Guidance on the management of left ventricular assist device (LVAD) supported patients for the non-LVAD specialist healthcare provider: executive summary

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POSITION PAPER

Guidance on the management of left ventricular assist device (LVAD) supported patients for the non-LVAD specialist healthcare provider: executive summary

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The accepted use of left ventricular assist device (LVAD) technology as a good alternative for the treatment of patients with advanced heart failure together with the improved survival of patients on the device and the scarcity of donor hearts has significantly increased the population of LVAD supported patients. Device-related, and patient–device interaction complications impose a significant burden on the medical system exceeding the capacity of LVAD implanting centres. The probability of an LVAD supported patient presenting with medical emergency to a local ambulance team, emergency department medical team and internal or surgical wards in a non-LVAD implanting centre is increasing. The purpose of this paper is to supply the immediate tools needed by the non-LVAD specialized physician — ambulance clinicians, emergency ward physicians, general cardiologists, and internists — to comply with the medical needs of this fast-growing population of LVAD supported patients. The different issues discussed will follow the patient's pathway from the ambulance to the emergency department, and from the emergency department to the internal or surgical wards and eventually back to the general practitioner.

Keywords Advanced heart failure • Mechanical circulatory support • Left ventricular assist device • Non-LVAD specialist

Introduction

The prevalence of patients with advanced heart failure (HF) is increasing comprising an estimated number of 1–10% of the overall HF population.[1,2] The gold standard for treatment of these patients is heart transplantation (HTx), but this option is limited by the restricted supply of donor organs and by the presence of contraindications to HTx.[3] Mechanical circulatory support (MCS), primarily by left ventricular assist devices (LVADs), has become an important tool for treating patients with advanced HF. The estimated total number of durable continuous flow LVADs implanted worldwide exceeds 100 000 of which 18 539 are reported in the Interagency Registry for Mechanically Assisted Circulatory Support (Intermacs) (2008–2017)[4] and 16 286 reported in the global IMACS registry collecting data from the United States, Europe, Japan and the United Kingdom (2013–2017).[5] Although the actual number of living LVAD supported patients is not reported, the 60% 4-year survival reported in the IMACS registry[5] is expected to improve with the increased global use of the new technologies. The traditional three major indications for MCS: bridge to transplantation (BTT), destination therapy (DT) and bridge to recovery (BTR) are expected to become less evident due to the combination of improved survival on LVAD support and the severe donor organ shortage. HTx is performed to the sicker and unstable end-stage HF patients whereas those implanted with the BTT indication will not be transplanted evolving practically to the DT group.[6]

The survival of patients supported with the new generations of LVADs is constantly improving with recently reported 2-year survival rates of more than 80%.[7] Thus, more patients are expected to be supported with LVADs for longer periods of time. The improved survival and ageing of patients on LVAD support, resulting in longer exposure to MCS, extends the risk for device-related complications as well as for the occurrence of a variety of chronic diseases and comorbidities. These patients require medical services from a broad range of healthcare providers, including family physicians, nurses, emergency medical service (EMS) teams, emergency department (ED), internal and surgical wards, anaesthesiologists, and cardiologists (both in the ambulatory and hospital setting). Many of those health providers are unfamiliar and uncomfortable with the specific issues that may be presented by the LVAD recipient.

The aim of this executive summary is to summarize knowledge and experience related to LVAD support in order to provide practical management guidance to healthcare professionals who are not dealing with LVAD technology on a day to day basis.

Left ventricular assist device system description

The LVADs most frequently used in Europe and the United States and discussed in this document include the HeartWare™ HVAD™ (HW, Medtronic, Minneapolis, MN, USA), HeartMate II™ (HMII) and HeartMate 3™ (HM3, Abbott, Abbott Park, IL, USA). These are all continuous flow devices; the HW and HM3 have a centrifugal and the HM II has an axial flow rotor mechanism. Although in June 3rd Medtronic, the manufacturer of HW has abruptly pulled the device from the market, the company announced it is establishing a programme to support the approximately 4000 patients that are currently supported with the device. The components of the LVAD system are presented schematically in *Figure 1*. The inflow cannula connects the left ventricular (LV) cavity to the pump. The pump, housing a frictionless rotor, transfers the blood from the LV cavity to the ascending aorta through the outflow graft. The driveline, a cable that exits the body at the lower abdominal wall, connects the pump to the external controller and to the energy supply. The controller is the system's computer, connected to the driveline and to the power sources that consist of rechargeable batteries lasting between 6–19 h, or an external power source. The actual extracorporeal parts of the system including batteries and controller are presented in *Figure 2* (HM3) and in *Figure 3* (HW).

