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REVIEW ARTICLE

Remote monitoring for better management of LVAD patients: the potential benefits of CardioMEMS

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Abstract

Left ventricular assist devices (LVAD) are frequently used in the treatment of end-stage heart failure (HF), and due to the shortage of heart donors and destination programs, it is likely to keep on growing. Still, LVAD therapy is not without complications and morbidity and rehospitalization rates are high. New ways to improve LVAD care both from the side of the patient and the physician are warranted. Remote monitoring could be a tool to tailor treatment in these patients, as no feedback exists at all about patient functioning on top of the static pump parameters. We aim to provide an overview and evaluation of the novel remote monitoring strategies to optimize LVAD management and elaborate on the opportunities of remote hemodynamic monitoring with CardioMEMS, at home in these patients as the next step to improve care.

Keywords Heart failure · LVAD · CardioMEMS · Remote monitoring · Telemonitoring

Introduction

Epidemiological data on end-stage heart failure (HF) is scarce. Estimations performed by the America Heart Association suggest that < 1% of all HF patients are in end-stage HF [1]. Other studies estimated that approximately 5–10% of the HF population develop at some moment in life advanced HF despite optimal medical treatment [2]. These patients become refractory for medical therapy and are frequently hospitalized and have high mortality rates, leaving heart transplantation or left ventricular assist device (LVAD) implantation as the only treatment options. Due to shortness in available heart donors, LVAD implantation rates continue to rise [3, 4].

Despite new LVAD designs and technological improvements, LVAD care remains very complex and associated with high mortality and with many rehospitalization and outpatient contacts [3, 5, 6]. The main reason for hospitalization is gastrointestinal (GI) bleeding or LVAD-related (driveline) infection, followed by decompensated HF and arrhythmia [7, 8]. Due to the growing number of patients treated with a LVAD, combined with the high hospitalization and complication rates, LVAD care places a high burden on hospital resources, with many logistical challenges with available hospital beds, as many other departments are not familiar with LVAD devices, so LVAD patients preferably are admitted at a cardiology ward despite non-cardiac admission indications.

It is difficult for pump optimization to be available in a short time at the outpatient clinic and so it is only based on echocardiographic images and static pump parameters.

Patient self-management and remote monitoring is an important part of chronic HF care, to prevent admission. Due to the complexity of LVAD care, remote monitoring has the potential to provide valuable information to help the physician in structured decision making. It has been suggested that remote monitoring of pump parameters, combined with remote monitoring of blood pressure, pacemaker-related parameters, coagulation values, and driveline exit parameters could improve LVAD care [9]. However, many of these investigations are still unexplored, and not yet tested in large populations. We aim to provide an overview of these new technological advances for the remote monitoring of LVAD patients.

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The LVAD and hemodynamics

Different LVAD designs, pump mechanisms (axial or centrifugal), and implantation techniques are used. The two most common used LVADs are the HeartMate 3 (HM3, Abbott Inc, Atlanta, GA, USA) and the HVAD (Medtronic Inc, Framingham, MA, USA) (Fig. 1. Both are centrifugal pumps, placed in the pericardial space. The HM3 uses a fully magnetic levitated pump rotor, whereas the HVAD uses passive magnetic and hydrodynamic thrust bearings [10–12].

Common LVAD-related complications

LVAD care can be lifesaving, however, it is also associated with several LVAD-related complications, such as right ventricular (RV) failure, LVAD-related infection, cardiac arrhythmia, hemolysis and thrombosis, GI bleeding due to angiodysplasia and renal dysfunction [13]. An overview of the incidence rates of common LVAD complications in HM3 and HVAD LVADs is presented in Table 1.

RV failure is a serious hemodynamic complication, occurring in up to 20–30% of the LVAD patients [14–17]. Signs of RV failure are elevated central venous pressure (CVP) and manifestations of elevated CVP, such as edema, ascites or increasing renal dysfunction [18].

Tamponade, which can develop shortly after LVAD implantation, is a feared complication, occurring in up to 20% of the LVAD patients [19]. Symptoms usually occur in a late stage, and common hemodynamic signs, such as tachycardia, shock or pulsus paradoxus can be masked by the LVAD pump [20]. Late tamponade can be hard to visualize on echocardiography until the patient is in shock, and the first sign might be a drop in pump parameters [21, 22].

