EDITORIAL

Prognostic scores in advanced heart failure: where are we now and where are we going?

Jadwiga Nessler, Paweł Rostoff

Department of Coronary Disease and Heart Failure, Faculty of Medicine, Jagiellonian University Medical College, The John Paul II Hospital, Kraków, Poland

Heart failure (HF) is a complex and heterogeneous clinical syndrome, which is characterized by increasingly high prevalence, unfavorable prognosis, and poor quality of life.[1-3] It is estimated that HF affects approximately 38 million adults worldwide, including at least 15 million Europeans.[2,4] In Poland, about 600 000 to 700 000 people suffer from HF.[5] Data from cohort studies showed that from 5% to 10% of patients with HF develop an advanced stage of the disease with an average life expectancy of 6 to 12 months.[4] In patients with end-stage HF (advanced, stage D), treatment options are relevantly limited, morbidity is usually progressive, and survival is extremely short with a 1-year mortality rate of approximately 50%.[6,7] In the REMATCH multicenter trial (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure), patients with end-stage HF who were ineligible for heart transplantation showed a mortality rate of 75% in the first year and virtually no survival at 2 years of follow-up.[6] Similarly, in the INTREPID study (Investigation of Nontransplant-Eligible Patients Who Are Inotrope Dependent), patients with end-stage HF on optimal pharmacological treatment had survival rates of 22% at 6 months and 11% at 1 year.[6] In addition, inotrope-dependent patients with end-stage HF had the most unfavorable prognosis and survival rate of only 6% at 1 year.[6]

Various definitions and criteria of diagnosis have been proposed so far for advanced HF.[1,6-8] Unfortunately, there is no unique parameter to define this clinical condition. It was postulated that escalation of diuretic doses, intolerance or reduction of doses of neurohormonal antagonists, refractory arrhythmias, development of end-organ dysfunction, malnutrition/cardiac cachexia, and repeated hospitalizations, all indicated advanced HF and refractoriness to traditional therapies.[6] The European Society of Cardiology defines advanced HF as a chronic clinical syndrome with severe symptoms of HF, objective evidence of severe cardiac dysfunction, episodes of fluid retention, severe impairment of functional capacity, and history of 1 or more hospitalizations for HF in the past 6 months, despite optimized medical, surgical, and device therapy.[1,8]

Despite recent advances in the treatment of end-stage HF, morbidity and mortality rates are still unacceptably high. Effective risk stratification and evaluation of prognostic markers are the key elements of the management of HF. The precise identification of HF patients at the highest risk of disease progression or death would enable physicians to intensify medical, surgical, and device therapy, including mechanical circulatory support implantation and heart transplantation, thus improving the prognosis of these individuals.[1,6] In addition, estimating prognosis for morbidity and mortality may help patients and their families understand the nature of illness and the reasons for a referral to supportive or palliative care in selected cases.[1,6] Many univariate predictors of poor prognosis in HF have been identified, including high New York Heart Association functional class, reduced left ventricular ejection fraction, abnormal right ventricular function, concomitant diastolic dysfunction, low peak oxygen consumption during cardiopulmonary exercise testing, and signs of reduced tissue perfusion (eg, low mean arterial pressure, renal dysfunction, and neurohormonal activation).[1,6,9]

It is well known that comorbidities influence the pathophysiology, management, and prognosis of advanced HF, contributing to increased morbidity and mortality.[1-6] Murad et al[10] demonstrated that 60% of elderly patients with HF had at least 3 comorbidities, while only 2.5% of them had none. Renal and liver dysfunction significantly increases mortality associated with HF.[6] The pathophysiology of cardiorenal syndrome in end-stage HF involves neurohormonal and hemodynamic imbalance between the heart and kidneys.[6] It results in the stimulation of the sympathetic nervous system and activation of the renin–angiotensin–aldosterone

Correspondence to:
Prof. Jadwiga Nessler, MD, PhD, Oddział Kliniczny Choroby Wieńcowej i Niewydolności Serca z Pododziałem Intensywnego Nadzoru Kardiologicznego, Wydział Lekarski, Uniwersytet Jagielloński, Collegium Medicum, Krakowski Szpital Specjalistyczny im. Jana Pawła II, ul. Prądnicka 80, 31-202 Kraków, Poland, phone: +48 12 614 22 18, e-mail: jnessler@interia.pl
Received: April 22, 2017.
Accepted: April 22, 2017.
Published online: April 27, 2017.
Conflict of interest: none declared.
Pol Arch Intern Med. 2017; 127 (4): 235-237
doi:10.20452/pamw.4013

