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Predicting Short-Term Mortality in Advanced Decompensated Heart Failure

– Role of the Updated Acute Decompensated Heart Failure/N-Terminal Pro-B-Type Natriuretic Peptide Risk Score –

Domenico Scrutinio, MD; Enrico Ammirati, MD; Andrea Passantino, MD; Pietro Guida, PhD; Luciana D'Angelo, MD; Fabrizio Oliva, MD; Marco Matteo Ciccone, MD; Massimo Iacoviello, MD; Ilaria Dentamaro, MD; Daniela Santoro, MD; Rocco Lagioia, MD; Simona Sarzi Braga, MD; Daniela Guzzetti, MD; Maria Frigerio, MD

Background: The first few months after admission are the most vulnerable period in patients with acute decompensated heart failure (ADHF).

Methods and Results: We assessed the association of the updated ADHF/N-terminal pro-B-type natriuretic peptide (NT-proBNP) risk score with 90-day and in-hospital mortality in 701 patients admitted with advanced ADHF, defined as severe symptoms of worsening HF, severely depressed left ventricular ejection fraction, and the need for i.v. diuretic and/or inotropic drugs. A total of 15.7% of the patients died within 90 days of admission and 5.2% underwent ventricular assist device (VAD) implantation or urgent heart transplantation (UHT). The C-statistic of the ADHF/NT-proBNP risk score for 90-day mortality was 0.810 (95% CI: 0.769–0.852). Predicted and observed mortality rates were in close agreement. When the composite outcome of death/VAD/UHT at 90 days was considered, the C-statistic decreased to 0.741. During hospitalization, 7.6% of the patients died. The C-statistic for in-hospital mortality was 0.815 (95% CI: 0.761–0.868) and Hosmer-Lemeshow X^2=3.71 (P=0.716). The updated ADHF/NT-proBNP risk score outperformed the Acute Decompensated Heart Failure National Registry, the Organized Program to Initiate Lifesaving Treatment in Patients Hospitalized for Heart Failure, and the American Heart Association Get with the Guidelines Program predictive models.

Conclusions: Updated ADHF/NT-proBNP risk score is a valuable tool for predicting short-term mortality in severe ADHF, outperforming existing inpatient predictive models. (*Circ J* 2015; **79:** 1076–1083)

Key Words: ADHERE logistic model; ADHF/NT-proBNP risk score; Advanced decompensated heart failure; GWTG-HF risk score; OPTIMIZE-HF risk score

Heart failure (HF) is a lethal disease and a leading cause of hospitalization in developed countries. Worsening chronic HF is the most common clinical presentation at admission, accounting for 70% of all admissions, and is associated with increased mortality compared with de novo HF.[1,2] Approximately 12–15% of the patients hospitalized for acute HF die within 12 weeks, and 30% within 12 months of admission,[1,3–7] with severe left ventricular (LV) systolic dysfunction substantially worsening prognosis.[1,8] In addition, 24–30% of the patients are readmitted within 60–90 days after discharge.[3,4]

Accurate estimation of absolute risk, combined with expert clinical judgment and supplementary evaluations, is essential to developing a tailored management plan including discharge planning, continuity and transition of care, outpatient follow-up, use of advanced treatment, and end-of-life issues.[6,9,10] Risk

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Division of Cardiology and Cardiac Rehabilitation, "S. Maugeri" Foundation, IRCCS, Institute of Cassano Murge, Bari (D. Scrutinio, A.P., P.G., D. Santoro, R.L.); Cardiothoracic and Vascular Department, Niguarda Ca' Granda Hospital, Milan (E.A., L.D'A., F.O., M.F.); San Raffaele Hospital and Vita-Salute University, Milan (E.A.); Cardiovascular Diseases Section, Department of Emergency and Organ Transplantation (DETO), University of Bari, Bari (M.M.C., M.I., I.D.); and Division of Cardiology and Cardiac Rehabilitation, "S. Maugeri" Foundation, IRCCS, Institute of Tradate, Varese (S.S.B., D.G.), Italy

Mailing address: Domenico Scrutinio, MD, Fondazione "S. Maugeri", IRCCS, Istituto di Cassano Murge, 70020 Cassano Murge (Bari), Italy. E-mail: domenico.scrutinio@fsm.it

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Table 1. Variables Incorporated in the Predictive Models

