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JACC COUNCIL PERSPECTIVES

Evaluation for Heart Transplantation and LVAD Implantation

JACC Council Perspectives

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ABSTRACT

Timely referrals for transplantation and left ventricular assist device implantation play a key role in favorable outcomes in patients with advanced heart failure. Nonetheless, evaluation usually occurs at advanced heart failure centers and is obscured from referring physicians. The purposes of this review are to explain the decision-making process for candidacy for advanced therapies and to describe the potential impact of the new organ allocation algorithm on center decision making. The document first addresses the signs of advanced heart failure, specifically focusing on the importance of the syndrome of low cardiac output as a key feature of advanced heart failure, and then summarizes the evaluation as a 3-step process addressing the following questions: 1) Is transplantation or durable assist device placement indicated? 2) Are there contraindications to either intervention? 3) How can one choose between transplantation and left ventricular assist device implantation if advanced therapies are indicated and not contraindicated?
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The care of patients with advanced heart failure (HF) can be challenging, not only because of the underlying disease but also because of the presence of multiple comorbid conditions in these patients. Application of guideline-directed medical therapy and management of reversible conditions (such as arrhythmia and conduction disorders, coronary stenoses, valvular lesions, etc.) are often challenging in patients with New York Heart Association (NYHA) functional class IV, American College of Cardiology (ACC)/American Heart Association (AHA) stage D disease. When medical management becomes inadequate, mechanical circulatory support (MCS) and heart transplantation become the only options for meaningful prolongation of life.

Although it is assumed that all cardiologists and most internal medicine physicians recognize that patients with advanced HF should be referred to a transplantation or MCS center, referrals are commonly delayed, sometimes beyond the point of

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ABBREVIATIONS AND ACRONYMS

ACHD = adult congenital heart disease

AHFTC = advanced heart failure and transplantation center

EDP = end-diastolic pressure

EDV = end-diastolic volume

HF = heart failure

HFrEF = heart failure with reduced ejection fraction

LV = left ventricular

LVAD = left ventricular assist device

MCS = mechanical circulatory support

NYHA = New York Heart Association

PVR = pulmonary vascular resistance

RV = right ventricular

SV = stroke volume

VAD = ventricular assist device

candidacy for either intervention. Moreover, although indications for advanced therapies have not changed much over the years, age restrictions and contraindications have become less strict and can vary according to institutions. As a result, practicing clinicians may not be aware of the current criteria regarding whom to refer or when to refer for advanced therapies in HF.

Several reputable organizations have described the process of evaluation for transplantation or left ventricular assist device (LVAD) placement, including the International Society for Heart & Lung Transplantation (ISHLT) (1–3) and individual papers addressing the changing paradigm (4). Unfortunately, the documents guiding the process lack consistency: in the ISHLT guidelines, listing for heart transplantation relies primarily on cardiopulmonary exercise stress testing, whereas in the revised 2018 Organ Procurement and Transplantation Network (OPTN) allocation scheme, criteria for the most urgent statuses focus on the need for MCS and the severity of hemodynamic compromise. Therefore, the overall process can be challenging to be clearly understood for referring physicians. Accordingly, the present review has 2 major objectives (**Central Illustration**): 1) to remove the "veil of mystery" from the evaluation process for transplantation and LVAD placement and to outline for general cardiologists and primary care clinicians a clear approach to decision making with regard to patient candidacy; and 2) to find common ground and harmonize the different documents providing guidance on the evaluation process.

The essence of the evaluation process can be summarized in 3 major steps: 1) Is transplantation or LVAD placement indicated? 2) Are there any contraindications? 3) If the patient is deemed a transplantation candidate, when should an implantable LVAD be considered as a bridge to transplantation? If the patient is deemed not a transplantation candidate, can he or she still benefit from and qualify for a long-term LVAD?

In the present review, we discuss only approaches to adult patients. Discussion of pediatric referrals is outside of the scope of this paper.

SCOPE OF THE PROBLEM

As a result of new pharmacological agents, improved surgical techniques, and device-based interventions, the number of patients living with some degree of HF continues to climb. In the United States, the estimated overall prevalence of HF with reduced ejection fraction (HFrEF) in the adult population, extrapolated from 2010 U.S. Census Bureau data, is 3.1 million.

HIGHLIGHTS

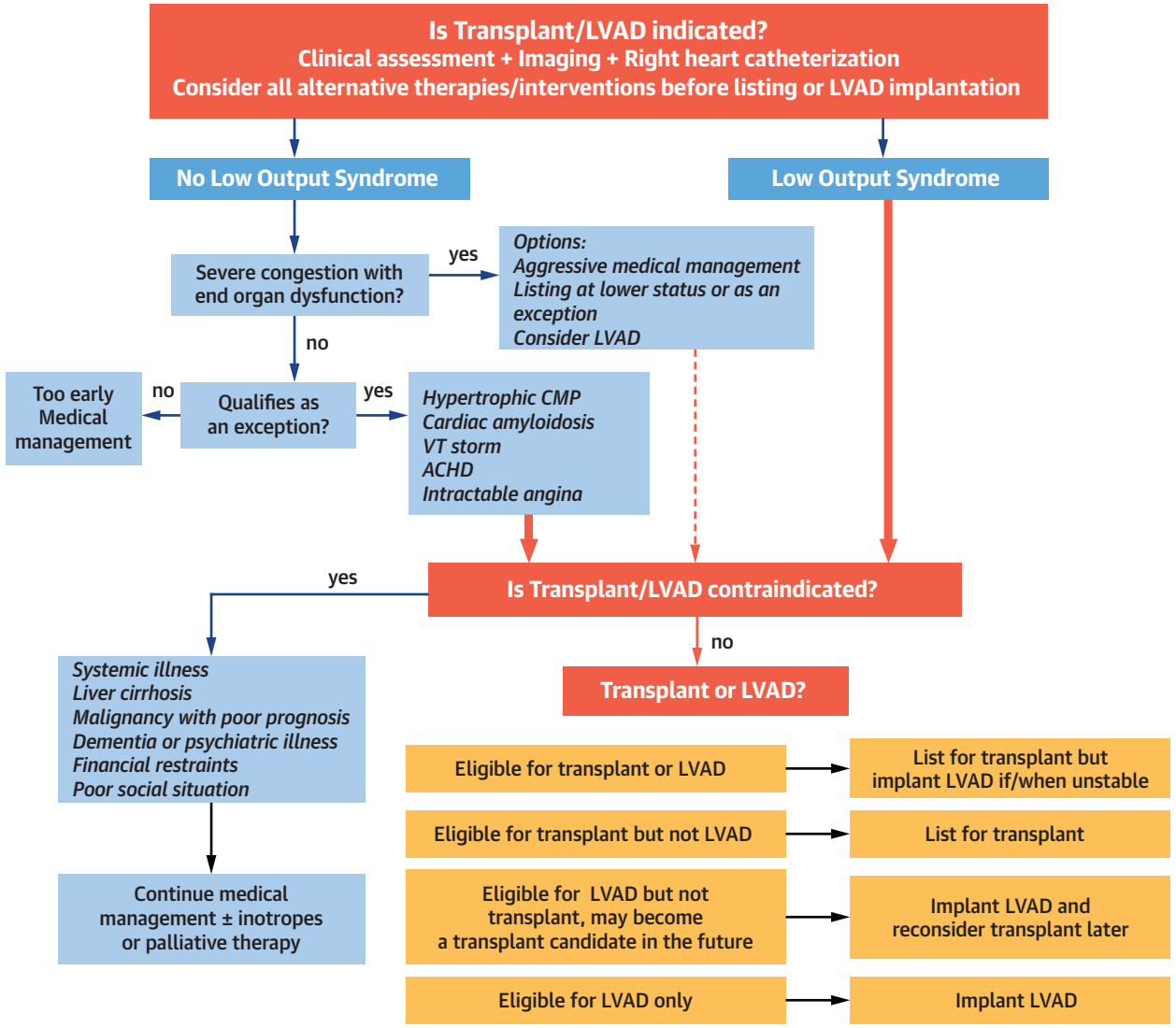
- Evaluation for transplantation or LVAD placement is an evolving process that needs to be transparent for referring providers.
- The evaluation process is structured to establish patient eligibility for transplantation or LVAD placement, rule out contraindications, and choose between transplant and durable support.
- Presence of low cardiac output syndrome is a main indication for transplantation or LVAD placement, with some exceptions.
- Timely referral is a key to good outcomes of transplantation and LVAD placement.

