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EDITORIAL

The Art of Timing: Recognizing Signs and Symptoms of Advanced Heart Failure to Guide Timely Referral to Advanced Heart Failure Specialists

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Heart failure is a clinical syndrome with symptoms and signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion [1]. It affects approximately 6.7 million Americans aged 20 or older, with prevalence expected to rise to 10.3 million by 2040 [2]. Given its increasing prevalence, heart failure patients are often managed by multiple providers, including internal medicine physicians, family medicine physicians, and cardiologists. Heart failure patients can range from stable patients with minimal symptoms with activity, to very ill patients requiring inotropic support or advanced therapies. Timely recognition of disease progression and appropriate referral to advanced heart failure specialists is critical, as delayed referral may limit eligibility for life-prolonging therapies such as durable mechanical circulatory support or heart transplantation. Early involvement of advanced heart failure cardiologists enables optimal risk stratification, guideline-directed therapy optimization, and proactive planning before irreversible end-organ dysfunction occurs. This article is intended to be a practical narrative overview to help frontline clinicians recognize the signs of advanced heart failure to facilitate timely referral to advanced heart failure specialists.

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Heart Failure Classification and Stages of Progression

The American College of Cardiology/American Heart Association/Heart Failure Society of America (ACC/AHA/HFSA) classifies heart failure (HF) into four progressive stages (A through D) that focus on disease development and progression [3]. Stage A (At Risk for HF) includes patients at risk of heart failure but without symptoms, structural heart disease, or cardiac biomarkers of stretch or injury. Stage B (Pre-HF) represents patients with no symptoms or signs of heart failure but with evidence of structural heart disease, evidence of increased filling pressures by invasive hemodynamics or noninvasive imaging, or patients with risk factors and elevated natriuretic peptides or persistently elevated cardiac troponin in the absence of competing diagnoses. Stage C (Symptomatic HF) includes patients with structural heart disease and current or previous symptoms of heart failure. Stage D (Advanced HF) represents patients with marked heart failure symptoms that interfere with daily life, and recurrent hospitalizations despite attempts to optimize guideline-directed medical therapy [3, 4]. Mortality rates increase progressively with each stage of heart failure, with 1-year

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all-cause mortality rates of approximately 8–12% for Stage A, 15–18% for Stage B, 21–27% for Stage C, and 30–40% for Stage D [5]. Patients who fit into advanced Stage C or Stage D heart failure would benefit from referral to an advanced heart failure specialist, as they will likely require intensive medical management and evaluation for advanced therapies.

Furthermore, the New York Heart Association (NYHA) functional classification categorizes heart failure patients into four classes (I-IV) based on symptom severity and functional limitation. Class I patients have no limitation of physical activity; ordinary activity does not cause undue fatigue, dyspnea, or palpitations. Class II patients have a slight limitation of physical activity; comfortable at rest, but ordinary activity results in symptoms. Class III patients have marked limitations; comfortable at rest; symptoms occur with less than ordinary activity. Class IV patients are unable to perform any physical activity without discomfort; symptoms are present at rest [6]. Mortality rates increase progressively with worsening NYHA class. Annual mortality ranges from 3–25% for Class II, 10–45% for Class III, and exceeds 50% (potentially as high as 77%) for Class IV patients [7]. Patients with class III symptoms and class IV symptoms should also be considered for referral to advanced heart failure specialists.

Signs and Symptoms of Advanced Heart Failure

In 2017, the I NEED HELP mnemonic was developed to help health care providers recognize advanced heart failure patients who would benefit from referral to advanced heart failure specialists [8] (Figure 1). It is comprised of 9 criteria that are easy to define and contribute to an increased mortality in heart failure patients. This review will discuss the rationale behind each criterion and its association with worse outcomes.

Initiation of intravenous inotropic support, including dobutamine and milrinone, is a sign that the failing heart requires exogenous support to maintain basic function. Inotropes are associated with a significant increase in mortality, up to 70% within one year of initiation [9]. The dangers of inotropic support include hypotension, arrhythmia, and sudden cardiac death [9]. Therefore, it is reasonable to involve advanced heart failure specialists to help determine whether patients would be a candidate for advanced therapies, such as mechanical circulatory support or heart transplantation.

Patients with persistent NYHA class IIIb or IV symptoms should alert providers of advanced disease, as they are linked to worse outcomes [7]. In addition, persistently elevated brain natriuretic peptides (BNP) despite medical management signify a stressed heart and are linked with worse mortality. Each 100-pg/mL increase in BNP is associated with a 14–35% increase in mortality risk, while a 1-log-unit increase confers a 51% increased hazard of death. For N-terminal pro B-type natriuretic peptide, levels >1,000 pg/mL are associated with markedly increased morbidity and mortality in chronic heart failure [10]. End-organ dysfunction (particularly renal and hepatic) signals hemodynamic compromise and is associated with poor prognosis and possible need for multiorgan transplant. Progressive deterioration in renal function reflects inadequate cardiac output and venous congestion, and when severe enough, may preclude candidacy for advanced therapies like transplantation or ventricular assist devices. Patients with creatinine ≥1.8 mg/dL or blood urea nitrogen ≥43 mg/dL are considered high-risk [11].

