Acute Heart Failure in the Emergency Department: What Is the Prognosis?

Heart failure (HF) is and will continue to be a major clinical problem in the United States, with an estimated prevalence of 6.5 million that is projected to increase to 8 million by 2030. Persons with HF account for about 1 million acute care hospitalizations, 2 million outpatient visits, and at least 500 000 emergency department (ED) evaluations annually (1). Patients with HF typically are older than 55 years and fragile and have multiple comorbid conditions, such as hypertension, coronary artery disease, atrial fibrillation, diabetes, and chronic renal insufficiency. Only about half have systolic dysfunction (ejection fraction <0.40), for which treatment guidelines for long-term care are well-established. The remainder have similar symptoms but normal or near-normal systolic function. Best practice for long-term care of those with preserved systolic function has been elusive (2, 3). Regardless of the underlying mechanism of HF, many of these patients have minimal functional reserve to cope with the various life stresses they encounter and spin out of control into acute heart failure (AHF).

The ED is uniquely positioned to provide immediate care for all levels of intensity of AHF. The ED physician must rapidly triage a wide range of AHF presentations. About 5% of patients arrive in cardiogenic shock that requires immediate high-level care in the intensive care unit. A second group presents with specific acute etiologies that require immediate intervention, such as acute coronary syndromes, hypertensive emergencies, severe arrhythmias, acute structural heart decompensation, or pulmonary embolism (3). However, the vast majority of patients require therapy for acute management of various severities of congestion. How should they be classified? Can they be treated rapidly and discharged from the ED, or do they require hospitalization? Does knowing the patient's prognosis help manage these decisions and subsequent care?

The first major attempt to classify the clinical status of patients with HF was published by Forrester and colleagues in 1976 (4). They used right heart catheterization–derived hemodynamics to define 4 categories of congestion (pulmonary capillary wedge pressure >18 or ≤18 mm Hg) and perfusion (cardiac index >2.2 or ≤2.2 L/min/m^2) for patients with acute myocardial infarction: warm and dry (good perfusion and no congestion), cool and dry (poor perfusion and no congestion), warm and wet (good perfusion and significant congestion), and cool and wet (poor perfusion and significant congestion). Short-term prognosis was poorer with congestion and was worst with poor perfusion combined with congestion (4). In 2003, Nohria and colleagues (5) adapted this concept to patients with HF by using clinical symptoms and examination. They reaffirmed over 18 months of observation that no congestion is better than congestion and poor perfusion combined with congestion carries a grave prognosis.

This classification scheme is the cornerstone of initial evaluation of AHF and is incorporated into current guidelines (2, 3). Its greatest use is in defining initial treatment in the ED: Patients in the "warm and dry" category are candidates for discharge to home, whereas those in the "cool and wet" category are immediately admitted for high-level care. The dilemma resides in patients in the middle 2 groups, who need either rehydration or decongestion. The rate of symptom resolution varies greatly, and the safety of discharge is difficult to determine. In the United States, the default is hospital admission, which occurs about 80% of the time. Many of these 24- to 48-hour admissions seem marginally effective at best, and they consume most of the $30 billion spent on HF care annually (1). Paradoxically, in Canada, the ED admission rate for AHF is much lower (40% to 60%). The dilemma in Canada is concern about an excess of significant outpatient adverse events after ED discharge. A need exists to more effectively identify ED patients with poor prognosis for admission (6).

In this issue, Miró and colleagues report a rigorous and well-conceived predictive study of 30-day mortality in patients with AHF (7). The data come from the Epidemiology of Acute Heart Failure in Emergency Departments (EAHFE) registry, an established registry that involves 34 Spanish EDs with high and low patient volumes drawn from a diverse group of EDs that range from community facilities to academic centers. All patients with a confirmed HF diagnosis are included, except those with acute ST-segment elevation myocardial infarction. The derivation set of 4867 ED patients was analyzed to choose 13 final prognostic variables (out of 88 candidate variables) for the model, which was tested against outcomes in the original cohort and in an independent validation population of 3229 patients gathered 3 years later from the same EDs. The model was superior to a previously published Canadian ED prognosis model (8). The variables that were chosen are all readily available and familiar, except for the Barthel index of patient functionality, which may not be commonly used in the ED. A drawback is the need to use a Web site for the calculation, but the equation could conceivably be embedded into an electronic medical record that automatically populates most of the variables. The model divides the population into 6 risk groups, with the lowest 2 groups having 30-day mortality less than 2% and the top group having a mortality rate of 45%. It also works well in all ED settings.

This is the fourth major study aiming to define ED prognosis (7–10). All of them claim excellent discrimination between high and low risk. Of note, only 3 vari-

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ables (positive troponin level, oxygen saturation, and renal function) are common to all 4 trials. Derivation methods in each trial vary considerably, which may explain why each model has some nonintuitive variables. If any of these models are to gain acceptance, they will need to be prospectively tested in diverse populations. That is the easy part; the next steps are more challenging. If 40% of ED patients with HF are truly at very low risk, we must find commonalities among them. This information may guide development of an alternate infrastructure to successfully treat these patients out of the hospital. The vast diversity of medical care delivery across North America will necessitate unique innovation at almost every institution.

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Annals of Internal Medicine ORIGINAL RESEARCH

Predicting 30-Day Mortality for Patients With Acute Heart Failure in the Emergency Department

A Cohort Study

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Background: Physicians in the emergency department (ED) need additional tools to stratify patients with acute heart failure (AHF) according to risk.

Objective: To predict mortality using data that are readily available at ED admission.

Design: Prospective cohort study.

Setting: 34 Spanish EDs.

Participants: The derivation cohort included 4867 consecutive ED patients admitted during 2009 to 2011. The validation cohort comprised 3229 patients admitted in 2014.

Measurements: Eighty-eight candidate risk factors and 30-day mortality.

Results: Thirteen independent risk factors were identified in the derivation cohort and were combined into an overall score, the MEESSI-AHF (Multiple Estimation of risk based on the Emergency department Spanish Score In patients with AHF) score. This score predicted 30-day mortality with excellent discrimination (c-statistic, 0.836) and calibration (Hosmer–Lemeshow P = 0.99) and provided a steep gradient in 30-day mortality across risk groups (<2% for patients in the 2 lowest risk quintiles and 45% in the highest risk decile). These characteristics were confirmed in the validation cohort (c-statistic, 0.828). Multiple sensitivity analyses did not find important amounts of confounding or bias.

Limitations: The study was confined to a single country. Participating EDs were not selected randomly. Many patients had missing data. Measurement of some risk factors was subjective.

Conclusion: This tool has excellent discrimination and calibration and was validated in a different cohort from the one that was used to develop it. Physicians can consider using this tool to inform clinical decisions as further studies are done to determine whether the tool enhances physician decision making and improves patient outcomes.

