treatment centers, and cardiac rehabilitation programs. Each will need to be trained in caring for a VAD patient. Though this can be time consuming, this can be a great way to connect with the community and teach them about VAD therapy, taking the mystery out of the machine. Asking a VAD patient from that specific community is very useful to demonstrate the equipment but to also show the stability of a VAD patient. When possible, consider asking the specific VAD patient being referred to the treatment center to attend the training as a means of introduction.

Conclusion

In conclusion, excellent outcomes are the essence for success of a VAD program. The financial stability of the program, new or continued referral patterns, and support of hospital administrators are dependent on positive results. Sharing the program successes via media releases, leadership forums, and professional conferences or publications will inform all stakeholders of the value of the therapy. Furthermore, implementing a systematic interdisciplinary patient management approach from the point of patient selection to long-term care improves outcomes for LVAD recipients, and thus lends to the continued success of the program [3, p. 515].

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Psychosocial and Palliative Aspects of VAD Care

Martha Abshire Saylor and Shunichi Nakagawa

Psychosocial Risk at Selection

Beyond biological needs, end-stage heart failure patients experience a high degree of psychosocial needs as they are undergoing VAD evaluation. Many patients experience increased depression and anxiety as other physical symptoms worsen [1]. Quality of life for patients prior to VAD implant is often quite low [2, 3]. As heart failure patients experience increased functional decline, they are increasingly relying on their families and support network to meet medical needs, such as medication management and support to attend clinic visits, but also basic needs including food, housing, financial support, etc. In addition, the uncertainty surrounding the VAD evaluation can be unsettling for families [1, 4]. Many pre-implant psychosocial characteristics, such as adherence to treatment plan, mental health, substance use, and social support, influence clinical outcomes post implant [5].

The ethical evaluation of patients for MCS is rooted in a long history of exploring the ethics related to transplant allocation. Evaluation procedures vary between hospitals as does the composition of the teams who do the evaluations. Common multi-disciplinary team members include a psychiatrist, social worker, financial counselor and palliative care physician in addition to the cardiology and cardiac surgery teams. Recent guidelines have provided more structure for VAD centers on which to base their psychosocial evaluation of patients [5–7]. Regardless of the

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procedures for evaluation, it is critical that VAD centers continually ensure equity in their evaluation process and assess if the psychosocial evaluation is yielding the information necessary to support successful patient outcomes.

The psychosocial evaluation often times will begin with a thorough assessment including cognition, mental illnesses, substance use disorder, suicidal ideation or self-injury and other psychological history [5, 8]. During this psychological evaluation, it is also critical that clinicians evaluate the patient's knowledge of the VAD and ability to operate the device. It is also important for the VAD team to begin to understand how the patient coped with their heart failure so that they can better support them as they cope with their VAD.

The social components of VAD evaluation include several features like financial and health insurance evaluation, home safety and access to reliable electricity, and social support [5, 8]. The identification of a full-time caregiver is a limiting criteria for many patients who would otherwise benefit from a VAD. However, most centers maintain a strict criterion for this full-time caregiver at least through the first few months post implant. The rationale for this criterion is rooted in experience, but there is little evidence to support this criterion among VAD patients.

While the patient is of course the focus of the psychosocial evaluation, it is critical to also evaluate the caregiver and social support [5, 8]. Caregivers will be relied upon after VAD implant to provide physical care, learn equipment management, provide household ADL and IADL support, and provide emotional support while themselves giving up much of their own professional and personal lives. While patient quality of life increases after VAD, caregiver quality of life often decreases [9]. Caregivers can experience burden depression and even trauma following the implant of a VAD [4, 10]. There is little ongoing assessment of caregivers and even less support to caregivers provided by the VAD team. Improving family-centered models of VAD care would include annual assessment of caregivers, changes in the home context and family, re-evaluation of financial concerns, and assessment of quality of life in both the patient and the caregiver. Re-evaluation of patients and families is common for bridge to transplant patients, however, it is less common among destination therapy patients. This highlights the importance of maintaining a relationship with the palliative care team as supportive therapies may benefit not only the patient but also the caregiver and their family.

Stress, Coping, and Support After VAD Implant

The care and management of a VAD patient is intensely medical. The focus of the care team on the medical aspects VAD management is essential to positive clinical outcomes. However, equally critical is a focus on the psychosocial coping and adaptation of VAD patients and their caregivers as they learn to manage this complex therapy. Normalizing the transitions that many VAD patients experience can help patients and caregivers set realistic expectations for themselves as they manage the VAD in the chronic setting.

Four phases have been described that are typical in adjustment to VAD: pre-VAD, implant hospitalization, early home, and late home adaptation phases [11]. Many patients will compare the pre-VAD phase to all later phases. Psychosocial aspects of the pre-VAD phase include experiences like cognitive impairment, existential crisis, trauma, and stress management while waiting for the device [12, 13]. Socially during the pre-VAD phase, patients and caregivers have had significant role changes and the family is providing a large amount of support while the patient experiences severe functional impairment [13, 14]. While in the hospital, after implant surgery, patients initially experience a significant adjustment to their own self-image including scarring, driveline appearance, and dependency on batteries. Stresses include equipment management, fear of transition to home, and some patients experience post-implant depression or even post-implant trauma [15, 16]. During the implant hospitalization, social aspects of VAD adjustment include increased dependence on the VAD team and involvement of the caregiver in equipment training [12, 13, 17].

Discharge from the implant hospitalization is extremely burdensome and scary for both patients and caregivers [12, 15, 17]. Many caregivers report feeling completely overwhelmed in the transition to home and patients are reliant on their caregivers which can be difficult for their relationship. Caregivers report not being able to sleep for fear of missing VAD alarms and having a sense of constant vigilance [4, 10, 18]. Patients focus on the difficult surgical recovery and feeling overwhelmed at the thought of managing this complex device for the rest of their lives [12, 13, 15–17]. Patients in early home transition slowly develop confidence with the basic device skills. Often they'll have increased functional capacity and will be able to engage more and more with family and friends. Patients and caregivers during the early to home transition phase are very connected to the VAD care team and will build a strong bond with their VAD coordinators. During this time, they need reinforcing education about the device, medication management, anticoagulation, and careful expansion of daily activities, especially bathing [19]. Social challenges include introducing the VAD to people who do not understand it, including non-VAD team healthcare providers, and managing these social interactions can sometimes be difficult.

After about 3 months, most patients will enter the late home adaptation phase. This is when VAD management becomes chronic and where the focus is on establishing normal routines, re-establishing family roles, and increasing independence. Often as patients approach 6 months past VAD, they are able to express gratitude for the device, their decreased symptoms, and reflect on how their fear has decreased as they have become more comfortable. In many cases, they are also able to describe increased intimacy, even physical intimacy, with their partners after having faced such a difficult journey together [20]. Charging and changing batteries becomes second nature, medicines are better understood and driveline management becomes more routine. Socially patients can increase outings, may return to work and establish a "new normal" [11, 15]. Also, implant strategy can influence this late home adaptation phase. There is some evidence that destination therapy patients, despite the challenges of not having additional therapies as an alternative, may reach a

higher quality of life than those who are waiting for a heart transplant [21]. This is attributed to the uncertainty in the period while waiting for a heart.

VAD coordinators and teams should be prepared to assess and support psychosocial adaptation to the VAD. Understanding the challenges that patients and caregivers face especially when transitioning to home is critical to supporting their needs. Building in assessment of patient stress, depression, anxiety, and quality of life is common if VAD clinics participate in registries such as STS-INTERMACS. However, resources to address these needs can be scarce, and it is easy for the VAD team to focus on medical needs above psychosocial needs. For this reason, it is critical to engage the multidisciplinary team, including palliative care, which can support ongoing assessment and identification of resources to help support patients. It may be helpful to address coping in two ways through problem-focused and emotion-focused coping. After assessment and careful evaluation of patient needs, VAD coordinators and teams can prioritize problems and co-develop strategies to address them. For instance, because the transition to home following hospital discharge is so difficult, perhaps the VAD team would consider video calls to help caregivers with initial equipment setup. Or perhaps the caregiver is struggling to do driveline dressing changes and a home health nurse could be consulted for additional teaching. Emotion-focused coping can be complex and often takes more time. Patient and family education that helps establish realistic expectations for recovery and adaptation to living with a VAD can be very supportive. In addition, normalizing the emotional sequelae after VAD is a powerful tool. Many patients may benefit from outside resources such as a therapist, counselor, or even meeting members of the religious community of the patient.

