

Conference paper

# Heart transplant candidate assessment: Contemporary principles, multidimensional evaluation and implications for organ utilisation

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## Abstract

Heart transplantation remains the definitive treatment for selected patients with advanced heart failure, yet appropriate identification and evaluation of candidates is increasingly complex. Contemporary practice requires integrating objective markers of cardiac disease severity with a holistic assessment of comorbidities, psychosocial readiness, and long-term capacity to benefit from transplantation. Modern guidelines—particularly the 2018 ESC Heart Failure Association position statement and the 2024 ISHLT candidate evaluation guidelines—have reshaped the conceptual framework for transplant candidacy, emphasising the interplay between disease severity, reversible and irreversible contraindications, frailty, and dynamic assessment over time. This review synthesises current principles guiding transplant evaluation and discusses how these decisions influence broader organ utilisation strategies. A narrative, clinically grounded approach highlights the importance of recognising patients who are sufficiently unwell from heart failure to derive benefit, yet not so compromised by end-organ failure or other high-risk features that transplantation becomes futile. Through a multidimensional model encompassing medical, functional, psychological, and social domains, modern transplant programmes aim to optimise individual outcomes while safeguarding equitable and efficient use of scarce donor organs.

## Introduction

Heart transplantation has evolved into a highly effective treatment for advanced heart failure, offering exceptional survival and quality-of-life benefits for appropriately selected patients (1-6). Despite advances in guideline-directed medical therapy, device therapy, and mechanical circulatory support, a substantial number of patients progress to a stage where conventional therapies no longer provide adequate symptom control or prognosis. At the same time, donor organ availability remains limited, creating a stringent need for careful and ethically grounded candidate selection.

Modern evaluation is neither purely cardiac nor solely physiological; it is a multidimensional and holistic process that considers medical suitability alongside psychosocial resilience, adherence potential, frailty, cognitive status, nutrition, and social support. The 2018 ESC definition of advanced heart failure provides a foundation for recognising patients whose disease severity

warrants consideration of advanced therapies, while the 2024 ISHLT guidelines supply a comprehensive blueprint for assessing transplant candidacy across medical, surgical, and psychosocial domains.

Importantly, transplant assessment cannot be understood in isolation from the broader context of organ utilisation. Listing decisions influence not only individual outcomes but also the efficiency and fairness of the entire transplant ecosystem. This review synthesises contemporary principles of transplant evaluation, integrating guideline-based recommendations with pragmatic clinical interpretation, while exploring how candidate assessment interacts with the challenge of stewarding scarce donor organs.

## Defining advanced heart failure and the need for transplantation

Modern definitions of advanced heart failure emphasise the persistent and severe nature of symptoms despite appropriate therapy. Patients typically exhibit NYHA class III–IV functional limitation, recurrent congestion, objective markers of significant ventricular dysfunction, and impaired exercise tolerance. These findings, when persistent despite optimised pharmacological and device therapy, identify individuals who may benefit from advanced interventions such as transplantation or durable mechanical circulatory support.

Advanced heart failure is a clinical syndrome, not a single parameter. Contemporary guidelines stress the integration of symptoms, objective markers of disease severity, cardiac reserve, end-organ involvement, and the presence of comorbidities. The ESC definition frames the population in whom transplantation may be relevant (Figure 1), whereas the ISHLT guidelines refine how to determine whether transplantation is appropriate and feasible.

All the following criteria must be present despite optimal guideline-directed treatment:

1. Severe and persistent symptoms of heart failure [NYHA class III (advanced) or IV].
2. Severe cardiac dysfunction defined by a reduced LVEF  $\leq 30\%$ , isolated RV failure (e.g. ARVC) or non-operable severe valve abnormalities or congenital abnormalities or persistently high (or increasing) BNP or NT-proBNP values and data of severe diastolic dysfunction or LV structural abnormalities according to the ESC definition of HFpEF and HFmrEF.<sup>9</sup>
3. Episodes of pulmonary or systemic congestion requiring high-dose intravenous diuretics (or diuretic combinations) or episodes of low output requiring inotropes or vasoactive drugs or malignant arrhythmias causing  $>1$  unplanned visit or hospitalization in the last 12 months.
4. Severe impairment of exercise capacity with inability to exercise or low 6MWT ( $<300$  m) or  $pVO_2$  ( $<12$ – $14$  mL/kg/min), estimated to be of cardiac origin.