The association between left ventricular ejection fraction (LVEF) and mortality follows a near-linear pattern below 45%, with each 10% reduction in LVEF conferring a 39% increase in all-cause mortality risk in one study [12]. It is important that providers optimize guideline-directed medical treatment to provide patients with the best chance of improving their ejection fraction. Many patients with heart failure, particularly those with ejection fractions less than 35%, qualify for implantable cardiac defibrillators for primary prevention of sudden cardiac death. However, both appropriate and inappropriate shocks have been linked to heightened sympathetic activation, myocardial injury, and progressive ventricular dysfunction, which may further exacerbate heart failure progression. Recurrent shocks are also associated with significant psychological distress, reduced quality of life, and increased healthcare utilization, and could be a sign of advanced heart failure [13].

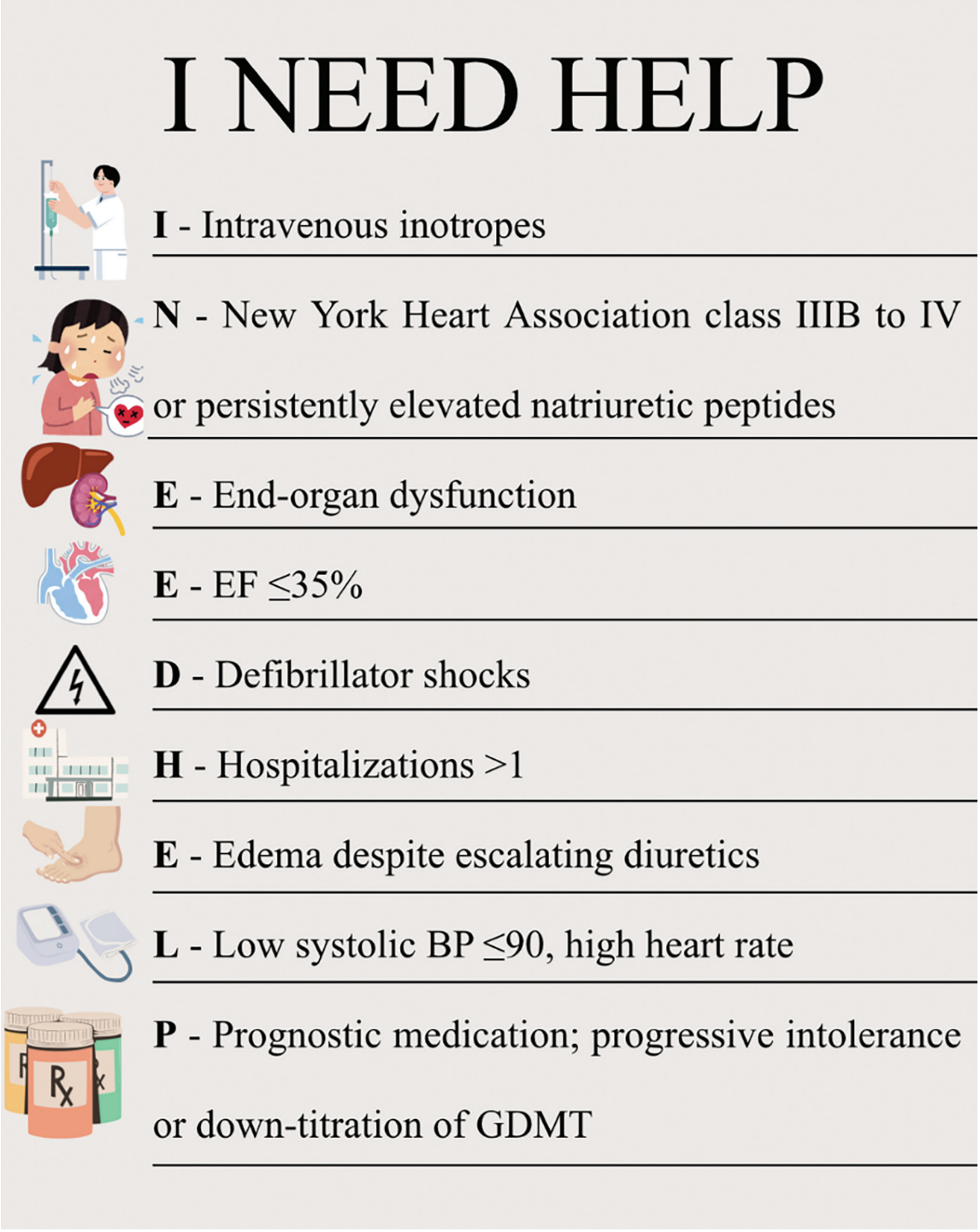

Figure 1 Pictorial Representation of the I NEED HELP Mnemonic, to Help Providers Recognize Signs and Symptoms of Advanced Heart Failure.