The exact number of patients with ACC/AHA stage C (NYHA functional class IIIB) and stage D (NYHA functional class IV) HF is harder to calculate, but on the basis of estimates from Olmsted County, Minnesota, the numbers range from 93,600 to 124,800 and from 15,600 to 156,000, respectively (5). NYHA functional class IIIB is vaguely defined in published research but includes patients who are very symptomatic with minimal exertion but are still less sick than those in class IV (6). These estimates are in line with other reports in which the U.S. adult population with advanced HF (ACC/AHA stage D) is described as ranging from 100,000 to 300,000 (7,8). Unfortunately, even with contemporary therapy, 1-year mortality is still estimated at 33% for stage D HF (9).

The annual incidence of new HF events per 1,000 subjects increases by decade of age, regardless of sex and race. Although both sexes are affected, the incidence of HFrEF is higher in men, and that of HF with preserved ejection fraction is higher in women (5). Most registries for heart transplantation and LVAD implantation typically reveal that >80% of recipients are men.

At present, heart transplantation remains the definitive therapy for end-stage HF with respect to reducing mortality and improving quality of life. Unfortunately, the epidemiological impact of this intervention is trivial, as only about 3,000 transplantations are performed annually in the United States and about 5,000 worldwide. Moreover, despite advances in other aspects of HF management, there has not been any significant increase in the number of

CENTRAL ILLUSTRATION **Advanced Heart Failure Center: Decision Making**



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The process within the advanced HF center consists of 3 main parts: identification of indications for heart transplantation and/or left ventricular assist device (LVAD) implantation, ruling out contraindications, and deciding on the strategy: proceed with listing, proceed with LVAD placement, continue management, or administer palliative care. In the latter 2 scenarios, the patient may be sent back to the referring center or comanaged by both teams. ACHD = adult congenital heart disease; CMP = cardiomyopathy; VT = ventricular tachycardia.

donor hearts (at least until recently, when a small increase was noted, likely related to the opioid epidemic and expanded use of donors with hepatitis C) (10). Even so, the staggering number of patients living with end-stage HF has created a supply-demand mismatch.

Over the past 30 years, LVADs have evolved from short-term, extracorporeal, and pulsatile devices containing valves and mechanical bearings into the smaller, intracorporeal, centrifugal-flow devices currently in use. As a result, during the 10-year period from 2009 to 2019, there has been an approximately 10-fold increase in the rate of LVAD implantation. Determining which patients with advanced HF are appropriate candidates for surgical therapies and when to refer these patients will undoubtedly evolve as HF specialists continue to gain experience with these patients and newer pumps.

SURVIVAL WITH TRANSPLANTATION VERSUS LVAD PLACEMENT

Although short-term survival rates on LVAD support are approaching survival after transplantation, long-term outcomes still favor heart transplantation. There have been relatively few trials comparing the safety and efficacy of MCS devices against heart transplantation. In transplantation-eligible patients, there appears to be equipoise between heart transplantation and LVAD implantation with respect to 1-year post-operative survival (11).

The matter was most recently reviewed in a 2018 meta-analysis in which a total of 8 studies constituted the 7,957-patient analysis. The pooled estimates demonstrated no difference in 1-year mortality regardless of strategy (12). These findings were, not unexpectedly, concordant with the findings of a 7,298-patient retrospective review of the United Network for Organ Sharing database in which the investigators found no significant difference between patients with LVAD support against recipients of marginal donor hearts. The 1- and 2-year survival rates were 89% and 85% for both the LVAD and marginal heart cohorts (13). In the recently published MOMENTUM 3 (Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy With HeartMate 3) trial, 1- and 2-year survival rates for the HeartMate 3 (Abbott, Abbott Park, Illinois) were 86.6% and 79.0%, consistent with the findings of the meta-analysis and competitive with transplantation (14).

Of course, the real issue is not 2-year survival but rather long-term survival, which remains to be defined. The improved short-term outcomes with the HeartMate 3 device provide a better option for patients who are less than optimal heart transplantation candidates. Additionally, as the new OPTN allocation scheme now prioritizes critically ill patients on temporary support devices, this could potentially prolong waiting times to transplantation for patients with LVADs without complications.

Refinements in patient selection, improvements in surgical technique and myocardial protection, better immunosuppressive and antimicrobial agents, and the use of right ventricular (RV) endomyocardial biopsy and gene expression profile testing to identify allograft rejection have resulted in an outstanding median survival of 12.2 years following heart transplantation (15). Mean survival on continuous-flow LVAD support, not including the HeartMate 3, is 7.1 years (16), and there are more hospitalizations after LVAD placement than after heart transplantation. As a result, long-term and event-free survival at the present time is better after transplantation compared with MCS. In addition, until devices become totally implantable, the risk for infection and driveline damage will persist, even though LVADs now have decreased rates of pump thrombosis and strokes. Unfortunately, although the supply of LVADs and other prosthetic pumps is controlled by industry, regulations, and insurers, and can be adjusted on the basis of need, the supply of donor hearts is naturally limited, which leads to the obvious need to be certain that in our decision-making process, patients deemed candidates for heart transplantation are those likely to have good outcomes.

TIMING OF REFERRAL FOR EVALUATION

As survival and quality of life have improved with both LVAD placement and heart transplantation, it is important that all patients with residual or ongoing HF symptoms be considered for referral to advanced HF and transplantation centers (AHFTCs), unless severe irreversible comorbidities or irremediable frailty is present (17). This specifically applies to ambulatory patients with advanced HF, who are at particularly high risk for disease progression, which, if not addressed appropriately, may render them ineligible for advanced therapies (18).

Referral to an AHFTC also ensures ongoing risk assessment, patient education, an opportunity to participate in investigational trials, and an open discussion about prognosis. The last point is particularly important, as patients tend to underestimate the risk for poor outcomes compared with their providers (19).

It is critical to understand that the presence of comorbidities such as renal insufficiency, liver dysfunction, frailty, cachexia, RV dysfunction, and fixed pulmonary hypertension should not preclude referral. Not infrequently, many of these conditions are reversible. Nonetheless, treatment options and long-term survival are still best if the patient is referred prior to the onset of end-organ disease.