Social isolation, fractured relationships with caregivers, depression, and even suicidal ideation have been reported after VAD implantation. These psychosocial challenges can negatively impact clinical outcomes and should be addressed early to mitigate negative consequences.

To date, there have been no randomized control trials testing interventions to address the psychosocial needs of patients and caregivers after VAD implantation. However, VAD clinics internationally have complex programs which incorporate many features of psychosocial support. Some components to integrate psychosocial support within VAD programs include regular support groups for patients and caregivers and annual trainings to reinforce teaching regarding driveline care and equipment management. In addition, understanding the challenges of stress and coping with the VAD highlights the importance of a multidisciplinary team to address these challenges. Engaging social workers, case management, home health, psychologists, palliative care, and chaplains can lighten the burden on the VAD team while also increasing the breadth of resources provided to the patients and their families.

There are also several ways for VAD patients and caregivers to connect via social media. MyLVAD.com is one source but there are also Facebook groups and local support groups for patients to connect. Common topics discussed include figuring out inventive ways to wear VAD equipment so that the weight is not too burdensome or to facilitate fashion or style. In these forums, many patients also discuss waiting for a heart and how difficult it is living with that uncertainty. Sometimes caregivers

will disclose their fears differently to other caregivers which can be supportive. Living with a VAD poses unique challenges but these online communities provide a sense of normalcy, creativity, and resourcefulness.

Palliative Care Consultation Before LVAD Implantation

LVAD patients are heavily burdened physically, psychologically, psychosocially, spiritually, and financially [11, 22]. When patients face the end of life, LVADs can pose unique challenges because of their peculiar characteristics as life support [10, 23]. Joint Commission and Center for Medicare and Medicaid Services [24, 25] have announced the regulatory mandate for the involvement of palliative care specialists in the care of DT LVAD patients. Both ISHLT and AHA/ACC guideline suggests palliative care consultation before LVAD implantation for both DT and BTT [6, 26, 27]. Yet, there is no consensus regarding the degree of involvement of palliative care team, and it is highly variable depending on institutions.

In palliative care consultation before LVAD implantation, advance care planning to address LVAD-related issues is particularly important, because LVAD therapy can pause its unique challenges after implantation. While the technology of devices has been advancing and the rate of complications decreased, there are still risks of catastrophic LVAD-related complications or device malfunction [28]. Multiple complications and prolonged hospitalizations could cause an inadequate post-LVAD quality of life. Furthermore, even if LVADs work perfectly, other debilitating medical problems such as dementia or cancer could occur. Specialized type of advance care planning to address these challenges is referred to as "preparedness planning" [29, 30].

Multiple semi-structured scripts have been developed for these pre-implant advance care planning [31, 32]. Reports in 2010–2011 showed that the prevalence of advance care planning conversation was between 28.9% and50.0% [33], but more recent reports between 2017 and 2018 showed it is 71–89% [30, 31, 34]. A single-center study showed that palliative care consultation with the use of semi-structured script was feasible in both bridge to transplant and destination therapy, and it helped increase the family's awareness of patient's unacceptable health states [31].

While there may be some concerns about the palliative care team's involvement before LVAD implantation, studies have shown that this pre-implant palliative care consultation resulted in positive outcomes. Advance directive completion before LVAD implantation increased [30, 31]. A qualitative study showed that the LVAD team has overall highly positive impressions of palliative care specialists, with perceptions of improved patient and family experience and decreased burden on LVAD team members [35]. Another study showed palliative care consultation before LVAD implantation was associated with fewer deaths in the intensive care unit and less use of mechanical ventilation and renal replacement therapy at the end of life [36]. On the other hand, challenges of preparedness planning have also been pointed out. While it is reported that palliative care consultation occurs within 1–9 days

before the LVAD implantation [30, 31, 36, 37], the best timing of preparedness planning has not been well established. It has also been pointed out that preparedness planning takes time and the time constraints of palliative care teams could become a barrier, and that palliative care providers sometime lack understanding of VAD preparedness planning [37]. A future direction for consults could be nurse or coordinator-led palliative care consultation; this approach has been tested in a small pilot with nurses with basic palliative care skills [32].

End of Life with LVAD

Many patients with LVADs experience end of life with the device in place. This is not avoidable with DT patients, and it is also very likely with BTT patients when they have a catastrophic event before undergoing heart transplantation. It is very challenging to provide end-of-life care to LVAD patients, especially to clinicians who are not familiar with the management of LVAD devices, because of the increasing symptom burden and the frequent need for medical care. As such, while some hospice agencies are willing to take care of LVAD patients at the end of life [38, 39], the rate of hospice enrollment is still very low [40–42]. A study from the INTERMACS database reported that, among 4769 deceased patients with LVADs, 76.9% died in the hospital and that out-of-hospital death increases with longer duration of survival after LVAD implantation (i.e., <1 month, 2.3%; 1–12 months, 16.8%; and >12 months, 37.4%) [40]. Other smaller studies from single institutions reported patients' death frequently occur in the hospital (75.9–77.6%) and most of them died in the ICU (83.3–87.7%) [36, 42]. Cause of death varies depending on the time from LVAD implant. While multisystem organ failure, neurological dysfunction, and right heart failure are most common <1-month post implant, neurological dysfunction and device infection dominate >12 months [40].

What makes the end of life of LVAD patients peculiar is considerations around withdrawal of LVAD support. While some patients continue LVAD therapy until they die, other patients, or their surrogates, may request withdrawal of LVAD therapy. INTERMACS database reports "Death Following Withdrawal of Support" as the third most common cause of death [40], and it is reported that 43–60% of deceased patients with LVADs died after the withdrawal of LVAD therapy [41, 42].

LVAD therapy is unique as a life-sustaining treatment because it is continuous and long-term, and it also takes over an essential function of the organ that cannot be provided for itself. Often this uniqueness may cause discomfort on clinicians with the withdrawal of LVAD therapy. It is known that cardiologists and palliative care physicians have different perspectives regarding LVAD deactivation. One survey showed that while 60% of cardiology clinicians think a patient should be imminently dying to deactivate an LVAD, only 2% of palliative care clinicians do so [43–45]. Some clinicians consider that deactivation of the device under any circumstances is more akin to "killing" than "allowing to die" because

a patient with a VAD does not have a terminal illness [46, 47]. Cardiology clinicians were noted with lower levels of comfort with deactivating a device (26%), high rates of refusing to deactivate an LVAD (17%), and greater concern that turning off an LVAD is akin to euthanasia or physician-assisted suicide (13%) [43, 44].

However, LVAD therapy is generally accepted as life-sustaining treatment and is regarded as the same as mechanical ventilation, renal replacement therapy, and artificial nutrition or hydration. Basic ethical principles in Western countries include that a patient with decision-making capacity has the legal right to refuse or request the withdrawal of any medical treatment regardless of whether s/he is terminally ill. Also, ethically and legally, there is no distinction between withholding therapy and withdrawal of therapy [48]. Pellegrino suggested a question-based algorithm for withdrawing life-sustaining treatment, and two important questions are "Who decides?" and "By what criteria?" [49]. Each patient weighs the benefits and burdens of treatment based on their unique goals and values. Accordingly, as long as the burden of the LVAD therapy outweighs the benefits, in other words, if the quality of life which is achieved by LVAD therapy is not good enough, the patient (or their surrogates if the patient is incapacitated) has the right to request the deactivation. Clinicians should not impose their values on patients. If clinicians feel uncomfortable due to their moral views, they should not be compelled to participate in the process of withdrawal, but in that case, they should not abandon the patient and should look for a clinician who is willing to deal with the issue [48].