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Annual hospitalizations due to acute heart failure (AHF) in Europe and the United States exceed 1 million in each region and account for most of the costs of heart failure–related care (1, 2). The emergency department (ED) has a central position in the management of AHF because about 90% of patients with this condition visit an ED for their symptoms (3, 4). Once initial treatments have been administered in the ED and their effects have been checked, decisions are made about subsequent patient management; specifically, does the patient need to be hospitalized, or can they be discharged to home with proper treatment and follow-up? As a result of a mainly subjective, empirically driven assessment, a highly variable proportion of patients with AHF are discharged directly to home from the ED (16.3% in the United States [5], 23.9% in Spain [4], and 36.2% in Canada [6]).

Although decision making in the ED is critically important, emergency physicians currently do not stratify patients by risk during this process. Some biomarkers, including heart-specific markers (such as natriuretic peptides and troponin) and nonspecific markers (such as glucose or creatinine), are associated with prognosis but cannot by themselves predict outcomes with sufficient reliability to aid decision making (7, 8). Several AHF risk scores have been developed (9, 10), but these scores were based on hospitalized patients, thus ignoring the many patients with AHF (more than a third in some countries [6]) who are managed entirely in the ED and discharged to home. To our knowledge, only 3 risk scores have been developed specifically for use in the ED: 2 in Canada (the Ottawa Heart Failure Risk Scale [OHFRS] and the Emergency Heart Failure Mortality Risk Grade [EHMRG] [11, 12]) and 1 in the United States (the Improving Heart Failure Risk Stratification in the Emergency Department [STRATIFY] scale [13]). However, the OHFRS and the STRATIFY scale were not externally validated, the OHFRS and the EHMRG were constructed from administrative data, the EHMRG was based on a sample that excluded palliative patients, the OHFRS was based on a nonconsecutive sample with multiple exclusion criteria, and the OHFRS and the STRATIFY scale were derived from databases of limited size (n = 557 and 1033 patients, respectively). Therefore, we believe that additional tools are needed to

See also:

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help physicians in the ED stratify patients with AHF according to risk.

METHODS

The Epidemiology of Acute Heart Failure in Emergency Departments (EAHFE) Registry

The EAHFE registry collects detailed information on consecutive patients attending 34 Spanish EDs with a final diagnosis of AHF (14, 15). University and community hospitals; EDs with high, medium, or low patient volume (>300, 200 to 300, or <200 patients per day, respectively); and hospitals from all areas of the country participate in the EAHFE registry voluntarily. Attending emergency physicians use Framingham clinical diagnostic criteria (16) to identify patients for the registry. The diagnosis is then double-checked by the principal investigator at each center, who makes the final adjudication of AHF diagnosis on the basis of a review of medical charts and all complementary tests done during the ED stay and hospitalization. The diagnosis was confirmed by natriuretic peptide measurement or echocardiography (17) in the 92% of patients included in the EAHFE registry. We excluded patients who had a concurrent diagnosis of ST-segment elevation myocardial infarction (approximately 3%).

For every patient, data on demographic characteristics, clinical history, presentation, and treatments were routinely collected on specific case record forms. Interventions, treatments, and patient placements (hospital admission or discharge) were based entirely on the decision of the attending emergency physician. Subsequent follow-up through telephone contact and consultation of medical records was performed between days 31 and 90. The EAHFE registry complies with the Declaration of Helsinki and was approved by the ethical committees of all participating centers, and all patients gave informed consent. About 2% of patients who met the inclusion criteria declined to participate.

Study Design

During the design of the EAHFE registry, we planned to develop a model that could stratify patients according to their risk for adverse outcomes. We wanted this model to be used as soon as possible after arrival in the ED by the first emergency physician who saw the patient, using variables routinely available in most EDs. When developing the model, which we named MEESSI-AHF (Multiple Estimation of risk based on the Emergency department Spanish Score In patients with AHF), we selected registry patients admitted during May 2009 and between November and December 2011 for the derivation cohort and patients admitted in January and February 2014 for the validation cohort (**Appendix Figure 1**, available at Annals.org). We used patients in the derivation cohort to generate a 30-day mortality risk model and patients in the validation cohort to measure the robustness of the model.

Statistical Analysis

We first identified 88 candidate predictor variables (**Appendix Table 1**, available at Annals.org) that described baseline demographic characteristics, medical history, and status at admission and could have prognostic implications. To develop the risk score, we used logistic regression (without interaction terms) with checks for nonlinearity and forward stepwise variable selection, with an entry criterion of a P value less than 0.010. We used multiple imputation with chained equations (18) to produce 50 imputed data sets for estimating missing values. Once we identified a predictor, we then identified a cutoff value based on clinical information about the predictor's value (for example, serum potassium level) or the linear trend (for example, serum creatinine level and systolic blood pressure). In the final model, we placed each continuous variable into ordered categories to facilitate their use in practice. We measured the model's discrimination with the c-statistic and the model's calibration by comparing observed versus model-derived mortality risk using the Hosmer–Lemeshow statistic. We conducted sensitivity analyses by type of hospital (university vs. community); by daily ED census (low to medium vs. high volume); and for alternative models that did not include values for Barthel index score, *N*-terminal pro–B-type natriuretic peptide (NT-proBNP) level, or troponin level (in any combination) because these values were unavailable for many patients. We compared our model with the EHMRG model (12) in a merged data set of both derivation and validation cohorts by comparing the areas under the receiver-operating characteristic curves for 30-day mortality with the DeLong test. We used Stata, version 13.1 (StataCorp), for all analyses.

Role of the Funding Source

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RESULTS

The derivation cohort comprised 4897 consecutive patients admitted to an ED with AHF during May 2009 and from November to December 2011 (**Appendix Figure 1**). Thirty patients were excluded from the analysis due to lack of follow-up, and 48 patients with censored data (<30 days of follow-up) were included. At arrival in the ED, mean age of the patients was 79.7 years; 57.1% were female; comorbidities were frequent (83.4% had hypertension, 42.2% had diabetes mellitus, 39.4% had dyslipidemia, and 29.9% had ischemic heart disease); 89.5% had New York Heart Association class III or IV disease; 56.5% had some dependency for activities of daily living (Barthel index score <100 points); and 41.5% had a left ventricular ejection fraction less than 0.50, with 52.4% of them receiving β-blockers, 62.9% receiving angiotensin-converting enzyme inhibitors or angiotensin II–receptor blockers, and 29.1% receiving mineralocorticoid-receptor antagonists. Patients who

Table 1. Multivariable Predictive Model for 30-Day Mortality Using Logistic Regression in 4867 Patients*