Predictive model	Risk markers	C-statistic	Follow-up	Mortality rate
Updated ADHF/ NT-proBNP[24]	Age / Prior admission for HF / COPD / SBP / eGFR / Sodium / Hb / NT-proBNP / LVEF / TR	0.748 (entire cohort) / 0.784 (patients aged ≤70 years)	12 months	32.4% (VAD/UHT: 15.5%)
ADHERE logistic model[14]	Age / SBP / BUN / Heart rate	0.759 (logistic model)	In-hospital	4.2% derivation cohort / 4.0% validation cohort
OPTIMIZE-HF[12]	Age / HF as primary cause of admission / Heart rate / SBP / Sodium / SCr / LVEF <0.40	0.753	In-hospital	3.8%
GWTG-HF[15]	Age / Non-black race / COPD / SBP / BUN / Heart rate / Sodium	0.75	In-hospital	2.86%
Rohde et al[16]	Age / Cancer / SBP / Sodium / BUN / SCr	0.77	In-hospital	10%
Euro Heart Failure Survey[1]	Age / Degree of LVSD / SCr / Treatment at discharge	NR	12 weeks	13%

ADHERE, Acute Decompensated Heart Failure National Registry; ADHF, acute decompensated heart failure; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; GWTG-HF, American Heart Association Get with the Guidelines Program; Hb, hemoglobin; HF, heart failure; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic dysfunction; NR, not reported; NT-proBNP, N-terminal pro-B-type natriuretic peptide; OPTIMIZE-HF, Organized Program to Initiate Lifesaving Treatment in Patients Hospitalized for Heart Failure; SBP, systolic blood pressure; SCr, serum creatinine; TR, tricuspid regurgitation.

markers are poorly discriminative when used individually.[11] Thus, several robust prognostic models, most of which used in-hospital mortality as an outcome measure, have been developed to predict outcome in patients with acute HF.[12–18] Nonetheless, clinical translation remains challenging. Given the phenotypic and prognostic heterogeneity of acute HF syndromes,[19] a one-size-fits-all approach to risk stratification may not be optimal to estimate absolute risk of death. Predictive models derived from unselected populations, although highly generalizable, may be miscalibrated when applied to specific clinical phenotypes at higher risk, with underestimation of absolute mortality risk. In addition, mortality risk may be influenced by different factors in patient subpopulations, such as age, cardiac function, comorbidities, and therapeutic options. Moreover, new potent risk markers are continuously being identified and validated.[20] Finally, in-hospital mortality may be a potentially biased endpoint.[21]

The acute decompensated HF (ADHF)/N-terminal pro-B-type natriuretic peptide (NT-proBNP) risk score was originally derived from patients hospitalized for worsening chronic HF with a wide range of LV ejection fractions (LVEF) and was validated in a truly external population.[22] Updating a predictive model is a desirable process.[23] Recently, the ADHF/NT-proBNP risk score was updated by adding age and ≥1 HF-related hospitalization within the 6 months preceding the index admission and applied to patients with advanced ADHF to predict 12-month mortality.[24] The risk score efficiently predicted 1-year mortality, performing particularly well among younger patients.

Patients with ADHF are, however, particularly vulnerable to death in the first few months after admission[2] and hospital clinicians may be more concerned about short-term than long-term risk of death. This concern is compounded by the imprecision of physician clinical judgment in estimating risk of death.[25] Thus, accurately assessing short-term prognosis at admission is a crucial step. The purpose of this study was to assess the value of the updated ADHF/NT-proBNP risk score for predicting short-term mortality in a larger population with advanced ADHF and compare its performance with other existing prognostic scores quoted in the most recent disease-specific Guidelines.[6]

Methods

This was a multicenter study. The subjects consisted of patients admitted for acute decompensation of chronic, established HF with New York Heart Association (NYHA) III/IV symptoms and evidence of severe LV systolic dysfunction (LVEF ≤0.30 on 2-D echocardiography) at admission. Patients were initially identified using a computer-generated list obtained from our administrative database and via review of electronic and paper medical records, and selected according to the following criteria. Inclusion criteria: current hospitalization for worsening of chronic, established HF; history of HF of at least 1 year; chronic treatment with evidence-based therapy; and need for i.v. diuretic and/or inotropic treatment. Exclusion criteria: symptoms and signs suggestive of acute coronary syndromes; angina pectoris; recent cardiac surgical or percutaneous procedures; planned coronary revascularization; no NT-proBNP recorded at admission; congenital heart disease; valvular heart disease. One thousand, one hundred and ninety-four ADHF patients fulfilling the aforementioned criteria were admitted between April 2006 and April 2014. Of these patients, 701 had both NYHA III/IV symptoms and evidence of severe LF systolic dysfunction (LVEF ≤0.30) at admission and were included in the study. Clinical and laboratory data were collected at admission. LVEF was assessed on 2-D echocardiography early during hospitalization.