GI bleeding is a common complication in LVAD patients, affecting up to 20–30% of the patients [14–17, 23–25]. GI bleeding has different presenting symptoms, 50% of patients present with melena, 25% with unexplained anemia, 15% with hematochezia and 10% with hematemesis [26].

LVAD-related infections occur in 10–25% of the LVAD patients in the first 3 months after LVAD implantation [14–16, 23–25, 27]. Presenting symptoms are fever, erythema at the driveline site, or purulent fluids from the driveline exit site.

Pump thrombosis affects approximately 15% of axial-flow LVAD, and 1% of centrifugal-flow LVADs [14–16, 23, 25]. Pump thrombosis is characterized by signs of worsening HF in the patients, which cannot be explained otherwise, abnormal pump parameters and signs of hemolysis in laboratory results, such as elevated LDH [28, 29].

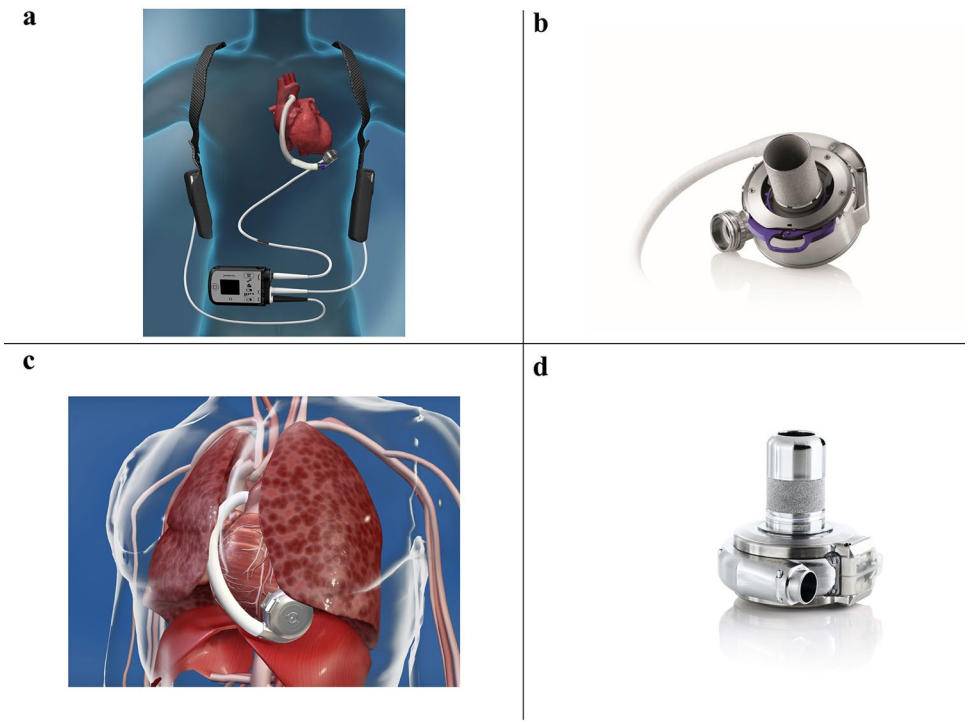

Fig. 1 Schematic presentation of the HeartMate 3 (**a**) and HeartWare LVAD (**c**), and close-ups of the pump house and inner work (**b**, **d**, resp) Courtesy of Abbott, Inc. and Medtronic, Inc. to provide the illustrations

