Inpatient Mortality Risk Scores and Postdischarge Events in Hospitalized Heart Failure Patients

A Community-Based Study

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BACKGROUND: The Acute Decompensated Heart Failure National Registry (ADHERE) and Get With The Guidelines (GWTG) registries have developed simple heart failure (HF) in-hospital mortality risk scores. We hypothesized that HF scores predictive of in-hospital mortality would perform as well for early postdischarge mortality risk stratification.

METHODS AND RESULTS: In this single-center, community-based, retrospective study of all consecutive primary HF hospitalizations (6203 hospitalizations in 3745 patients) from 2000 to 2013, the ADHERE and GWTG risk scores were calculated from admission data. There were 176 (3.0%) and 399 (6.7%), 869 (14.7%), and 1272 (21.5%) deaths in-hospital and at 30, 90, and 180 days postdischarge, respectively. The GWTG but not ADHERE risk score was well calibrated for in-hospital mortality. Both the ADHERE (C statistic 0.66 and 0.67, 0.64, and 0.64) and GWTG (C statistic 0.74 and 0.73, 0.71, and 0.70) HF risk scores were similarly predictive of in-hospital and 30-, 90-, and 180-day postdischarge mortality. The ADHERE risk score identified 10% and the GWTG risk score identified 20% of hospitalizations where 180-day postdischarge mortality was 50%, a prognostic bench mark for hospice referral. In contrast, hospitalizations characterized as lowest risk by the ADHERE (57% of hospitalizations; 180-day mortality 16.2%) or GWTG score (20% of hospitalizations; 180-day mortality 8.0%) had substantially lower mortality (odds ratios high versus low risk of 5–8 [ADHERE] and 11–18 [GWTG] across time points; $P<0.0001$ for all).

CONCLUSIONS: The simple ADHERE and GWTG scores stratify hospitalized HF patients for both inpatient and early postdischarge mortality risk, allowing comprehensive risk assessment on admission.

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WHAT IS NEW?

- Several scores have previously been developed for risk prediction but most focus on in-hospital mortality and are complex and, therefore, underutilized.
- Both the Acute Decompensated Heart Failure National Registry and Get With The Guidelines scores are relatively simple to calculate using variables available at the time of admission and can be extended, as we show in this study, to mortality and readmissions ≤180 days after discharge.

WHAT ARE THE CLINICAL IMPLICATIONS?

- Heart failure hospitalizations account for a significant proportion of the rising financial pressure on healthcare systems.
- Using risk scores to identify the group of patients at highest risk of mortality and postdischarge events early during the hospitalization facilitates targeting of limited resources and allows time for care coordination and discharge planning, and may guide discussions about long-term prognosis.

Patients hospitalized for heart failure (HF) are at risk for prolonged hospitalizations, in-hospital mortality, and early postdischarge death and readmission.[1] Given the high cost of inpatient HF care and expanding at-risk population,[2] there is an urgent need for strategies to shorten length of stay, prevent readmissions, and provide the care appropriate for each patients' stage in the HF natural history. Critical therapeutic decisions must frequently be made in the hospital where providers and patients have limited understanding of prognosis.[3,4] Palliative care consultation can improve quality of life and assist patients in defining their goals of care. Care transition programs or appropriate hospice referral may reduce readmissions but require predischarge coordination of care and are resource intensive.[3,5] Thus, such programs are ideally considered soon after admission and focused on patients at highest risk. However, existing risk assessment tools for inpatients with HF primarily assess in-hospital mortality, are often complex, and are uniformly underutilized.[4,6]

The Acute Decompensated Heart Failure National Registry (ADHERE) Classification and Regression Tree (CART) algorithm used 3 admission variables (blood urea nitrogen, systolic blood pressure, and creatinine) to stratify patients into 5 groups at incremental risk of in-hospital mortality (Figure 1).[7] The Get With The Guidelines (GWTG) HF risk score used 7 admission variables (blood urea nitrogen, systolic blood pressure, age, heart rate, sodium, race, and presence of chronic obstructive pulmonary disease) to predict risk of in-hospital mortality (Figure 2).[8] Both scores were developed from voluntary national registries wherein diverse institutions self-reported data on an uncertain percent of HF admissions. As data were available only in aggregate,[9] multiple events experienced by the same patient could not be linked, and only in-hospital mortality was assessed. We hypothesized that HF patients at heightened risk of in-hospital mortality would also be at increased risk of early (up to 6 months) postdischarge mortality and, thus, that scores predictive of in-hospital mortality would perform as well for early postdischarge mortality. Accordingly, our objective was to evaluate the performance of these 2 parsimonious risk scores in a community-based sample of all consecutive HF admissions, using longitudinal data on mortality and readmissions to estimate risk of mortality during and after each admission.