The updated point-based ADHF/NT-proBNP risk score for each patient was calculated as detailed in our previous study.[24] Briefly, the score incorporates age, chronic obstructive pulmonary disease (COPD), ≥1 hospitalization for HF within the 6 months preceding the index admission, and systolic blood pressure (SBP), estimated glomerular filtration rate (eGFR), serum sodium, hemoglobin, NT-proBNP, LVEF, and moderate-severe tricuspid regurgitation (TR) at admission.[24] The score assigns 2 points to COPD; 1 point to SBP ≤100 mmHg; 3 points or 1 point to eGFR <30 or 30–59 ml/min/1.73 m^2, respectively; 3 points to serum sodium ≤135 mmol/L; 3 points to hemoglobin <13.0 g/dl in men and <12.0 mg/dl in women; 3 points to NT-proBNP >5,180 pg/ml; 5 points or 3 points to LVEF ≤0.20 or 0.21–0.30, respectively; and 2 points to moderate-severe TR. The score for each patient is the sum of the points assigned to each risk marker. The predicted mortality

Table 2. Baseline Characteristics

Variables	
Age (years)	63±13
Age >70 years	217 (31)
Male sex	587 (83.7)
BMI (kg/m^2)	27±5
Hypertension	279 (39.8)
Diabetes	245 (35.0)
COPD	164 (23.4)
Previous CVE	67 (9.5)
Known dysthyroidsm	153 (21.8)
Chronic liver disease	69 (9.8)
Ischemic etiology	354 (50.5)
Previous CABG/PTCA	265 (37.8)
NYHA IV class at admission	322 (46)
On waiting list for HTx at the time of admission or listed during hospitalization	65 (9.3)
Referred for transplantation evaluation	13 (1.9)
≥1 hospitalization in the prior 6 months	397 (56.6)
≥1 hospitalization in the prior 12 months	492 (70.2)
Atrial fibrillation	217 (31.0)
ICD	514 (73.3)
CRT	253 (36.1)
Heart rate (beats/min)	82±18
SBP (mmHg)	106±18
SBP ≤100 mmHg (n=674)	343 (50.1)
DBP (mmHg)	68±10
SCr (mg/dl)	1.5±0.74
eGFR (ml/min/1.73 m^2)†	59 (26)
eGFR <60 ml/min/1.73 m^2	381 (54.4)
eGFR <30 ml/min/1.73 m^2	80 (11.4)
BUN (mg/dl)	35±22
NT-proBNP (pg/ml)†	5,418 (2,501–10,633)†
NT-proBNP >5,180 pg/ml	362 (51.4)
Serum sodium (mmol/L)	137.9±4.8
Serum sodium ≤135 mmol/L	187 (26.7)
Serum potassium (mmol/L)	4.23±0.57
Hb (g/dl)	12.5±1.9
Hb <13 g/dl in men, <12 g/dl in women	382 (54.5)
Total cholesterol (mg/dl)	139±44
LVEF (%)	23.1±4.7
LVEF ≤20%	260 (37.1)
Moderate to severe TR	228 (32.5)
I.v. diuretics	677 (96.6)
I.v. inotropic drugs	290 (41.4)
Ventilator support	77 (11)
Intra-aortic balloon pump	8 (1.1)
In-hospital VAD implantation	12 (1.7)
In-hospital UHT	6 (0.9)
ADHF/NT-proBNP risk score	10.1 (4.1)
LoS	14 (8–21)†
Treatment at discharge for patients discharged alive:	
RAAS-I	474 (73.2)
β-blockers	524 (80.9)
Furosemide	640 (98.7)
Aldosterone antagonists	516 (79.6)

Data given as n (%), mean±SD or †median (IQR). BMI, body mass index; CABG, coronary artery bypass surgery; CRT, cardiac resynchronization therapy; CVE, cerebrovascular events; DBP, diastolic blood pressure; HTx, heart transplantation; ICD, implantable cardioverter defibrillator; IQR, interquartile range; LoS, length of stay; NYHA, New York Heart Association; PTCA, percutaneous coronary angioplasty; RAAS-I, renin-angiotensin-aldosterone system inhibitor; UHT, urgent heart transplantation; VAD, ventricular assist device. Other abbreviations as in Table 1.