Not surprisingly, this process to explore patient's unique goals and values requires sensitive communication, and palliative care specialists could be most helpful. The patient's unique goals and values must continue to be shared with surrogates and clinicians throughout the disease trajectory, ideally starting pre-LVAD implant. When withdrawal of LVAD therapy is considered, while patients' unique goals and values have to be prioritized, it is ideal that surrogates and clinicians are in agreement that the patient is suffering and continuing the LVAD therapy is more burdensome than beneficial. Conflicts typically occur when there is a misunderstanding among patients, surrogates, and clinicians regarding the medical condition, prognosis, and goals and values of patients. Conflicts may be resolved by negotiation, ethics consultation, pastoral or psychological counseling [50], or palliative care consultation, but it could take some time. One study reported that the majority of LVAD deactivation happened in the ICU (83.6%) and the time for conflict resolution was significantly longer outside the ICU. Especially, it is more challenging when patients with decision-making capacity requested withdrawal of LVAD therapy, and it took 46 days outside the ICU compared with the 1 day in the ICU [41].

In a recent assessment, less than half of institutions have protocols for LVAD deactivation [50]. An interdisciplinary team checklist for the deactivation of LVADs is available to support teams needing to develop institutional protocols [51]. The actual process of deactivating the device is akin to that of ventilator withdrawal [52]. But clinicians should be aware that most patients die in a relatively short

period, just minutes to hours [42], that symptoms such as dyspnea, agitation, or anxiety will have a rapid onset after the device deactivation and, additionally, that the time to peak effect of the medication will be delayed due to the diminished circulation [52]. Accordingly, it is advised that enough opioid and benzodiazepine is given to the patient before deactivation so that the symptoms will be well controlled during the dying process. The palliative care team is an excellent resource to provide the best symptom management as well as the maximum psychosocial support to families throughout the dying process.

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Professional Organizations in the Mechanical Circulatory Support Community: An Opportunity to Network

Michael Petty

Organizing Your Search

Identifying which groups MCS clinicians should seek membership can be complicated. Societies with an interest in mechanical circulatory support—either solely or as part of their larger mission—are wide-ranging. MCS overlaps clinical fields, such as heart failure, heart transplantation, artificial organs, biomedical engineering, cardiology, cardiac surgery, pediatrics, nursing, social work, and more. As a result, MCS may have a smaller or larger footprint in any one organization.

Membership in professional organizations often involves membership dues. Meetings will also mean incurring expenses for travel, registration, housing, and meals. Each of those factors may help you to rule out an organization because it is "not in the budget." However, before crossing one off your list, consider the cost/benefit ratio. Perhaps selecting one organization with significant benefits as described above will be more effective for you than joining three organizations with lesser costs but also fewer benefits related to your goals for membership.

Often the first step to narrowing your list of options is to ask colleagues about the organizations they have joined and which meetings they find the most relevant to their practice. From those recommendations, you can begin to focus your search and learn which organizations would meet your specific interests and needs. Another strategy is to identify groups that focus on addressing the needs of MCS professionals with similar credentials to your own.

The following are three possible approaches for finding your way through the variety of organizations linked to MCS and provides illustrations in each category. This list of examples is not intended to be exhaustive rather to identify a few of the notable organizations from each search strategy.

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Technology-Specific Search

One organization whose name most directly reflects its focus on the MCS clinician is the **International Consortium of Circulatory Assist Clinicians (ICCAC)** (https://iccac.global). Founded in 2007 by VAD coordinators from across the United States, ICCAC is dedicated to sharing information; educating, supporting, and mentoring individuals in the MCS field to achieve optimal outcomes for patients; and promoting clinical research and development. Its membership is global and its leaders have come from North America, Europe, and Australia. ICCAC holds its annual meeting in collaboration with other organizations (ASAIO, ISHLT), offering educational content relevant to practitioners.

The International Society for Mechanical Circulatory Support (ISMCS) (www.ismcs.org) is specifically focused on science and research around the use of rotary blood pumps and publishes in the journal *Artificial Organs*. The annual EUropean Mechanical Support Summit (EUMS) (https://www.congresseums.com/) meeting brings together physicians, engineers, inventors, and MCS clinicians interested in mechanical circulatory support. This conference is held in collaboration with the journal *Artificial Organs*.

ASAIO (https://asaio.org/) was originally called The American Society of Artificial Internal Organs. They retained the acronym but have updated their title to "Science, Medicine and Industry—Innovating for the Future." ASAIO was founded more than 60 years ago and cites its mission as "saving lives one medical device at a time." The organization has dedicated specific space in their annual meeting and scientific sessions to mechanical circulatory support and the clinicians and engineers involved in technological development and refinement. Membership includes a subscription to the *ASAIO Journal* which contains many articles on MCS.

Similar to ASAIO, The European Society for Artificial Organs (ESAO) (https://www.esao.org/) brings together an international representation of clinicians, engineers, and inventors dedicated to improving lives through technical innovation. Also with a journal (*International Journal for Artificial Organs*), ESAO collaborates with the International Federation for Artificial Organs (IFAO) (https://ifao.org/), co-sponsoring meetings of mutual interest. Many of the topics on the agenda of their annual meetings and webinars are related to mechanical circulatory support.

Nursing Community of Practice-Specific Search

In the United States, the **American Association of Heart Failure Nurses (AAHFN)** (https://www.aahfn.org/) is comprised of nurses at the staff nurse and advanced practice nurse levels focused on the care of patients in all stages of heart failure. Their focus encompasses not only education and development of their members, but they also dedicate significant energy to educational materials for patients with heart failure. They publish the journal *Heart and Lung: The Journal of Acute and Critical Care*. Their annual meeting regularly includes speakers on topics related to mechanical circulatory support.

The **Canadian Council of Cardiovascular Nurses (CCCN)** (http://www.cccn.ca/) focuses on the care of patients with needs across the spectrum of cardiac care. CCCN publishes the *Canadian Journal of Cardiovascular Nursing*. Members attend the CCCN-sponsored spring conference as well as the Canadian Cardiovascular Society's (CCS) annual Canadian Cardiovascular Conference in the fall.

In Europe, the **Association of Cardiovascular Nursing and Allied Professions (ACNAP)** (https://www.escardio.org/Sub-specialty-communities/Association-of-Cardiovascular-Nursing-&-Allied-Professions) is affiliated with the European Society of Cardiology. Since its inception in 2006, it has grown in its international representation across Europe and beyond. They also publish the *European Journal of Cardiovascular Nursing* with manuscripts from across the continent. They sponsor an annual conference with extensive programming on a variety of heart disease topics.

The **Australasian Cardiovascular Nursing College (ACNC)** (https://www.acnc.net.au/home) provides an opportunity for nurses interested in cardiovascular care including MCS to collaborate. Affiliated with the ACNAP in Europe, the ACNC is dedicated to collaborating and promoting the advancement of cardiovascular nursing practice, research, and education. MCS coordinators looking for more local/regional connections in transplant may look to the **Transplant Society of Australia and New Zealand** (TSANZ) (https://tsanz.com.au/) or the **Transplant Nurses' Association (TNA)** (https://transplantnurses.org.au/).

Interdisciplinary-Specific Search

When thinking on a larger scale of organizations in which nurses are actively involved but which address a broader audience than heart failure/mechanical circulatory support, four organizations consistently top the list.

- The American Heart Association (AHA) (https://professional.heart.org/) (Journal: *Circulation*)
- Canadian Cardiovascular Society (CCS) (https://ccs.ca/) (Journal: *Canadian Journal of Cardiology*)
- European Society of Cardiology (ESC) (https://www.escardio.org/) (Journal: *European Heart Journal*)
- Heart Failure Society of America (HFSA) (https://hfsa.org/) (Journal: *Journal of Cardiac Failure*)

Each unites clinicians, educators, researchers, and scientists investigating and trialing treatments and interventions to improve the quantity and quality of life of patients in the heart disease space. You might join local/regional affiliates as well as the national organization. Their annual meetings include presentations on topics related to MCS among many other cardiology topics. Attendance is commonly large, drawing professionals from across the globe. Each has a nursing council within them: **AHA's Council on Cardiovascular and Stroke**

Nursing (CCSN) (https://professional.heart.org/en/partners/scientific-councils/cvsn); **CCS's Canadian Council of Cardiovascular Nursing (CCCN)** (see above); the **ESC's Association of Cardiovascular Nursing and Allied Professionals** (see above), and the **HFSA's Nursing Committee** (https://hfsa.org/hfsa-committees). Each of these councils hold sessions as part of the larger organization's annual Scientific Sessions.