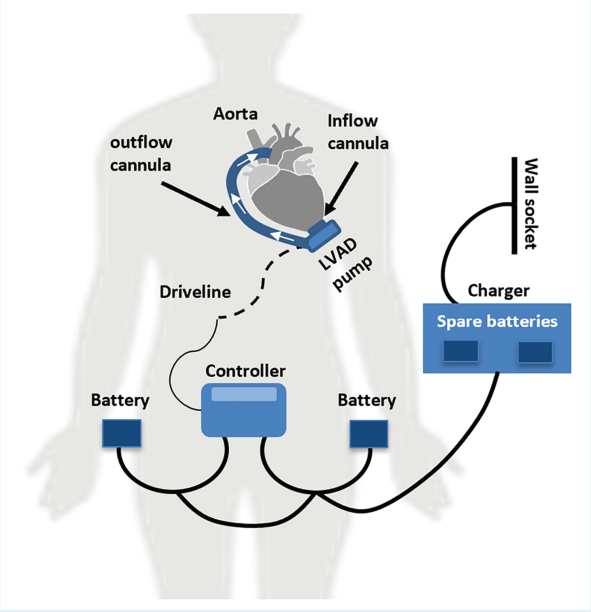

Figure 1 Illustration of a left ventricular assist device (LVAD) with its components. Components of the LVAD system: (i) inflow cannula — stationed inside the left ventricle connects the left ventricular cavity to the pump and directs blood into the pump; (ii) pump — the body of the LVAD, located at the apex of the left ventricle, houses the impeller (magnetically levitated frictionless rotor), connected to the ascending aorta via the outflow graft; (iii) outflow graft — flexible conduit that directs blood from the pump to the ascending aorta; (iv) driveline — the pump is connected by the driveline, a cable subcutaneously tunnelled from the pump exiting the body at the lower abdominal wall, to the external controller and the energy supply. The cable contains double set of wires that provide power and operating details to the pump from the controller; (v) external controller — the controller is the system's computer. It monitors pump function (flow, speed, power), controls pump speed and power supply, records pump data and alarms; displays battery life and function. The controller is connected to the driveline and to the power sources (the batteries or external power supply like the wall socket); (vi) batteries — two lithium batteries.

Typical left ventricular assist device operating parameters (*Table 1*)

Pump speed

This is the speed of the internal rotor spin and is displayed as revolutions per minute. The different devices have different ranges of working device speeds and speed change increments. Pump speed is fixed and set for each device by the LVAD team using specialized equipment. Current devices are programmed to temporarily reduce the speed to a set value in case of diminished blood flow to the device. This lower speed is also set by the LVAD team.

Figure 2 The extracorporeal parts of the HeartMate 3 system including batteries and controller.

Figure 3 The extracorporeal parts of the HeartWare system including batteries and controller.

Table 1 Typical left ventricular assist device operating parameters and picture

Picture	HeartMate II	HeartMate 3	HVAD
Typical speed, rpm	8000–10 000	5000–6000	2400–3200
Speed adjustment increment, rpm/increment	200	100	20
Flow, L/min	4–7	4–6	4–6
Power, W	5–8	4.5–6.5	3–7
Pulsatility index (peak to trough)	5–8	3.5–5.5	2–4

Pump flow

The amount of blood flowing through the pump is reported on the system controller in litres per minute. Notably, the flow is an estimated value based on pump speed and the power needed to exert that speed. The flow estimation may not be accurate in case of physiologic derangements such as aortic insufficiency or LVAD dysfunction, including pump thrombosis.

Pump power

The LVAD pump power (watts) is a measure of the current and voltage applied to the motor and varies directly with pump speed and flow.

Pulsatility index

The pulsatility index (PI) corresponds to the magnitude of flow pulse through the pump and is determined by pump speed and the patient's native heart function. The controller measures temporal power fluctuations to give an estimate of pulsatility through the pump in numbers for the HeartMate devices and represented graphically as a waveform for the HW device. Magnitude of the PI value is related to the amount of assistance provided by the pump: higher values indicate more ventricular filling and higher LV pulsatility while lower values indicate less ventricular filling and lower pulsatility. The PI fluctuates with changes in the volume status and in the heart contractility. It increases when LV preload and contractility increase and decreases when blood volume and LV afterload are reduced and when there is an obstruction to the inflow cannula or to the outflow graft that causes low flow and abnormal power. PI values are routinely monitored and should not vary significantly during resting conditions.

Initial assessment of the left ventricular assist device supported patient in the ambulance and/or emergency department

The initial evaluation of an LVAD supported patient includes assessment of non-LVAD-related and LVAD-related clinical characteristics. Among the non-LVAD-related features are the presence of typical advanced HF characteristics including dyspnoea, fatigue, volume overload and cachexia as well as other comorbidities and all related medical and device therapies. The LVAD-related characteristics include clinical manifestations of LVAD complications or possible malfunctioning of the LVAD system which may trigger specific alarms necessitating an urgent response.

Medical history

Determine the manufacturer and model of the device, the date of its implantation, and identify the LVAD implanting centre with contact phone number. Ask the patient or his/her close caregiver for any recent alarms and record the type. Assess the specific pump parameters such as pump speed power and flow. Following this LVAD specific information, other clinical issues must be addressed:

- Re-occurrence of HF signs and symptoms?
- Bleeding event?
- Driveline infection?
- Any discharges from the defibrillator (if present)?
- Any change in urine colour? (dark urine?)

Flow adequacy and patient clinical assessment

Automated blood pressure (BP) devices and pulse oximeters will be effective in approximately 50% of LVAD supported patients.[5] If monitoring the patient with these basic devices fails, use Doppler techniques for measuring mean arterial pressure (MAP). The optimal MAP range for LVAD supported patients is 70–90 mmHg.[6] A capillary refill of more than 2 s indicates pathologic low BP as well as cool and abnormal skin colour. Evaluate the patient's respiratory status – normal, agonal, or apnoea.

Auscultate to the patient's chest. The normal hum produced by the LVAD is clear, loud, and easily heard; the presence of a hoarse LVAD hum may be an indication of device malfunction whereas complete absence of the hum means that the device is not functioning.

Suction events

A suction event occurs when there is reduced preload and reduced filling of the pump causing part of the LV wall to be sucked over the inflow cannula. The system will sound an alarm and the speed will decrease to release the sucked ventricular wall. Suction events are caused by hypovolaemia, right ventricular (RV) failure or tamponade and may lead to low LVAD flows and can trigger ventricular arrhythmias. Management of a suction event includes decreasing the pump speed and re-hydration.