TABLE 1 The Model for End-stage Liver Disease (MELD) and MELD-variant scores (modified from references no. 12–15)

MELD	9.57 × ln (creatinine [mg/dl]) + 3.78 × ln (bilirubin [mg/dl]) + 11.2 × ln(INR) + 6.43
MELDNa	MELD – Na (mmol/l) – (0.025 × MELD × (140 – Na [mmol/l]) + 140; Na range = 125–140 mmol/l
MELD-Na	MELD + 1.59 × (135 – Na [mmol/l]); Na range = 120–135 mmol/l
MELD-XI	5.11 × ln (bilirubin [mg/dl]) + 11.76 × ln (creatinine [mg/dl]) + 9.44
modMELD	If serum albumin >4.1 g/dl: 1.12 × (ln 1) + 0.378 × ln (bilirubin [mg/dl]) + 0.957 × ln (creatinine [mg/dl]) + 0.643 If serum albumin <4.1 g/dl: 1.12 × (ln [1 + (4.1 – albumin)]) + 0.378 × ln (bilirubin [mg/dl]) + 0.957 × ln (creatinine [mg/dl]) + 0.643
iMELD	MELD + (age [years] × 0.3) – (0.7 × Na [mmol/l]) + 100
Updated MELD	1.27 × ln (1 + creatinine [mg/dl]) + 0.94 × ln (1 + bilirubin [mg/dl]) + 1.66 × ln (1 + INR)
MESO	(MELD / Na [mmol/l]) × 100
UKELD	5 × {1.5 × ln(INR) + 0.3 × ln(creatinine [μmol/l]) + 0.6 × ln(bilirubin [μmol/l]) – 13 × ln (Na [mmol/l]) + 70}

Abbreviations: INR, international normalized ratio; Na, sodium

system, upregulation of inflammatory cytokines, and sodium and water retention.[6] Advanced HF may also lead to cardiohepatic abnormalities including congestive hepatopathy, ischemic hepatitis, and cardiac cirrhosis.[6]

In recent years, numerous prognostic risk scores have been developed by multivariate survival analyses in adult patients with HF. In these multivariate predictive models, relative weights are assigned to each parameter with the aim of calculating the probability that a specific event (ie, death) will happen in the future.[11] Prognostic scoring systems help clinicians estimate prognosis and predict therapeutic response, translating the result of prognostic studies to everyday clinical practice.[11] Furthermore, the analysis of these models is fundamental for public health policy, comparative effectiveness research, and health technology assessment of therapies.[11] However, the clinical utility of prognostic scores is not unlimited.[1,6] The main limitation of the current prognostic models is the interpatient variability of the clinical course and progression of HF, which significantly impairs the adequacy of derivation samples and validation in specific patient cohorts.[1,6] In addition, the population-based risk may not reflect individual patient risk. Although prognostic scales significantly correlated with survival in large populations, their usefulness to predict survival in individual patients with HF is generally less clear. Most prognostic models in HF focused on the single clinical outcome, particularly on mortality. There is evidence that prognostic scores may help predict death in HF patients, but remain less useful for the prediction of HF hospitalizations or decreased quality of life.[1] The results of meta-analyses and systematic reviews evaluating over 200 prognostic models showed only a moderate accuracy for predicting deaths, and even poorer estimation precision for predicting hospitalization or the combined endpoint of death from, or hospitalization for, HF.[1]

There are several well-validated prognostic scores frequently used to predict mortality in patients with advanced HF, including the Seattle Heart Failure Model (SHFM), Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) risk calculator, and the Heart Failure Survival Score (HFSS).[12,13] The SHFM estimates the effect of adding newer HF therapies (eg, ultrafiltration, implantable cardioverter defibrillator/cardiac resynchronization therapy, and left ventricular assist devices) on mortality, but it may overestimate survival, especially in patients with severe HF.[12,13]

Recently, numerous studies have shown that the Model for End-Stage Liver Disease (MELD) score and its variants (**TABLE 1**) constitute valuable tools for estimation of cardiorenal and cardiohepatic interactions and predict mortality in individuals with HF, after Fontan surgery, with end-stage liver disease, and in cirrhotic patients undergoing cardiac and noncardiac procedures.[12-14] The classic MELD score uses 3 noncardiac biomarkers that reflect the severity of liver (international normalized ratio, serum bilirubin) and renal (serum creatinine) dysfunction.[12-14] In individuals receiving vitamin K antagonists (eg, warfarin) due to concomitant atrial fibrillation/flutter, the use of the "modified MELD" (modMELD) or "MELD excluding INR" (MELD-XI) scoring systems is recommended (**TABLE 1**).[12,13] The prognostic value of MELD scores in patients with HF receiving non-vitamin K antagonist oral anticoagulants remains unknown.[13]