In addition to the above, extra-cardiac organ dysfunction due to heart failure (e.g. cardiac cachexia, liver, or kidney dysfunction) or type 2 pulmonary hypertension may be present, but are not required.

Criteria 1 and 4 can be met in patients who have cardiac dysfunction (as described in criterion #2), but who also have substantial limitation due to other conditions (e.g. severe pulmonary disease, non-cardiac cirrhosis, or most commonly by renal disease with mixed aetiology). These patients still have limited quality of life and survival due to advanced disease and warrant the same intensity of evaluation as someone in whom the only disease is cardiac, but the therapeutic options for these patients are usually more limited.

ARVC, arrhythmogenic right ventricular cardiomyopathy; BNP, B-type natriuretic peptide; ESC, European Society of Cardiology; HFA, Heart Failure Association; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; LV, left ventricular; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association;  $pVO_2$ , peak exercise oxygen consumption; RV, right ventricular; 6MWT, 6-minute walk test distance.

**Figure 1. HFA-ESC criteria for defining advanced heart failure.** Eur J Heart Fail. 2018 Nov;20(11):1505-1535. doi: 10.1002/ejhf.1236. Epub 2018 Jul 17

In clinical practice, several recurrent features help identify patients whose disease is progressing despite therapy. These include intolerance to guideline-directed medical therapies due to hypotension or renal dysfunction, recurrent unprovoked heart failure hospitalisations, escalating diuretic requirements, persistent congestion, increasing arrhythmia burden including appropriate ICD therapies, declining renal or hepatic function, and evidence of cardiac cachexia or frailty. The appearance or accumulation of these markers signals advancing disease severity and highlights the need for timely referral for advanced heart failure assessment. The HFA-ESC group proposed a useful mnemonic rule to aid in the identification of patients with advanced heart failure, labelled as “I NEED HELP” (Figure 2).

I	Inotropes	Previous or ongoing requirement for dobutamine, milrinone, dopamine, or levosimendan
N	NYHA class/natriuretic peptide	Persisting NYHA class III or IV and/or persistently high BNP or NT-proBNP
E	End-organ dysfunction	Worsening renal or liver dysfunction in the setting of heart failure
E	Ejection fraction	Very low ejection fraction <20%
D	Defibrillator shocks	Recurrent appropriate defibrillator shocks
H	Hospitalizations	More than 1 hospitalization with heart failure in the last 12 months
E	Edema/escalating diuretics	Persisting fluid overload and/or increasing diuretic requirement
L	Low blood pressure	Consistently low BP with systolic <90 to 100 mmHg
P	Prognostic medication	Inability to up-titrate (or need to decrease/cease) ACEI, beta-blockers, ARNIs, or MRAs

ACEI, angiotensin-converting enzyme inhibitor; 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; NYHA, New York Heart Association.  
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**Figure 2. HFA-ESC I NEED HELP.** Eur J Heart Fail. 2018 Nov;20(11):1505-1535. doi: 10.1002/ejhf.1236. Epub 2018 Jul 17

Patients considered for transplantation typically fall into a category where, despite maximal therapy, predicted survival without advanced intervention is limited. The purpose of evaluation is therefore twofold: to confirm that the patient's heart failure is sufficiently severe to justify transplantation, and to ensure that other medical, surgical, or psychosocial factors do not render transplantation excessively risky or unlikely to succeed.