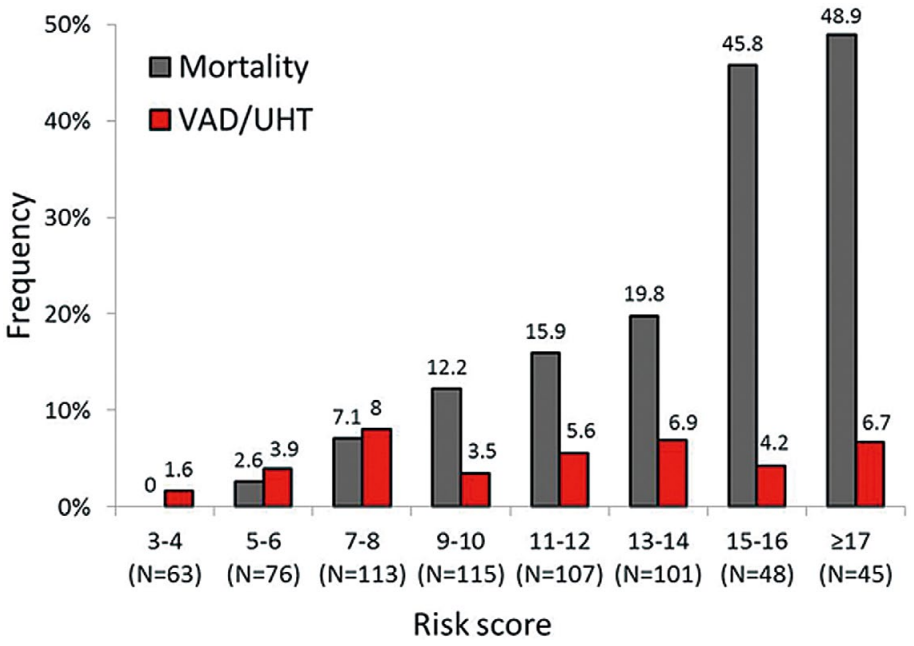

Figure 1. Incidence of death or urgent heart transplantation (UHT)/ventricular assist device (VAD) implantation within 90 days of admission as a function of acute decompensated heart failure/N-terminal pro-B-type natriuretic peptide risk score.

risk for the summed score is then adjusted for age and ≥1 HF-related hospitalization in the previous 6 months.[24] The risk score calculator can be downloaded to iPAD®/iPHONE® and is available at the App Store website by searching for "ADHF/NT-proBNP risk score calculator".

The primary objective of this study was to assess the association of updated ADHF/NT-proBNP risk score with all-cause mortality within 90 days of admission. Death was ascertained by linking with the regional Health Information Systems or by telephone follow-up. For purposes of comparison, we also assessed the association of risk score with in-hospital mortality. The secondary objective of the study was to assess the association of updated ADHF/NT-proBNP risk score with the occurrence of the combined outcome of all-cause death, urgent heart transplantation (UHT), or ventricular assist device (VAD) implantation as a first event within 90 days of admission.

Statistical Analysis

Data are reported as mean±SD for continuous variables or number (%) for categorical variables. Data were 98.9% complete. Missing data included body mass index (11.4% missing), heart rate (9.4% missing) and SBP (3.8% missing) at admission, and use of inotropes (3.4% missing). Missing SBP were replaced with the median.

The association of updated ADHF/NT-proBNP risk score with in-hospital and 90-day mortality was assessed with logistic regression modeling, using the score and prior hospitalizations as covariates. Based on data from our earlier study,[24] a survival function was constructed using regression techniques. To limit the loss of information associated with grouping, particularly at extreme risk, predicted and observed mortality rates were compared in risk subgroups stratified according to the 16th, 50th, and 84th centiles of the prognostic index.[26] Quoting Lee and Ezekowitz, a prognostic model "might be of far greater utility if a particularly high or low risk group can be identified".[25] Survival curves were based on Kaplan-Meier analysis. The patients who underwent HT or VAD implantation were censored. A secondary analysis was performed to assess the association of the risk score with the occurrence of death, UHT, or VAD implantation as a first event within 90 days of admission.