Unfortunately, an accurate assessment of prognosis is difficult, and no single clinical, hemodynamic, or laboratory variable, test, or risk score can perform this role accurately. Although no specific guidelines exist and there is a lack of evidence on the optimal timing for referral to an AHFTC, a recently published expert consensus document suggests certain case scenarios that should trigger a referral (18).

Although a number of prognostic tools (**Table 1**) help in risk stratification, these tools are better suited for use at an AHFTC than by the primary cardiologist (20). The primary physician should rely on simple,

easy-to-access, and universally available variables. A recently published consensus document on the care of patients with HF identified a simple acronym, I NEED HELP (Table 2), with listed variables as a trigger for referral (21). In Table 2, we have changed the originally suggested left ventricular (LV) ejection fraction of <20% to <25%, because we think that at this point, patients should be already considered for evaluation for advanced therapies.

LOW CARDIAC OUTPUT AS A KEY FEATURE OF ADVANCED-STAGE OF HF

In patients with NYHA functional class III or ACC/AHA stage C HF, congestion typically dominates the picture. Practically all hospitalizations for HF during this stage occur because of volume overload (the patients are "wet") (22). It is not until patients with HFrEF have progressed to stage D that a reduction in stroke volume (SV) becomes evident, often accompanied by further LV dilation (Figure 1). This is caused by progressive impairment in LV systolic function, which is frequently associated with varying degrees of functional mitral regurgitation, further impairing forward SV. Notably, there may be individual differences in the hemodynamic progression of HFrEF, and abnormal hemodynamic parameters are not the sole determinants of HF severity.

For reference, ejection fraction is defined as the ratio of LV SV to LV end-diastolic volume (EDV). In asymptomatic patients with ACC/AHA stage B HFrEF, the reduction in LV ejection fraction is due primarily to an increase in LV EDV despite a generally normal SV (Figure 1). In symptomatic stage C patients, the reduction in ejection fraction is again driven by the increased EDV. However, in contrast to stage B patients, these patients also have elevated LV end-diastolic pressure (EDP), which affects pulmonary pressures, right heart function, and systemic venous congestion and explains the progressive exercise limitation. As well, although cardiac output is generally normal at rest in stage C patients, it typically fails to augment appropriately under the stress of exercise (Figure 1). Thus, it is not surprising that the bedrock of treatment for stage C HF is diuretic agents to mitigate congestion (reduce EDP), allowing a reduction in pulmonary artery pressures, fewer symptoms, reduced frequency of hospitalization, and slower progression to more advanced stages. Neurohormonal antagonists, which are proved to prolong survival, are used as well to promote reverse remodeling (reduction in EDV) or at least prevent progression (stable EDV). During this stage, congestion may occur with increasing frequency and increasing resistance to diuretic agents, frequently with declining renal function, despite resting cardiac output that is not severely reduced when measured after decongestion. Eventually the disease progresses to its terminal phase.

TABLE 1 Clinical, Biochemical, Imaging, Hemodynamic Markers, and Risk Score Markers for Advanced Heart Failure

Category	Signs
Clinical	Cardiogenic shock
	>1 HF hospitalization in past 6 months
	NYHA functional class III or IV
	Intolerance of guideline-directed medical therapy
	Increased diuretic agent dose
	Poor performance on metabolic stress test or 6-min walk
	Lack of response to cardiac resynchronization therapy
	Cachexia, unintentional weight loss
	Poor quality of life on Kansas City Cardiomyopathy Questionnaire or Minnesota Living With Heart Failure Questionnaire
Biochemical	Rising blood urea nitrogen and/or creatinine
	Hyponatremia
	Elevated B-type natriuretic peptide
	Anemia
	Rising bilirubin
	Low albumin
Imaging	Low left ventricular ejection fraction
	Increasing left ventricular dimensions
	Right ventricular dysfunction
	Moderate to severe valvular regurgitation
	Dilated inferior vena cava without respiratory variation
Hemodynamic	Low cardiac output/index
	Reduced pulmonary arterial saturation
	Elevated right or left ventricular filling pressures
	Elevated pulmonary pressures
	Seattle HF model predicted survival <80% at 1 yr

Modified with permission from Crespo-Leiro et al. (25)
HF = heart failure; NYHA = New York Heart Association.

The signs and symptoms reflected in the I NEED HELP mnemonic that should prompt a referral for transplantation evaluation (such as a decline in functional status, the need for inotropes, development of resistance to diuretic therapy, appearance of hypotension, and inability to up-titrate or maintain previously well-tolerated drugs) point in the same direction regarding the development of end-stage HF. This stage has different characteristics, a different course, and requires different treatment.

The 2013 ACC/AHA guidelines (17) refer to the definition of advanced HF from the previous 2009 Heart Failure Society of America guidelines: "patients with truly refractory HF who might be eligible for specialized, advanced treatment strategies, such as MCS, procedures to facilitate fluid removal, continuous inotropic infusions, or heart transplantation or other innovative or experimental surgical procedures, or for end-of-life care, such as hospice" (23).

TABLE 2 Simplified Signs Prompting Referrals to Advanced HF Center

I	Inotropes	Previous or ongoing requirement for dobutamine, milrinone, dopamine, or levosimendan
N	NYHA class/natriuretic peptides	Persisting NYHA functional class III/IV and/or high BNP or NT-proBNP
E	End-organ dysfunction	Worsening renal or liver dysfunction
E	Ejection fraction	Very low ejection fraction (<25%)
D	Defibrillator shocks	Recurrent appropriate defibrillator shocks
H	Hospitalizations	At least 1 hospitalization with HF in the past 12 months
E	Edema/escalating diuretic agents	Persistent fluid overload and/or increased diuretic requirement
L	Low BP	Consistently low BP (systolic <90 to 100 mm Hg)
P	Prognostic medications	Inability to up-titrate (or need to decrease/cease) ACE inhibitors, beta-blockers, ARNIs, or MRAs

Modified with permission from Baumwol (21).

ACE = angiotensin-converting enzyme; ARNI = angiotensin-receptor neprilysin inhibitor; BNP = B-type natriuretic peptide; BP = blood pressure; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N-terminal pro-B-type natriuretic peptide; other abbreviations as in Table 1.

The European Society of Cardiology defines advanced HF as a combination of features including NYHA functional class III or IV, low ejection fraction, elevated wedge and right atrial pressures, frequent hospitalization, increased B-type natriuretic peptide, fluid retention, and low peak oxygen consumption on stress testing (24). The most recent position statement from the European Society of Cardiology updates the criteria without major alterations (25).

Lacking from all the definitions is the recognition that advanced HF requires different treatment strategies for the simple reason that a key component in many patients with advanced stages of the disease is the decreased forward flow that defines the syndrome of low cardiac output.