Variable	Patients, *n (%)*	Death Within 30 Days, *n (%)*	Odds Ratio (95% CI)	Missing, %
Barthel index score at admission				28.4
≥75 points	1556 (44.6)	60 (3.9)	1.00 (reference)	–
50–74 points	912 (26.2)	76 (8.3)	1.52 (1.07–2.16)	–
25–49 points	614 (17.6)	98 (16.0)	2.34 (1.61–3.38)	–
<25 points	404 (11.6)	125 (30.9)	3.99 (2.69–5.92)	–
Systolic blood pressure				2.0
≥155 mm Hg	1443 (30.3)	89 (6.2)	1.00 (reference)	–
140–154 mm Hg	991 (20.8)	81 (8.2)	1.52 (1.08–2.15)	–
125–139 mm Hg	986 (20.7)	105 (10.7)	2.06 (1.48–2.86)	–
110–124 mm Hg	845 (17.7)	114 (13.5)	2.56 (1.85–3.56)	–
95–109 mm Hg	357 (7.5)	56 (15.7)	2.52 (1.67–3.78)	–
<95 mm Hg	146 (3.1)	41 (28.1)	3.03 (1.82–5.06)	–
Age				0.3
<75 y	1227 (25.3)	61 (5.0)	1.00 (reference)	–
75–79 y	911 (18.8)	71 (7.8)	1.59 (1.08–2.33)	–
80–84 y	1116 (23.0)	112 (10.0)	1.74 (1.22–2.49)	–
85–89 y	1054 (21.7)	139 (13.2)	1.72 (1.21–2.45)	–
≥90 y	546 (11.3)	117 (21.4)	2.62 (1.79–3.83)	–
NT-proBNP level				59.8
<8000 ng/L	1412 (72.2)	84 (6.0)	1.00 (reference)	–
8000–15 999 ng/L	285 (14.6)	38 (13.3)	1.64 (1.08–2.49)	–
16 000–23 999 ng/L	110 (5.6)	26 (23.6)	2.04 (1.25–3.34)	–
≥24 000 ng/L	148 (7.6)	42 (28.4)	2.59 (1.68–3.99)	–
Potassium level				4.9
<3.5 mmol/L	249 (5.4)	32 (12.9)	1.48 (0.95–2.30)	–
3.5–4.9 mmol/L	3536 (76.5)	284 (8.0)	1.00 (reference)	–
5.0–5.5 mmol/L	508 (11.0)	73 (14.4)	1.35 (0.98–1.87)	–
>5.5 mmol/L	332 (7.2)	78 (23.5)	2.09 (1.48–2.94)	–
Positive troponin level†	1286 (45.1)	198 (15.4)	1.75 (1.32–2.30)	41.4
NYHA class IV disease at admission	2148 (46.1)	340 (15.8)	1.63 (1.28–2.09)	4.2
Respiratory rate				29.5
<25 breaths/min	2305 (67.2)	189 (8.2)	1.00 (reference)	–
25–29 breaths/min	540 (15.7)	76 (14.1)	1.35 (0.96–1.88)	–
≥30 breaths/min	585 (17.1)	109 (18.6)	1.69 (1.23–2.32)	–
Low-output symptoms‡	792 (17.5)	161 (20.3)	1.48 (1.15–1.90)	6.9
Oxygen saturation				4.0
95%–100%	1830 (39.2)	127 (6.9)	1.00 (reference)	–
90%–94%	1675 (35.8)	159 (9.5)	1.19 (0.90–1.56)	–
85%–89%	689 (14.7)	98 (14.2)	1.34 (0.97–1.86)	–
<85%	479 (10.3)	98 (20.5)	1.67 (1.18–2.36)	–
Episode associated with ACS§	134 (2.8)	36 (26.9)	2.02 (1.25–3.27)	2.9
Hypertrophy on ECG‖	290 (6.2)	38 (13.1)	1.59 (1.05–2.40)	3.4
Creatinine level				1.8
<133 μmol/L (<1.5 mg/dL)	3401 (71.1)	263 (7.7)	1.00 (reference)	–
133–212 μmol/L (1.5–2.4 mg/dL)	1054 (22.1)	156 (14.8)	1.27 (0.99–1.64)	–
>212 μmol/L (>2.4 mg/dL)	326 (6.8)	67 (20.6)	1.46 (1.00–2.13)	–

ACS = acute coronary syndrome; ECG = electrocardiography; NT-proBNP = *N*-terminal pro–B-type natriuretic peptide; NYHA = New York Heart Association.

* Quantitative predictor variables have been grouped into appropriate categories. The odds ratio for each category is the change in the odds of death within 30 d relative to the reference category (e.g., age <75 y). The coefficient for each variable is the log of the odds ratio. Multiple imputation using chained equations was used for missing data. The intercept was −5.40, which is the log of the odds of death within 30 d for a patient in the reference category for each variable. Such a patient has the most favorable characteristics and a low probability (0.5%) of death within 30 d. Percentages may not sum to 100 due to rounding.

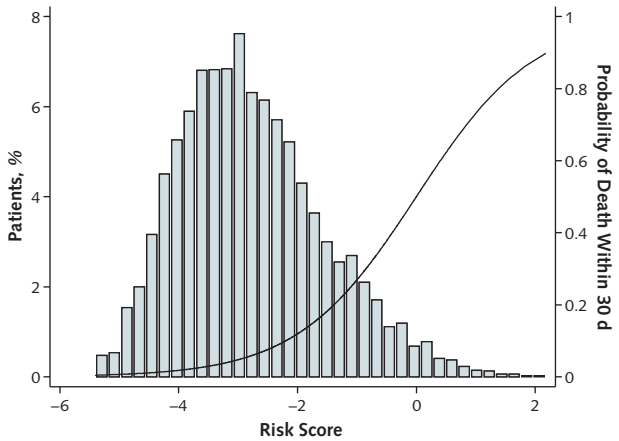
† Defined as a value above the upper limit of normal provided by the assay manufacturer.

‡ Defined as confusion; weakness; cold periphery; and ≥1 of the following: poor peripheral perfusion, anuria, or oliguria.

§ Defined as the presence of ≥2 of the following: chest pain, abnormalities on ECG, and positive troponin level.

‖ Defined using the Sokolow-Lyon index.

Figure 1. Modeled risk score distribution (*bars*) and predicted 30-d mortality risk (*line*) in the derivation cohort.



For a patient in the reference category of each variable in **Table 1**, the log of the estimated odds of death within 30 d is −5.40 (intercept of the logistic model), meaning that the risk for death within 30 d for a patient at the lowest risk (−5.40) is 0.5%. The log of a patient's odds of death within 30 d (referred to as "x") is equal to the sum of their relevant coefficients in **Table 1** and this intercept value. Their probability of death within 30 d can then be calculated as $e^x/(1 + e^x)$. This calculation can be done for any patient at http://MEESSI-AHF.risk.score-calculator-ica-semes.portalsemes.org.

were subsequently hospitalized (75.6%) had a median length of stay of 7 days. The remaining characteristics of the study population are presented in **Table 1**.