- Due to the continuous flow physiology, almost half of LVAD patients do not have a palpable pulse and measuring BP and oxygen saturation may be difficult.
- Use Doppler techniques for measuring MAP, optimally between 70–90 mmHg.
- Use clinical evaluation to assess the patient.
- A capillary refill >2 s and or cool and abnormal skin colour indicates pathologic low blood pressure.
- Respiration: normal, agonal, or apnoea.
- Auscultation to the patient's chest: clear, hoarse, or totally absent hum indicating normal, device malfunctioning or non-functioning, respectively.

Cardiopulmonary resuscitation for left ventricular assist device supported patients (*Figure 4*)

The cause for unconsciousness in an LVAD supported patient is not necessarily of cardiac origin. If the device is functioning and no alarm is heard, it is unlikely that the cause is cardiac: it could be related to a neurologic event such as intra-cranial bleeding. In such cases, no benefit is expected from chest compressions.

In the LVAD patient with non-functioning device and circulatory arrest, first inspect the cables, controller, and batteries. Expose the abdomen of the patient and look for the integrity of the driveline exiting the abdominal wall.

Concomitantly, try to contact the ventricular assist device centre without delaying emergency treatment. In the absence of signs of life, the first in contact with the patient is encouraged to immediately start cardiopulmonary resuscitation (CPR).

Chest compression

Evidence regarding the utility of CPR in LVAD supported patients is scarce. In the very few cases reported, none have used mechanical

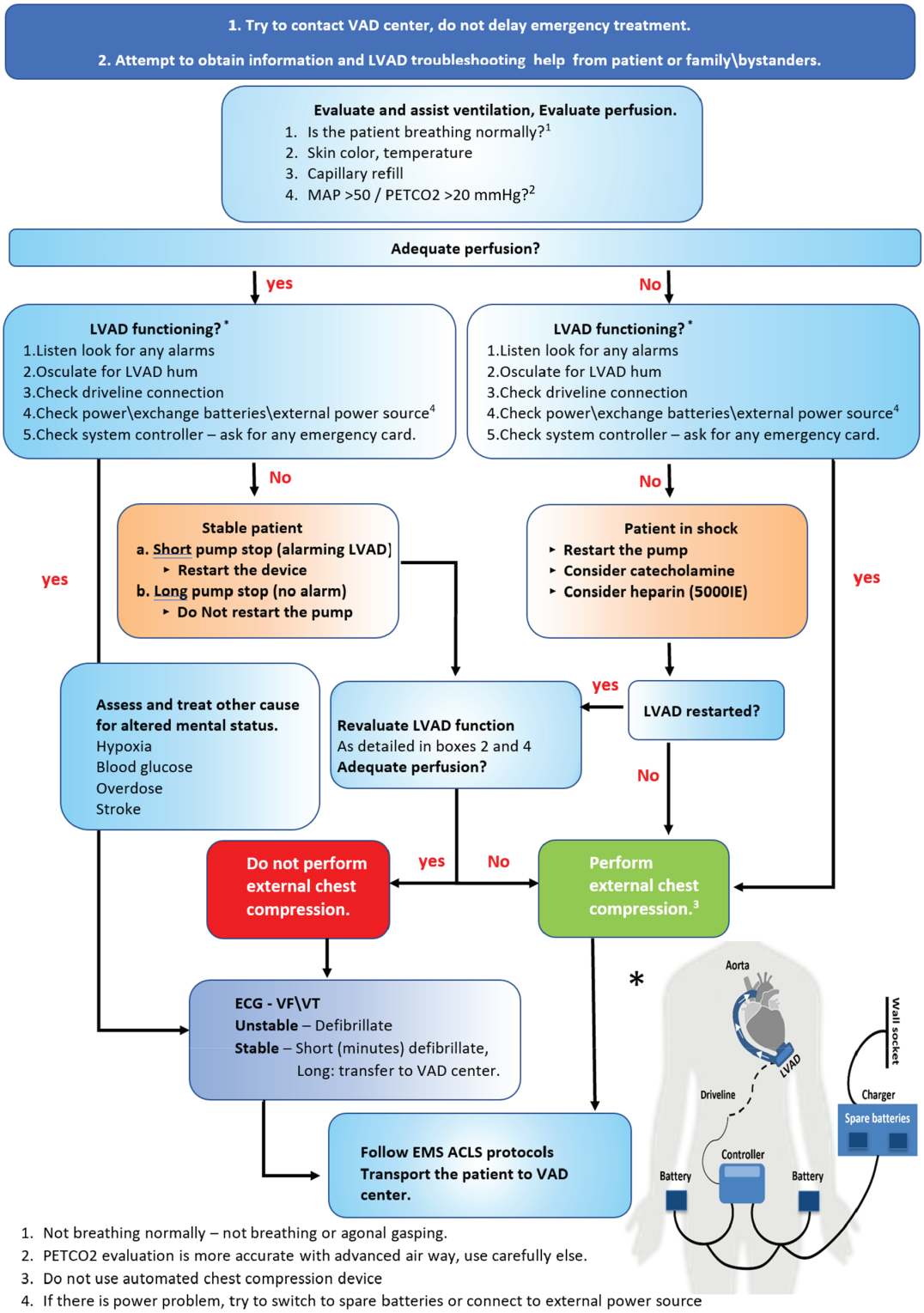

Figure 4 Initial assessment and management of the unstable left ventricular assist device (LVAD) supported patient. ACLS, advanced cardiac life support; ECG, electrocardiogram; EMS, emergency medical service; MAP, mean arterial pressure; $PETCO_2$, end-tidal carbon dioxide partial pressure; VAD, ventricular assist device; VF, ventricular fibrillation; VT, ventricular tachycardia.

chest compression. It is assumed that CPR with manual chest compression in LVAD patients is safe and might even be helpful[5–7] but being much more aggressive with mechanical compressions, probably will be of no help.