In stage D, a reduction in SV becomes evident, often accompanied by further LV dilatation (26,27) (Figure 1). This progressive impairment in LV systolic function is frequently associated with varying degrees of functional mitral regurgitation, which further impairs forward SV. In turn, the decreased SV triggers additional neurohormonal and autonomic activation and compensatory tachycardia. The neurohormonal activation drives sodium and water retention, increased EDP, and right heart overload, which further interfere with LV diastolic filling and systolic function. As the process progresses, the exercise-induced SV and cardiac output reductions, which are objectively measurable as a reduction in peak oxygen consumption and impairment in ventilatory efficiency (28), become evident at rest as well. Eventually, a reduction in systemic blood pressure is observed as the adaptive mechanisms can no longer compensate for the loss of cardiac function (17), and patients become unable to tolerate conventional neurohormonal antagonists (29). These are the patients who clearly merit careful consideration for advanced therapies, including LVAD placement and heart transplantation. However, it is important to remember that any patient with advanced HF whose prognosis is predicted to be worse than that following heart transplantation or LVAD therapy may still be a candidate for advanced therapies. Patients with intractable ventricular arrhythmia, complex adult congenital heart disease (ACHD), or restrictive cardiomyopathy fall into this category.

Therefore, in the first stage of the evaluation process for transplantation or LVAD placement, one question must be answered: is the patient's prognosis on tolerated medical therapy poor enough that advanced therapies should be considered? In other words, is heart transplantation or LVAD placement indicated?

EVALUATION PROCESS

IS HEART TRANSPLANTATION OR LVAD PLACEMENT INDICATED (DOES THE HEART REQUIRE ASSISTANCE WITH MECHANICAL SUPPORT OR REPLACEMENT)? As previously noted, several documents outline the processes of evaluation for heart transplantation and MCS. The 2006 ISHLT guidelines place the cardiopulmonary stress test data and the risk assessment scores at the forefront of the listing process (30). The signs and symptoms of advanced HF, as outlined earlier, are essential because they determine poor prognosis. Although much of this work is accomplished by referring providers, reevaluation must be done by the advanced HF team to optimize candidate selection and minimize the chance of error. Some tools are more appropriate for use by advanced HF centers, as the interpretation of the results depends on experience and expertise. Such tools primarily include invasive hemodynamic assessment and cardiopulmonary stress testing.

In the previously published documents, the role of hemodynamic data from right heart catheterization is limited to determination of the presence, severity, and reversibility of pulmonary hypertension (30). The 2013 ISHLT guidelines on LVAD therapy also do not endorse any specific hemodynamic criteria that need

to be met but do underscore the need to determine candidacy for heart transplantation before considering LVAD placement (1).

In contrast to the ISHLT and LVAD guidelines, the OPTN heart transplantation status criteria that came into effect in 2018 prioritize hemodynamic compromise and the need for MCS. Although transplantation centers can add patients to the waiting list at their discretion, meeting stringent hemodynamic criteria are now required to list a patient at a certain status. There are 6 active statuses, which are discussed in detail later in this document. Patients can be placed into 2 top-priority statuses if they are already supported by some means of mechanical circulation (such as extracorporeal membrane oxygenation, a ventricular assist device [VAD], an intra-aortic balloon pump, etc.), or if they have intractable ventricular tachycardia.

Previously, hospitalized patients on high-dose inotropes and requiring invasive hemodynamic monitoring with a Swan-Ganz catheter could be listed in the top-priority status. Under current policies, they can be listed only as status 3, and only if following hemodynamic criteria are met: 1) systolic blood pressure <90 mm Hg; 2) cardiac index <1.8 l/min/m^2 off inotropes within 7 days of inotropes or <2.0 l/min/m^2 on inotropes or MCS; and 3) pulmonary capillary wedge pressure >15 mm Hg.

To extend status 3, a program must demonstrate that a patient cannot be weaned off inotropes because weaning attempts within 48 h of status expiration result in one of the following: 1) cardiac index <2.2 l/min/m^2 on current medical regimen; 2) cardiac index <2.2 l/min/m^2 during inotrope dose reduction; 3) increase in serum creatinine by 20% over the value immediately prior to, and within 24 h of, inotrope dose reduction; 4) increase in arterial lactate to >2.5 mmol/l during dose reduction; and 5) mixed venous oxygen saturation <50% measured using a central venous catheter.

Patients who are on inotropes at home, previously eligible for second-priority status, now qualify only for status 4. Thus, it becomes apparent that under the present paradigm, transplantation evaluations generally need to include right heart catheterization in order to answer the questions, Is low cardiac output present? Is the heart so weak that it needs either assistance or replacement (**Central Illustration**)? If the answer is no, candidates can still be listed, but their priority will be lower.

Of course, all clinical, laboratory, and imaging data are thoroughly reviewed at the advanced HF center. All potentially reversible conditions must be properly addressed (ablation of persistent atrial fibrillation or frequent ventricular ectopic beats, cardiac resynchronization in the presence of left bundle branch block or mandatory RV pacing, correction of severe mitral regurgitation and aortic stenosis, revascularization in coronary artery disease, etc.).

Patients with normal cardiac output but with other features of advanced HF, primarily refractory severe congestion with end-organ dysfunction, deserve special consideration. These patients may be very close to requiring transplantation or LVAD implantation. In fact, a single measurement of cardiac index can be erroneous, and repeat procedures may be justified. Several options can be considered, including aggressive medical management, which can be different than at the referring center. Patients remaining clinically unstable despite all efforts must be very closely monitored even when cardiac output is preserved but congestion is present and end-organ function may become labile. Elective transplantation listing as a status 6 (lowest priority), surveillance right heart catheterization, or LVAD implantation at INTERMACS level 4 to 6 is an option to be explored, with in-depth dialogue and shared decision making.

Exercise testing and measurement of peak oxygen consumption are considered essential when evaluating patients with HF. The relationship between cardiac output and oxygen consumption during exercise is assumed to be linear (31). Thus, for most patients with reduced cardiac output, the results of exercise testing will be abnormal. There are exceptions in which a patient's exercise capacity and/or cardiac output may be preserved; this is uncommon and may require specialized consideration (e.g., heart transplantation patients with severe coronary disease with intractable angina and no revascularization options, restrictive cardiomyopathy such as amyloidosis with preserved cardiac output, hypertrophic cardiomyopathy, adult congenital disease, benign cardiac tumors, and a few other conditions).

Once the indications for heart transplantation are established, the evaluation process moves to the next step: consideration of potential contraindications.

ARE THERE CONTRAINDICATIONS TO TRANSPLANTATION? It is important to realize that exact boundaries of contraindication have not been scientifically established and are expected to vary according to institutional practice and that grounds for ineligibility are much more often based on integration of more than one relative contraindication than on a single absolute contraindication.

Systemic diseases with poor survival, such as advanced connective tissue diseases, systemic amyloidosis, metastatic or aggressive malignancies,

and liver cirrhosis, usually exclude patients from consideration for advanced therapies. In most cases, however, the candidacy decision is not straightforward and requires careful assessment.

Age. As recipient age remains a strong predictor of mortality after transplantation (32), heart transplantation is usually reserved for younger patients. Most programs adhere to 70 years of age as an upper limit for listing, although there is no absolute rule. In a recent online survey, 83.7% of programs reported that they have an absolute contraindication for heart transplantation for patients older than 80 years (33). Meanwhile, about 14% of LVADs are implanted in patients older than 70 years, and their survival up to 2 years was not statistically different from that of younger patients (65% vs. 70%) (34). Regardless of whether there is a specific chronologic age for exclusion, patients age >70 years are frequently found to have substantial burden of other comorbidities. As reflected in consideration for other major cardiac procedures, the decreased resilience of older patients may become more obvious after the first postoperative complication leads to a cascade of deterioration. The support system also may face more jeopardy when dependent on an older spouse.