Table 1 Common LVAD-related complications

	HeartMate 3			HeartWare		
	Short term	Medium term	Long term	Short term	Medium term	Long term
RV failure	8.0	10.0–14.7	14.0–31.7	–	25.4	–
Resulting in RVAD implantation	4.0	4.0–6.7	3.2–4.0	2.1–4.0	1.4–3.3	6.0
Bleeding	30.0	25.1–38	42.9–50.0			
GI bleeding	4.0	6.0–8.0	20.0–27.0	3.3–4.3	9.9–12.7	–
Resulting in surgical intervention	12.0	10.2–14.0	12.2–16.0	12.0–16.0	14.3–14.8	20.0
Infection	20.0	35.2–36.0	52.0			
Driveline infection	2.0	11.7–16.0	23.8–24.0	0.0–3.6	12.1–16.9	18.0
Sepsis	8.0	9.1–16	13.8–22.0	2.0–3.0	11.4–17.2	10.0
Suspected or confirmed pump thrombosis	0.0	0.0	1.1	0.0	2.1	–
Resulting in surgical intervention	–	–	0.0	0.3	4.2	–
Stroke	4.0	5.4–12.0	10.1–24.0			
Ischemic	0.0	3.9–4.0	6.3–24.0	3.3–5.0	7.1–14.1	4.0
Hemorrhagic	4.0	1.5–8.0	4.2–8.0	0.0–2.1	5.7–12.7	8.0
Cardiac arrhythmia	28.0	34.0	37.6	–	–	–
Ventricular	–	–	23.8	2.0–10.2	20.7–20.8	4.0
Supra-ventricular	–	–	17.5	14.8–15.0	20.0–21.4	–
Organ dysfunction						
Renal dysfunction	10.0	10.0	13.2	5.1–10.0	8.6–9.6	10.0
Hepatic dysfunction	2.0	2.0	4.2	1.8–2.1	2.9–4.8	6.0
Respiratory dysfunction	14.0	16.0	23.8	14.0–16.0	20.0–22.0	16.0
References	[24]	[15, 17, 24]	[15, 16, 26]	[25, 28]	[18, 25, 26]	[28]

Short term defined as < 1 month; medium term defined as 6–12 months; long term defined as 2 years; – data not available

RV right ventricle, *RVAD* right ventricular assist device, *GI* Gastrointestinal

Quality of life

All the above-mentioned LVAD-related complications affect the mortality and morbidity of LVAD patients. However, the complications and the hospitalizations due to these complications also affect the quality of life of LVAD patients. Especially in patients with an LVAD as the destination therapy, quality of life should be the main focus [30]. Remote monitoring of LVAD patients could aid in improving the quality of life of LVAD patients. By earlier detection of LVAD-related complications, earlier intervention is possible, potentially reducing the number of rehospitalizations. Additionally, LVAD settings and the patient's status could be better monitored, allowing for better optimization of the pump settings, improving the pump function [31].

Monitoring strategies

Non-invasive remote monitoring

An overview of remote monitoring strategies in LVAD patients is showed in Table 2. One of the keystones in traditional ambulant HF management is the active participation of patients with their medical care team. The use of non-invasive remote monitoring, or structured telephone monitoring in HF patients, has been investigated in multiple trials showing different results [32]. A recent Cochrane review showed that the use of non-invasive and structured telephone remote monitoring reduced mortality and HF-related hospitalizations [32].

At this moment, there is one study that investigated the use of a structured telephone remote monitoring system in LVAD patients [33]. This retrospective study investigated 96 LVAD patients, among who 25 received bi-weekly telephone calls, consisting of an inquiry about LVAD parameters, alarms, blood pressure, INR, body weight, temperature, driveline exit status, symptoms and presence of edema. They found after 2 years a better overall survival in the intervention group (89% vs. 57%, $p = 0.027$), however, there was no effect on time free of readmission between the groups.

Remote antithrombotic monitoring

LVAD care is associated with thromboembolic complications, such as pump thrombosis, which could be a life-threatening complication, thus showing the need for adequate chronic anticoagulation [7]. However, LVADs are also