Left ventricular assist device reconnection

Restarting the pump after an episode of loss of power and pump stop carries the risk of pump thrombosis and embolization. In case of pump stop:

(i) Short pump stop (minutes; LVAD still alarming)
  – re-start the device immediately

(ii) Long pump stop (hours; no alarm sounds) and stable patient
  – Do not re-start the pump
  – Transport to the nearest LVAD centre

(iii) Short or long pump stop and unstable patient (shock or non-responsive)
  – Re-start the pump immediately
  – Treat underlying condition of shock, start vasopressors
  – If there is no overt bleeding, start intravenous (IV) heparin.

For the emergency medical service teams

(i) If no sign of life: immediately start CPR.
(ii) Take a quick history if possible, from the patient, caregiver or bystanders.
(iii) Check for the device manufacturer — look for the 'identity document' bracelet.
(iv) Contact the LVAD centre (LVAD coordinator).
(v) Check the device equipment from the driveline exit site through the controller to the batteries.
(vi) Ask for the emergency card.
(vii) Ask the family for all the LVAD equipment.
(viii) Ask the family's help with troubleshooting the device.

- When evaluating LVAD patients in the acute scenario, look for any identification, ask the patient and/or caregiver for help and try to contact the LVAD centre.
- When indicated, start CPR as soon as possible.
- Chest compression is safe in LVAD patients. Avoid using automated devices.

Following the life saving measures applied by the EMS and ED teams aimed at achieving temporal clinical stabilization, the ED team will be challenged by the medical emergencies presented in their unique form by the LVAD supported patients such as arrhythmias, bleeding, neurologic events, pump thrombosis, chest pain, syncope and more.

The initial assessment and management of the unstable LVAD patient is presented schematically in *Figure 4*.

Arrhythmias

Arrhythmias are common in LVAD recipients, leading to hospitalization in 30–40% of the patients within the first 2 years after LVAD implantation.[8] In most LVAD supported patients, atrial fibrillation (AF) is not manifested clinically and anticoagulation is rarely an issue for most of the patients who receive vitamin K antagonists as part of their regular LVAD management. In rare cases, AF may become acutely symptomatic if RV function is marginal and in others it may lead to poor exercise capacity. Treatment of AF follows the principles applied in non-LVAD supported patients,[8] but ablation is rarely considered.

Ventricular tachycardia or fibrillation (VT/VF) is reported in 20–50% of LVAD recipients.[9] The main predisposing factor for VT/VF post-LVAD implantation is ventricular arrythmias prior to the implant.[10] VT/VF may arise because of the underlying heart disease, from scar tissue related to the LVAD operation or due to mechanical irritation of the LV inflow cannula, especially if excessive LV unloading is present ('suction' events).

Sustained VT or even VF does not necessarily lead to acute haemodynamic compromise in LVAD patients.[11] During sustained VT or VF, although RV function is impaired, systemic blood flow can persist if LV preload is maintained.

The management of LVAD patients with VT/VF depends on the clinical presentation of the patient. Electrocardiogram (ECG) monitoring and IV access must be ensured. If the patient has an implantable cardioverter defibrillator (ICD), and is awake, immediately place a magnet over the ICD to prevent discharges. If the VT/VF in the LVAD supported patient results in haemodynamic instability, immediate sedation and emergent cardioversion are indicated. Defibrillating a LVAD supported patient will not harm the device and the location of the pad placement on the chest is like the non-LVAD patient. In the haemodynamically stable patient, IV amiodarone (300 mg) and reduction in pump speed (if possible, echo guided) are advised. If the patient is dehydrated and echocardiography suggests an unfilled left ventricle, administer IV fluids. In patients not responding to these measures, sedation and cardioversion must be performed together with correction of acidosis, hypokalaemia and hypomagnesaemia if present. Further treatment includes optimization of beta-blocker doses, prolonged antiarrhythmic therapy (often amiodarone) and ablation in refractory cases.[12]

(i) AF may present as RV failure. In such cases, cardioversion might be clinically beneficial.
(ii) Stable LVAD patients presenting with VF/VT need to be immediately transferred to a hospital with a cardiology centre.
(iii) Haemodynamically unstable patients presenting with VT/VF should undergo emergency cardioversion.

Bleeding

Bleeding complications are common in LVAD carriers with an incidence ranging between 32–44%.[13,14] The underlying pathophysiology is complex, but involves anticoagulation therapy, acquired von

Willebrand syndrome and development of (mainly gastrointestinal) arteriovenous malformations possibly due to low arterial pulsatility. Risk factors for bleeding include older age and female gender,[15] lower body mass index, history of bleeding prior to LVAD implant, smoking, elevated international normalized ratio (INR) and a low platelet count.[16]

Depending on bleeding severity, temporary interruption of anticoagulation or, if deemed clinically justified, even reversal of anticoagulation might be necessary.[17] These decisions are better made in close collaboration with experienced HF cardiologists or the LVAD team, due to the possible adverse outcomes (i.e. device thrombosis).

Gastrointestinal bleeding

Gastrointestinal bleeding can occur in any part of the gastrointestinal tract, but most often in the upper small intestine, proximal to the Treitz ligament.[17]

Invasive procedures

Diagnostic and treatment options include upper and lower gastrointestinal tract endoscopies, video capsule endoscopy, or deep enteroscopy.[17,18]

If these are not able to locate the bleeding site, angiography could be performed (in unstable patients, interventional radiology might be a good option), or scintigraphy with tagged red blood cells.