Nutrition and obesity. Both poor nutritional status (cachexia) and obesity are associated with poor outcomes. The 5-year mortality can double in obese patients compared with normal-weight patients (35,36). Many programs limit transplantation candidacy to patients with body mass index of <35 kg/m^2. Those same programs, however, do not necessarily limit body mass index for LVAD implantation. Obese patients on LVAD support have similar survival compared with nonobese VAD recipients (37). For the morbidly obese, bariatric surgical interventions such as sleeve gastrectomy can be safely performed in patients on LVAD support or even simultaneously with LVAD implantation (38,39).

Frailty. Frailty, or decreased physiological reserve, is prevalent in patients with advanced HF and is associated with increased mortality and poor outcomes. Frailty assessment includes one or more tools, including Fried's frailty phenotype, handgrip strength, and gait-speed testing. Fried's frailty phenotype is based on 5 domains—exhaustion, grip strength or weakness, mobility, poor appetite or unintentional weight loss, and physical activity—with each domain scored 0 or 1. A score of more than 3 is associated with frailty. The addition of cognitive testing increases sensitivity to predict short-term and long-term outcomes after LVAD implantation. Postoperative complications such as mortality, length of ventilator support, in-hospital stay, intensive care unit stay, and time to discharge are adversely affected by frailty (40). Handgrip has been shown to be a particularly effective predictor of survival (41). Assessment of frailty is becoming standard in most programs. The addition of cognitive impairment assessment may add further discrimination. Importantly, more research is needed to distinguish between cardiac and noncardiac causes of frailty. It is reported that there is an opportunity to reverse some of these changes with rehabilitation and postoperatively as well, and the disqualification of patients on the basis of frailty alone may not be ideal (42,43).

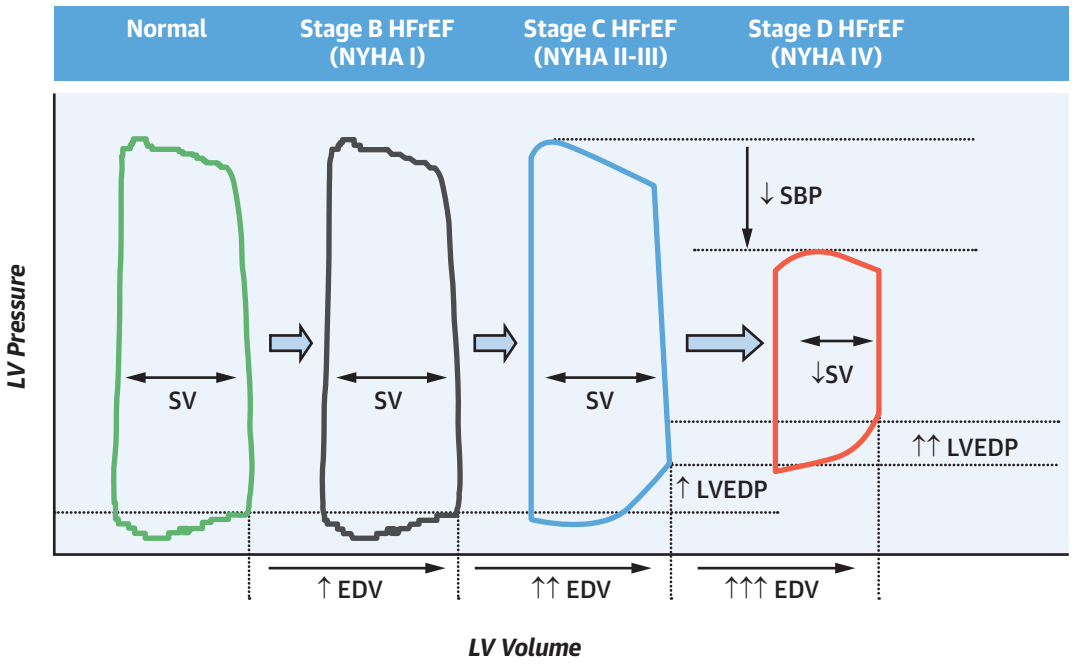
Pulmonary hypertension and RV failure. As previously noted, the elevated LV EDP seen in patients with HF results in elevated pulmonary venous and then pulmonary arterial pressure. Initially, normalization of intracardiac pressures (e.g., with diuretic agents) leads to normalization of pulmonary pressures. However, if the elevated LV EDP persists for a long time, vasoconstriction and structural changes in the pulmonary vasculature result in elevated pulmonary vascular resistance (PVR). At least initially, the increase in PVR is reversible with medical therapy to a generally acceptable value of <3.5 Wood units. Patients who are able to achieve PVR <2.5 Wood units with vasodilator therapy have excellent surgical outcomes, indicating that reversibility of pulmonary vascular disease is important. Nitroprusside, intravenous prostanoids, and inhaled nitric oxide may be used to dilate the pulmonary vasculature prior to and following heart transplantation (44,45).

In patients in whom PVR reaches 5 to 6 Wood units, transplantation may be contraindicated for the simple reason that the healthy right ventricle of the donor heart is not conditioned to handle the pulmonary hypertension and may fail in the operating room or early post-operative period. Early recognition of this problem and an increased use of pulmonary vasodilators such as inhaled nitric oxide and/or inhaled prostacyclins have decreased its incidence, but it remains a significant factor in determining suitability for and timing of transplantation.

For some patients, because of the presence of an irreversible increase in PVR, the only realistic short-term option might be an LVAD. It has been known for many years that decompressing the left ventricle with a VAD creates conditions that may result in complete or partial reversal of elevated PVR (46), allowing the patient to become a transplantation candidate.

Although pulmonary hypertension is not a contraindication to LVAD implantation, RV failure (because of pulmonary hypertension, native cardiomyopathy,

FIGURE 1 Hemodynamic Progression of HF



Typical course of heart failure (HF), evolving from normal status to asymptomatic left ventricular (LV) dysfunction with elevated LV end-diastolic volume (EDV) and normal filling pressures, to symptomatic stage with elevated LV end-diastolic pressure (LVEDP) but still normal systemic blood pressure and stroke volume (SV), and finally to advanced disease with severely enlarged left ventricle, severely elevated filling pressures, and decreased systemic pressure and SV (low cardiac output). HFrEF = heart failure with reduced ejection fraction; NYHA = New York Heart Association.

or chronic volume overload) is. LVADs provide substantial hemodynamic unloading of the left ventricle but do little to assist the right ventricle. Moreover, in the period soon after device placement, increased systemic blood flow immediately increases RV workload. This situation is exacerbated further by the septal shift to the left secondary to acute unloading of the left ventricle, which increases RV EDV and alters RV geometry and function. Multiple risk scores and hemodynamic parameters have been used to predict the likelihood of RV failure after LVAD implantation (47-49). Decreased parameters of RV performance as estimated using echocardiography (decreased tricuspid annular plane systolic excursion), low fractional area change and stroke work index, increased central venous pressure, low systolic pulmonary arterial pressure, elevated liver enzymes, and increased creatinine may all suggest RV dysfunction. Pulmonary artery pulsatility index (calculated as: [pulmonary artery systolic pressure − pulmonary artery diastolic pressure]/right atrial pressure) has gained popularity in recent years. A lower pulmonary artery pulsatility index is predictive of higher odds of RV failure after LVAD placement, and many surgeons would avoid implantation if the index is <2 (47).