Heart failure hospitalizations carry a high burden for patients, their care providers, and hospital systems. Inpatient hospitalizations make up nearly 50% of the direct cost of heart failure care [14]. In addition, hospitalization for heart failure carries a mortality risk comparable to myocardial infarction and stroke [15]. Multiple hospitalizations carry an even greater risk of mortality, and therefore, are a sign for primary physicians to consider referral. Oftentimes, patients require either medical optimization, consideration of cardiac resynchronization therapy, or, potentially, advanced heart failure

therapies. Most advanced heart failure practices incorporate a practice that promotes close follow-up with specialized advanced practitioners who aim to prevent readmission through outpatient diuretic adjustment and follow-up calls with patients. This modality of care is invaluable for patients who need a closer follow-up to ensure medication and dietary compliance, and that might be challenging to do with the high workload and long wait times in most primary care practices.

Diuretic resistance is defined as persistent congestion despite escalating doses of loop diuretics, with furosemide ≥80 mg once or twice daily. It confers a higher risk of hospitalization and mortality in heart failure patients [16]. It can be a sign of low cardiac output, worsening kidney function, increased gut edema, and renal tubular resistance. Oftentimes, patients with persistent congestion are hospitalized in the hope that receiving intravenous diuretics would help them achieve euvolemia. However, many large studies found that patients do not lose a significant amount of weight during hospitalizations for volume overload from heart failure. In fact, about 20% of patients gain weight by the time of discharge [17]. Before attempting to target multiple nephron segments, it is reasonable to refer these patients to advanced heart failure specialists. These patients might require invasive hemodynamics to assess right atrial pressures and cardiac output. In addition, they might be progressing to renal failure and could benefit from expediting their evaluation for advanced therapies before end organ dysfunction ensues.

Hypotension (systolic blood pressure ≤90 mmHg) and resting tachycardia are both well-established independent predictors of poor prognosis in heart failure. Chronic hypotension in heart failure reflects impaired myocardial contractility and inability to generate adequate cardiac output, signaling worse prognosis despite the paradox that hypertension is a risk factor for developing heart failure. Initial systolic blood pressure <120 mmHg was independently associated with a 1.81-fold increased risk of long-term mortality (OR 1.81, 95% CI 1.35–2.42), while diastolic blood pressure <80 mmHg conferred a 2.24-fold increased risk (OR 2.24, 95% CI 1.65–3.05) [18]. Providers are more likely to stop or down titrate important guideline-directed medical therapy (GDMT) for borderline blood pressures, stripping patients of the benefit gained with these medications. In addition, resting tachycardia is an independent predictor of mortality and heart failure hospitalization in patients with reduced ejection fraction in sinus rhythm. Each 10-bpm increase in heart rate was associated with a 12% increased risk of cardiovascular death or heart failure hospitalization (HR 1.12, 95% CI 1.09–1.16) [19].

Progressive intolerance of GDMT is another poor prognostic marker for patients with heart failure. The likely causes of intolerance include hypotension, bradycardia, electrolyte imbalances, and progressive worsening of renal function. In this modern era of GDMT, the addition of newer classes of medications such as sodium glucose transport inhibitors and angiotensin receptor neprilysin inhibitor therapies markedly improved mortality and morbidity of patients with heart failure, ultimately leading to a survival benefit. Many studies show that discontinuation of renin angiotensin system inhibitors and beta blockers was associated with an increase in mortality [20]. The inability to tolerate GDMT reflects the underlying hemodynamic fragility of advanced heart failure—these patients have such marginal cardiac reserve that even evidence-based therapies designed to improve outcomes cannot be sustained.

Real-world validation of the I NEED HELP mnemonic comes from the HELP-HF Registry, which evaluated 1,149 patients with at least one I NEED HELP criterion. This study found that a higher cumulative number of criteria was independently associated with worse outcomes (adjusted HR 1.19 per additional criterion, $P < 0.001$). Patients with >5 criteria had the worst prognosis. The individual criteria with independent prognostic impact were: need for inotropes, NYHA class III-IV or elevated natriuretic peptides, end-organ dysfunction, >1 hospitalization in the past year, persistent edema or escalating diuretics, and low blood pressure [21].