Medical treatment

(i) Initiation of IV proton pump inhibitors is indicated,[19] especially when involvement of the gastric mucosa is suspected.
(ii) Octreotide, a synthetic somatostatin analogue, has also been tried in gastrointestinal bleeding not responding to other measures.[20]

Other forms of bleeding that might be encountered in LVAD carriers include bleeding from the nasal or oral mucosa, seen usually as epistaxis, after teeth extraction, skin bruising, or haematuria.[15] Managing such bleeding episodes follows the principles applied to non-LVAD supported patients and only if considered severe or long standing, referred to the relevant specialist.

(i) Gastrointestinal bleeding is the most frequent source of bleeding in LVAD supported patients.
(ii) When reversal of the anticoagulation is needed, opt for less aggressive means such as oral vitamin K or fresh frozen plasma (FFP) depending on bleeding severity to reduce the risk of pump thrombosis.
(iii) In moderate blood loss, try to avoid blood transfusion in the BTT group and, when possible, prefer IV iron supplements.

Neurological events

Patients on LVAD support are routinely treated with a vitamin K antagonist targeting INR levels of 2–2.5 in most institutions (in others 2–3). Despite proper, or due to over anticoagulation, stroke is a leading cause of significant morbidity in patients with LVAD hampering future cardiac transplantation.[21,22] In a large cohort of LVAD patients, during a follow-up of 0.02–34.96 months (median 9.79), 9.2% had at least one stroke yielding an estimated incidence rate of 0.123 strokes per patient-year.[21] Approximately half of the strokes were ischaemic and half haemorrhagic; infection significantly increased the risk of stroke in these patients.[22]

In LVAD patients with new neurological symptoms, cerebrovascular injury is highly suspected, and cerebral computed tomography (CT) scanning be performed with no delay.

Ischaemic stroke

The efficacy of IV recombinant tissue plasminogen activator has not been assessed in LVAD-related strokes.[22] Thrombolysis may be ineffective since emboli from within the LVAD may have a composition (fibrin and denatured protein) that may not be amenable to thrombolysis. Endovascular stroke therapy, including in selected cases even mechanical thrombectomy, may provide specific clinical and diagnostic benefits in patients with an LVAD.[23] The risk of haemorrhagic transformation with endovascular stroke therapy appears like that of systemic thrombolysis.[23]

Haemorrhagic stroke

There are several possible causes of haemorrhagic stroke in patients with LVAD, such as anticoagulation, haemorrhagic conversion after ischaemic stroke, acquired von Willebrand syndrome and rupture of histologically fragile vessels caused by the non-physiological continuous pulseless flow.[24,25]

Pre-implant risk factors for haemorrhagic stroke include heparin-induced thrombocytopenia, treatment with intra-aortic balloon pump and female sex.[21]

The presentation of haemorrhagic stroke in LVAD supported patients ranges from mild neurological signs to deep unconsciousness that, due to the pulseless nature of the continuous flow, might be mistaken for circulatory arrest. The mainstay of therapy in haemorrhagic stroke or intra-cranial haemorrhage (ICH) is reduction of excessive BP and reversing coagulopathy. The acute treatment of BP elevations in the LVAD patient with an ICH is not well established. Reduction of MAP to <90 mmHg is advised.[26] Reversal of warfarin can be obtained with FFP, prothrombin complex concentrate (PCC), vitamin K, or a combination. PCC is beneficial in neurosurgical emergencies, given its faster effect.[22]

Depending on the severity of presentation, some patients will require surgical treatment, such as craniotomy with drainage.[6] Routine administration of platelets is avoided in ICH, since adverse outcomes have been noted, but it might be beneficial in patients undergoing neurosurgical intervention.[22]

(i) When a patient with LVAD presents with an ischaemic stroke, infection or sepsis might be the potential causes.
(ii) Beware of haemorrhagic conversion.

(iii) Treatment of haemorrhagic stroke includes lowering MAP to below 90 mmHg, and reversion of anticoagulation with FFP, or PCC.

Suspected pump thrombosis

Pump thrombosis may occur in up to 10% of LVAD supported patients (lifelong risk),[27] although considerable differences in incidence between devices exist. Pump thrombosis refers to the development of a clot within the flow path of any component of the pump: the inflow cannula, the rotor, or the outflow graft. The thrombus can be created within the LVAD or it can travel from either the left atrium or the left ventricle and lodge into any of the pump components.

Inflow cannula and intra pump thrombus is suspected in the setting of any of the following: signs of worsening HF (progressive dyspnoea on exertion), acute changes in LVAD parameters ('low flow' alarms and LVAD power spikes), haemolysis: lactic dehydrogenase increase, haemoglobin drop, plasma free haemoglobin rise and darker urine, and signs of distal embolization.

In case an LVAD thrombus is suspected, the LVAD alarms and power spikes need to be explored. If the decrease of power and flow happens in a short period of time, an inflow pump thrombosis is the more reasonable diagnosis. The suspicion of intra device or inflow cannula thrombus can be confirmed using the following tools:

- Transthoracic echocardiogram
  - LV enlargement
  - Opening of the aortic valve in each cycle
  - Worsening mitral regurgitation
  - Inflow cannula turbulence
  - Visible thrombus
- CT angiography (CTA): no outflow graft obstruction.

Outflow graft obstruction/thrombosis

Although the outflow graft is the less prevalent site of a pump thrombosis, the diagnostic process is very similar to the one of an inflow cannula thrombosis with some modification.