MALIGNANCY. An active or recent (within 5 years from listing) malignancy is usually a contraindication to heart transplantation, and all high-risk heart transplantation candidates should be screened for the presence of an occult malignancy. It is widely accepted that post-transplantation immunosuppression greatly increases the risk for a malignant growth. A remote history of treated malignancy without evidence of recurrence and tumors localized to the heart are not contraindications to heart transplantation (50). Also, some patients with low-grade prostate cancers or other slow-growing cancers with overall favorable prognosis may be acceptable transplantation candidates. Oncology consultation is usually required to clarify the tumor status and potential of growth or recurrence. A plasma cell dyscrasia that has caused cardiac amyloidosis is not an absolute contraindication to heart transplantation, even if chemotherapy or subsequent stem-cell transplantation is needed. However, enhanced coordination with the hematology and oncology team is

required under these circumstances, and consideration for heart transplantation may depend on other organ involvement (51).

Infection. Infection, like malignancy, may reactivate with immunosuppression. The presence of an active infection is usually a temporary contraindication to heart transplantation until it is adequately treated. The only exception to this rule is an infection of the VAD, which is usually "cured" with explantation of the device and heart transplantation. Patients with infective endocarditis without metastatic infection may also be considered for transplantation (52).

Hepatitis B, hepatitis C, and cytomegalovirus serologies are usually obtained as part of the pre-transplantation evaluation. Acquired immunodeficiency syndrome, properly treated, is not an absolute contraindication to transplantation (53,54), and the majority of heart transplantation programs do not exclude patients with human immunodeficiency virus infection from consideration. Also, with the recent development of curative treatment for hepatitis C, this infection is no longer a contraindication to either transplantation or LVAD placement. In patients without hepatitis C infection who received transplanted hearts from donors with hepatitis C viremia, treatment with an antiviral regimen, initiated before or after transplantation, has been reported to prevent the establishment of hepatitis C infection (55).

Diabetes. Diabetes with end-organ damage other than nonproliferative retinopathy or poor glycemic control (glycated hemoglobin >7.5) is a relative contraindication to transplantation (56). In practice, evolving therapies in endocrinology, better means of glucose control, and an increase in the prevalence of diabetes in the general population have resulted in a more liberal approach, and many programs list patients with diabetic neuropathy or nephropathy. LVAD implantation with subsequent hemodynamic and metabolic optimization can improve the course of diabetes with decrease of fasting glucose and insulin requirements (57).

Renal dysfunction. When it comes to evaluation of renal function, differentiation between cardiorenal syndrome and intrinsic kidney disease may be difficult. Although renal dysfunction related to impaired renal perfusion secondary to HF (decreased perfusion and/or congestion) may diminish with optimization of therapy with inotropic or vasodilating agents, or after LVAD placement, underlying intrinsic renal disease may represent a significant comorbidity compromising survival. It is reasonable to consider the presence of irreversible renal dysfunction (glomerular filtration rate <30 ml/min/1.73 m^2) as a relative contraindication for heart transplantation alone (56), especially considering the renal toxicity of some immunosuppressants. Combined heart and kidney transplantation may be considered in younger patients. Dialysis-dependent renal failure is no longer an absolute contraindication to LVAD insertion. Nonetheless, it is prudent to confirm future acceptance of such a patient by a local dialysis center prior to proceeding with LVAD implantation.

Peripheral vascular disease and carotid disease. If severe peripheral vascular disease results in walking difficulty, it may limit function after transplantation or LVAD placement and needs to be addressed with surgery or percutaneous intervention. Also, clinically severe symptomatic cerebrovascular disease, with resultant cognitive or neurological deficit or severe or recurrent symptoms, may be considered a contraindication to transplantation (56). Aortopathies with ascending aortic or aortic root aneurysm or dissection would require a multidisciplinary approach for determination of appropriate interventions.

Hepatic dysfunction. Transaminase levels more than twice their normal value with or without elevated bilirubin and associated coagulation abnormalities may reflect right HF or passive congestion and may diminish with therapy, decongestion, or mechanical support. However, primary liver disease, in particular cirrhosis, needs to be excluded, which sometimes requires a liver biopsy (58).

Irreversible hepatic cirrhosis is considered an absolute contraindication to heart transplantation, unless combined with liver transplantation. Combined heart and liver transplantation is a rare, lifesaving procedure for concomitant end-stage heart and liver disease. Outcomes of combined heart and liver transplantation have been demonstrated to be comparable with outcomes of isolated heart and isolated liver transplant (59).

Pulmonary disease. Chronic lung disease is a common comorbidity seen in patients with HF and is associated with increased mortality (60). The complex relationship between chronic obstructive pulmonary disease and HF, including overlapping symptoms, contributes to difficulties in making the diagnosis of one in the presence of the other, and it may be difficult to ascertain the severity of lung disease in the presence of lung congestion with HF (61). Pulmonary function testing is a standard part of evaluation for transplantation or LVAD placement, although its significance is not well established. When patients before LVAD implantation were stratified into 5 groups by forced expiratory volume in 1 s and diffusing capacity for carbon monoxide, ranging from <40% predicted to normal, there was no

association with survival, suggesting that abnormal pulmonary function test results alone should not exclude patients from consideration for MCS (62).

Combined heart and lung transplantation can be considered for patients with HF with advanced pulmonary disease such as severe pulmonary hypertension (in ACHD), pulmonary arterial hypertension, cystic fibrosis, chronic obstructive pulmonary disease, and interstitial lung disease.

Surgical contraindications. Surgical input for heart transplantation remains a critical part of the multidisciplinary team-based approach to ensuring optimal outcomes. Evidence-based or guideline-supported surgical contraindications to heart transplantation are somewhat difficult to define. As such, most transplantation programs endorse their center-derived sets of surgical contraindications. With that statement made, however, patients with reoperative sternotomy, prior mediastinal radiation, and ACHD pose some of the greatest technical challenges for surgeons. Although at high risk, these patients, especially those with ACHD, may also derive some of the greatest benefit from transplantation. Thus, an overarching theme of this document is that each patient must be individually considered and evaluated to determine whether heart transplantation is appropriate from a surgical perspective.

The first consideration is the number of prior sternotomies or invasive chest procedures that a particular transplant candidate may have undergone. Controversy surrounds the question of whether reoperative sternotomy is associated with mortality. Two single-center reports (63,64) failed to demonstrate an association between prior cardiac surgery and mortality after transplantation. However, 2 large registry-based analyses of United Network for Organ Sharing data (65,66) and 1 analysis of a larger number of patients transplanted at Johns Hopkins and Barnes-Jewish Hospital (67) showed an early and late mortality risk for patients undergoing transplantation after prior sternotomy. From a purely technical point of view, it is well recognized that mediastinal adhesions from prior cardiac surgery lead to increased bleeding, more blood transfusions, and longer cardiopulmonary bypass times, all of which logically could lead to higher mortality.

Prior mediastinal radiation is a relative surgical contraindication to transplantation. In particular, patients who have had a prior sternotomy and radiation-induced valvular heart disease have exceptionally high post-transplantation mortality (65). However, in this group of patients, often the only surgical solution for advanced HF is transplantation.