The **International Society for Heart and Lung Transplant (ISHLT)** (https://www.ishlt.org) (Journal: *Journal of Heart and Lung Transplant*) draws clinicians, researchers, and scientists from around the world with interest in four interdisciplinary networks: heart failure and transplantation; lung failure and transplantation; mechanical circulatory support; and pulmonary vascular disease. Members in each of those networks are drawn to the organization's foundation of ten professional communities including the Nursing and Allied Health Professional Community (https://ishlt.org/membership-networking/professional-communities/nursing-and-allied-health). Members of each professional community align with and participate in the work of one of the four interdisciplinary networks. Like the other organizations, ISHLT's annual meetings include presentations of interest to all the networks and professional communities.

Once you have had the opportunity to explore the professional organizations that hold particular interest for you and have decided which you want to join, you will automatically be connected with other professionals working in the MCS community. The opportunity to network with those clinicians will be an invaluable experience.

Additional Benefit to Professional Organizations: Networking

Most professionals will report that their primary reason for attending meetings and workshops of their specialty organizations (whether regional, national, or international) is to enhance their knowledge, learn the results of the latest research, and identify strategies to translate that research into practice. However, taking advantage of the opportunity to meet and connect with others in your field during those conferences can be equally as valuable. It is in those extracurricular networking encounters that access to new opportunities can appear, the potential for collaboration can be identified, solutions to shared challenges can be discovered, and the chance to become a mentor or mentee can evolve. Engaging in those discussions, you will be noticed by others in your community. You have a chance to build your communication skills, enhance your self-confidence, and receive advice and support. Imagine all the interesting people you can meet.

The benefits of networking cannot be overestimated. Professional networking involves building connections and relationships in the workplace and in your identified community of practice [1]. It allows you to increase your understanding of changes happening in your profession, improve your opportunity for career advancement, communicate with other professionals, encounter new ideas, and become

involved in creating policies and standards in your field [1]. The premise of successful networking is a mutually beneficial interaction either between individuals or between individuals and groups [2]. Goolsby and Knestrick reported that in the literature, professional networking has been associated with reductions in staff turnover in primary care, clarified the value of roles in healthcare systems and within interdisciplinary teams, enhanced clinical autonomy, and facilitated the achievement of policy goals [2]. Importantly, in a world where such encounters may be face-to-face or virtual, we need to be open to taking advantage of opportunities in either format.

Networking starts with speaking up and being planful. It can involve something as simple as striking up a conversation with the person sitting next to you before a session starts or with a person in line with you for snacks or a meal [2]. When you look at the program of any large conference, you should be intentional to identify sessions and speakers in which you have specific interest. If you see an abstract or hear a presentation that particularly stimulated your thinking or with which you particularly resonated, make it a point to seek out the presenter. Take the opportunity to ask a question or engage in a brief discussion about their topic and how it related to your work or experience. Ask to share business cards. Offer to help them with reviewing an article, sharing a resource, or supporting their work. When social events are planned, make time in your schedule to attend them and introduce yourself to others in the room. Make an effort to learn what brings others to the meeting, what they are passionate about, what attracted them to their current job.

One of the important tools to create an effective network is involvement in professional societies [1, 3]. In those environments, you will encounter opportunities to volunteer on projects large and small. Like anything else involving relationships with others, networking takes time and continued effort. Involvement in professional organizations can be a path to regular connections with others in your community of practice. It can also provide a forum for introducing new members or colleagues, serve as a reminder to follow up on previous contacts or discussions, and provide ongoing opportunities to find new ways to connect with colleagues.

Summary

This chapter has reviewed the reasons MCS clinicians join one or more professional organizations, strategies for selecting which one(s) to join, and the benefits associated with the networking opportunities that are inherent in such membership. It is important for MCS clinicians to recognize the vast resources available to our practice community through connections with these organizations. When we encounter challenges or difficulties in the care of our patients or the organization of our team, it is highly likely that someone else has faced— and solved—a similar dilemma before you. Leveraging their knowledge in your work can reduce stress, save you time, and allow you to keep your focus on improving the quality and quantity of life for your patients. In addition, through these connections you can identify ways for you to grow in your career.

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Clinical Research and Applications to Mechanical Circulatory Support

Pamela S. Combs

Basics

Forming the Research Idea

The research idea is a conception that the inquisitive mind of the researcher sets out to explore. But, where does one start? The literature review is the first step in initiating the research process. Carrying out the review helps to provide a context of the idea, along with informing the researcher of past methodologies. Of note, if the trial replicates an already published trial, the odds of publishing are close to nil dependent upon the goal of the trial. Thus, the expended energy dedicated to the project might have been for nothing.

Failure to conduct an in-depth literature review is associated with several problems including: (1) the research not grounded in theory, (2) the production of a weak methodology, and (3) failing to expand knowledge beyond a single event [1]. Asking peers and mentors within the VAD community for feedback concerning the research idea is highly recommended. Their suggestions can be extremely invaluable as there are many great research mentors that are willing to guide the novice researcher. However, negative feedback does not represent the need to cease forward movement of the plan. The research topic may still have potential and simply need modification. Many researchers, who forged ahead, even though being discouraged by peers, have published monumental, LVAD benchmark studies. Thus, the final "take home" in this message is heed the advice of peers, but do not think your idea is not worth further investigation.

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Principal Investigator

The assurance that objective research that generates independent, high quality, and reproducible results occurs is charged to the Principal Investigator (PI) [2]. Additionally, the PI is responsible for the direction and oversight of compliance, financial, personnel, and other related aspects of the research. In simple terms, the PI is required to ensure that the research follows an ethical manner. Research is to be in alignment with all federal, state, and local laws, regulations, institutional policies, and the requirements of the ethics committee/institutional review board (IRB). It is advised to confirm with the researcher's affiliated organization's regulations if nurse, perfusionist, bioengineer PI assignment is allowed. For instance, some organizations do not allow LVAD non-physician clinicians to be a designated PI (yes, that still exists in some places!).

Protocol

Research team meetings should take place at the initial phase to clearly define the roles of each member; these members can encompass various LVAD roles such as perfusionists, pharmacists, and social workers. Thereafter, the trial team then writes the protocol, a written plan of the trial. No trial-related steps should take place until the regulatory board gives approval to the trial. A protocol describes the following: (1) the goal of the trial, (2) who is eligible to take part in the trial, (3) protections against risks of the trial, (4) possible benefits of the trial, (5) details about tests, (6) interventions, procedure, (7) duration of trial, and (8) information to be collected [3]. After the proposed protocol is submitted to the regulatory board for approval, the waiting begins. The regulatory board will review the application and the following are possible decisions: (1) approval, (2) minor changes required, (3) tabled for re-review, or (4) disapproval. If questions from the board occur, prompt yet detailed responses are required. It can be easy to take the board's determination personally, as the PI is very passionate about the proposed trial, but remaining focused on forward movement is crucial to the process. Simply put, do not regard it personally.

Types of Trials

In the protocol, design description is integral to clarity of the research plan. In the situation when industry leads the clinical trial, the project is referred to as an "industry-sponsored clinical trial." These entities are responsible for initiating, managing, or financing the clinical trial, but do not actually conduct the research [4]. Conversely, a clinical trial where the PI is the protocol author and leads the trial is termed a "PI-initiated clinical trial." Trials can involve a sole center or many centers. Because collaborations between programs and a large sample size (n) provide a level of generalizability, multi-center trials are encouraged. If it is a first-time trial

for the researcher, a single center trial is advised to assist in increasing confidence and knowledge in the process. Trials can occur at sites as varied as hospitals, universities, and in communities, to name a few.

Trial design can follow a retrospective or prospective design. The retrospective design typically involves a chart review or collection of data that occurred in the past [5]. Prospective designed trials collect data in "real time" and are considered the most desired between the two. With prospective design, consent is required.