The patient presentation will be very similar with progressive dyspnoea on exertion, 'low flow' alarms and LVAD power spikes but occurring gradually for a longer period of time. Haemolysis may be absent. The suspicion of an outflow graft obstruction can be confirmed using the following tools[28]:

- Transthoracic echocardiogram
  - LV enlargement
  - Opening of the aortic valve in every cycle
  - Worsening mitral regurgitation
  - Outflow graft turbulence
  - No thrombus is seen inside the left ventricle

Table 2 Differences between inflow and outflow pump thrombosis

	Inflow and intra pump thrombosis	Outflow pump thrombosis
Signs and symptoms	Progressive exertional dyspnoea	Signs of distal embolization
LVAD parameters	Low flow alarms	Power decrease in spikes
Duration	Short	Gradual, longer
Haemolysis	LDH increase Haemoglobin drop Plasma free haemoglobin rise Darker urine	May be absent
Echocardiography	LV enlargement Aortic valve opens every cycle Worsening MR Inflow cannula turbulence Visible thrombus	LV enlargement Aortic valve opens every cycle Worsening MR Outflow cannula turbulence No visible thrombus inside the LV
CTA	No outflow graft obstruction	Outflow graft stenosis present Outflow graft obstruction present Identification of the cause
IVUS	Not indicated	Outflow graft internal diameter Intraluminal tissue/external pressure

CTA, computed tomography angiography; IVUS, intravascular ultrasound; LDH, lactic dehydrogenase; LV, left ventricle; LVAD, left ventricular assist device; MR, mitral regurgitation.

- CT angiography
  - Outflow graft stenosis present
  - Outflow graft obstruction present
  - Identification of the cause for the outflow graft obstruction
  - Intravascular ultrasound (IVUS): identification of the nature of the outflow graft internal diameter
  - Narrowing: intraluminal tissue growth or external pressure.

For differences between intra and outflow pump thrombosis, see *Table 2*.

There are no randomised studies on the treatment of LVAD pump thrombosis, therefore, it is advised to discuss and coordinate the therapeutic strategy with the hub LVAD centre. The presented interventions are based on anecdotal case reports[29]:

- First, adjust INR levels to 2.5–3.5.
- Second, try continuous heparin infusion to a partial thromboplastin time (PTT) goal of 80–100 s. The use of bivalirudin is preferred by some centres and generally in the presence of heparin-induced thrombocytopenia.[29]
- Third, if non-responsive so far or unstable, try thrombolytic therapy. If non-responsive yet or becoming unstable the patient might need pump exchange.

(i) Pump thrombosis is a life-threatening event that must be addressed immediately — contact the implanting centre.
(ii) Stabilize the patient, confirm the diagnosis and promptly initiate medical treatment.

(iii) Use increased anticoagulant therapy and stenting in outflow graft thrombus.
(iv) If medical treatment fails, contact the implanting centre for an advanced therapy.

Chest pain

Chest pain in patients with LVADs is commonly encountered and can have cardiac and non-cardiac causes.[30] In most cases, the pain is of non-cardiac origin with a broad differential diagnosis: post-pericardiotomy syndrome, mechanical pain from device-intrathoracic wall contact in slim patients or children, pneumonia/pleuritis, pneumothorax, pneumomediastinum, oesophageal spasm or oesophagitis, cholecystitis or biliary colic, pancreatitis, peptic ulcer, costochondritis, or rib injury or fracture. In some patients, chest pain is caused by carrying the accessory bag on one shoulder only. Local infection must be ruled out if pain is combined with fever or increased inflammatory activity. Rule out myocardial infarction but if myocardial infarction is confirmed, promptly perform transoesophageal echocardiogram for the potential presence of aortic root thrombus.

(i) Chest pain in most cases is of non-cardiac origin and difficult to diagnose.
(ii) Chest pain from cardiac origin in LVAD patients is uncommon but should immediately be ruled out.
(iii) Acute myocardial infarction is rare, and, in its occurrence, suspect embolization from an aortic root thrombus.

Syncope

Syncope and orthostatic symptoms like dizziness, blurry vision, confusion and nausea can be challenging in LVAD patients[6] (*Table 3*). Up to 30% of those patients suffer from orthostatic hypotension. Differential diagnosis for syncope in these patients includes orthostatic hypotension, cardiac factors like arrhythmias, vaso-depressive neurogenic and device-specific mechanical factors. Further contributors to orthostatic hypotension include low intravascular volume state, medications with vasodilator properties, poor RV function and comorbidities like diabetes leading to secondary autonomic failure. Device-specific factors like malposition of the inflow cannula need special attention.

Diagnosis includes careful history taking, thorough physical examination, supine and standing BP measurements, ECG monitoring, and routine blood tests (anaemia).

Therapy must be individually tailored according to the underlying reasons for syncope. In cases of orthostasis, correction of low volume status (higher fluid intake, blood transfusion), removal of vasodilatory drugs or drugs associated with dysautonomia (amiodarone) might prove beneficial.

(i) LVAD patients are prone to syncope, mainly due to orthostatic hypotension.

Table 3 Syncope and orthostatic hypotension: symptoms and differential diagnosis

	Syncope	Orthostatic hypotension
Symptoms	Dizziness Blurry vision Confusion Loss of consciousness	Dizziness Blurry vision Confusion Nausea
Differential diagnosis	Orthostatic hypotension Arrhythmias Vaso-depressive Device-specific mechanical factors Malposition of the inflow cannula	Low intravascular volume Vasodilating medications Right ventricular dysfunction Autonomic failure (diabetes)

(ii) Evaluate the patients for dehydration, anaemia and arrhythmia using ECG, echocardiography, blood tests and pacemaker interrogation.
(iii) When a suction event is suspected, apply fluid resuscitation and consult the LVAD specialist.