The performance of the ADHF/NTproBNP risk score to predict 90-day mortality was compared with that of the Euro Heart Failure Survey (EHFS) risk score.[1] In addition, the performance of the risk score to predict in-hospital mortality was compared with that of the Acute Decompensated Heart Failure National Registry (ADHERE) logistic regression model[14] and the Organized Program to Initiate Lifesaving Treatment in Patients Hospitalized for Heart Failure (OPTIMIZE-HF),[12] the American Heart Association Get with the Guidelines Program (GWTG-HF),[15] and the Rohde et al[16] risk scores, all of which are quoted in the most recent disease-specific Guidelines.[6] The variables incorporated in each model are reported in **Table 1**. Each risk score was introduced into a logistic regression model to estimate the association of raw score with outcome. Tests of overall model fit, discrimination, and calibration were used to compare the prognostic models. Discrimination was assessed by calculating the C-statistic. Calibration was assessed with the Hosmer-Lemeshow statistics. Given that the equation to estimate risk was reported only in the ADHERE study,[14] predicted mortality across risk categories could be estimated only for the ADHERE logistic model. Overall model fit was assessed with Bayes information criterion (BIC) and Akaike information criterion (AIC), which describe the distance between actual and predicted outcome. Lower values indicate better fit.[27] Analysis was conducted using Stata 12 (StataCorp, College Station, TX, USA).

Table 3. Discrimination, Calibration, and Model Fit for the Risk Scores

	C-statistic (95% CI)	Differences in C-statistics between the models with and without NT-proBNP	H-L χ^2 (P-value)	AIC	BIC
90-day mortality					
Updated ADHF/NT-proBNP risk score	0.810 (0.769–0.852)	–	1.05 (0.984)	500.5	514.1
EHFS risk score	0.714 (0.673–0.765)	–	8.89 (0.064)	542.8	551.9
EHFS plus NT-proBNP	0.756 (0.708–0.804)	0.042	8.86 (0.181)	519.9	533.5
In-hospital mortality					
Updated ADHF-NTproBNP risk score	0.815 (0.761–0.868)	–	3.71 (0.716)	327.6	341.2
ADHERE	0.758 (0.699–0.817)	–	9.96 (0.126)	345.1	354.2
ADHERE plus NT-proBNP	0.785 (0.730–0.840)	0.027	3.25 (0.776)	331.3	345.0
OPTIMIZE	0.771 (0.711–0.830)	–	5.66 (0.462)	338.9	348.0
OPTIMIZE plus NT-proBNP	0.793 (0.734–0.849)	0.022	3.69 (0.718)	328.5	342.1
GWTG	0.776 (0.720–0.832)	–	7.58 (0.271)	337.5	346.7
GWTG plus NT-proBNP	0.798 (0.744–0.852)	0.022	3.38 (0.760)	325.3	338.9
Rohde et al	0.749 (0.689–0.809)	–	6.92 (0.140)	339.8	348.9
Rohde plus NT-proBNP	0.787 (0.735–0.839)	0.038	8.14 (0.228)	327.3	340.9

NT-proBNP dichotomized at 5,180 pg/ml. The differences in C-statistics between the ADHF/NT-proBNP risk score and the other risk scores plus NT-proBNP were not statistically significant. AIC, Akaike information criterion; BIC, Bayesian information criterion; EHFS, Euro Heart Failure Survey; GWTG-HF, American Heart Association Get with the Guidelines Program; H-L, Hosmer-Lemshow. Other abbreviations as in Table 1.

Results

Descriptive statistics for baseline variables are reported in Table 2. Mean age was 63 years; 56.6% of the patients had had at least 1 hospitalization for HF in the prior 6 months; 50 patients (7.1%) were on the waiting list at the time of admission, 15 (2.1%) were listed during hospitalization, and 13 (1.9%) were referred for transplantation evaluation at discharge; 73.3% had an implanted cardioverter defibrillator and 36.1% had an implanted resynchronization device; mean SBP, LVEF, blood urea nitrogen, and eGFR were 106±18 mmHg, 23.1±4.7%, 35±22 mg/dl and 59±26 ml/min/1.73 m^2, respectively; median NT-proBNP was 5,418 pg/ml (IQR, 2,501–10,633 pg/ml); and 41.4% of the patients required i.v. inotropic therapy. Of the patients without in-hospital events, 73.2% were discharged on renin-angiotensin-aldosterone system inhibitors and 80.9% on β-blockers. Descriptive statistics across risk subgroups are reported in Table S1.