# A multidimensional and holistic assessment model

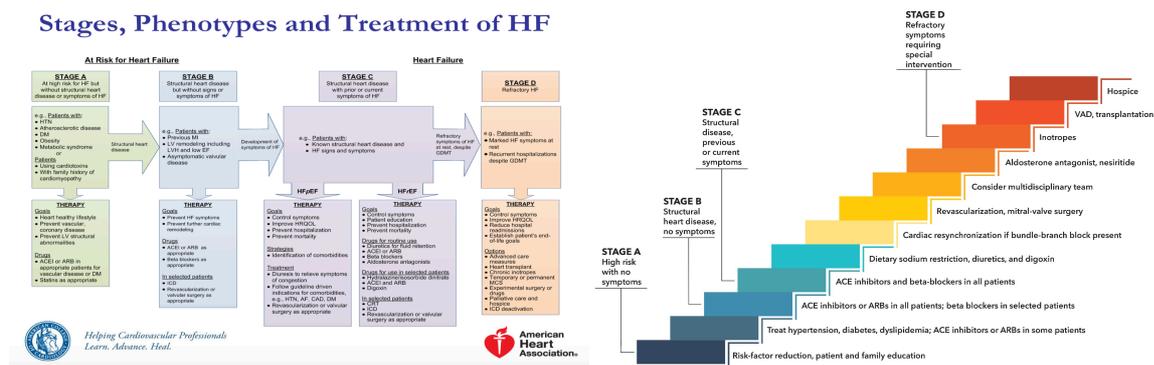
Contemporary evaluation for heart transplantation is founded on the principle that suitability cannot be judged based on haemodynamics or ejection fraction alone. Instead, the process requires comprehensive assessment across interconnected domains: cardiac status, pulmonary hypertension and haemodynamics, end-organ function (renal, hepatic, pulmonary), comorbidities, frailty, nutrition, psychological readiness, adherence, social support, substance use history, and surgical feasibility. In practice, the weight of these domains is cumulative rather than absolute, and candidacy reflects their combined influence rather than any single factor [ISHLT 2024].

These domains, considered collectively, determine whether a patient is likely to survive the transplant procedure, recover satisfactorily, and maintain long-term graft health. They also help to distinguish between patients whose poor prognosis derives primarily from heart failure—where transplantation offers substantial benefit—and those whose prognosis is driven by systemic comorbidities less amenable to correction.

The assessment is rarely static. Instead, it is dynamic and iterative, involving serial evaluation over time to detect improvement or deterioration, clarify ambiguous findings, and allow optimisation of reversible risk factors.

## Determining whether the patient is sufficiently ill from heart failure

A central question in transplant evaluation is whether the patient’s heart failure is severe enough to justify transplantation. This requires assessing the trajectory of the disease, the presence of prognostic markers, and the likelihood of continued decline despite maximal therapy.



**Figures 3 & 4. Disease staging and the HF continuum.** Reproduced from: Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol 2013; 62:e147. Table used with the permission of Elsevier Inc. All rights reserved

## Clinical indicators

Patients approaching end-stage heart failure typically display recurrent symptoms and frequent episodes of decompensation despite good adherence to therapy. A history of repeated unprovoked hospital admissions strongly predicts adverse outcomes. Intolerance to guideline-directed medical therapies due to hypotension, renal dysfunction, or other side effects may signal diminishing cardiac reserve.

### **Functional capacity and cardiopulmonary exercise testing**

Cardiopulmonary exercise testing (CPET) is a cornerstone of prognostic assessment. A peak  $\text{VO}_2 \leq 14$  mL/kg/min in patients not on beta-blockers—or  $\leq 12$  mL/kg/min in those receiving beta-blockers—identifies impaired cardiac reserve. Percentage-predicted values provide additional granularity, with  $<50\%$  predicted indicating significant limitation, especially in younger patients. The  $\text{VE}/\text{VCO}_2$  slope, with thresholds  $\geq 35$ , reflects ventilatory inefficiency and is strongly associated with adverse outcomes, particularly when maximal effort is not achieved. A  $\text{VE}/\text{VCO}_2$  slope exceeding 40 is particularly concerning, especially in older individuals or in tests where a maximal respiratory exchange ratio ( $\text{RER} \geq 1.05$ ) is not achieved.

### **Invasive haemodynamics and pulmonary vascular status**

Right heart catheterisation provides essential information about cardiac output, filling pressures, and pulmonary vascular loading conditions, all of which have major prognostic and perioperative implications. In particular, pulmonary hypertension arising from long-standing left-sided heart failure may become fixed and unresponsive to vasodilatory therapy, creating a prohibitive risk of acute right ventricular failure following transplantation. Contemporary ISHLT guidance provides specific thresholds beyond which isolated heart transplantation is generally unsafe: a pulmonary artery systolic pressure (PASP) persistently  $>50$ – $60$  mmHg, a transpulmonary gradient (TPG)  $\geq 15$  mmHg, and a pulmonary vascular resistance (PVR)  $\geq 3$  Wood units, especially when these abnormalities fail to improve with vasodilator testing or left ventricular unloading. The distinction between reversible and irreversible pulmonary vascular disease is therefore critical.