Randomization

Randomization for a controlled trial is widely accepted as the best design for evaluating the efficacy of a new intervention because of the advantages of random allocation. Randomization is when two or more alternative treatments are assigned to volunteers by chance instead of choice. It eliminates accidental bias, including selection bias, and provides a base for allowing the use of probability theory [6]. An extension to randomization is the double-blind randomized controlled trial. Both randomization and blinding are common methods to assure higher quality outcomes of trials by preventing any subjective biases.

The term double-blind refers to the fact that both the researcher and the patient do not know which randomization group the patient is allocated. The advantage of this blinding is twofold: the researcher cannot affect the outcome of the study by knowing group assignment and the patient is not influenced by knowing their group assignment. The most common and basic method of simple randomization is flipping a coin. Other randomization methods are utilized within computer software programs.

Regulatory

Regulatory bodies govern trials in order to assure human protection of subjects is accomplished [7]. Typical criteria for board approval of protocols include (1) risks to subjects are minimized and have reasonable benefits; (2) selection of subjects is impartial and fair; (3) informed consent obtained is appropriate; (4) sufficient provisions for data monitoring exist to maintain the safety of subjects; (5) adequate mechanisms are utilized to ensure subject confidentiality; and (6) rights and welfare of vulnerable populations are protected [8]. Of note, some regulatory boards charge fees for submission so preparation for payment and/or budgeting of this fee will be necessary.

Good Clinical Practice (GCP) is an international standard that governments can transpose into regulations for clinical trials involving human subjects. GCP guidelines include standards on how clinical trials should be conducted and a definition of the roles and responsibilities of clinical trial sponsors, clinical research investigators, and monitors [8]. In performing ANY research, the LVAD clinician should know GCP as it is an underlying standard and foundation of research.

Data Collection

Quantitative

Quantitative research requires the reduction of an event to numerical values in order to carry out statistical analysis [9]. REDCap is a web-based software tool developed at Vanderbilt University in Nashville, Tennessee, USA, and is a very common tool used in data collection [10]. REDCap allows the researcher to choose and define their data elements thus tailoring the database to the particular trial at hand. Electronic medical records (EMRs) have assisted researchers in utilizing the desired data more efficiently and precisely. Such EMRs like EPIC provide the data that the researcher collects for the database.

Facilitated by rapid advances in data science and driven by everlasting effort to use up-to-date information, we are now facing a big data revolution [11]. There is tremendous potential for their utility in research. As we move on to the next era of data-driven medicine, big data research and health informatics will assist in new insights of caring for our patients. Examples of past quantitative research are those that review adverse events, lab results, and LVAD drug comparisons.

Qualitative

Qualitative research is a "situated activity," meaning that the research observations are made within the real world or real-life situation. Additionally, qualitative research "turns the world into a series of representations" by describing the observations. Qualitative data can take the form of words, pictures, documents, and other symbols. Lastly, qualitative researchers seek to "make sense" of the meanings that research subjects bring from different experiences. This allows for a greater understanding of those phenomena [12]. Quantitative trials were and still are very common in the LVAD field, however, more and more qualitative trials are being published in current literature. Finding a trained qualitative expert is not easy. Many novice researchers believe they can easily perform qualitative research without a qualitative-trained mentor or without receiving any training. This action will only set the researcher up for failure. An example of LVAD qualitative research are those that describe the experiences of LVAD caregivers' transition to home.

Data Analysis

Data analysis is a process that relies on methods and techniques to transforming raw data into metrics, facts, and figures; thus, interpreting the results to enhance understanding [13]. This aspect entails an in-depth process too large to briefly discuss. Many resources offer detail on this step of research that can be found in published materials.

The Report

The goal in writing a report is to communicate a scientific result while providing an interpretation of the aforementioned results [14]. In order to ensure this transparency and accuracy of reporting medical research, several guidelines have been gradually introduced to the field. There are consensus guidelines for randomized trials (CONSORT), registry analyses (STROBE), meta-analyses (PRISMA), and prediction analyses (TRIPOD) [14–16]. Competent reviewers of reports that are submitted for journal publication will expect all components of the relevant guideline to be included in a manuscript.

Authorship

Authorship can be a great source of conflict among collaborating investigators. Journals now are implementing a contributorship policy. Specifically, because authorship does not communicate what contributions qualified an individual to be an author, some journals now request and publish information about the contributions of each person named as having participated in a submitted trial.

The individuals who conduct the work are responsible for identifying who meets these criteria and ideally should do so when planning the work, making modifications as appropriate as the work progresses. It is the collective responsibility of the authors, not the journal, to determine that all people named as authors contributed to the work; it is not the role of journal editors to determine who qualifies or does not qualify for authorship or to arbitrate authorship conflicts. The criteria used to determine the order in which authors are listed on the byline may vary and are to be decided collectively by the author group and not by editors. In the past, some authors add colleagues who did not take any part of the research project or writing. This is inappropriate and opposes the mantra of respecting the research team members who donated the time and effort to the project. If authors request removal or addition of an author after manuscript submission or publication, journal editors should seek an explanation and signed statement of agreement for the requested change from all listed authors and from the author to be removed or added.

The corresponding author is the individual who owns the primary responsibility for communication with the journal during the manuscript submission, peer review, and publication process. The corresponding author ensures that all the journal's administrative requirements, such as providing details of authorship, ethics committee approval, clinical trial registration documentation, and disclosures of relationships and activities, are properly completed and reported, although these duties may be delegated to one or more coauthors. The corresponding author should be available throughout the submission and peer review process to respond to editorial queries in a timely way and should be available after publication to respond to critiques of the work and cooperate with any requests from the journal for data or additional information should questions about the paper arise after publication [16].

Abstract

Most peer-reviewed journals offer detailed instructions regarding abstract structure and format. Be sure to read the journal's guidelines before writing. The abstract should mirror both the structure and the focus of the manuscript, which may only be evident after the manuscript is completed. Thus, most researchers prefer to write the abstract after the manuscript.

The basic elements of an abstract are the background section, the methods section, the results section, and the conclusions section. The background section should be brief, encompassing one or two sentences. The methods section should state the population studied, the basic methodologies in the trial, and the statistical analysis utilized. The results section should state the number of subjects studied and the key findings including confidence intervals, effect sizes, and *P* values. The conclusions section should only state in one or two sentences. Since few studies are definitive, avoid claiming that a theory is proven true or false [17].

Methods

The methods section is, said by many, the most important part of a research report; as it represents the framework for reproducibility. It is the PI's duty to describe the methods in sufficient detail so that another future investigator can reproduce the trial if desired.

The methods area may be the easiest part of a research report to write as one can cut-and-paste them from the protocol. Specific references to published methods, techniques, or procedures should be cited rather than repeated. In a clinical trial, "standard-of-care" details do not need to be reported. Typically, the methods section consists of four subsections: subject selection, protocol, measured variables, and data analysis.

Results

The results follow the organization of the methods section. Start by describing the population, typically this is entailed in the demographics section. Give an overview of the data. Then address each measurement and discuss what was discovered. From there, progress to your primary and secondary outcomes. Every report should include a "takeaway figure" that captures the primary result. This is the figure that others will find very helpful in describing the research in future review articles, book chapters, and refresher courses. Non-statistical significance can be just as important as statistical significance, do not consider it non-fruitful!

Implementation of Research

Grant Applications

Grant funding can be helpful in providing financial support to a research trial that might not occur without the means. Carefully reading the call for funding is key as a vast amount of time is expended in an application, and if a grant reviewer finds the applicant does not fit the eligibility, the application is immediately declined. A biosketch or Curriculum Vitae (CV) of all involved in the trial may be requested along with description of each member's role within the study. Knowing the deadline of the applications is highly recommended as late submissions are not accepted. Some professional organizations within the LVAD field offer LVAD Coordinator research grants such as ICCAC and ISHLT.