Table 2 Remote monitoring strategies

	Number of patients	Main findings	Refs.
Non-invasive remote monitoring			
Schloglhöfer et al.	96	At 2 years of follow-up, using bi-weekly telephone calls (consisting of an inquiry about LVAD parameters, alarms, blood pressure, INR, body weight, temperature, driveline exit status, symptoms and presence of edema), the overall survival was significantly better compared to standard care (89% vs. 57%, $p=0.027$); but no significant difference in time free of readmission	[32]
Remote antithrombotic monitoring			
Dionizovik-Dimanovski et al.	50	Moderate correlation between INR measured using a POC device and in a central laboratory(correlation coefficient of 0.83)	[34]
Joshi et al.	41 samples	Good correlation between INR measured by a POC device and in a central laboratory(correlation coefficient of 0.96)	[35]
Bishop et al.	11	Using a POC-INR measurement device at home leads patients to be more often within therapeutic range compared with regular INR measurements at a central laboratory (44% vs. 31%, $p=0.026$)	[36]
Gavalas et al.	956 samples	The statistical performance of positive urine hemoglobin to predict LDH $\geq$ 600 IU/L is: sensitivity 60.4%; specificity 85.5%; PPV 42.7%; NPV 92.4%	[39]
Remote pump monitoring			
Pektok et al.	5	Demonstrates the feasibility of remote pump parameter monitoring, providing additional information to the treating clinicians	[41]
Kawahito		Adding a vibration sensor to an LVAD could adequately detect pieces of silicone, acting like thrombi, at the four most common thrombus locations	[43]
Bishop et al.	6	In patients with no or minimal AoV regurgitation, adding a specific algorithm could adequately predict AoV opening	[47]
Intrathoracic impedance			
Bartoli et al.	1	Demonstrates the potential utility of intrathoracic impedance measurements in a patient with an LVAD, with an increased intrathoracic impedance preceded intravascular volume depletion and dangerous LVAD dysfunction	[49]
Implantable hemodynamic monitoring devices			
Feldman et al.	27	Using remote monitored PAP, by the CardioMEMS, leads to a large reduction of PAP and an optimized timing of LVAD implantation compared to those receiving standard care	[54]
Hubert et al.	4	Significant correlation between left atrial pressure sensor, and pump speed, LV and LA size and pulmonary capillary wedge pressure ($r=0.92$–0.99, $p<0.05$)	[55]

POC point-of-care, *LDH* lactate dehydrogenase, *PPV* positive predicting value, *NPV* negative predicting value, *AoV* aortic valve, *LVAD* left ventricular assist device, *PAP* pulmonary artery pressure, *LV* left ventricle, *LA* left atrial

associated with bleeding events, particularly GI bleeding, thus requiring a small target window of chronic anticoagulation to minimize the risk of bleeding events [7, 34]. The development of accurate point-of-care (POC) INR monitors made patient self-testing possible. In patients with other indications for anticoagulation therapy, self-testing led to a higher percentage of time in the therapeutic range [35]. Two studies showed a moderate to good correlation between the INR measured by the POC system and laboratory results [36, 37]. Bishop et al. [38] compared 11 LVAD patients using a POC-INR monitoring system or regular laboratory INR monitoring in the outpatient setting. Patients using a POC system were significantly more frequently tested (7.4 vs. 21.4 days, $p<0.01$), and were more often within the therapeutic range (44% vs. 31%, $p=0.03$). Furthermore, they investigated the potential differences in the number of bleeding or thromboembolic events, however, due to the small sample size, no significant difference was found. Self-testing in LVAD patients has the potential to increase the frequency of INR monitoring. By doing so, dosage changes can be made more often, leading to a higher percentage of "time in therapeutic INR range". This could contribute to reducing the number of thromboembolic and bleeding events in LVAD patients, but has not been shown yet.

The diagnosis of pump thrombosis is complex, consisting of an evaluation of symptoms of HF, pump parameters,

echocardiographic analysis and serum lactate dehydrogenase (LDH). LDH is a sign of hemolysis, and probably one of the most reliable markers of pump thrombosis [39, 40]. LDH monitoring is usually only performed during regular outpatient clinic follow-up visits, leading to potential delays in pump thrombosis detection of weeks. Gavalas et al. [41] demonstrated a good correlation between a simple dipstick urine analysis for urine hemoglobin and serum-measured LDH. Absent of urine hemoglobin had a negative predicting value for LDH ≥ 600 IU/L (significant hemolysis) of > 90%, thus indicating the potential use for easy remote monitoring at home of pump thrombosis in LVAD patients.

Remote pump monitoring

Although experience with remote monitoring especially in ICDs and CRTs is growing [42], experience with a remote monitoring function within an LVAD system is limited. However, the first experiences with remote monitoring of pump parameters have been described [43, 44]. The HeartAssist 5 and aVAD LVADs have these remote monitoring functions, allowing to transmit pump parameters, such as pump speed, rounds per minute (rpm) and pump flow, as well as errors, to a website accessible to the care team. This new information can be used in earlier detection of pump complications. Hypovolemia and LVAD thrombosis could be detected by a downward LVAD flow trend [44].