Patients with ACHD present unique challenges for heart transplantation. It is well established that early survival after transplantation for patients with ACHD is inferior to that of patients without ACHD. However, for patients who survive this early mortality risk, their long-term outcomes may be superior to those of patients without ACHD (68). A healthy discussion in the transplantation community continues regarding whether patients with ACHD should be transplanted primarily at pediatric-based hospitals or adult hospitals, with the surgical team being led by an experienced ACHD surgeon (69). A strong recommendation, however, is that the technical features of the heart transplantation operation should be performed by a cardiac surgeon with ACHD experience.

Several other factors come into play when LVAD implantation is considered. Small LV chamber dimensions pose challenges for the implantation of an LVAD. The left ventricle should be large enough to accommodate the inflow cannula without the interventricular septum being sucked into it. This situation is relevant in the setting of patients with restrictive cardiomyopathy or just small hearts. LV end-diastolic dimension <4.5 cm has been proposed as an exclusion criterion for LVAD insertion, and a single report described a small LV chamber as a risk factor for VAD thrombosis and suction events (70).

ETHICAL, SOCIAL, AND FINANCIAL CONSIDERATIONS. Apart from the medical and surgical contraindications just discussed, there are a host of social, financial, and ethical situations to be considered when evaluating a patient for heart transplantation or LVAD placement. The psychosocial assessment for VAD implantation and transplantation is an important, albeit controversial, aspect of this process. Psychosocial contraindications vary and remain particularly nebulous and are driven by institution-specific practices. Any cognitive or functional issue affecting a patient's ability to self-care or maintain adherence is a relative contraindication in the absence of robust care at home. Although conditions such as mental retardation, stroke with significant residual deficits, and dementia suggest poor candidacy, they should not be absolute contraindications. Instead, these conditions should be triggers for an in-depth functional capacity and self-care assessment.

Another contraindication to VAD placement and transplantation is chemical dependency. The guidelines state that it is reasonable to consider active tobacco smoking as a relative contraindication to transplantation. Active tobacco smoking during the previous 6 months is a risk factor for poor outcomes after transplantation (30). Drug and alcohol abuse have the potential to interfere with patients' ability to

care for themselves and are thus justifiably contraindicated for heart transplantation and for VAD insertion. Efforts should be made to offer and implement social contracts combined with frequent laboratory-based checks to monitor for relapse or abstinence. Only if a patient demonstrates an ability to adhere to these contracts should he or she be considered a candidate for advanced therapies. A structured rehabilitation program may be considered for patients with recent (within 24 months) histories of alcohol abuse if transplantation is being considered. Patients who remain active substance abusers should not undergo heart transplantation (30).

Also, post-operative complications are often associated with considerable anxiety and altered self-image (71). That said, psychiatric conditions, in and of themselves, are not absolute contraindications, and many patients with known psychiatric disorders have had good post-operative results after appropriate intervention and social support. Poor compliance with drug regimens remains a risk factor for graft rejection and mortality. Patients who have demonstrated an inability to comply with drug therapy on multiple occasions should not undergo transplantation (30).

As a society, we desire to maximize graft success after transplantation, and the importance of social support in achieving this goal cannot be overstated (71). Similarly, in the case of a durable VAD, in fact perhaps to an even greater extent, caregivers are crucial in helping family members or friends manage and adapt to the new device and lifestyle. The absence of support is associated with higher rates of nonadherence, and patients who perceive low levels of support report high rates of depression and anxiety (71). Thus, inadequate social support is considered a strong relative contraindication, if not an absolute contraindication, to both therapies.

Finally, the financial burden of these therapies should be taken into account. Although the decision can be ethically and emotionally challenging, patients without the financial means or adequate insurance coverage may have tremendous financial fallout and should not be considered candidates.

Research examining the specificities of the psychosocial factors associated with poor outcomes for VAD implantation are lacking. The Stanford Integrated Psychosocial Assessment for Transplantation has been a reproducible tool for assessing negative outcomes in transplantation. More recently, its efficacy has been assessed among VAD patients as well. Although score on this tool was not associated with mortality or time to first adverse event, it did predict cumulative adverse events. This score needs to be further validated among patients with VADs in prospective studies and combined with strategies to reduce any assessed risk (72).

Recently, the ISHLT published its first set of consensus-based recommendations on the content and process of the psychosocial evaluation of candidates for heart transplantation and long-term MCS implantation. It is expected that these recommendations will be tailored to fit local and regional mandates and needs (73).

DECISION PATHWAY FOR LVAD PLACEMENT AND/OR TRANSPLANTATION

With all considerations in mind, after the completion of evaluation for transplantation or LVAD implantation, and in the absence of absolute contraindications, the pathway for the patient is delineated by the medical review board at the AHFTC. The decision process is rarely straightforward, as each patient is unique. In fact, decisions are very difficult in many cases and are required to be made with substantial multidisciplinary input documented in decision meetings. Generalizing the overall approach, the algorithm in the **Central Illustration** gives an idea of the typical process.

1. If the patient is eligible for heart transplantation but not eligible for LVAD placement, then list for transplantation with no intention to implant an LVAD. In general, biventricular or RV failure favors transplantation, as a failing right ventricle may not be able to tolerate increased workload created by the LVAD. Although implanting a second VAD for RV support or implanting a total artificial heart as a bridge to transplantation may be an option, patients who require such surgery are generally sicker than those who can be supported with an LVAD alone and have poorer outcomes. Likewise, the presence of intractable ventricular tachycardia favors transplantation listing, because LVAD implantation may not affect the proarrhythmic milieu. Total artificial heart implantation may be considered. Common scenarios for such patients include the following: 1) RV failure; 2) restrictive cardiomyopathy; 3) hypertrophic cardiomyopathy; 4) any cardiomyopathy with small (<4.5 cm) LV end-diastolic dimension; 5) patient refusal of LVAD implantation; and 6) contraindications to long-term anticoagulation.
2. If the patient is eligible for both transplantation and LVAD placement, then list for transplantation but proceed to LVAD placement if the patient is unstable and/or has evidence of impending or progressive end-organ damage. This path is commonly called bridge to transplantation. This approach may be particularly relevant if the

patient is too unstable to wait or is sufficiently stable has characteristics that suggest that the waiting time could be prolonged, including hemodynamic compromise, blood type O, large body size, or sensitization.

It is worth noting that terms "bridge to transplantation" and "destination therapy" are mostly maintained by insurance carriers, whose coverage may differ on the basis of one of these determinations. The professional community increasingly prefers to avoid such terms, as patients can easily shift from "bridge" to "destination" after experiencing disabling strokes or if they demonstrate noncompliance (e.g., resume smoking, alcohol, or using drugs after receiving an LVAD). Weight gain beyond acceptable standards for a given program also may preclude a former candidate from ever undergoing transplantation. On the contrary, reversal of previously severe pulmonary hypertension, favorable changes in social situation, elapsing of a required 5-year period after treated malignancy, or sufficient weight loss may change the status from "destination" to "bridge." Not surprisingly, in the latest landmark MOMENTUM 3 trial, the investigators avoided these terms altogether, using the terms "short-term cohort" and "long-term cohort" instead (14). Ironically, on the basis of the positive results of that trial, the HeartMate 3 was still approved for "bridge to transplantation" and "destination therapy."