A more recent study published in 2025 compared many risk prediction tools including I NEED HELP and machine learning modules in their assessment of 1 year mortality and found that the risk prediction tools failed to predict 1 year mortality. It is interesting to note that the vector machine-based model had the best area under the curve, but only slightly outperformed most traditional risk scores. This study suggested that while I NEED HELP is

valuable as a screening tool for identifying patients who warrant referral to advanced heart failure specialists (its intended purpose), it performs poorly as a quantitative risk prediction model [22]. Modern electronic health record-based machine learning models offer a transformative capability that simple mnemonics cannot: continuous, automated risk updating as clinical status evolves, detecting deterioration before it becomes clinically obvious and predicting heart failure hospitalization up to 3 years in advance [23]. However, machine learning models face substantial implementation barriers including poor interpretability, lack of external validation, and requirements for sophisticated data infrastructure. Rather than replacing the mnemonic, modern data-driven tools can be used to augment it, preserving its accessibility while adding predictive power. In summary, the I NEED HELP mnemonic should be used as a screening and referral trigger tool, rather than a quantitative risk assessment tool. It does not substitute formal risk scores, specialist assessment, or advanced therapy eligibility evaluation.

Referral to Advanced Heart Failure Specialists

Once providers recognize the signs and symptoms of advanced heart failure using the information above, the next step is to determine which patients would benefit most from referral. Having an in-depth discussion with patients regarding their goals of care is a crucial step to complete. Ideal patients for an advanced heart failure center are those who are motivated to pursue intensive evaluation, potentially invasive procedures such as a heart catheterization, cardiac biopsies, implantation of mechanical circulatory support, and/or heart transplantation. Additionally, patients should have a suitable environment for success, including stable housing, and supportive family members and care givers. Substance abuse patients should be offered necessary interdisciplinary help from addiction specialists to help them quit prior to referral to advanced heart failure. A history of substance abuse does not preclude patients from consideration for advanced therapies, and with the right help, abstinence can increase their chances of being suitable candidates for advanced therapies. If patients have significant comorbidities such as dementia and advanced cancer, they would likely not be eligible for advanced therapies. If providers are not comfortable discussing the different therapies offered by advanced heart failure specialists, a referral for patient education is encouraged and can be beneficial for patients to determine whether further pursuit of this avenue aligns with their goals of care.

Advanced heart failure providers can offer patients a multitude of services, aside from advanced therapies and transplant. These services include palliative inotropes that can help patients feel better in their last days of life. In addition, patients can have access to ongoing clinical trials and opportunities to take part in research. They also play a critical role in expanding patient access to novel therapies that can significantly improve outcomes and quality of life. Through careful patient selection, they can offer innovative technologies such as CardioMEMS, which enables remote pulmonary artery pressure monitoring to guide proactive, individualized diuretic management and reduce hospitalizations, and Barostim therapy, which modulates autonomic imbalance to improve symptoms and functional capacity in patients with advanced disease [24, 25].

Timeliness of Referral

Timely referral to advanced heart failure care is crucial, as delayed referral has been consistently associated with increased morbidity and mortality [26]. When patients are referred later in the course of their disease, they are more likely to have developed multi-organ dysfunction, including renal, hepatic, and pulmonary impairment, which can preclude candidacy for advanced therapies or heart transplantation. In many cases, a missed opportunity for referral allows progressive deconditioning to occur, leading to frailty—a condition that is itself a strong marker of poor prognosis. Frailty not only reflects advanced disease severity but also significantly limits therapeutic options and tolerance of advanced interventions, further narrowing pathways for disease-modifying or life-prolonging treatment [27].

Timely recognition and referral to advanced heart failure specialists empowers patients with access to comprehensive, multidisciplinary care and life-prolonging therapies, preserving both survival and

quality of life. The I NEED HELP mnemonic is a practical and easy to use bedside tool that can be incorporated into daily practice, to serve as a mental checklist to screen for advanced heart failure. Once referred, most heart failure practices provide patients with a supportive framework to navigate their disease, including dietitians, pharmacists, physical therapists, social workers, therapists, and support groups. When a patient becomes plugged into a heart failure practice, they are more likely to receive optimal medical therapy. They will be closely monitored for the appropriate timing of advanced therapies before end-organ dysfunction occurs. Early referral does not signify therapeutic failure, but rather facilitates comprehensive multidisciplinary care, optimization of guideline-directed medical therapy, and proactive evaluation for advanced therapies before irreversible end-organ damage limits options. Collaboration between primary care physicians, general cardiologists, and advanced heart failure teams is essential to ensure appropriate patient selection, shared decision-making, and goal-concordant care. Ultimately, timely referral to advanced heart failure programs offers patients the best opportunity to alter the natural trajectory of this life-limiting disease and improve both survival and quality of life.

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Conflict of Interest

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