Furthermore, new technologies and algorithms are developed which use the LVAD parameters and help with troubleshooting, and patient monitoring. Detection of vibrations as a sign of mechanical failure is widely used in the biomechanical industry, however, it is not yet used in LVAD management. Kawahito [45] investigated the use of a vibration sensor in combination with an LVAD detect pump thrombosis. This study investigated vibration signals caused by pieces of silicon, acting like actual thrombi, attached at the four most common locations for thrombus in an LVAD: the total area of the bottom of the impeller, an eccentric shape on the bottom of the impeller, a circular shape around the shaft top and an eccentric shape on the top of the impeller. Thrombi at these specific locations can be detected by specific vibration signals, indicating the potential use for early detection of pump thrombosis in LVAD patients.

The aortic valve opening rate is an important aspect of LVAD care. When the aortic valve is not opening the risk of adverse cerebrovascular events increases [46] and commissural fusion can occur, one of the causes of aortic valve regurgitation [47]. Bishop et al. [48] described a novel algorithm to analyze in patients with no or minimal aortic valve regurgitation whether the aortic valve is opening or not. This algorithm uses the electric current waveforms provided by the HeartMate-II LVAD and analyzes this data using a modified Karhunen–Loève transformation. The algorithm could accurately predict aortic valve opening and closing. This algorithm can also be used in an automatic regulation program which can automatically change the rpm settings of the LVAD based on this physiological feedback to maintain a predefined aortic valve opening rate.

Intrathoracic impedance

Remote intrathoracic impedance monitoring is possible in the newer ICD and CRT devices. A drop in intrathoracic impedance is seen during pulmonary congestion, as an early sign of HF decompensation. Due to the remote monitoring function of newer ICD and CRT devices, the intrathoracic impedance can be used to detect HF decompensation at an earlier stage. Multiple studies investigated whether remote monitoring of intrathoracic impedance could lead to a better outcome in chronic HF patients. A recent systematic review [49] showed that intrathoracic impedance was associated with lower health care costs due to a reduction in planned hospital visits, despite a slight increase in unplanned visits. However, the use of remote impedance monitoring did not affect all-cause or cardiac mortality.

At this moment, there is only one case report [50] describing the use and potential benefits of remote monitoring of intrathoracic impedance in LVAD patients. This patient experienced shortly after LVAD implantation an increase in the impedance as a sign of intravascular fluid depletion. The patient was admitted and treated with fluid repletion and the impedance was increased. This case showed that intrathoracic impedance measurements in LVAD patients might provide some information on their fluid status. However, the use of remote monitoring of impedance in chronic HF holds limited additional value, and it is unclear whether this will be better in LVAD patients.

Implantable hemodynamic monitor devices

Due to the failure of simple non-invasive and intrathoracic impedance remote monitoring strategies to improve the outcome of chronic HF patients, new, wireless implantable hemodynamic monitor systems were developed. These systems measure filling pressures, and work according to the hypothesis that filling pressures will increase before other signs of decompensated HF occur, as shown in Fig. 2. As has been shown, intracardiac pressures will rise weeks before patients are hospitalized due to decompensated HF [51]. Recently, Abraham provided an overview of multiple implantable hemodynamic monitor devices, which were developed in recent years [52]. In chronic HF patients, one of the most promising techniques is the CardioMEMS system (Abbott Inc, Atlanta, GA, USA) (Fig. 3). This device is implanted in the pulmonary artery during right-heart