METHODS

Study Population

This study was approved by the Mayo Clinic Institutional Review Board and restricted to appropriately consented patients residing within 40 miles of Rochester, Minnesota. Using the Data Discovery and Query Builder (IBM, Armonk New York; Methods in the Data Supplement) to search patient's electronic medical records, we identified all HF consecutive hospitalizations occurring between January 1, 2000, and December 31, 2013, at Mayo-affiliated hospitals in Rochester, Minnesota. The Data Discovery and Query Builder includes all clinical patients in the electronic health record at Mayo Clinic Rochester. During the registration process at Mayo, patients sign a general consent to allow use of their deidentified medical record data for research and have several opportunities to opt out during registration or by mail afterward. However, an extremely small number of patients opt out, and in our study, only 0.16% of eligible patients opted out. A HF hospitalization was defined as the primary (first listed) reason for hospitalization using appropriate *International Classification of Disease* codes (Table I in the Data Supplement). Comorbidities, medications, echocardiographic, and laboratory results from each admission were extracted using Data Discovery and Query Builder and relevant laboratory, pharmacy, and echocardiographic databases. The Data Discovery and Query Builder *International Classification of Disease* code search strategy has been demonstrated to have excellent specificity for detection of medical conditions.[10] Left ventricular ejection fraction (EF) was determined from the echocardiogram closest to the admission date. The Charlson Comorbidity Index[11] was assessed with higher values indicative of greater comorbidity burden.[12]

Risk Stratification

Risk stratification was performed for each hospitalization using admission data according to the ADHERE CART algorithm[7] (Figure 1) and the GWTG HF risk score[8] (Figure 2). In-hospital and postdischarge mortality was assessed across the 5 ADHERE risk groups and across the quintiles of the GWTG score observed in our cohort. While the risk scores

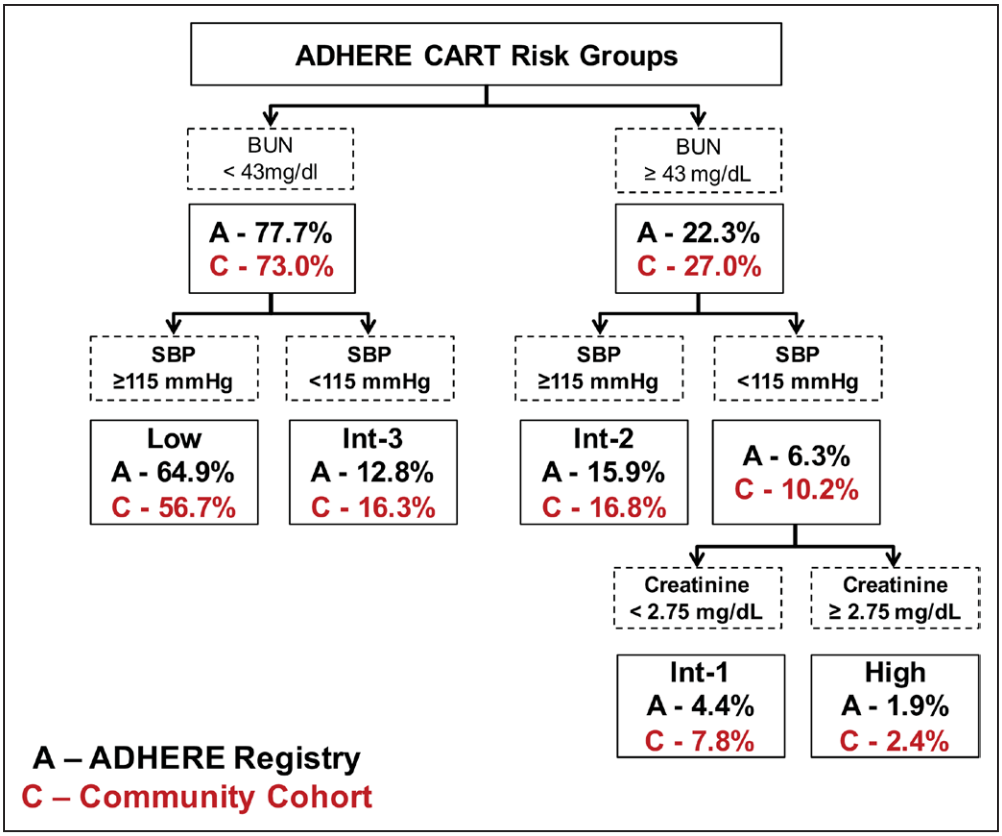

Figure 1. Distribution of community heart failure patients across Acute Decompensated Heart Failure National Registry (ADHERE) Classification and Regression Tree (CART) risk groups.
According to the ADHERE CART risk algorithm, community patients were divided into five 5 groups (low, intermediate 3, intermediate 2, intermediate 1, and high) at each hospitalization using their admission blood urea nitrogen (BUN), systolic blood pressure (SBP), and serum creatinine. The distribution of ADHERE registry and community patients across the ADHERE CART risk groups is shown.

were not designed to predict readmissions, as mortality and readmission risk are at least loosely associated, the association of risk scores and readmission rates was also described.