In this issue of the *Polish Archives of Internal Medicine* (*Pol Arch Intern Med*), Szyguła-Jurkiewicz et al[15] report their single-center experience with 1-year survival in ambulatory patients with end-stage HF who were placed on the heart transplant waiting list. The mortality rate during the study follow-up was 43.3%.[15] Based on the univariate and multivariate logistic regression analyses, the authors found that the modMELD score, as well as serum levels of high-sensitivity C-reactive protein, sodium, and uric acid were independent predictors of death in the study population.[15] In addition, they demonstrated that the modMELD score of more than 10 predicts HF mortality with a sensitivity of 82% and specificity of 77% (area under the receiver operating characteristic curve, 0.868; 95% CI, 0.821–0.915).[15] However, this interesting finding needs to be confirmed in future prospective studies.

In summary, several risk scoring systems are available to predict mortality in patients with end-stage HF. All of them provide additional, prognostic information and can be used to evaluate the outcome in patients with advanced HF. The newly proposed, simple, and accurate prognostic model, modMELD score, seems to be a clinically useful tool in predicting survival in end-stage HF. However, further studies are required to better stratify and identify high-risk patients with advanced HF who would benefit from additional, more aggressive interventions.

REFERENCES

1 Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016; 37: 2129-2200.

2 Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. Nat Rev Cardiol. 2016; 13: 368-378.

3 Konduracka E, Gajos G. Clinical characteristics of elderly patients with heart failure: what else do we need to know? Pol Arch Med Wewn. 2016; 126: 463-464.

4 Aleksova N, Demers C, Strachan PH, et al. Barriers to goals of care discussions with hospitalized patients with advanced heart failure: feasibility and performance of a novel questionnaire. ESC Heart Fail. 2016; 3: 245-252.

5 [Heart failure in Poland – a 2016 report]. [Informational materials of the Heart Failure Section of the Polish Cardiac Society]. http://www.niewydolnosc-serca.pl/barometr.pdf. Accessed April 20, 2017. Polish.

6 Fang JC, Ewald GA, Allen LA, et al. Advanced (stage D) heart failure: a statement from the Heart Failure Society of America Guidelines Committee. J Card Fail. 2015; 21: 519-534.

7 Friedrich EB, Böhm M. Management of end stage heart failure. Heart. 2007; 93: 626-631.

8 Metra M, Ponikowski P, Dickstein K, et al. Advanced chronic heart failure: A position statement from the Study Group on Advanced Heart Failure of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2007; 9: 684-694.

9 Colucci WS. Predictors of survival in heart failure due to systolic dysfunction. http://www.uptodate.com/contents/predictors-of-survival-in-heart-failure-due-to-systolic-dysfunction. Accessed April 20, 2017.

10 Murad K, Goff DC Jr, Morgan TM, et al. Burden of Comorbidities and Functional and Cognitive Impairments in Elderly Patients at the Initial Diagnosis of Heart Failure and Their Impact on Total Mortality: The Cardiovascular Health Study. JACC Heart Fail. 2015; 3: 542-550.

11 Passantino A, Monitillo F, Iacoviello M, et al. Predicting mortality in patients with acute heart failure: Role of risk scores. World J Cardiol. 2015; 7: 902-911.

12 Szyguła-Jurkiewicz B, Zakliczyński M, Andrejczuk M, et al. The Model for End-Stage Liver Disease (MELD) can predict outcomes in ambulatory patients with advanced heart failure who have been referred for cardiac transplantation evaluation. Kardiochir Torakochirurgia Pol. 2014; 11: 178-181.

13 Eisen HJ. The MELD scoring system and the prediction of outcomes in heart failure patients: what we have learned from the hepatologists. J Am Coll Cardiol. 2013; 61: 2262-2263.

14 MELD-based calculators. Bologna Liver Oncology Group (BLOG). Università di Bologna, Bologna. http://www.livercancer.eu/calculators.html. Accessed April 20, 2017.

15 Szyguła-Jurkiewicz B, Szczurek W, Skrzypek M, et al. One-year survival of ambulatory patients with end-stage heart failure: the analysis of prognostic factors. Pol Arch Intern Med. 2017; 127: 254-260.