Within 30 days of ED admission, 500 patients (10.3%) died. We used a logistic regression model with forward stepwise variable selection to identify 13 highly significant independent predictors of death that we then included in the MEESSI-AHF risk score. These variables are listed in **Table 1** in descending order of their statistical strength of prediction (Barthel index score at admission was the most highly significant), and each odds ratio is adjusted for all other variables. **Appendix Figure 2** (available at Annals.org) displays the independent effect of each predictor on mortality risk based on the model in **Table 1**, and **Appendix Table 2** (available at Annals.org) shows comparisons of key predictor variables in patients with and without missing values.

The multivariable risk score for a specific patient can be determined by summing the relevant risk coefficients and the intercept coefficient in **Table 1**, which is the log of the patient's predicted odds of death within 30 days. The distribution of this risk score for all 4867 patients is shown in **Figure 1**. Also, the curve in **Figure 1** relates a patient's risk score to their probability of death within 30 days of ED admission (median, 0.051 [range, 0.005 to 0.898]). We have created a Web site to facilitate the calculation of any patient's risk for death within 30 days, including those who do not have values for Barthel index score, troponin level, or NT-proBNP level (http://MEESSI-AHF.risk.score-calculator-ica-semes.portalsemes.org). On the Web site, values for the relevant items can be entered, and the percentage of patients with these values who are predicted to die within 30 days will be calculated.

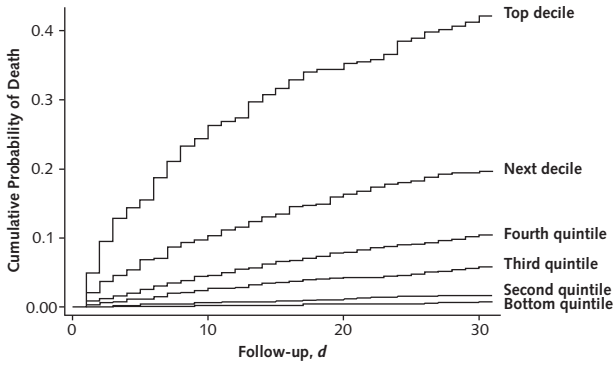
Figure 2 shows cumulative mortality over 30 days for patients classified into 6 risk groups based on the bottom 4 quintiles and the top 2 deciles of the risk score's distribution in the derivation cohort. Good discrimination of the model was achieved, with a c-statistic of 0.836 (95% CI, 0.818 to 0.853). There was a steep gradient in 30-day mortality across risk groups, with 45% mortality for the top decile and about 0.7% for the bottom quintile. Similar discrimination was observed in university and community hospitals and in low- to medium-volume and high-volume EDs (**Table 2**). **Figure 3** (*top*) depicts the goodness of fit of the model in this derivation cohort, comparing observed and model-predicted 30-day mortality risk across the 6 risk groups. A useful nomenclature is "low risk" for the first and second quintiles, "intermediate risk" for the third and fourth quintiles, "high risk" for the second-highest decile, and "very high risk" for the highest decile. Sensitivity and specificity of every possible risk threshold are plotted on the receiver-operating characteristic curve in **Appendix Figure 3** (available at Annals.org). Models that did not include Barthel index score, troponin level, or NT-proBNP level (in any combination) also showed good discrimination, with c-statistics ranging from 0.784 to 0.829 (**Appendix Table 3**, available at Annals.org).

Finally, we validated our risk score in a cohort of 3229 patients recruited during January and February 2014. In this validation cohort, 299 (9.26%) patients died within 30 days of ED admission. Four patients were excluded from the analysis because of lack of follow-up, and 6 patients with less than 30 days of follow-up were included. Comparisons of key predictor variables between the derivation and validation cohorts are provided in **Appendix Table 4** (available at Annals.org). **Appendix Figure 4** (available at Annals.org) shows the distribution of the MEESSI-AHF score in the validation cohort. **Figure 3** (*bottom*) compares the observed and model-predicted mortality in the validation cohort. The model fit and extent of risk discrimination were similar in the derivation and validation cohorts. For example, the c-statistic in the validation cohort was 0.828 (CI, 0.802 to 0.853), and the Hosmer–Lemeshow test for the validation cohort yielded a P value of 0.122. When we compared the EHMRG score, which was developed to predict 7-day mortality (12), with the MEESSI-AHF score for predicting 30-day mortality, the MEESSI-AHF score had superior discrimination overall (c-statistic, 0.830 vs. 0.750; $P < 0.001$) (**Appendix Figure 5**, available at Annals.org).

DISCUSSION

Our findings are based on a large prospective population-based cohort of consecutive patients with AHF who were admitted to 34 hospital EDs across Spain. Patients with many types of AHF were included, except those developing AHF during ST-segment elevation myocardial infarction, and all data were re-

Figure 2. Cumulative mortality for 6 risk groups.



Risk	Intervals	Patients, *n*	Probability of Death Within 30 d
Low	Bottom quintile	974	0.5%–2.1%
	Second quintile	973	2.1%–3.9%
Intermediate	Third quintile	974	3.9%–7.0%
	Fourth quintile	973	7.0%–14.5%
High	Second-highest decile	487	14.5%–25.7%
Very high	Highest decile	486	25.8%–89.8%

The first 4 risk groups correspond to quintiles 1 to 4, with the top quintile divided into 2 deciles.

corded shortly after arrival at the ED. The 13 predictors of 30-day mortality we identified should be readily available in routine clinical practice worldwide, and we have provided a Web-based calculator (http://MEESSI-AHF.risk.score-calculator-ica-semes.portalsemes.org) to make it easier for physicians to calculate risk for a specific patient. Using such a calculator, emergency physicians will now be able to determine whether a patient is at high (or low) risk for death within 30 days, which in turn might allow for better patient management. Our score may be particularly useful in the 10% of patients at very high risk (around 45%) for death at 30 days and in the 40% of patients at low risk (<2%). Identification of both groups has important management implications. For a patient with very high risk, attention should be focused on ensuring that the patient and their relatives are aware of the severity of the situation. In addition, the patient should receive prompt and aggressive treatment if appropriate, with an emphasis on early admission to an intensive care unit. For a patient with low risk, attention should be focused on treatment that will lead to early discharge from the ED to home, which is consistent with a recent consensus opinion about patients with less than 2% all-cause mortality who undergo sufficient observation in the ED (19).

In the United States, the overall rate of heart failure hospitalization decreased by 29.5% between 1998 and 2007 (20). We suggest that this decrease could be due to better ambulatory care that avoids patient decompensation and allows proper treatment of less severe AHF episodes without hospitalization. There is an increasing perception that more patients with AHF who are at low risk for adverse outcomes should avoid hospitalization (4, 21), and recent consensus opinions by clinical experts advocate this approach (19, 22). Specifically, one group recommends that 20% to 40% of patients diagnosed with AHF should be discharged directly from the ED (depending on whether the ED has a specific observation area) (19). These figures match well with patients in our low-risk category.