90-Day Mortality

Of the 701 patients, 668 had a 90-day complete follow-up. During the 90-day follow-up, 105 patients (15.7%) died and 35 (5.2%) underwent VAD implantation (n=20, 3%) or UHT (n=15, 2.2%). Fifteen additional patients (2.2%) underwent elective HT. Cumulatively, the occurrence of death, VAD implantation, and urgent or elective HT as a first event within 90 days of admission was 23.2%. Figure 1 shows the incidence of death or UHT/VAD implantation within 90 days of admission as a function of the risk score at 2-point intervals. Mortality rate rose linearly with increasing risk score, with a steep increase for score >14. Such a pattern was not observed for UHT/VAD implantation. Among the 93 patients with risk score >14, 44 (47.3%) died within 90 days of admission. Among the 139 patients with risk score <7, mortality rate was as low as 1.4%.

Table 3 lists measures of discrimination, calibration, and global model fit for the ADHF/NT-proBNP risk score and the EHFS risk score. The ADHF/NT-proBNP risk score had a C-statistic for 90-day mortality of 0.810 (95% CI: 0.769–0.852). After excluding the patients with missing data for SBP (n=27, 3.8%), the C-statistic was 0.815 (95% CI: 0.774–0.856). Hosmer-Lemeshow chi-square was 1.05 (P=0.984), indicating excellent calibration. Calibration plot of predicted vs. observed 90-day mortality across risk subgroups is shown in Figure 2. Figure 3 shows transplant-free and VAD-free Kaplan-Meier survival curves of the risk subgroups. The rate of VAD implantation or UHT across categories of increasing risk were 3.9%, 4.9%, 5%, and 7%. The EHFS risk score had a C-statistic of 0.714 (95% CI: 0.673–0.765). The Hosmer-Lemeshow statistic was 8.89 (P=0.064). Adding NT-proBNP dichotomized at 5,180 pg/ml to the EHFS risk score led to an increase in C-statistic of 0.042 (Table 3).

The C-statistic of the ADHF/NT-proBNP risk score for predicting the occurrence of the combined outcome of death, VAD implantation, or UHT as a first event within 90 days of admission was 0.741 (95% CI: 0.696–0.786). The Hosmer-Lemeshow statistic was 3.73 (P=0.713).

In-Hospital Mortality

During hospitalization, 53 patients (7.6%) died. Cumulatively, the in-hospital occurrence of death, VAD implantation, and UHT as a first event was 10.1%.

Measures of discrimination, calibration, and model fit of the predictive models are reported in Table 3. The ADHF/NT-proBNP risk score had a C-statistic for in-hospital mortality of 0.815 (95% CI: 0.761–0.868). After excluding the patients with missing data for SBP (n=27, 3.8%), the C-statistic was 0.824 (95% CI: 0.7734–0.876). The Hosmer-Lemeshow chi-square was 3.71 (P=0.716), indicating good calibration. The C-statistic of the ADHERE logistic model was 0.758 and that of the OPTIMIZE-HF, GWTG-HF, and Rohde et al risk scores was 0.771, 0.776, and 0.749, respectively. The Hosmer-Lemeshow chi-square was 9.96 (P=0.126), 5.66 (P=0.462), 7.58 (P=0.271), and 6.92 (P=0.140), respectively. Adding NT-proBNP dichotomized at 5,180 pg/ml to the predictive models led to an increase in C-statistic in the range 0.022–0.038 (Table 3). Figure 2 shows calibration plots of predicted vs. observed in-hospital mortality across risk subgroups for

