Criteria for Status 4 Eligibility in LVAD complications

Michael McDonald, Mustafa Toma, Nakul Sharma, Jennifer Conway, Rohit Singal, Kim Anderson, Brian Clarke

on behalf of the Canadian Cardiac Transplant Network

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Preamble

Left ventricular assist device (LVAD) therapy improves survival and quality of life for patients waiting for heart transplantation. While life-threatening complications are rare, there are several clinical scenarios where urgent heart transplantation is warranted. The contents of this document outline the eligibility criteria for Status 4 listing for LVAD patients on the heart transplant waiting list in Canada.

These criteria are based on currently available scientific evidence and consensus of the Canadian Cardiac Transplant Network. There are several overarching guiding principles that are universally applied in all scenarios where Status 4 eligibility for LVAD complication is considered:

1) The LVAD complication causes an imminent life-threatening scenario

2) The patient continues to be deemed a transplant candidate

3) Mandatory discussion (as per CCTN policy) between the donor and recipient site at the time of an offer in cases of interprovincial sharing, in appropriate clinical situations

4) To be eligible for high status, LVAD patients must be, and remain ill enough, to warrant ongoing hospitalization

5) If the surgical team feels that revision or exchange of the LVAD will be too hazardous for technical reasons, then it may be reasonable to consider high status listing as the upfront preferred approach in certain LVAD complication scenarios.

This document outlines eligibility for Status 4 in the following areas of LVAD complication:

1) Pump Thrombosis
2) Infection
3) GI Bleeding
4) Arrhythmia
5) Right Heart Failure

Pump Thrombosis

Continuous flow devices (any 1 of the following)

1) Failure of medical management of a pump thrombosis **AND** contraindication to pump exchange
2) Previous pump exchange **AND** new pump thrombosis despite adequate anticoagulation
3) Pump thrombosis with a thromboembolic event with no significant limiting neurologic deficit and contraindication to pump exchange **OR** previous pump exchange

Pulsatile Devices (Pediatrics) (any 1 of the following)

1) Ischemic Stroke (given the 30% stroke risk and risk of subsequent events)
2) Recurrent pump exchanges itself **should not** be considered a factor for Status 4 listing given the various thresholds for pump exchanges

Definition of pump thrombosis:

Hemolysis associated with alteration in device performance (alterations in pump parameters and other device-specific indicators of device dysfunction)

Definition of hemolysis:

2 separate samples measured within 48 hours confirming markers of active hemolysis as evidence by at least 2 of the following criteria:

- LDH $\geq$ 2.5x ULN
- Plasma free hemoglobin $\geq$ 20mg/dL
- Hemoglobinuria

Infection

The patient must be hemodynamically stable without evidence of septic shock to qualify for status upgrade in the setting of infection. Any 1 of the following enables Status 4 listing:

1) Persistent Blood Stream infection OR IV antibiotic dependence, due to any device-related infection.

    - There should be reasonable expectation that the infection is treatable with low likelihood of serious sequelae post transplant

2) Bacteremia with imaging evidence of pocket, device, cannular, or outflow graft infection
    i. CT imaging
    ii. PET imaging
    iii. Ultrasound

    - Listing should be delayed until effective antimicrobial therapy has been initiated and bacteremia has cleared x 72hours.

3) Positive culture material from the pump pocket of an implanted device

4) Persistent cannula infection with resistant organisms

***Device related blood stream infections with *Candida, Pseudomonas, Staph aureus* does not preclude status 4 listing when there is agreement that post transplant treatment success is expected without serious sequelae.

GI Bleeding

All of the following criteria must be met:

1. At least **3 eligible episodes** of gastro-intestinal bleeding in a period of **6 months or less.**

2. To be eligible, an episode of gastro-intestinal bleeding must meet ALL the following criteria

    i. Each episode must happen while the patient is supported by a continuous flow LVAD.

    ii. Each single episode required a minimum of 4 units of packed red blood cells (PRBC) transfusion to maintain an Hb of $\geq$ 90g/L

    iii. The cause of bleeding must be related to the continuous-flow LVAD support with the reasonable expectancy to resolve by the recovery of a pulsatile flow and removal of the high shear stress induced by the LVAD, which would be possible only with a cardiac transplantation. As such, other causes of bleeding unrelated to LVAD support must have been eliminated.

    iv. Bleeding event happening solely while anticoagulation is supra-therapeutic should not qualify if resolution occurs when the INR is reduced to the target limits established for the device.

3. Thorough investigations were undertaken to identify the source of bleeding and must include updated upper and lower gastro-intestinal imaging as well as small bowel investigation (for gastro-intestinal bleed).

4. All medical therapies have been exhausted with continued bleeding episodes. Active collaboration with a gastroenterologist is mandatory.

5. Bleeding episode within 7 days after LVAD implantation is not eligible.

Definition of a gastro-intestinal bleeding event:

Either criterion 1 OR 2 is sufficient to fulfill the definition:

1) Overt bleeding from the upper or lower GI tract manifested by melena, hematochezia or hematemesis prompting hospitalization and endoscopic or radiologic evaluation

2) Occult bleeding, with a ≥20 g/L drop in hemoglobin from recorded baseline values and hemoccult positive stool with no alternative explanation for anemia and no hemolysis.

The end of an individual GI bleed episode will be defined as passage of non melenic stool and absence of hematochzia and hematemesis for at least 48h.

In patients where this would be difficult to assess, absence of transfusion requirement for 5 days will be considered as the end of an episode of GI bleeding (as most GI bleeding episode resolves in 4 days).

Arrhythmia

Refractory sustained ventricular arrhythmia (>3 episodes sustained ventricular arrhythmia in 24 hours) despite attempts at medical suppressive therapy with beta blockers and at least 1 anti-arrhythmic drug infusion and electrophysiological ablation, OR not a candidate for ablation as deemed by the electrophysiology team, causing any ONE of the following:

1) VAD malfunction
2) Right heart failure (see criteria below)
3) Severe Hemodynamic deterioration
   3.1. Sustained MAP <60mmHg during ventricular arrhythmia
4) ICD shocks for electrical storm ($\geq$ 3 shocks in 24 hours)

Right Heart Failure

1) Patient meets the INTERMACS criteria for Severe RV failure (see below) at least 3 months post LVAD implant.

   AND

2) Despite appropriate management (pulmonary vasodilators, inotropic support and/or mechanical intervention) has:

   i) ***Declining*** VAD and/or hepatic/renal dysfunction ***despite*** RV optimization with optimal medical therapy, which must include inotropes.

   Or

   ii) Right heart failure requiring RVAD

INTERMACS Definition of SEVERE Right Heart Failure Definition:

Symptoms or findings of persistent right ventricular failure characterized by **both** of the following:

1) Documentation of elevated central venous pressure (CVP) by:
   - Direct measurement (e.g., right heart catheterization) with evidence of a central venous pressure (CVP) or right atrial pressure (RAP) > 16 mmHg.

2) Manifestations of elevated central venous pressure characterized by:
   - Clinical findings of peripheral edema (≥2+ either new or unresolved), **OR**
   - Presence of ascites or palpable hepatomegaly on physical examination (unmistakable abdominal contour) or by diagnostic imaging, **OR**
   - Laboratory evidence of worsening hepatic (total bilirubin > 2.0mg/dL, 34.2μmol/L) or renal dysfunction (creatinine > 2.0mg/dL, 177μmol/L).

PLUS:

Need for inotropes for >14 days **OR** 2 or more readmissions for intravenous diuretics/vasodilators to treat RHF **OR** RVAD.