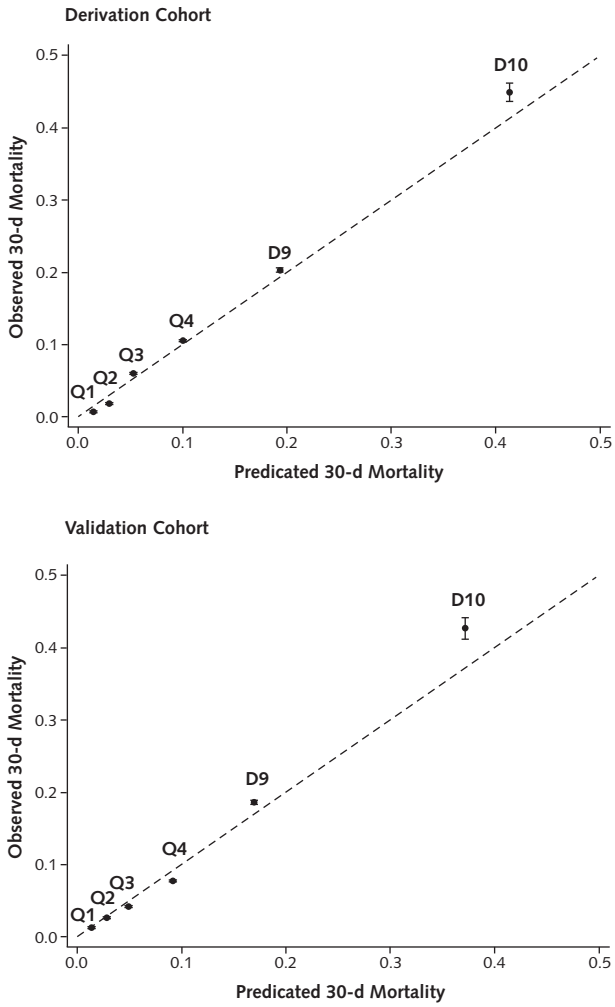
Avoiding hospitalization is not only a matter of improving health care system efficiency and saving costs. Hospitalization could expose the patient to such hazards as nosocomial infection, medication errors, acute reactive psychosis, and deteriorating functional status, all of which are distressingly common among elderly patients in the hospital. Patients with AHF are typically of advanced age, with a median age around 80 years in most series (4, 12). However, we are not aware of any formal tools that are currently being used to aid risk stratification for patients with AHF in the ED. Thus, some have argued that direct discharge of patients without objective risk stratification puts some patients at an unacceptably high risk for adverse events (6, 23). This situation contrasts with improvements achieved in other prevalent ED conditions, such as community-acquired pneumonia and acute coronary syndromes, for which risk scores have been developed (24, 25) and

Table 2. Analysis of 30-Day Mortality, by Hospital Type and ED Patient Volume

Risk Group	Death Within 30 Days, *n (%)**		*P* Value†	Death Within 30 Days, *n (%)*‡		*P* Value†
	University Hospitals	Community Hospitals		High-Volume ED	Low- or Medium-Volume ED	
Bottom quintile	6 (0.7)	1 (0.7)	0.65	2 (0.3)	5 (1.3)	0.74
Second quintile	15 (1.8)	3 (2.4)		11 (1.8)	7 (2.0)	
Third quintile	50 (5.9)	8 (6.7)		36 (6.0)	22 (6.0)	
Fourth quintile	83 (9.9)	19 (15.5)		64 (10.4)	38 (10.8)	
Second-highest decile	86 (20.5)	12 (19.1)		66 (20.9)	32 (19.3)	
Highest decile	193 (45.8)	24 (38.7)		142 (44.5)	75 (45.7)	

ED = emergency department.
* The c-statistic for our model in university hospitals was 0.839 (95% CI, 0.820–0.858), similar to that in community hospitals (0.812 [CI, 0.761–0.862]). 4193 patients (with 433 outcomes) were admitted to university hospitals, and 626 patients (with 67 outcomes) were admitted to community hospitals.
† From the Mantel–Haenszel test.
‡ The c-statistic for our model in high-volume EDs was 0.842 (CI, 0.820–0.863), similar to that in low- or medium-volume EDs (0.824 [CI, 0.791–0.867]). 3045 patients (with 321 outcomes) were admitted to high-volume EDs, and 1774 patients (with 179 outcomes) were admitted to low- or medium-volume EDs.

Figure 3. Assessment of risk discrimination and goodness of fit of the model in 6 risk groups (4 quintiles and the top 2 deciles) from low to very high risk for the derivation cohort (*top*) and the validation cohort (*bottom*).



D = decile; Q = quintile.

are being widely applied to discharge patients with less severe disease who previously would have been hospitalized. We believe that the MEESSI-AHF score can provide similar help in the management of patients with AHF, especially elderly patients who are more challenging to evaluate (15).

The 13 variables we found to be predictive have been reported to influence the prognosis of patients with AHF (1, 11–13, 15, 26–28). However, in our study, more than 25% of values were missing for 4 of these variables. We adjusted for these missing values by using multiple imputation. Moreover, to match our score to real-world practice, our Web site calculator provides a risk score even when values for Barthel index score, troponin level, and NT-proBNP level are not available, and we have shown that these risk scores perform as well as the regular ones (Appendix Table 4).

Our model compares favorably with other risk models. For example, it had c-statistics of 0.836 in the derivation cohort and 0.828 in the validation cohort, which were higher than when we calculated the EHMRG score in 2137 patients who had all of the data necessary to calculate it. The EHMRG model focuses on a shorter-term perspective (7-day mortality) (12); we believe that a longer perspective (30-day mortality) provides a better framework to create a model to aid emergency physicians. Moreover, palliative patients (who have a higher risk for adverse events) were excluded when the EHMRG score was developed, which could limit its generalizability. Patients receiving only palliative care are not uncommon; 10.2% of our patients had a Barthel index score of 0 to 20 points (indicating complete dependence for activities of daily living), and an additional 32.8% had a Barthel index score between 21 and 60 points (indicating severe dependence), and palliative care may be appropriate for many of them, although this was not directly recorded in our study. However, we have previously shown that excluding patients for whom palliative care may be appropriate did not significantly change the discriminatory capacity of the model (c-statistic decreased from 0.741 to 0.729) (29). Our findings, in line with previous work in this field (30), affirm that the Barthel index is a key outcome predictor, adding value to previously developed risk scores. Thus, it is important to recognize that patient frailty and dependence are key aspects that should be considered in every disease affecting elderly persons, including AHF. Finally, our model was developed with data that were prospectively recorded using a standardized pro forma at the time of admission to the ED instead of using retrospective extraction from administrative reports, as was done for the EHMRG model. The latter strategy could limit reliability and completeness of the data. All of the aforementioned limitations also apply to the OHFRS model, which was developed using more extensive patient exclusion criteria and a smaller sample and had a c-statistic of 0.77 (11). On the other hand, although the STRATIFY scale (13) was developed using prospectively recorded data, it was derived from a limited number of cases and was not externally validated, and discriminatory capacity was moderate (c-statistic, 0.68) (13).