Project Budget

Many LVAD clinicians are unaware of research study budgets as a whole. Budgets of industry-sponsored clinical trials are clearly negotiated and agreed upon by contracting departments within the research institutions; thus, the budget is solidified and agreed upon preceding the researcher study activities. Negotiating an acceptably profitable budget depends on careful line-by-line itemization of the practice's costs and overhead expenses. Conversely, grant funded trials have a budget, which requires a budget description/justification with the application submission. The applicant composes this through the subjective lens concerning what is predictive of the research continuum. Examples of budget line items may include statistician labor, software, travel to conference where the trial results will be presented. It is crucial to spend all of the monies given by the grant along with providing receipts of all monies spent (Table 1).

Table 1 Examples: budget line items

Line item	Amount	Justification
Administrative	$500	Purchasing: Printing, flyers, interview snacks, water, etc.
Data analysis software and equipment	$8000	Software educational multi-user license 5 users. This will serve as the primary software for data analysis
Transcription costs	$2000	Digital audio recorders
Travel	$2000	Audio recorded interviews professionally transcribed in Spanish and translated to English
Total	$125,000	

Timely Completion of Data Points

Successful and timely completion of subject data points assure the initial research plan's success. Importantly, humans are involved with trials and events, such as pandemics, may slow down enrollment causing completion of a trial to be delayed. Communication of a delay to sponsors, funding agencies, the IRB to name a few is vital to assure of adhering to all regulatory standards. When the protocol is submitted to the IRB, study duration is detailed. Changes to this timeline can be addressed by submitting amendments that detail the change of timeline and the rationale of change.

Monitoring, Auditing, Inspection

Effective monitoring of clinical investigations by sponsors is critical to the protection of human subjects and the conduct of high-quality studies. Companies typically conduct on-site monitoring visits at approximately 4–8-week intervals, with 100% verification of all data. This has historically been the Food and Drug Administration's preferred way for sponsors to meet their monitoring obligations. In contrast, academic coordinating centers, cooperative groups, and government organizations use on-site monitoring less extensively [18].

While the PI must ensure that the study is conducted according to the approved protocol, in some cases (e.g., low risk studies, not blinded), it may be acceptable for the PI of the study (PI or Co-Investigator) to also be responsible for carrying out the monitoring plan. Areas assessed are typically the following: (1) PI oversight, (2) informed consent process, (3) source data verification, (4) adverse events, (5) protocol adherence, and (6) study endpoints.

The process of monitoring ensures that study activities are being carried out as planned and deficiencies addressed and corrected promptly. It is thus a quality control tool. Conversely, an audit is not frequent. It can be done at any time during the conduct of the study (ad hoc) or "for cause" (for a specific purpose). An audit is essentially a quality assurance activity undertaken by personnel independent of the trial.

An inspection is a regulatory audit. It is conducted by the regulatory authority and assesses whether the investigator and sponsor are conducting the study as per applicable statutory and regulatory requirements. In the event that noncompliance is found, the regulator can suspend/cancel the trial and even debar the sponsor and/or investigator from conducting future studies. Thus, preparedness of the study site at all times must be ensured. Unlike audits and monitoring, an inspection can be sudden or with very little warning. The preparedness for inspection is in no way different from that of an audit or monitoring [19].

Dissemination of Research

Oral Presentation of the Report

Presenting at conference/professional events have long been the traditional method of disseminating research results. If delivered effectively, it can be an invaluable opportunity to present your research trial in front of peers as well as receive feedback. Many LVAD forums are either for an LVAD Coordinator audience or a varied audience that includes surgeons, cardiologists, and bioengineers, for example.

Although order may vary slightly depending on the type of research you are presenting, the typical structure is as follows:

- Opening slide (title of trial, authors, institutions, and date). Be sure to add a footer that indicates what event you are presenting; for example, "ISHLT 2021."
- Background
- Aims
- Methodology
- Results
- Discussion (including limitations of the trial)
- Conclusions
- References

It is important to avoid clutter within the slides, specifically too much text or pictures. Using no more than five bullet points per slide, with no more than five words per bullet point maintains a visually appealing presentation. It is also good to break up the slides with those that include diagrams or graphs. This can also help convey results in a more visual and easy-to-understand fashion. The researcher should practice their presentation before the conference, making sure that adherence to the allocated time is followed. Oral presentations are usually short (around 8–10 min maximum), and it is, therefore, easy to not adhere to the allotted time if not rehearsed. Aiming to spend around 1 min per slide is usually a good guide but some slides require more time depending on the purpose the researcher wishes to communicate.

Presenting to colleagues, mentors, and fellow professionals is useful as it allows the opportunity for questions from the audience; thus, preparing the presenter for the sort of questions at the upcoming presentation event. If asked a question, thanking the audience member shows professionalism. Additionally, repeating what the individual asked to the rest of the audience is encouraged as it helps the audience, as a whole, hear the question. If the presenter does not know, then they should say so. Becoming defensive is not productive, but being excited that an opportunity to clarify issues issue offered is encouraged. Occasionally, having to agree of a weakness in the research projects is realistic but being gracious as possible only lends to the fact that future research projects will be more thorough [19].

Delegating a peer who is in the audience to write down the questions is useful, as the presenter may not remember everything during the presentation. Some of the conferences are out of the country where the researcher resides, thus, costs and time away from work needs to be evaluated for assurance the research does get presented.

Poster Presentation of the Report

The conference/professional event usually provides guidelines how to compose the poster, some more detailed than others. Additionally, the researcher's organization may have guidelines to follow also; for instance, using the organization's logo and type of poster color, etc. When creating poster presentations, researchers need to be aware of design standards that improve visual impact in order to maximize content dissemination. Despite the numerous how-to articles available in the literature, there is little research evidence on the characteristics that influence viewers' decisions to read a particular poster or interact with a particular poster presenter. Siedlecki (2017) surveyed 96 nurses regarding their perspectives of poster presentations. Among the poster variables, each of which was rated on an 11-point scale, nurses considered visual appeal the top priority. When asked respondents, what poster presenters could do to improve dissemination, suggestions stated that business card distribution and copies of the poster to take home and reread at their leisure were highly desired. Although the researcher's presence at the poster session was important to many respondents, many reported a preference for viewing the posters without having to interact with the presenter [20]. Knowing what day/time the poster will be presented is crucial as to not miss this very important event. The researcher should also be prepared on how to hang the poster as some events do NOT provide hanging fasteners, and trips to the nearest office supply store can be an undesired occurrence.

During an open poster session, posters with various topics are displayed in an assigned physical area. Posters may be grouped categorically; for instance, one poster session may be "Nursing and Allied Health." The poster may be displayed during the entire conference/event or for a short duration. It is crucial to be present at the poster showing. Those presenters who are not in attendance show a substandard level of professionalism.

Manuscript Publication of the Research

Impact factors (IF) may be the guide of the researcher's choice of journal. IF is an approach that quantifies the prestige level of a journal. A metric used by many authors, universities, and funding agencies, it is now a variable to assess those who wish to be promoted, receive funding, and considered for tenure [20]. The issue at hand is that this metric is gameable and may not truly measure the impact of a paper. Examples of gaming includes self-citations; thus, citing their own past paper. Another reality not truly taken into account, some papers take decades before the

true impact of the observation is recognized by the field. The unequivocal goal should be to publish the best research, obtain timely reviews, and disseminate the research at hand [21, 22].

Conclusion

The arena of clinical research field offers an exciting combination of scientific inquiry, multi-disciplinary collaboration, and patient advocacy. Clinical researchers come from a wide range of educational and professional backgrounds offering diversity in research topics that take the field forward. For those who wish to become clinical researchers, it is important to first seek the education, mentoring, and do not stray from perseverance. In summary, this venue within the LVAD field is very rewarding and exciting!

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Mechanical Circulatory Support in the Era of COVID-19

Christina Marie Silva and Scott Stewart

Introduction

As mentioned, COVID was first identified in December 2019 in Wuhan, China. The virus was identified using a polymerase chain reaction to sequence the genetic material noting that it had uniquely shaped spikes on its surface causing it to resemble a crown and thus lending itself a member of the other coronavirus families [1, 2]. Because the virus had not previously been known, it was named the 2019-novel Coronavirus/SARS-CoV-2 and more colloquially known as COVID-19. Variations of coronaviruses have been previously known and identified and been responsible for the prior epidemics including severe acute respiratory syndrome (SARS) in 2003 and the middle eastern respiratory distress syndrome (MERS) [2, 3]. Contact tracing of those infected revealed the suspected origin within a wholesale wet market in Wuhan, but the exact source of transmission—animal to animal and subsequently to people—has yet to be confirmed [3]. According to the World Health Organization (WHO), COVID-19 is spread through respiratory droplets from an infected person's oral and nasal cavities [4].