Patients with unfavourable pulmonary haemodynamics may benefit from targeted optimisation strategies prior to listing. These include aggressive diuresis, temporary inotropic support, and selective use of pulmonary vasodilators in carefully supervised settings. In a subset of patients, Mitral Transcatheter Edge-to-Edge Repair (TEER) or mechanical circulatory support (MCS)—most commonly durable left ventricular assist devices—can effectively unload the left heart, reduce left-sided filling pressures, and allow re-evaluation of PVR after an appropriate period of support. Demonstrated reversibility under these conditions may transition a patient from ineligible to acceptable transplant candidacy. Conversely, persistent elevation in PVR despite optimal unloading suggests fixed pulmonary vascular disease and remains a contraindication to isolated heart transplantation.

### **Determining whether the patient is not too sick from other perspectives**

While severe heart failure is necessary to justify transplantation, excessive illness from other causes may render the intervention futile. End-organ function, comorbidities, frailty, psychosocial stability, and surgical feasibility must be considered collectively.

## **Diabetes**

Diabetes, especially when accompanied by end-organ involvement, is associated with increased post-transplant morbidity and reduced long-term survival. The presence of proliferative retinopathy, severe neuropathy, advanced nephropathy, autonomic dysfunction, or poor glycaemic control despite optimised therapy identifies a population at significantly higher risk of infection, poor wound healing, renal deterioration, and accelerated allograft vasculopathy. While diabetes itself is not a contraindication, poorly controlled disease (e.g., HbA1c persistently >8.5–9%) and established microvascular complications require careful consideration and optimisation prior to listing. Patients with diabetes-related end-organ damage may still be considered for transplantation when metabolic control is demonstrably improved and comorbidities are stabilised, but more severe disease may prompt exploration of alternative strategies such as combined heart–kidney transplantation when renal involvement is dominant and irreversible.

## **Peripheral vascular disease**

Peripheral vascular disease (PVD) also carries major prognostic implications. Significant PVD reflects widespread atherosclerotic burden and is associated with impaired wound healing, increased perioperative morbidity, and higher rates of cerebrovascular and limb ischaemic events post-transplant. Severe or symptomatic PVD—particularly with prior interventions, claudication limiting daily activity, or involvement of mesenteric or cerebrovascular beds—may represent a relative or absolute contraindication depending on severity. ISHLT guidance emphasises the importance of a detailed vascular assessment, including non-invasive imaging and functional testing when appropriate, to clarify the extent of disease. When vascular pathology is limited or can be corrected, transplantation may still be reasonable; however, diffuse or multi-territory disease with impaired perfusion reserves substantially diminishes expected benefit.

## **Malignancy**

Malignancy requires especially nuanced evaluation, balancing the risk of recurrence under immunosuppression with the potential for meaningful survival gain. ISHLT recommendations focus on tumour type, stage, biological behaviour, and time from remission. Cancers with a high recurrence rate, evidence of metastatic potential, or insufficient disease-free interval remain contraindications to transplantation, given the profound immunosuppression required post-operatively. Many low-risk malignancies—including successfully treated skin cancers, certain prostate cancers, or early-stage solid tumours—may be compatible with listing once an appropriate disease-free window has elapsed, typically 2–5 years depending on tumour biology. Increasingly, oncology collaboration and the use of personalised prognostic tools allow more tailored assessment. Ultimately, malignancy does not universally preclude transplantation, but its presence requires rigorous, evidence-based appraisal to ensure that the anticipated transplant benefit exceeds the risk of cancer recurrence.

## **End-organ function**

Renal and hepatic dysfunction are common manifestations of advanced heart failure, yet their prognostic implications differ depending on reversibility and severity. Cardiorenal and cardiohepatic syndromes may improve substantially following haemodynamic optimisation, whereas intrinsic kidney or liver disease, once advanced, may preclude isolated heart

transplantation. Most programmes consider chronic kidney disease with an estimated GFR  $<30$  mL/min/1.73 m<sup>2</sup> as a relative contraindication and GFR  $<20$  mL/min/1.73 m<sup>2</sup> as a threshold at which isolated heart transplantation becomes inappropriate unless clear reversibility is demonstrated. In patients with sustained renal dysfunction, combined heart–kidney transplantation may be considered when end-organ damage is deemed irreversible. The presence of significant proteinuria often supports a diagnosis of intrinsic chronic kidney disease rather than cardiorenal syndrome and therefore carries important implications for the feasibility of isolated heart transplantation.