3. If the patient is eligible for LVAD placement but cannot undergo transplantation at present and may be able to undergo transplantation in the future, then implant a long-term LVAD and reevaluate for transplantation later. This path is commonly called bridge to decision. The common scenarios for such patients include the following: 1) severe pulmonary hypertension with PVR >6 Wood units; 2) questionable psychosocial status (recent smoking or other substance use); 3) marginal compliance; 4) recent (<5 years) malignancy with favorable prognosis; 5) body mass index >35 kg/m^2 (or other weight cutoff for an individual program); and 6) glycated hemoglobin >7.5.
4. If the patient is not eligible for transplantation, and transplantation candidacy is not anticipated, but is eligible for LVAD placement, then implant a long-term LVAD with no intention to consider transplantation. This path is called destination therapy and includes following typical scenarios: 1) age greater than the heart transplantation program-specific age cutoff; and 2) other contraindications to heart transplantation, such as significant comorbidities precluding consideration for heart transplantation but not VAD placement.

This algorithm represents only an outline of the decision-making process, as this is a rapidly evolving area, with ongoing changes based upon the collective experience in the field, new discoveries, and technological progress.

If serious contraindications are found, the choice is between the continuation of medical management including inotropes or palliative care or hospice, depending on the patient's and family preferences.

NEW ORGAN ALLOCATION SYSTEM

Since 1984, the Health Resources and Services Administration has contracted with the United Network for Organ Sharing to run the OPTN, which is responsible for the allocation of solid organs for transplantation in the United States.

For heart transplantation, a 3-tier allocation algorithm (1A, 1B, and 2) had operated since 2006. Unfortunately, between 2006 and 2015, the waiting list doubled and the proportion of status 1A patients increased by 548% (74). These candidates were 3 times more likely to die on the waiting list than patients with any other status.

In addition, certain populations were not well served by the system, because of large variability in patient acuity within each individual status, prompting a large number of exception requests, 90% of which were approved (75). Typically, these exceptions were requested for patients with congenital heart disease, ventricular arrhythmias, and an inability to tolerate inotropes and/or indwelling pulmonary artery catheters.

Moreover, the use of MCS as a bridge to transplantation had expanded significantly, such that in 2019 half the patients undergoing heart transplantation were on mechanical support (76). The traditional allocation system did not accurately prioritize patients on MCS or distinguish on the basis of type of mechanical support.

The revised heart allocation policy was approved and implemented on October 18, 2018 (77). There are now 6 active tiers, with status 1 being the most urgent and status 6 being the least urgent. Inactive patients are placed in status 7. Patients may also be placed in a temporarily inactive status (**Table 3**). Patients who are not supported with any devices can qualify at best for status 3.

The new statuses 1 to 3 correlate with prior status 1A, subcategorized into 3 groups of decreasing acuity. Status 4 generally defines prior status 1B, and statuses 5 and 6 define prior status 2. MCS complications

TABLE 3 New Listing Criteria for Heart Transplantation

Status	Qualifying Criteria
1	ECMO (up to 7 days) Nondischargeable BiVAD Mechanical circulatory support with life-threatening ventricular arrhythmia
2	Intra-aortic balloon pump (up to 14 days) Acute percutaneous endovascular circulatory support device (up to 14 days) Ventricular tachycardia/ventricular fibrillation, mechanical support not required Mechanical circulatory support with device malfunction/mechanical failure Total artificial heart, BiVAD, or RVAD Nondischargeable surgically implanted LVAD
3	LVAD for up to 30 days Multiple inotropes or single high-dose inotrope with continuous hemodynamic monitoring (up to 14 days) Mechanical circulatory support with device-related complications such as right heart failure, device infection, hemolysis, pump thrombosis, bleeding, aortic insufficiency, or thromboembolism
4	Diagnosis of congenital heart disease Diagnosis of ischemic heart disease with intractable angina Diagnosis of hypertrophic cardiomyopathy Diagnosis of restrictive cardiomyopathy Stable LVAD candidates after 30 days Inotropes without hemodynamic monitoring Diagnosis of amyloidosis Retransplantation
5	Combined organ transplantations
6	All remaining active candidates
7	Inactive

BiVAD = biventricular assist device; ECMO = extracorporeal membrane oxygenation; LVAD = left ventricular assist device; RVAD = right ventricular assist device.

are more precisely defined, reducing the need for exception requests. An important aspect of the new system is broader sharing for the sickest patients, with allocation of donor organs to status 1 and 2 candidates within 500 miles of the donor hospital. Additionally, subpopulations deemed to be at higher risk for waiting-list mortality are now recognized for prioritization (status 4) if specific and stringent hemodynamic or clinical criteria are met: patients with congenital heart disease, intractable angina, cardiac amyloidosis, hypertrophic or restrictive cardiomyopathy, or redo transplantation. Patients with life-threatening ventricular arrhythmias get priority, especially with complicating MCS (status 1) or if intractable (status 2).

There remain concerns regarding the new allocation scheme. Broader sharing will be associated with increased travel costs and risk to donor procurement teams. Longer ischemic times may affect post-transplantation outcomes. The highest status for patients on extracorporeal membrane oxygenation may reduce waiting-list mortality at the expense of decreased post-transplantation survival. Although more stringent criteria have been placed to define cardiogenic shock, many fear an increase in the use of temporary MCS devices and intra-aortic balloon pumps to facilitate higher priority listing. Patients on MCS without complications will likely wait longer for transplantation. Access for patients with pure restrictive or hypertrophic cardiomyopathy may be compromised, as these patients are frequently not suitable for MCS.

Despite a large percentage of allosensitized patients, the new scheme did not prioritize these patients, citing a lack of data. Nonetheless, these patients have greater waiting-list times and mortality and a greater risk for being delisted (78). Prioritization and broader sharing resulted in an increased number of sensitized patients undergoing transplantation (79).

Data comparing the first 4 months of the new heart allocation system with a comparable time the prior year have recently been released (80). Although there is variability among centers and OPTN regions, there has been no substantial overall impact on the number of waiting-list registrations, transplantations, or heart utilization. During the first 4 months under the new heart allocation system, 8% of candidates were transplanted at status 1, 42% at status 2, and 27% at status 3, compared with 66% transplanted as status 1A under the previous policy. Although the impact of the new system is still uncertain, it is possible that it will increase waiting time for patients on home inotropes and patients in stable condition on LVAD support.

CONCLUSIONS

Advanced HF differs from other stages of the condition by having a worse prognosis, often related to the syndrome of low cardiac output. Transplantation and/or durable MCS prolong life and improve its quality in patients with advanced HF.

Timely referrals for evaluation for transplantation or LVAD placement, with incorporation of the patient's preferences and goals of care, play the key role in successful patient management. This document summarizes the indications, contraindications, and approach to the decision pathway for consideration for VAD implantation and/or heart transplantation for general cardiologists and primary care clinicians. The evaluation process starts with confirmation of indication for transplantation or LVAD placement, continues with ruling out contraindications, and ends with selecting the right path of transplantation without VAD placement, VAD placement followed by transplantation, VAD placement for bridge to decision, VAD placement as destination therapy, or ineligibility for VAD placement or transplantation with the requirement for referral for palliative care.

This review is the first document of this kind since recent changes in the donor organ allocation algorithm. How the new allocation process will affect listing practices, management of listed patients, and outcomes following heart transplantation remains to be determined.

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