Patients who are infected with COVID-19 can present as asymptomatic or symptomatic. Typically, patients manifested physical symptoms after an incubation period of 5 days post exposure [5]. Symptomatic presentation is multifaceted from mild to severe and include fever, dry cough, fatigue, shortness of breath, gastrointestinal distress, as well as loss of taste and loss of smell [5]. Of those infected and symptomatic, 39% of those people had disease progression to the point of acute respiratory distress syndrome (ARDS). ARDS requiring mechanical ventilation typically progressed at the patient's 10-day mark from the onset of symptoms. Many patients whose disease progressed to ARDS continued to become progressively ill

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despite attempts at therapeutic and supportive measures ultimately would go on to have multisystem organ failure leading to death [3].

COVID-19 began to spread outside of Wuhan into Europe, and subsequently, to the United States by January 2020. On January 22, 2020, the first case was identified in the United States from a patient who traveled from Wuhan, China. By March of 2020, the WHO declared COVID-19 a global pandemic, and the world began a global shutdown to limit spread and ensure hospital capacity would be able to handle patient volumes. The use of face masks and face coverings was highly encouraged, and in some countries, made compulsory. Businesses and restaurants were forced to redesign their delivery models as in-person meetings were heavily discouraged and take-out meals were strongly encouraged. Schools transitioned to remote and virtual styles for teaching, and hospitals were required to cancel elective procedures to make all beds available for the increased surge of COVID-19 patients. Many facilities required conversions of non-clinical space to acute care environments to accommodate this increased volume of hospitalized patients. As COVID19 was newly discovered, treatments remained supportive and geared toward management of secondary infections. Preventative measures became key to slowing the spread of the virus throughout populations. The WHO issued recommendations for slowing the spread of the virus including wearing a mask or face covering, staying at least 6 ft away from others with avoiding large events and mass gatherings, and washing hands often and for at least 20 seconds with either soap and water or a 70% alcohol-based solution [4].

Treatment for patients with COVID-19 remains supportive for those not deemed as critically ill. The WHO classifies critically ill or severe patients as those meeting criteria for ARDS, septic shock, and/or other conditions that would necessitate the use of life-sustaining therapies including but not limited to vasopressor therapy or mechanical ventilation. For the population requiring inpatient hospital care, the available treatments include antiviral therapies, antibody therapy, and in some patients, steroids [6].

COVID-19 and Cardiac Disease

COVID-19 has been indiscriminate with its ability to affect people. The severity of illness in specific populations varies based on a variety of factors. Individuals who are greater than 60 years old or who have comorbidities including diabetes, chronic respiratory disease, and cardiovascular diseases have a higher risk of developing a significant illness [7]. The exact mechanism by which the virus affects people with cardiovascular disease disproportionately is unknown but current hypothesis suggests the exacerbated systemic inflammation cascade and subsequent cytokine storm increases cardiac strain [8]. For patients with cardiovascular disease, COVID-19 infections present an additional layer to the demise of a healthy state. Patients with a concurrent cardiac injury or known cardiac disease increases the risk of mortality by four times than that of a person with no underlying cardiac disease [8].

Patients infected with COVID-19 during this inflammatory cascade are more prone to risks of myocardial strain due to the secondary complications including sepsis, hypoxia, and hypercoagulability due to microvascular clotting. These complications have the ability to enhance right ventricular dysfunction and strain as well as create an arrhythmogenic state. ARDS can also increase pulmonary pressures and put patients with an already compromised cardiac function at increased risk for right ventricular failure [8].

Initial concerns existed for patients with advanced heart failure due to the nature of COVID-19 virology as the entry point to the cell was via angiotensin-converting enzyme (ACE) 2. Guideline directed therapy for patients with advanced heart failure demonstrates use of ACE inhibitor therapy for reduction of mortality, however, it was thought use of these drugs would favor higher rates of COVID-19 infections. Concerns of this association created concerns and fears from patients prompting self-discontinuation of medication. The Heart Failure Society of America (HFSA), American College of Cardiology (ACC), and the American Heart Association (AHA) jointly created a position statement advising benefit of therapy was higher than risk of COVID infection therefore not recommending discontinuation of therapy although indicated those patients who were infected with COVID-19 should evaluate hemodynamic risks at that time [9].

MCS and COVID

Patients infected with COVID-19 present challenges to the MCS community. Treatment modalities traditionally used for acute cardiogenic shock were now being redeployed to patients in severe respiratory distress whereby maximum settings on invasive mechanical ventilation were no longer effective. The use of temporary mechanical circulatory support (MCS) devices such as extracorpeal membrane oxygenation (ECMO) were used for the COVID-19 population in severe ARDS who met certain criteria. Both venous-arterial (VA) and veno-venous (VV) ECMO proved to be necessary treatments for these patients. Based on high volume use, the Society of Critical Care published guidelines to help guide clinicians in selecting patients appropriate for ECMO therapy. The use of ECMO was recommended for critically ill patients who had little to no response to their current treatment plans on maximal ventilation. Because of the high risk of multisystem organ failure with severe COVID-19 infections and immense resources needed, patient selection should be prioritized towards patients with a higher likelihood of recovery and success. In order for ECMO to be successful, there must be a high functioning team of trained nurses, physicians, perfusionists, and other allied health professionals who are able to manage the patient. In the setting of COVID-19, consideration must be given to staffing capabilities and resource allocation such as personal protective equipment (PPE) as these may be limited and therefore should be a contributing factor in deciding if a patient is a candidate for ECMO therapy. The thought is that resources may be better served to areas where the most amount of people would receive benefit [8]. The American Society for Artificial Internal Organs (ASAIO)

has reported that the initiation of ECMO therapy should continue to be a measure taken only when all other therapeutic measures have been exhausted regardless of COVID-19 status. Mortality rate increases with prolonged mechanical ventilation time so early initiation of ECMO is recommended if deemed to be a feasible treatment option by the medical team [10]. Furthermore, ASAIO also recommends that implanting ECMO centers should create a system whereby exclusion criteria can be clearly determined for patients not suitable for ECMO as patients on prolonged support have a significantly higher mortality rate [10]. Patients with ECMO and mechanical circulatory support are at an already increased risk for thrombus formation due to the implanted device. COVID-19 is known to create a prothrombotic state, and therefore this patient population is at a disproportionate risk of thrombus formation compared to those without a device. It is important that MCS patients diagnosed with COVID-19 are assessed as early as possible so that anticoagulation is adequate.

Treatment for VAD Patients with COVID-19

At the time of this publication, treatment for patients infected with COVID-19 is an evolving process however some treatment methods initiated during the 2020 pandemic have demonstrated some benefit. The use of antiviral therapies, monoclonal antibodies, convalescent plasma, and limited steroid use showed some improvement in patients' condition. A mainstay of treatment for critically ill patients with COVID-19 was prone position with supplemental oxygenation or mechanical ventilation. The benefit of the prone position for patients in ARDS is that the right ventricle is unloaded allowing for improvement of pulmonary pressures and increased oxygenation capacity [7]. For the patients receiving critical care treatment for severe COVID-19 infections, proning became a treatment technique used often for 12–16 hours at a time. Patients with durable LVADs risk the potential for increased pressure on the right ventricle that can lead to right ventricular failure. This risk is partly due to possible compression of the outflow graft when the patient is laying on their abdomen and/or an interruption of venous return because of increased thoracic pressure [8]. Critical to the success of patients with an LVAD is adequate function of the right ventricle. Because LVADs are preload-dependent, it is essential that the right ventricle has enough contractility to supply blood flow to the pump. Any right ventricular dysfunction has the potential to disrupt the flow of the LVAD and negatively affect the patient. It is currently thought that the prone position would not have a significant enough effect on the right ventricle, but the risk should not be excluded [8]. Additional concerns of proning include potential of pressure injury due to extensive time laying on the driveline. Particular attention must be paid to supportive cushioning of both the driveline and controller to avoid risk of skin breakdown and driveline infection [11].