Our study has important limitations. Some significant predictors had a high number of missing values, which we have addressed with multiple imputation techniques and sensitivity analyses. A false-positive predictor may have entered the risk model, although use of a *P* value less than 0.010 as an entry criterion minimized this risk. Some variables, such as Barthel index score, New York Heart Association class, association with acute coronary syndrome, or low cardiac output, are partially based on subjective interpretation, but we tried to reduce this problem by providing all study centers with a dictionary of variables and holding meetings with all researchers before each recruitment phase. In addition, the precision of our model might change in the future, especially if new treatments for heart failure modify mortality, such as the combined

use of inhibitors against neprilysin and angiotensin II receptors, which were not available when this study was done. Finally, as with any study done in a single country, caution should be used in extrapolating findings to other countries. Moreover, EDs were not randomly selected but were participants in the EAHFE registry with special interest in AHF, so results could differ when applied to other EDs. We encourage others to validate our risk model in other countries and regions, although we believe it has the potential for widespread use.

In conclusion, our study shows that physicians can use 13 readily available items to estimate individual risk for death within 30 days for patients with AHF who are admitted to the ED. The tool we have developed has excellent discrimination and calibration and was validated in a different cohort from the one that was used to develop it. We believe that physicians can consider using this tool to inform clinical decisions as we conduct further studies to determine whether the tool enhances physician decisions and improves patient outcomes. To facilitate its use, we have provided access to a user-friendly calculator for specific patients (http://MEESSI-AHF.risk.score-calculator-ica-semes.portalsemes.org). We believe that this tool will be especially useful for identifying persons at lower risk, for whom further hospitalization may not be required.

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Reproducible Research Statement: *Study protocol:* The protocol for patient and date recruitment was approved by the Ethical Committee of the Hospital Universitario de Asturias (Oviedo, Spain) at every EAHFE phase, with the reference numbers 49/2010, 69/2011, 166/13, and 160/15. It can be consulted there. *Statistical code:* Restricted access is available by contacting Dr. Miró (e-mail, omiro@clinic.cat). *Data set:* Not available.

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Unless otherwise noted, members contributed to the article but did not author it.

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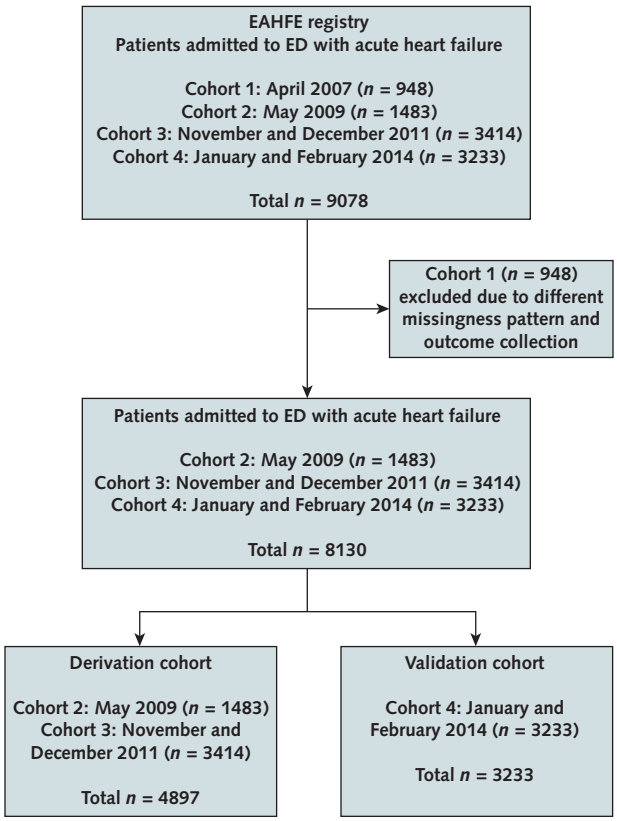
* Authored the article.

Appendix Figure 1. Patient flow diagram.



EAHFE = Epidemiology of Acute Heart Failure in Emergency Departments; ED = emergency department.

Appendix Table 1. Candidate Predictor Variables and Units/Definitions

Demographic characteristics
- Age (years)
- Gender (male/female)
- Body mass index (kg/m^2)

Vital signs
- Systolic blood pressure (mm Hg)
- Diastolic blood pressure (mm Hg)
- Heart rate (beats/min)
- Respiratory rate (breaths/min)
- Arterial oxygen saturation (%)
- Temperature (°C)

Transfer and triage
- Triage level (severity)
- Type of transfer to hospital
- Transfer to hospital with oxygen
- Transfer with diuretic, nitroglycerin, or invasive ventilation

Medical history
- Hypertension
- Diabetes mellitus
- Dyslipidemia
- Ischemic heart disease
- Chronic renal failure (creatinine level >2 mg/dL)
- Cerebrovascular disease
- Atrial fibrillation
- Peripheral arterial disease
- Valvular heart disease
- Chronic obstructive pulmonary disease
- Dementia
- Neoplasia
- Cirrhosis
- Current smoker
- Prior congestive heart failure
- Prior echocardiography
- Type of ventricular dysfunction
- Left ventricular ejection fraction on most recent echocardiogram (≤1 y before patient's inclusion)

Medical/social history
- Incontinence
- Hearing impairment
- Social support
- Prior falls

Status at admission
- Type of acute heart failure
- Symptoms of low output
- Cold skin
- Cutaneous pallor
- Delayed capillary refill
- Livedo reticularis
- Stupor or anxiety
- Dyspnea
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Increased jugular venous pressure
- Hepatomegaly
- Edema
- Tachycardia
- Third sound auscultation
- Pulmonary rales
- Cardiomegaly (on chest radiography)
- Pleural effusion

Continued on following page

Appendix Table 1–Continued

Scores
- Barthel index at baseline
- Barthel index at admission
- NYHA class at baseline
- NYHA class at admission