Death declaration in the emergency department

In a non-responsive LVAD supported patient brought to the ED the following strategy is suggested.

(i) If LVAD is functioning and the perfusion found to be appropriate, perform acute cerebral CT and consult a neurologist.
(ii) If the LVAD is not functioning, start CPR and re-connect the LVAD to electrical supply if possible.
(iii) Ventilate if not yet done by the EMS.
(iv) Perform an ECG.
(v) Perform basic echocardiography to assess heart function.
(vi) If asystole is not confirmed, assess organ perfusion by performing carotid and femoral Doppler.
(vii) If no perfusion, depending on the patient's status, the duration of CPR and comorbidities, veno-arterial extracorporeal membrane oxygenation is also an option.
(viii) Death declaration is to be performed according to the local law.

In the internal medicine ward

Blood pressure management

A pulse pressure of <15 mmHg is not palpable by physical examination and will not be detected by most automated BP cuffs. Approximately half of the LVAD patients have a low pulse pressure, and hence, no palpable pulse ('non-pulsatile'). If the automated BP cuffs method fails, apply the Doppler method in the following steps:

(i) Identify with the Doppler probe the brachial or radial pulse.
(ii) Manually inflate the cuff.
(iii) Deflate the cuff slowly while holding the probe above the artery.

(iv) The level of the heard pulse represents the MAP[30]:

- If no palpable pulse, use Doppler method and measures MAP
- Palpable pulse, use automated BP cuff and calculate MAP from systolic and diastolic BP.

Elevated BP is associated with cerebrovascular accidents, pump thrombosis, aortic regurgitation and ventricular arrhythmias.[31,32] The optimal BP for LVAD patients is MAP of 70–90 mmHg.[33,34]

Hypertension treatment

Hypertension is common among LVAD patients and is preferably managed with HF medications, such as angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, beta-blockers and mineralocorticoid receptor antagonists.[33,34] Special caution needs to be taken with beta-blockers in patients with RV failure, due to their negative inotropic effect. Second-line medication include calcium channel blockers, alfa-blockers, hydralazine and nitrates. Phosphodiesterase 5 inhibitors used for lowering pulmonary pressure should not be combined with nitrates.

(i) Target MAP to 70–90 mmHg.
(ii) Control BP preferably using HF drugs like renin–angiotensin–aldosterone system inhibitors.
(iii) Use beta-blockers in cases of tachyarrhythmia but be aware of the risk of worsening RV failure.

Anticoagulation

Current guidelines and position papers recommend anticoagulation with vitamin K antagonist for all patients on LVAD support targeting INR levels of 2–2.5 in most institutions (in others 2–3) and low-dose aspirin.[6,33] Long-term anticoagulation is tailored to the recipient and device type.

(i) Anticoagulation is mandatory for all settings of care followed by close monitoring.
(ii) New oral anticoagulant drugs are not to be used in this population

Heart failure exacerbation in left ventricular assist device supported patients

Late (right-sided mainly) HF develops in 15–20% of LVAD recipients.[35] Assessment of the LVAD patient with HF is like the non-LVAD patient with emphasis on interrogation of past events if possible. Treating HF exacerbation starts by deciding whether left or right failure predominate. Treatment includes increasing dosage of diuretics and if needed IV diuretics or inotropic support. In most cases it will be right-sided HF. In the cases of left-sided HF, evaluate device function and settings and maintain strict BP control. Consult with the LVAD centre in order to evaluate the pump history.

In the surgical ward

Anaesthesia for non-cardiac surgery of the left ventricular assist device supported patient

Approximately 30% of all LVAD supported patients will require non-cardiac surgery.[34] Several considerations must be made when planning surgery in LVAD recipients and except for emergency cases, preoperative communication with the LVAD centre is advised.[35]

(i) LVAD centres are preferred for major surgical procedures.
(ii) The LVAD patient is preload-dependent, and afterload-sensitive.
(iii) Critical factors influencing preload in these patients include blood volume, positioning, surgical technique (laparoscopic vs. open), arrhythmias, and RV function.
(iv) Minor cases can safely be monitored in the regular post-anaesthesia care unit whereas major cases require close surveillance in the intensive care unit.
(v) Establish BP monitoring before induction of general anaesthesia
(vi) Maintain MAP 70–90 mmHg.
(vii) Temporarily de-activate ICD.
(viii) Recommence IV heparin 24–48 h post-non-cardiac surgery until therapeutic INR levels.

During any hospitalization, medical or surgical, and at discharge

Infection

Definition of infections in LVAD supported patients can be differentiated according to the standardized classification of infections, formulated by the International Society for Heart and Lung Transplantation Infectious Disease Working Group in 2017.[36,37]

LVAD-specific infections

Only occur in LVAD patients and are directly related to the implanted hardware (i.e. pump, inflow cannula, outflow graft, driveline). These infections are often difficult to diagnose and to eradicate.

LVAD-related infections

May also occur in non-LVAD patients. However specific considerations apply if present in LVAD patients. The entities belonging to this group: endocarditis, blood stream infections, mediastinitis, and sternal wound infection.

Non-LVAD-related infections

Infections independent or not directly associated with the presence of an LVAD such as lower respiratory tract infections like pneumonia, blood stream infections, urinary tract infections, and gastrointestinal infections.

Driveline issues

The driveline is a vulnerable component of LVAD therapy. Infections are the Achilles heel of the LVAD system among which driveline infection is the most common, reported at a range of 15–40% in the 3 years post-LVAD implantation.