Antiviral therapies have been used in the treatment of prior coronavirus cases. Remdesivir specifically has been previously used to treat Middle East respiratory syndrome (MERS) and was thought to be beneficial for the COVID-19 population

as well because of its ability to target the virus in vitro and inhibit production [6]. Previous studies with Remdesivir in MERS have shown that when initiated promptly, there were reduced lung virus levels and lung damage [6]. In studies conducted using Remdesivir for the treatment of COVID-19, the patients who received Remdesivir did have a shorter time to recovery than those who had received the placebo and that receiving the drug may have contributed to preventing severe disease progression. Remdesivir received approval for emergency use (EUA) to treat patients with COVID-19 from the FDA on May 1, 2020 and in the European Union in July 2020 [12].

Patients with a durable VAD who have COVID-19 should be able to receive Remdesivir as part of their treatment plan but will require vigilant monitoring of their INR levels. Anticoagulation is essential for patients with a durable VAD to prevent the development of a thrombus on the pump [13]. While there is little data to support the notion that the use of Remdesivir can cause a patient to be supratherapeutic based on INR levels, there is a reported case study of a patient using warfarin therapy for atrial fibrillation where her INR level increased after initiation of the Remdesivir and remained elevated for the duration of her therapy even after the warfarin dose had been decreased [14]. Therefore, more vigilant monitoring of both INR levels and frequent warfarin dose adjustments must be considered when a patient is receiving both therapies.

The use of monoclonal antibody therapies has also been considered as an option for the treatment of COVID-19. Previously, monoclonal antibodies have been used in the treatment and management of other viral infections such as influenza, SARS, MERS, and Ebola and had resulted in a reduced mortality rate. The goal of monoclonal antibody therapy use is for the antibodies to have specific targets that, once identified, are able to act on those targets using specifically designed mechanisms and inhibit further replication of the virus [15]. Emergency use authorization (EUA) was granted to Eli Lilly and Company on November 9, 2020 and to Regeneron Pharmaceuticals Inc. on November 21, 2020 [16, 17] for use in the treatment of COVID-19.

Convalescent plasma is another treatment option for management of COVID-19 as it is thought to be transmission of recovered antibodies from person to person. Convalescent plasma is dependent on recovered donors and the amount of antibodies present in their donation specimen. Those who volunteer to donate plasma must have pre-donation blood testing done to determine if there is a sufficient amount of antibodies present for donation [18].

For patients in severe ARDS, steroid use has been shown to decrease mortality. Patients requiring supplemental oxygen would have less risk of their disease progressing to the point of requiring invasive mechanical ventilation and for those patients already requiring mechanical ventilation, steroid use would increase the chances of weaning the support [10]. The RECOVERY trial was performed in the United Kingdom in September 2020 which demonstrated efficacy of dexamethasone for COVID-19 patients. The results showed that the use of dexamethasone was indicated for patients with severe or critical COVID-19, however exacerbated disease in patients with non-severe COVID-19. While dexamethasone 6 mg IV or oral

is the preferred steroid for treatment of COVID-19, prednisone 40 mg, methylprednisolone 32 mg, and hydrocortisone 160 mg are also acceptable doses [19].

In December of 2020, the first COVID-19 vaccines were approved in the United States for use and became available for distribution. These vaccines were the Pfizer-BioNTech and Moderna vaccines which were mRNA vaccines and the Johnson and Johnson and Astrazeneca vaccines use as a viral vector. MRNA vaccines, or messenger RNA vaccines, had instructions that were injected into a person's immune cells through the muscle in the upper arm. These were instructions for how to make the protein that is unique to the COVID-19 virus. Once visible, the body's immune system would recognize the protein as foreign and the immune response would begin creating antibodies. In contrast, while mRNA vaccines provide the body with instructions on how to make the protein, viral vaccines inject a similar virus—not the COVID-19 virus—into the body that initiates the cell to create the COVID-19 protein the body can recognize as foreign and create antibodies against. To date, vaccines are the most effective method for reducing spread and decreasing severity of illness in COVID-19 [20, 21]. Both the Pfizer-BioNTech and Moderna vaccines require people to receive a two-shot series to be completely protected, and Johnson & Johnson is a single-dose vaccine. The European Union (EU) has approved the Vaxzevria, formerly the COVID-19 Astrazeneca vaccine for use in the prevention of COVID-19 [22].

In September of 2021, the U.S Food and Drug Administration gave emergency use authorization for only the Pfizer-BioNTech Covid vaccine booster shot and the Moderna and Johnson & Johnson vaccines received approval in October of 2021. The booster dose is a single dose that is administered at least 6 months after completion of the two shot initial vaccine series. At the time of this publication, the booster shot is indicated for high risk populations, or individuals 65 years of age and older, and/or individuals 18–64 years old who are at high risk for developing severe COVID-19 infection or who have frequent institutional or occupational exposure to the virus [23]. At the time of this publication, additional booster doses are being discussed for approval.

Implantation and Follow-Up of Durable MCS in the COVID Era

For non-COVID-19-infected patients with heart failure who require durable MCS implantation during the pandemic, more careful consideration is needed prior to implant of the device to ensure successful outcomes. During peak times of pandemic surges, elective surgery was canceled to allow for reduced risk of person-to-person transmission within the acute care environment and to increase available capacity for treatment of infected patients [24]. This adjustment led to delays in care, and hospitals began to see a rise in acuity post-pandemic recovery [25]. Before a patient can receive a durable VAD, a comprehensive workup and a significant amount of pre-implant education must be completed. This workup can include in-person family meetings, multidisciplinary appointments, and an elective admission to promote the best patient outcome [24]. Placement of a durable VAD is

indicated only after both the patient and family have been adequately prepared for the change living with a VAD will have on lifestyle [24]. Traditionally, comprehensive teaching is done in person where the patient and family members can see and feel the equipment, become familiar with the device, and ask questions as they arise once seeing the equipment in person. In the setting of COVID-19, hospital systems no longer allowed visitors into the hospitals, and increased restrictions were placed on in person meetings. While adjustments can be made to accommodate these meetings virtually, careful consideration must be given to each patient situation to ensure the preparation of family members of VAD patients is adequate. Immediately following VAD implant, many centers utilize discharge to subacute or acute rehab facilities however during the height of the COVID pandemic, many rehab sites closed for admissions to patients being discharged from the hospital and outpatient centers were shut down [26]. This created challenges for patient disposition and use of home therapy with more dedicated caregivers were essential for success.

VAD programs were tasked with the challenge to care for chronic VAD patients but also avoid risk of exposure by bringing patients to hospital-based clinics. For current patients at home living with VADs, the thought of contracting the virus during office visits became a real fear for patients and clinicians alike. Because routine care for VAD patients typically includes periodic office visits and blood work, it is essential for VAD centers to coordinate closely with their VAD patients to ensure the safest option for preventing infection. The use of telehealth and virtual appointments can be utilized to help with this population, as well as the use of home INR machines [27]. Patients should be encouraged to maintain constant communication with their implanting centers to prevent escalation of any issues that may lead to hospitalizations if not treated promptly. When the patients are able to come to the office, it is important to attempt to ensure the safest environment for the patients. Offices should follow the Center for Disease Control (CDC) guidelines for prevention of the spread of COVID-19.

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Correction to: A Guide to Mechanical Circulatory Support

Scott Stewart and Peggy Blood

Correction to:
Chapters 4 and 16 in: Stewart, S., Blood, P. (eds), *A Guide to Mechanical Circulatory Support,*
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Noted that the last name in Chapter 4 was spelled incorrectly. It should be Rhoades instead of Rhodes.

The book was inadvertently published with incorrect spelling of one of the authors of Chapter 16. It has been updated to Andrea Stuart, instead of Andrea Stewart as listed. This has been updated now.

The updated original version of this chapters can be found at
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