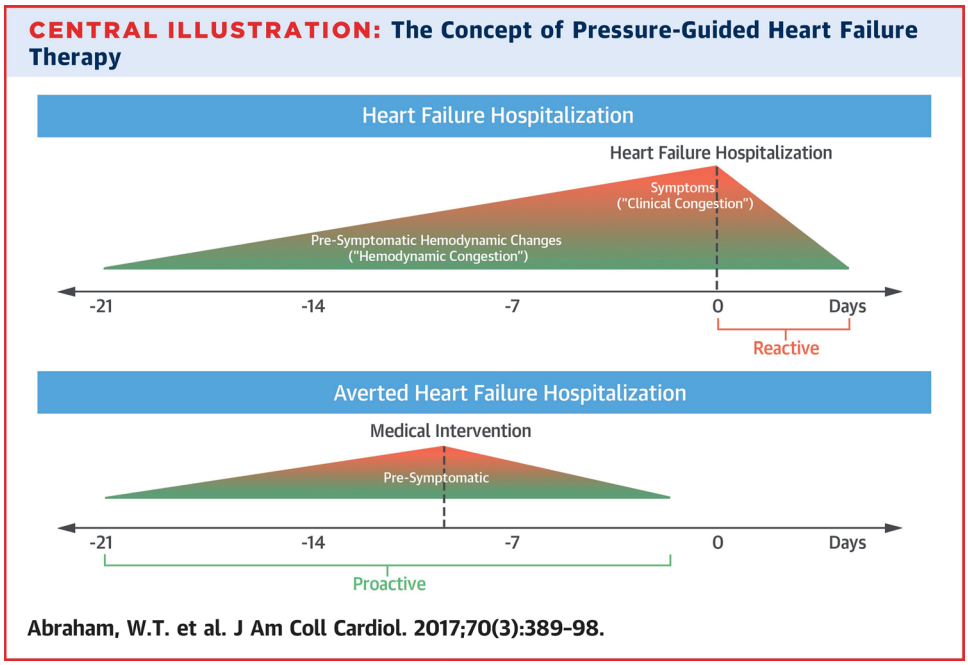

Fig. 2 Hypotheses of pressure monitored and guided heart failure management Reprinted from Abraham [52], 2017, with permission from Elsevier

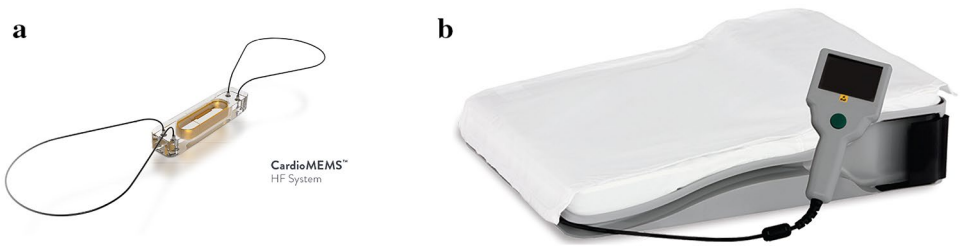

Fig. 3 CardioMEMS HF system, consisting of the pulmonary artery pressure sensor (**a**) and the patient electronics system (**b**) used to take daily pressure readings Courtesy of Abbott, Inc. to provide the illustrations

catheterization, and consists of a pressure-sensitive capacitor combined with a coil and can be powered by coupling this electrical circuit with an external antenna. When powered, the capacitor resonates, which is received by the external antenna. When pressure by the pulmonary artery pressure (PAP), is applied, the frequency of resonated energy changes via a characteristic pattern and can be converted into a pressure wave. This system has been shown in clinical trials as well as in real-world clinical practice to be effective in reducing HF hospitalization rates by maintaining normal PAP [53, 54].

A subgroup analysis of the CHAMPION trial, the initial clinical trial investigating the CardioMEMS, consisting of 27 chronic HF patients, who received an LVAD, showed that patients who received an LVAD were sicker, and had a higher PAP when compared to the group who did not receive an LVAD [55]. The intervention group received more medical changes, based on the hemodynamic feedback provided by the CardioMEMS compared to the control group. However, the PAP did not decrease significantly in the patients who received an LVAD, indicating that a lack of decrease of PAP can be a sign of refractory HF, and thus providing useful information in the timing of an LVAD implantation. Post-LVAD implantation, the PAP dropped in both groups, however, using the hemodynamic feedback in the intervention group, the PAP dropped even lower. This indicates that the use of the PAP provided by the CardioMEMS leads to a better and more optimal LVAD management, leading to a better pump function.

Hubbert et al. [56] investigated in four LVAD patients an implantable left atrial pressure (LAP) monitor, the Titan LAP monitoring system (ISS Inc. Ypsilanti, MI). They showed a significant correlation between LAP and pump speed, LV and left atrial size and the pulmonary capillary wedge pressure, thus indicating the potential use of pressures obtained by an implantable hemodynamic monitor for optimization of the pump settings during a ramped speed test.