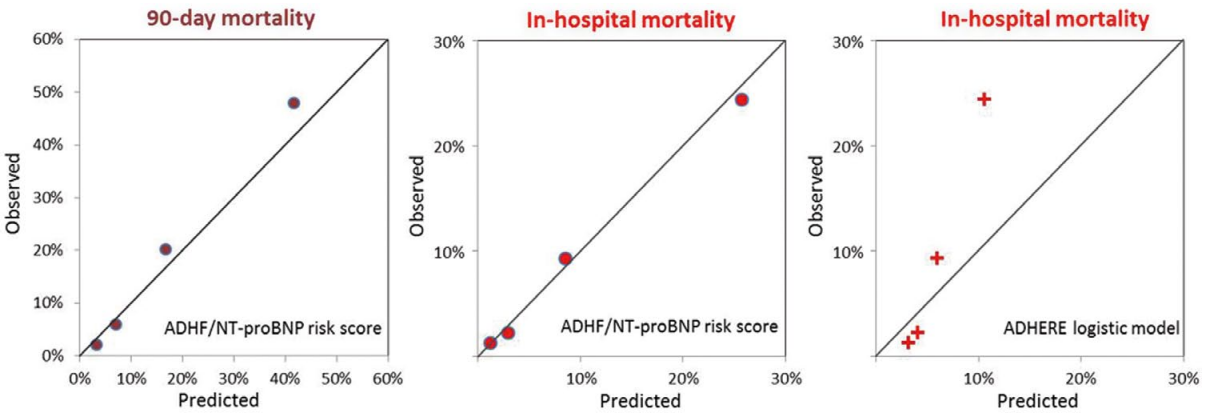

Figure 2. Calibration plots for the acute decompensated heart failure/N-terminal pro-B-type natriuretic peptide (ADHF/NT-proBNP) risk score and the Acute Decompensated Heart Failure National Registry (ADHERE) logistic model.

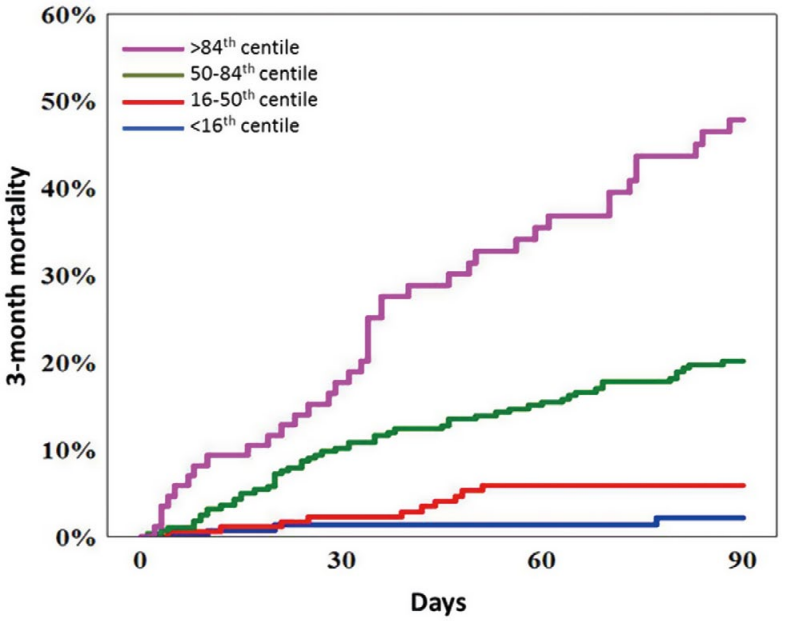

Figure 3. Kaplan-Meier mortality curves stratified by centiles of acute decompensated heart failure/N-terminal pro-B-type natriuretic peptide risk score.

the updated ADHF/NT-proBNP risk score and the ADHERE logistic model.

The equations to estimate risk for in-hospital and 90-day mortality with the ADHF/NT-proBNP risk score are reported in Table S2.

Discussion

Risk prediction in the setting of ADHF remains important but difficult.[10] There are 2 major findings of this study. First, the ADHF/NT-proBNP risk score reliably predicts short-term mortality in advanced ADHF. Compared with the other predictive models, the ADHF/NT-proBNP risk score demonstrated better overall performance, as judged using metrics of risk prediction. Discrimination for both in-hospital and 90-day mortality was excellent by current convention,[28] with a C-statistic >0.80. This threshold of discrimination has been suggested as adequate for predicting individual outcome and guiding medical decision making.[28,29] The ADHF/NT-proBNP risk score also was well calibrated, that is, predicted and observed mortalities were in close agreement. The patients in the highest risk category had an approximately 20-fold greater risk of dying in hospital or within 90 days of admission than those in the lowest risk category. Finally, the ADHF/NT-proBNP risk score demonstrated better overall model fit, as indicated by lower AIC and BIC. There is, however, no way of deciding if the difference is "large enough to translate into a clinically more useful model".[27] Discrimination, however, substantially decreased when the composite of death, VAD implantation or UHT was used as outcome measures. Although