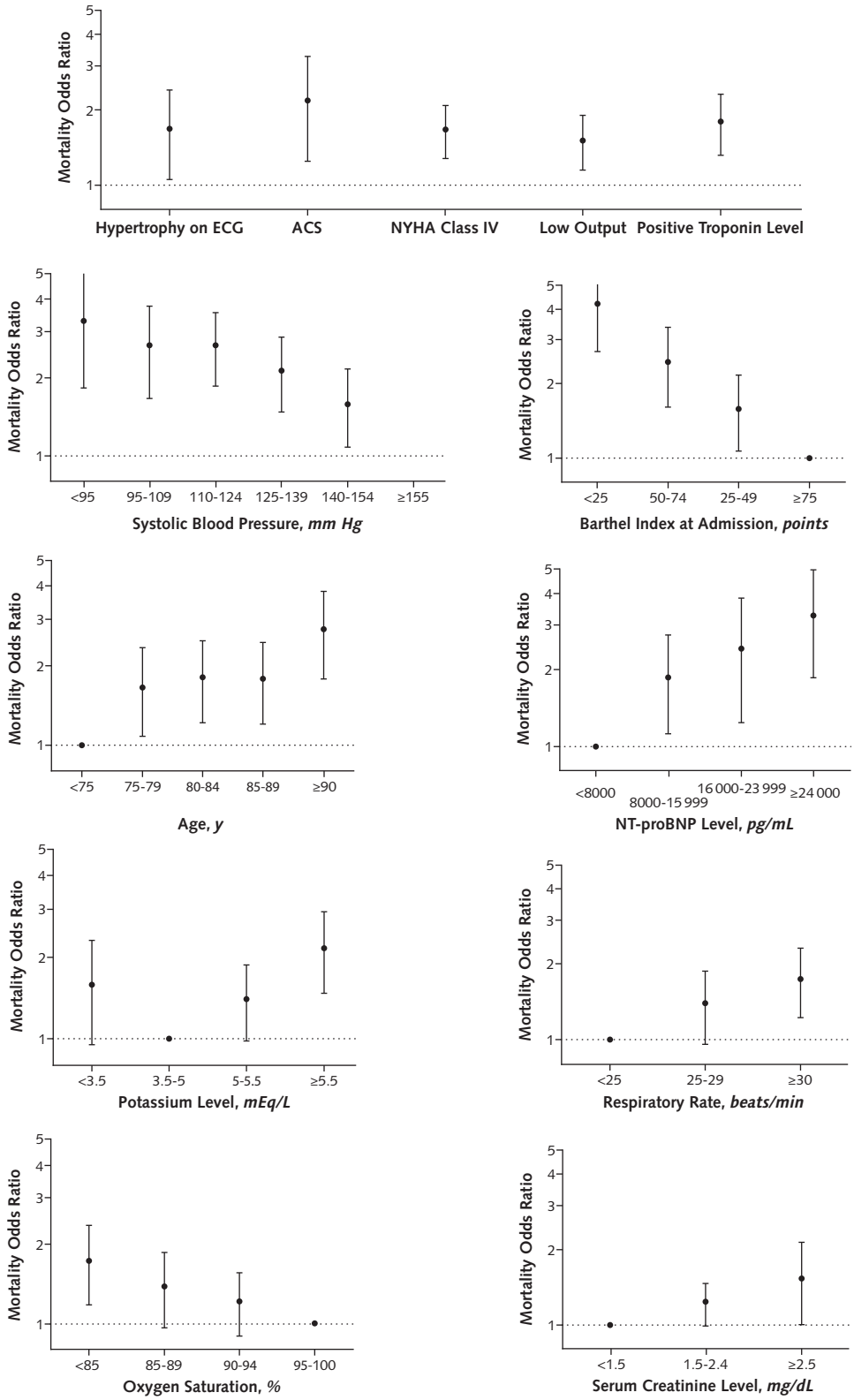
Precipitating factors
- Any
- Infection
- Rapid atrial fibrillation
- Anemia
- Hypertensive crisis
- Nonadherence to treatment
- Other

Blood tests
- Hemoglobin (g/dL)
- Hematocrit (%)
- Erythrocyte distribution width (%)
- Leukocyte count (cells/mm^3)
- Platelet count ($\times 10^9$ cells/L)
- Platelet volume (fl)
- Glucose (mg/dL)
- Urea (mg/dL)
- Creatinine (mg/dL)
- Sodium (mEq/L)
- Potassium (mEq/L)
- Troponin
- BNP (pmol/L)
- NT-proBNP (pmol/L)
- C-reactive protein (mg/dL)
- Procalcitonin
- $PaCO_2$ in arterial blood
- pH in arterial blood
- Lactic acid in blood (mmol/L)

ECG
- Sinus rhythm
- Atrial fibrillation
- Left ventricular hypertrophy (according to Sokolow–Lyon index)
- Left bundle branch block
- Pacemaker rhythm

BNP = B-type natriuretic peptide; ECG = electrocardiography; NT-proBNP = *N*-terminal pro–B-type natriuretic peptide; NYHA = New York Heart Association.

Appendix Figure 2. Mortality odds ratios for each variable in the predictive model.



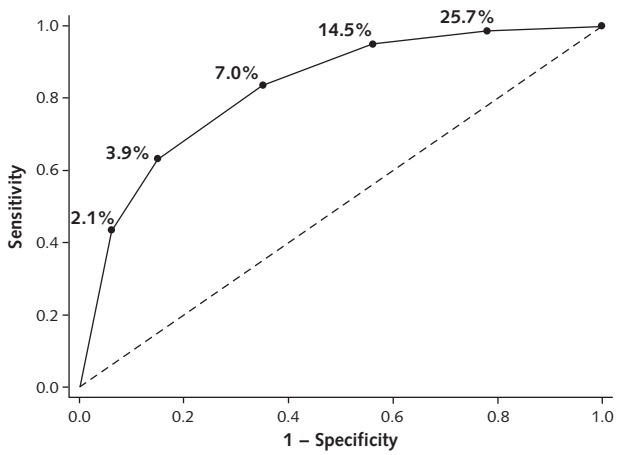
Error bars represent 95% CIs. Each odds ratio is adjusted for all other variables in the model. ACS = acute coronary syndrome; ECG = electrocardiography; NT-proBNP = *N*-terminal pro–B-type natriuretic peptide; NYHA = New York Heart Association.

Appendix Table 2. Collective Descriptive Missingness for Key Predictor Variables in the Derivation and Validation Cohorts

Variable	Missing, %	Death Within 30 Days, *n* (%)		*P* Value
		Missing Value	Nonmissing Value	
Barthel index score at admission	28.4	526 (9.8)	273 (10.3)	0.44
Age	0.3	0 (0)	799 (10.0)	0.40
Systolic blood pressure	2.0	18 (10.7)	781 (9.9)	0.73
NYHA class IV disease at admission	4.2	40 (11.3)	759 (9.9)	0.39
Potassium level	4.9	45 (11.0)	754 (9.9)	0.48
NT-proBNP level	59.8	478 (10.2)	321 (9.6)	0.44
Positive troponin level	41.4	335 (9.9)	464 (10.0)	0.92
Low-output symptoms	6.9	29 (8.5)	770 (10.0)	0.38
Respiratory rate	29.5	213 (8.6)	586 (10.5)	0.007
Episode associated with ACS	2.9	128 (9.7)	771 (9.9)	0.89
Oxygen saturation	4.0	30 (8.8)	769 (10.0)	0.48
Creatinine level	1.8	19 (13.8)	780 (9.9)	0.129
Hypertrophy on ECG	3.4	30 (11.5)	769 (9.9)	0.39

ACS = acute coronary syndrome; ECG = electrocardiography; NT-proBNP = *N*-terminal pro–B-type natriuretic peptide; NYHA = New York Heart Association.