Similarly, hepatic dysfunction requires careful discrimination between congestive hepatopathy—often reversible—and established cirrhosis. Patients with advanced fibrosis, portal hypertension, or synthetic dysfunction (elevated INR not attributable to anticoagulation, hypoalbuminaemia  $<30$  g/L) have significantly worse outcomes following isolated heart transplantation. For some, combined heart–liver transplantation may be the only viable advanced therapy. Thus, the evaluation of organ dysfunction requires not only an assessment of severity but also an understanding of trajectory and potential for recovery.

### **Surgical feasibility**

Complex chest anatomy, prior sternotomies, severe mediastinal adhesions, or pulmonary vascular abnormalities can substantially increase operative risk. Likewise, congenital anomalies, prior thoracic irradiation, or significant aortic pathology may necessitate more extensive surgical planning. Multidisciplinary input from transplant surgeons, anaesthetists, and imaging specialists is crucial to determine feasibility, anticipate intraoperative challenges, and integrate surgical risk into overall candidacy decisions.

### **Frailty and nutrition**

Frailty is a potent predictor of mortality, prolonged recovery, and postoperative complications. Distinct from chronological age, frailty reflects diminished physiological reserve and impaired functional capacity, and it is often modifiable through targeted rehabilitation and nutritional optimisation. Nutritional assessment includes evaluation of cachexia, sarcopenia, and body mass index (BMI). International guidelines recognise BMI  $>35$  kg/m<sup>2</sup> as a relative contraindication to isolated heart transplantation due to elevated perioperative risk and long-term metabolic complications, while BMI  $>40$  kg/m<sup>2</sup> is generally considered prohibitive in most programmes. Conversely, severe malnutrition or BMI  $<18$  kg/m<sup>2</sup> is also associated with poor outcomes. These thresholds, however, are not absolute, and selected patients may become acceptable candidates following structured weight optimisation, rehabilitation, or nutritional support. These thresholds, however, are not absolute, and selected patients may become acceptable candidates following structured weight optimisation, rehabilitation, or nutritional support.

### **Psychosocial evaluation**

Transplantation requires lifelong adherence to immunosuppression and follow-up. Psychosocial assessment therefore examines mental health, coping strategies, stability of caregiving arrangements, insight into disease, and adherence patterns. Substance use—past or present—requires structured evaluation with clear guidance for abstinence and monitoring. There is strong evidence that psychosocial instability, including poor adherence or inadequate support structures, is associated with worse graft survival and increased long-term morbidity.

## **Multidisciplinary decision-making and the evolution of candidacy**

Modern transplant programmes rely on a structured multidisciplinary approach, recognising that the complexity of advanced heart failure requires coordinated expertise. Multidisciplinary team (MDT) meetings bring together cardiologists, surgeons, anaesthetists, imaging specialists, psychologists, nurse specialists, and transplant coordinators, each contributing complementary insights that shape a balanced evaluation. This collective appraisal allows the integration of clinical, functional, psychosocial, and procedural considerations, helping determine the safest and most appropriate path for each individual.

Equally important is the close collaboration between referring centres and transplant centres. Shared-care pathways, early communication, and ongoing dialogue support timely identification of patients who may benefit from advanced therapies and ensure continuity across the patient journey. Candidacy evolves over time, improving with optimisation of reversible factors or declining with disease progression; therefore, dynamic reassessment within this collaborative framework has become essential. Together, these processes promote consistent decision-making, safeguard equity, and ensure that transplantation is offered to those most likely to achieve sustained benefit.

## **Implications for organ utilization**

Candidate assessment directly influences the efficiency and fairness of organ use. Optimal utilisation requires identifying patients who will derive durable benefit while avoiding transplantation in those unlikely to do well. Early referral allows optimisation of reversible factors, expanding the transplantable population. Equitable criteria prevent undue exclusion while safeguarding outcomes.

## **Discussion**

Heart transplant candidate assessment has advanced significantly, reflecting the growing evidence base and increasing complexity of the transplant population. The modern paradigm emphasises holistic evaluation, extending beyond heart failure severity to consider frailty, psychosocial resilience, comorbidities, surgical risk, and long-term trajectory.

## **Conclusion**

Heart transplant evaluation has evolved into a comprehensive, multidisciplinary process that integrates disease severity with broader physiological, psychosocial, and ethical considerations. The goal is to identify patients who are sufficiently ill from heart failure to benefit from transplantation, yet not so compromised by other factors that the procedure becomes unsafe or

futile. These principles remain essential foundations for sound candidate selection and responsible organ utilisation.

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