(i) In any suspected external damage to the driveline, contact the LVAD team or the manufacturer.
(ii) A fall or pull of the system bag are the primary causes of infection.
(iii) A good fixation of the driveline can reduce the incidence of driveline infection.
(iv) In any case of a significant line pull (bag fall), the healthcare provider is instructed to perform an assessment of the wound, start an empiric antibiotic course and consult the LVAD specialist.
(v) In case of erythema or discharge from driveline exit site, culture and be very liberal with starting empiric antibiotic therapy.
(vi) When empiric antibiotics are started, target the common pathogens as suggested by the LVAD centre.

Fever or other symptoms of infection

(i) Careful history and review of symptoms may prompt early suspicion of infection.
(ii) A detailed physical exam, including inspection of the driveline exit site and surgical wounds is warranted.
(iii) Lab test should include a complete blood count and serial assessment of C-reactive protein or erythrocyte sedimentation rate.
(iv) Take three sets of blood cultures at different time points within the first 24 h of suspicion, at least the first set *before* initiating antibiotic therapy.
(v) If a central or peripheral line is present, take two sets of blood cultures simultaneously, one from the central or peripheral line, the other from a non-related peripheral site.
(vi) Imaging: routinely perform chest X ray. Ultrasound can help detecting fluid collections and differentiate between local and extended infection. Positron emission tomography with CT may be very useful in diagnosing and/or differentiating LVAD-specific and LVAD-related infections. Patients with LVAD are precluded from performing magnetic resonance imaging.

Therapeutic approach

- Blood culture and swabs from the driveline exit site are to be taken prior to initiation of antibiotic therapy.
- Involve your LVAD centre when initiating antibiotic therapy.
- Even in cases of superficial infection without signs of systemic disease, initiation of antibiotic therapy is not to be deferred until the culture results are available but later modified accordingly.
- In case of clinical signs of infection and negative culture results, start empirical antibiotic therapy and assess the clinical response.
- In case of systemic disease or sepsis, empirical IV antibiotic therapy should cover Staphylococcus, Pseudomonas and Enterobacteriaceae species.
- Take the local (institutional) resistance profile into account when initiating antibiotic therapy.
- When using rifampicin adjust the vitamin K antagonists accordingly.

Aortic insufficiency following left ventricular assist device implantation

Aortic insufficiency may develop following implantation of a continuous flow LVAD. In the presence of an LVAD, aortic insufficiency leads to a futile circulatory loop since a portion of the LVAD output flow regurgitates back through the aortic valve to the left ventricle and then back through the device. This leads to ineffective forward flow and may cause organ malperfusion and increased LV diastolic pressures.

LVAD-associated aortic insufficiency is related to reduced valve opening, altered blood flow dynamics, pan cyclic transvalvular gradients, high shear stress, and leaflet malcoaptation.[38]

(i) *De novo* or progressing aortic insufficiency can be the cause for worsening HF symptoms in LVAD patients (perform transthoracic or transoesophageal echocardiogram)
(ii) Moderate and worse aortic insufficiency at the time of LVAD implants requires valve replacement (biological valve) or (rarely) aortic valve closure.
(iii) For LVAD patients with *de novo* severe aortic insufficiency, transcatheter aortic valve replacement can be an option.

Exercise training

Exercise training is beneficial in LVAD recipients. Based on the current consistent, though limited, evidence supporting the safety and benefit of early mobilization and exercise training in the LVAD population, the Heart Failure Association (HFA) of the European Society of Cardiology has developed practical advice on the modality of exercise implementation in LVAD patients.[39]

(i) Early mobilization post-LVAD implantation and 6 weeks of interval training are applied by most centres.
(ii) To optimize the workload prescription to the training LVAD patient, a symptom-limited cardiopulmonary exercise testing or 6-min walking test according to local availability is advisable.

Pre-discharge counselling: education and social support

Education and support of LVAD patients and their close caregiver is vital during the different phases of the LVAD trajectory.

Communication between healthcare providers, LVAD patients and their caregivers needs to address the practical, physical, psychological and social consequences of LVAD implantation.

Successful long-term LVAD support includes maintaining general health such as age-specific recommendations, routine vaccination and dental care[3,6] and a high degree of self-care by the patient and their caregiver requiring long-term support by a multi-disciplinary team.[40]

(i) LVAD patients require close support by a multi-disciplinary team addressing practical, physical, psychological and social consequences of LVAD implantation.
(ii) Instruct the patient and his caregiver on performing self-care maintenance, monitoring and management for best outcomes.

Palliative care and end-of- life issues in left ventricular assist device supported patients

The integration of a palliative approach into advanced HF management has been recommended both within international guidelines[1,3] and expert position papers.[2,41] Patients, prior to LVAD implantation, may derive benefit from the opportunity to discuss end of life concerns with a specialist palliative professional.[42] Including the patient's caregiver in discussions will enable realistic goal setting and provision of ongoing support for the patient.

(i) Provide an opportunity for a palliative consultation prior to LVAD implantation.
(ii) Openly discuss with the patient and family to ensure realistic goals and expectations about LVAD implantation as well as end of life decisions.
(iii) A documented advance plan of deactivation of the LVAD can be very helpful.

Conclusions

The increasing number of advanced HF patients treated with MCS and the improved survival of those patients supported with the new generation LVADs will result in longer support times and ageing of patients on MCS. Those patients will need medical assistance from a broad range of non-LVAD specialist healthcare providers in different clinical scenarios. A constant update of knowledge is needed to provide optimal care for this growing group of patients. The non-LVAD specialist healthcare provider encountering a LVAD supported patient should use this document to increase confidence and provide the necessary treatment in the appropriate clinical setting.

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