90-day mortality rose steeply across categories of increasing risk, VAD implantation and UHT events were uniformly distributed. Several reasons may be hypothesized to explain this finding. In parallel with the severity of HF, age and comorbid burden significantly increased across categories of increasing risk (Table S1), thus restricting the potential use of advanced treatments in the highest risk category. Unmeasured covariates, such as the pattern of clinical course, the degree of right ventricular dysfunction, reversibility of pulmonary hypertension, or sociocultural status[30] may have influenced clinical decision. In addition, it should be considered that the availability of a donor in an urgency condition is unpredictable. In contrast, the possibility that the clinical conditions of a patient may rapidly and severely deteriorate despite an apparently low risk profile at presentation cannot be excluded.

Second, the ADHERE logistic model (C-statistic 0.758)[14] and the GWTG-HF (C-statistic 0.776),[15] OPTIMIZE-HF (C-statistic 0.771),[12] and Rohde et al (C-statistic 0.749)[16] risk scores, although applied to a patient population with strikingly different baseline characteristics and level of risk (Table S3), accurately distinguished the patients who died in hospital from those who survived to discharge, with an accuracy very close to that obtained in the original studies. This is a notable finding, because the discriminative value of a predictive model usually tends to decline in truly external populations. Remarkably, adding NT-proBNP to these robust predictive models improved their discriminative ability, with an increase in C-statistic in the range 0.022–0.038. The predictive models also had adequate calibration, as judged by the Hosmer-Lemeshow statistics. Nonetheless, it should be considered that the ADHERE logistic model, the only model for which predicted mortality could be estimated, substantially underestimated absolute risk for in-hospital mortality in the highest risk category. Discrimination of the EHFS risk score for 90-day mortality was not reported in the original study.[1] In the present study, its ability to predict 90-day mortality was modest (C-statistic 0.714). Again, adding NT-proBNP to the model led to substantially improved discrimination (C-statistic 0.756). These findings emphasize the strong prognostic value of NT-proBNP.

The updated ADHF/NT-proBNP risk score and the existing predictive models share some potent risk markers including age, COPD, LV systolic dysfunction, SBP, renal function, and sodium concentration. The ADHF/NT-proBNP risk score also incorporates recent hospitalization for HF and NT-proBNP concentration, 2 of the most powerful predictors of outcome, and TR. Repeated hospitalization for HF may reflect the progressive loss of effectiveness of recommended therapies, NT-proBNP concentration is related to the stretching of failing myocardium and the degree of neurohormonal activation,[31] while moderate-severe TR has been associated with poor survival, independent of age, biventricular systolic function, and right ventricular size.[32] Renal impairment is a universally recognized powerful risk marker, common to all models tested. We recently showed that NT-proBNP is highly discriminative in patients with either poor renal function at admission or worsening renal function during hospitalization.[33] Thus, the combined use of NT-proBNP and a measure of renal dysfunction may result in improved risk prediction. These features may provide a basis to explain the overall better performance of the updated ADHF/NT-proBNP risk score compared with the existing predictive models.

Study Limitations

Limitations of existing predictive models for in-hospital mortality have been discussed by Peterson et al.[15] Some limitations of the present study should be acknowledged. As with most prognostic studies in HF,[21] the present study was retrospective in nature. Other unmeasured or non-documented factors may have influenced actual mortality risk. Women represented only 16.3% of the study population. Substantial gender-related differences exist in patients with HF.[34] The model can be applied only to worsening HF patients with severe symptoms and severely depressed LV systolic dysfunction at presentation, thus limiting the generalizability of the model. In-hospital results were based on a relatively low number of events; nonetheless, an impressive 19-fold greater in-hospital mortality rate was observed in the highest compared with the lowest risk category. We focused on mortality; from the patient perspective, quality of life also ranks high in importance. Finally, further validation of the updated ADHF/NT-proBNP risk score in separate populations is warranted.

Conclusions

The care of patients with acute HF involves accurate risk assessment. The updated ADHF/NT-proBNP risk score is a valuable tool for predicting short-term mortality in severe ADHF, thus extending our previous results at 1 year. Predicting outcome(s) in individuals remains, however, challenging.

Disclosures

Conflict of Interest: None declared.

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Supplementary Files

Supplementary File 1

Table S1. Baseline characteristics across risk strata

Table S2. Risk estimation equations

Table S3. Selected baseline characteristics

Please find supplementary file(s);
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