Potential impact of implantable hemodynamic monitoring

We believe that the implantable hemodynamic monitors hold more potential in LVAD patients than currently shown. Using the daily pressure readings, which provide real-time insight into patients' fluid status, the clinicians could optimize patients shortly prior to the LVAD implantation, thereby improving patients' status and their clinical outcome. Also, this hemodynamic information provides direct feedback on medical changes made. We believe that using this hemodynamic feedback will lead to better optimization, thus improving patients' status and potentially improving their clinical outcome [57]. Furthermore, optimizing patients will lead to a better decongestion and thereby better unloading of the RV, thus, reducing the impact of the LVAD implantation on the RV and reducing the risk of RV failure.

Changes in filling pressures post-LVAD implantation might indicate potential postoperative complications. An increase in filling pressures might indicate a tamponade, since the venous return reduces due to inflow obstruction due to elevated pressures in the pericardium. An earlier detection and thereby earlier intervention might prevent late-stage tamponade and more severe complications.

Multiple complications, such as pump thrombosis, hemodynamic important arrhythmias or aortic valve regurgitation, will lead to congestion. Similar to chronic HF patients, in LVAD patients filling pressures will rise as a result of congestion [58]. A rise in filling pressures might indicate one of these complications is occurring. Hospitalization and the worsening outcome can potentially be prevented by acting on rising filling pressures. Furthermore, investigating the waveforms and rhythm could provide insight into potential arrhythmias.

A drop in filling pressures might indicate a loss of circulating volume, which might point to a GI bleeding.

LVAD therapy will increase cardiac output, and thereby increase the renal perfusion and resolve the congestion, lowering the renal venous pressure and thereby improving the renal function [59]. Filling pressures might aid in optimizing LVAD therapy, and thus improve the renal function even further.

Fixed pulmonary hypertension is an absolute contraindication for heart transplantation. In these patients, the by ischemic stunned right ventricle will be unable to overcome the elevated afterload and is most likely to fail immediately after heart transplantation. In patients with fixed pulmonary hypertension, LVAD therapy can be used as a bridge to candidacy for heart transplantation, since LVAD therapy is more effective in treating fixed pulmonary hypertension, compared to medical therapy alone [60]. Pulmonary hypertension should be evaluated periodically using a right-heart catheterization, as recommended by the ISHLT guidelines to evaluate whether the patient has become eligible for heart transplantation [61]. However, remote hemodynamic monitoring could replace these periodically right-heart catheterizations, and provide daily feedback on hemodynamic changes. Providing continues insight when a patient could be considered eligible for heart transplantation.

Recently, it has been shown that preforming hemodynamically guided ramp testing could reduce the number of LVAD-related complications and the number of hospitalizations [31, 62, 63]. However, this technique is limited by the need for frequent Swan-Ganz measurements, which increases the risk of bleeding events. Using the hemodynamic information provided by the CardioMEMS, this limitation could be overcome and allowing for easy hemodynamic optimizing of LVAD pump settings.

Future perspectives: design of the HEMO-VAD study to guide LVAD management by hemodynamic feedback

To investigate the potential impact of an implantable hemodynamic monitor in LVAD patients, we designed the HEMO-VAD pilot study[64]. In this study, we will investigate ten consecutive end-stage HF patients, who are accepted for LVAD implantation. These patients will receive prior to LVAD implantation a CardioMEMS device, which will be used for daily hemodynamic monitoring to optimize patients prior to LVAD implantation and monitoring of complications and patient status after LVAD implantation.

Conclusion

Many remote monitoring strategies are currently investigated and developed for LVAD patients, ranging from non-invasive telephone monitoring programs to implantable hemodynamic monitoring systems. Based on results from trials investigating the use of remote monitoring of regular heart failure, it is warranted to study these devices in LVAD patients. This technique holds the potential to provide additional information for determining the optimal LVAD implantation window, optimizing the patients prior to and post-LVAD implantation, and monitoring for LVAD-related complications to identify the patients most likely to benefit from such therapy and for early discovery of its complications.

Compliance with ethical standards

Conflict of interest The author(s) declare that they have no competing interests.

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