Appendix Figure 3. Receiver-operating characteristic curve, with predicted 30-d risk for death labeled on the curve.



Sensitivity and specificity of the risk threshold for each category of the prediction model are plotted.

Appendix Table 3. Description of the Area Under the Receiver-Operating Characteristic Curve for the Full MEESSI-AHF Model and Alternative Models

Model	c-Statistic (95% CI)
Full model	0.836 (0.818–0.853)
Without NT-proBNP level	0.821 (0.803–0.840)
Without troponin level	0.829 (0.811–0.848)
Without Barthel index score	0.817 (0.797–0.836)
Without NT-proBNP level and troponin level	0.812 (0.792–0.831)
Without NT-proBNP level and Barthel index score	0.796 (0.776–0.816)
Without troponin level and Barthel index score	0.809 (0.789–0.829)
Without NT-proBNP level, troponin level, and Barthel index score	0.784 (0.762–0.805)

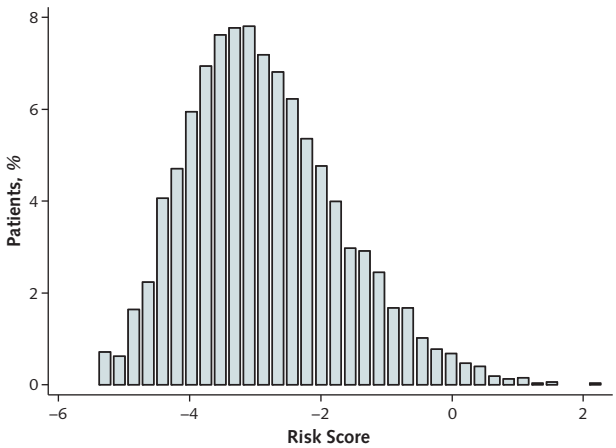
MEESSI-AHF = Multiple Estimation of risk based on the Emergency department Spanish Score In patients with Acute Heart Failure; NT-proBNP = *N*-terminal pro–B-type natriuretic peptide.

Appendix Table 4. Comparison of Key Predictor Variables Between Derivation and Validation Cohorts

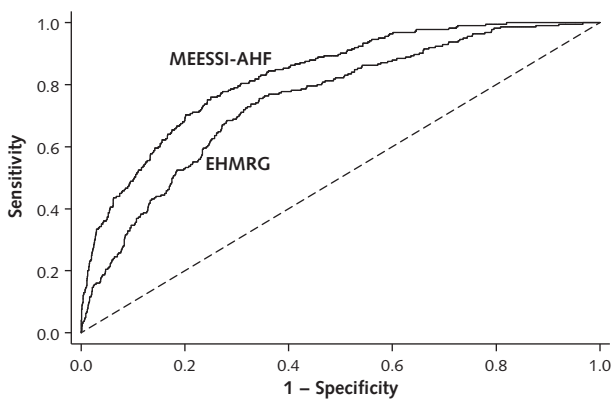
Variable	Derivation Cohort, *n* (%)	Validation Cohort, *n* (%)
Barthel index score at admission		
<25 points	404 (11.6)	171 (8.8)
25–49 points	614 (17.6)	286 (14.7)
50–74 points	912 (26.2)	520 (26.7)
≥75 points	1556 (44.6)	971 (49.9)
Systolic blood pressure		
≥155 mm Hg	1443 (30.3)	873 (27.6)
140–154 mm Hg	991 (20.8)	747 (23.7)
125–139 mm Hg	986 (20.7)	681 (21.6)
110–124 mm Hg	845 (17.7)	570 (18.1)
95–109 mm Hg	357 (7.5)	210 (6.7)
<95 mm Hg	146 (3.1)	77 (2.4)
Age		
<75 y	1227 (25.3)	783 (24.3)
75–79 y	911 (18.8)	580 (18.0)
80–84 y	1116 (23.0)	775 (24.0)
85–89 y	1054 (21.7)	657 (20.4)
≥90 y	546 (11.3)	429 (13.3)
NT-proBNP level		
<8000 ng/L	1412 (72.2)	1060 (75.4)
8000–15 999 ng/L	285 (14.6)	195 (13.9)
16 000–23 999 ng/L	110 (5.6)	61 (4.3)
>24 000 ng/L	148 (7.6)	90 (6.4)
Potassium level		
<3.5 mmol/L	249 (5.4)	150 (4.9)
3.5–4.9 mmol/L	3536 (76.5)	2397 (78.4)
5–5.5 mmol/L	508 (11.0)	311 (10.2)
>5.5 mmol/L	332 (7.2)	200 (6.5)
Positive troponin level	1286 (45.1)	983 (53.5)
NYHA class IV disease at admission	2148 (46.1)	1329 (43.2)
Respiratory rate		
<25 breaths/min	2305 (72.6)	1575 (67.2)
25–29 breaths/min	540 (11.6)	252 (15.7)
≥30 breaths/min	585 (15.8)	342 (17.1)
Low-output symptoms	792 (17.5)	628 (19.5)
Oxygen saturation		
95%–100%	1830 (39.2)	1292 (41.9)
90%–94%	1675 (35.8)	1098 (35.6)
85%–89%	689 (14.7)	398 (12.9)
<85%	479 (10.3)	294 (9.5)
Episode associated with ACS	134 (2.8)	62 (2.0)
Hypertrophy on ECG	290 (6.2)	61 (2.0)
Creatinine level		
<133 μmol/L (<1.5 mg/dL)	3401 (71.1)	2298 (72.3)
133–212 μmol/L (1.5–2.4 mg/dL)	1054 (22.1)	676 (21.3)
>212 μmol/L (>2.4 mg/dL)	326 (6.8)	203 (6.4)

ACS = acute coronary syndrome; ECG = electrocardiography; NT-proBNP = *N*-terminal pro–B-type natriuretic peptide; NYHA = New York Heart Association.

Appendix Figure 4. Risk score distribution in the validation cohort.



Appendix Figure 5. Comparison between the MEESSI-AHF and EHMRG scores.



Of note, the EHMRG score was conceived to predict death at 7 d, whereas the MEESSI-AHF score predicts death at 30 d. Between both validation and derivation cohorts, 2137 patients had available data to calculate the EHMRG score and perform the comparison between risk scores. The c-statistic was 0.830 (95% CI, 0.804 to 0.857) for our model and 0.750 (CI, 0.719 to 0.783) for the EHMRG score (DeLong test $P < 0.001$). EHMRG = Emergency Heart Failure Mortality Risk Grade; MEESSI-AHF = Multiple Estimation of risk based on the Emergency department Spanish Score In patients with AHF.