Ventricular Assistance Devices as Bridge to Transplantation

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KEYWORDS

• Ventricular assistance devices • Heart transplantation • Therapeutic strategies
• Posttransplant outcomes

KEY POINTS

- Bridge to transplantation is a major indication for ventricular assistance device (VAD) implantation both as a life-saving measure and in the elective setting.
- VAD implantation improves patients' status and can reduce operative risk.
- VAD implantation does not seem to adversely affect posttransplant outcomes, at least in selected patients.
- Bridge to transplantation by VAD can potentially be cost-effective in some patients groups.

BACKGROUND

Almost 50 years after the first procedure performed in 1967, heart transplantation still remains the gold standard for the treatment of advanced and refractory heart failure (HF) because of its excellent long-term outcomes. The number of procedures carried out worldwide dramatically increased in the early 1980s following the clinical employment of cyclosporine to prevent graft rejection. Since the 1990s, the total number of transplants slowly started to decrease, until reaching (since the 2000s) a stable number of about 4500 procedures per year.[1] Although transplants have remained stable, the number of patients waiting for a heart continues to increase and actually largely exceeds the available organs; in North America, 13.6% of patients die while on the waiting list for transplantation.[2]

Mechanical circulatory support (MCS) is an umbrella term that encompasses various devices that sustain or even replace cardiac function. The first clinical applications of MCS date back to the 1960s, mostly in the setting of postcardiotomy cardiogenic shock.[3] The development of durable, implantable MCS devices was initially conceived for indefinite support (destination therapy) in patients who were not eligible for heart transplantation. Concerns about the long-term performance and safety, however, led regulatory agencies to restrict the initial use of such devices to patients who were eligible for a transplant. This bias set the early stage for what has become the bridge to transplantation (BTT) indication.[4]

The devices typically used for BTT are ventricular assistance devices (VADs). These devices are pumps connected to the patients' circulation that partially or completely replace the function of the left or right side of the heart (or both). Both percutaneously and surgically implanted VADs are available. The first type (intravascular or extracorporeal) is intended for temporary, short-term use, whereas surgically implanted (intracorporeal or paracorporeal, axial or centrifugal) VADs are for

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midterm or long-term use. The first VADs were paracorporeal, bulky pulsatile pumps (mostly pneumatically driven) requiring hospitalization and allowing very poor patient mobilization. The development of continuous-flow, axial pumps (second-generation VADs) eliminated the reservoir chamber and valves needed for the first-generation pulsatile pump. This development has led to more reliable, smaller, and totally implantable devices, thereby allowing a quality of life that is comparable with normal. The magnetic and/or hydrodynamic levitation of the impeller without any contact bearings with the pump is the major advancement of the third-generation VAD.[5]

INDICATIONS FOR BTT

To date, there is no universal consensus on the indications for MCS as a BTT. The Heart Failure Society of America's comprehensive HF practice guidelines[6] state that patients awaiting heart transplantation who have become refractory to all means of medical circulatory support should be considered for an MCS device as a BTT (level of evidence B). Also, patients with refractory HF and hemodynamic instability and/or compromised end-organ function with relative contraindications to cardiac transplantation or permanent MCS expected to improve with time or restoration of an improved hemodynamic profile should be considered for urgent MCS as a bridge to decision (ie, in order to gain time for a further evaluation over the most appropriate strategy) (level of evidence C).

The European Society of Cardiology's 2012 guidelines for the diagnosis and treatment of acute and chronic HF recommend left VAD (LVAD) or biventricular assistance device support as BTT in selected patients with end-stage HF despite optimal pharmacologic and device treatment and who are otherwise suitable for heart transplantation to improve symptoms and reduce the risk of HF hospitalization for worsening HF and to reduce the risk of premature death while awaiting transplantation (class I, level of evidence B).[7]

Establishing the time frame for implantation of MCS is crucial to maximize the benefit and minimize the risk of MCS. The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) is a US registry that acquires data on patients supported with Food and Drug Administration–approved MCS devices. In the registry, patients in the New York Heart Association III to IV class are further classified into 7 clinical profiles according to their signs and symptoms (7 being the least and 1 the most severe profile) (**Table 1**). The prognostic implications of the INTERMACS profiles provide guidance for the indication for MCS; for the optimal timing of implantation; and ultimately, for the selection of the appropriate device.[8] INTERMACS 1 patients need MCS within hours; rapidly implantable devices, like intra-aortic balloon counterpulsation, percutaneously implanted VADs, or extracorporeal membrane oxygenation (ECMO) will bridge the patients to durable MCS devices or transplantation. Patients in the INTERMACS 2 profile require enrollment in the emergent transplantation list or, alternatively, MCS support to be provided within days; both short-term and surgically implanted VADs can be considered. INTERMACS 3 and 4 patients are in end-stage HF and are waiting for elective MCS implantation; surgically implantable devices are the devices of choice.

VAD AS BTT: SETTINGS AND CURRENT STATUS

In the current clinical practice, BTT is a major indication for VAD implantation. In the most recent publication from the INTERMACS registry, 54.1% of the primary VAD implantations were for BTT (with about half of the implanted patients listed for transplantation at the time of the device implantation).[9] Similarly, the 2010 International Society of Heart and Lung Transplantations' report shows that the incidence of VAD-supported cases at the time of transplantation increased from 11% in 1999 to 36% in 2011[1]; most of the cases (89%) are supported with LVAD, almost 10% require biventricular assistance, and only a small minority (1%) need right ventricular support.

Patients receive VAD as a BTT in 2 different settings. A consistent number of cases receive VAD in the setting of acute, unresponsive cardiogenic shock as a life-saving measure (INTERMACS 1 and 2 patients). In this setting, VAD implantation as a BTT seems associated with improved outcomes when compared with emergency transplantation.[10]

In others circumstances, patients who are already on the waiting list undergo device implantation in a more elective setting with the aim of preventing progressive hemodynamic deterioration and improving physical and nutritional status before transplantation.[11] A distinctive advantage of device implantation is the possibility to decrease pulmonary pressures leading to possible improvements in posttransplant outcomes and even to listing patients who were previously not listable (bridge to candidacy).[12] VAD implantation ameliorates end-organ perfusion and function and consents optimization of patients' fitness and nutritional status, but these advantages must be weighed against the potential risk of surgery