Heart failure remains a leading cause of morbidity and mortality, with increasing numbers of patients being affected annually. Developing models and approaches for predicting adverse outcomes and survival is of particular importance in determining when to initiate specific therapies, in particular those for advanced heart failure such as cardiac transplantation and mechanical circulatory support. The first approach was the New York Heart Association functional classification, which provided the ability to risk stratify patients by using the subjective assessment of exercise tolerance (1). To some degree, this classification has stood the test of time because it is still used to determine when to initiate therapies such as defibrillator implantation or cardiac resynchronization, but it is limited by its subjectivity. Efforts to improve prognostication in patients with heart failure include peak oxygen consumption during cardiopulmonary exercise testing in ambulatory heart failure patients (2). This parameter became an important way of identifying patients whose survival would be improved with cardiac transplantation.

As therapies for heart failure became more sophisticated, efforts were made to develop more sophisticated scoring models that would include a variety of clinical and laboratory parameters. One such model is the Heart Failure Survival Score (HFSS), which has 7 variables (3). The Seattle Heart Failure Model (SHFM) incorporates 24 variables, including clinical findings, laboratory parameters, and specific medical and device therapy (4). For both scoring models, patients can be placed into low-, medium-, or high-risk groups based on scores derived from these variables. SHFM is limited in that it may overestimate prognosis in patients with advanced heart failure, potentially failing to identify patients who would benefit from advanced therapies. The models seem to be most successful when combined for predicting adverse events in the medium-risk group. This group is probably the most critical for obtaining reliable prognosticators because the other groups have relatively few (low risk) or have frequent and significant (high risk) adverse events. It is prediction of outcomes in the medium-risk group that has been most difficult and problematic clinically, and the combination of the HFSS and the SHFM has provided some guidance; any additional information that could provide more robust predictive capabilities would be very important clinically.

Heart failure results from effects on the cardiovascular system of neurohormonal perturbations and also has systemic effects as a result of hemodynamic derangements such as congestion and diminished cardiac output. One consequence is hyponatremia as a result of activation of the renin-angiotensin and vasopressin systems. Hyponatremia has been identified as a predictor of poor outcome in hospitalized patients with heart failure (5–8). Serum sodium has been incorporated in both the HFSS and SHFM as part of the prediction algorithms.

Among the systemic effects of heart failure is hepatic congestion and subsequent abnormalities of hepatic function. These abnormalities identify a heart failure patient population at risk for worse outcomes, particularly death. Hepatologists have developed their own scoring system for hepatic function, the Model for End-Stage Liver Disease (MELD) in patients with end-stage liver disease being considered for liver transplantation; the goal is to determine their prognosis before transplantation and to prioritize listing for transplant based on this prognosis (9,10). The MELD uses 3 noncardiac biomarkers that reflect the severity of hepatic dysfunction on synthesis (international normalized ratio [INR]), metabolism (total bilirubin), and renal function (creatinine). MELD has been applied as a prognosticator for cirrhotic patients sent for cardiac surgery and to determine the prognosis of patients with stage D heart failure who are referred for mechanical circulatory support or heart transplantation (11–14).

In this issue of the Journal, Kim et al. (15) retrospectively studied 343 patients with ambulatory advanced heart failure undergoing evaluation for cardiac transplantation, 260 of whom had complete datasets. These datasets included clinical parameters, medication and device therapy information, and laboratory values as well as hemodynamic measures. The authors applied the MELD as well as 2 of its modifications, the MELDNa (which includes serum sodium levels) and the MELD-XI (which does not include INR and thus can be applied to heart failure patients with elevated INRs due to therapeutic anticoagulation with warfarin) (16). The various MELD scores were used separately and in combination with the HFSS and SHFM in this study. MELD scores alone were able to identify patients’ risk for...
the endpoint of death, heart transplantation, or ventricular assist device implantation. When MELD scores were combined with the HFSS and SHFM, low (<12) MELD scores were found to predict good outcomes and clinical stability in the low-risk group whereas high (>12) scores in the medium-risk group identified patients at higher risk for the aforementioned outcomes. MELD scores were independent of peak oxygen consumption and some of the other parameters in HFSS and SHFM. MELDNa scores also provided robust discrimination of patients into high and low risks for the outcome endpoints. The use of MELD-XI was potentially attractive because it might provide additional prognostic information in patients who received anticoagulation therapy with warfarin because this scoring system does not include the INR (16). Only this MELD scoring system was able to identify patients with diminished survival in anticoagulated patients, but the survival difference was more pronounced and hence the discrimination more robust for nonanticoagulated patients; the MELD and MELDNa scoring systems were of no use for anticoagulated patients.

The authors (15) are to be commended on applying what is a simply calculated scoring system using readily available laboratory data to an overlooked population with significant hepatic dysfunction, those with advanced heart failure. The question is what steps should be taken next to explore the utility of the MELD and how should cardiologists apply this information clinically. Certainly, calculation of the MELD and MELDNa scores is simple and, as was shown in the current study, can be done longitudinally to assess disease progression. The utility of MELD scoring in heart failure outcomes prognostication would be strengthened with a prospective study encompassing patients with a variety of severities of heart failure and with MELD scoring to assess response to initiation and/or optimization of heart failure medical therapies and devices as well as prognosis and relationship to clinical outcomes. It is not known at present, for example, whether optimization of medical therapy can lower the MELD scores. In addition, the utility of MELD-XI is apparently more limited because it seems to be only modestly predictive for patients receiving warfarin anticoagulation; the other 2 MELD scoring systems cannot be used in these patients because the INR is part of the score. This is not a trivial issue given the frequent coincident occurrence of heart failure and atrial fibrillation and the necessity of anticoagulation therapy in these patients. This situation may be mitigated in the future as newer antithrombotic agents such as dabigatran and rivaroxaban are used more frequently in patients with atrial fibrillation, resulting in less perturbations of INR. The utility of MELD scores in patients with heart failure who are receiving these agents is unknown. The utility of MELD scores specifically for predicting sudden cardiac death and arrhythmic events was not defined.

In summary, the addition of the MELD and MELDNa scores to the traditional heart failure outcome prediction models may provide additional data regarding risk that is independent of the traditional models such as HFSS and SHFM. Although the MELD is simple to use and its utility may be enhanced with MELDNa, prospective studies are needed to define its utility in a broad range of heart failure patients as well as its utility in monitoring changes in medical and device therapy. The application of MELD is more difficult in patients receiving anticoagulation therapy with warfarin.

**Key Words:** heart failure • liver dysfunction • MELD • prognosis.

**REFERENCES**