In the ADHERE registry cohort (enrolled 2001 to 2003), optimal predictor variables and partition values for inpatient mortality were derived through recursive partitioning analysis, a statistical technique suited to generating clinical decision rules.[13] In the GWTG registry cohort (enrolled 2005 to 2007), the GWTG-HF score was derived using multivariable logistic regression analysis. A 100-point risk score was established using the 7 predictor variables identified in the multivariable model.

Comparison to ADHERE and GWTG Derivation Cohorts

The distribution of admissions and in-hospital mortality in our cohort across ADHERE and GWTG risk groups were compared with those observed in the respective derivation cohorts. Calibration was assessed by comparing the predicted (from derivation cohort) versus observed (in our cohort) in-hospital mortality for each score group. Predicted in-hospital mortality for the ADHERE analysis was considered as that reported for the ADHERE derivation cohort. However, the GWTG derivation study reported in-hospital mortality by score deciles.[8] We used the same score cut points (F.A. Masoudi, MD, unpublished data, 2010) from that study to compare our observed in-hospital mortality with the original cohort for calibration. The remainder of the GWTG analysis was done with the quintiles of risk scores observed in our cohort.

Outcomes

Vital status was obtained from registration and billing data, inpatient records, and death certificates. Readmissions (all cause and for HF) to Mayo-affiliated hospitals were assessed. A period was classified as event-free only if sufficient follow-up time was available. For 30-day through 180-day postdischarge mortality analysis, a patient was censored if they died prior to discharge or were rehospitalized before the follow-up period because they then became a new (hospitalization) case. For readmission analysis, patients were also censored if they had died during the relevant interval or were lost to follow-up. The date of last known follow-up was derived from multiple sources, including inpatient and outpatient visits and patient correspondence. Follow-up was through December 31, 2013.

Statistical Analysis

Baseline characteristics of patients at their first HF hospitalization were compared across the 5 ADHERE CART risk groups

BUN	Points	SBP	Points	Age	Points	Sodium	Points	HR	Points	Black Race	Points	COPD	Points
≤ 9	0	50-59	28	≤ 19	0	≤ 130	4	≤ 79	0	Yes	0	Yes	2
10-19	2	60-69	26	20-29	3	131	3	80-84	1	No	3	No	0
20-29	4	70-79	24	30-39	6	132	3	85-89	3				
30-39	6	80-89	23	40-49	8	133	3	90-94	4				
40-49	8	90-99	21	50-59	11	134	2	95-99	5				
50-59	9	100-109	19	60-69	14	135	2	100-104	6				
60-69	11	110-119	17	70-79	17	136	2	≥ 105	8				
70-79	13	120-129	15	80-89	19	137	1						
80-89	15	130-139	13	90-99	22	138	1						
90-99	17	140-149	11	100-109	25	≥ 139	0						
100-109	19	150-159	9	≥ 110	28								
110-119	21	160-169	8										
120-129	23	170-179	6										
130-139	25	180-189	4										
140-149	27	190-199	2										
≥ 150	28	≥ 200	0										

Score	GWTG % Patients	Community % Patients
0-28	10%	2.9 %
29-32	10%	6.1 %
33-35	10%	8.2 %
36-37	10%	6.8 %
38-40	10%	12.1 %
41-42	10%	10.5 %
43-44	10%	10.5 %
45-47	10%	14.3 %
48-51	10%	13.7 %
52-87	10%	15.0 %

Figure 2. Distribution of community heart failure patients across GWTG heart failure risk score groups.
The Get With The Guidelines (GWTG) score ranges from 0 to 100 and is calculated from the admission blood urea nitrogen (BUN), systolic blood pressure (SBP), age, sodium, heart rate (HR), race, and presence of chronic obstructive pulmonary disease (COPD) as shown. The GWTG derivation study stratified patients according to deciles of score ranges. The distribution of community patients across the GWTG registry score deciles is shown.

or across GWTG score quintiles using linear (for continuous variables) or logistic (for dichotomous variables) regression. The odds of an outcome for each HF hospitalization were compared per risk group and versus the lowest risk group using univariate logistic regression. We performed analyses clustered by patient[14] and obtained robust standard errors to mitigate the effect of correlation between recurrent hospitalizations in the same person. Models were run with interaction terms for the 5 ADHERE CART risk groups or the GWTG quintiles and HF type to assess differences in risk stratification according to HF type (preserved [≥50%] or reduced [<50%] EF). We defined the predictive characteristics of the 5 ADHERE CART risk groups or the GWTG risk score for study outcomes using logistic regression and receiver operating characteristics curve analysis. Calibration for each score for the prediction of in-hospital mortality was assessed by visual comparison of expected and observed mortality. All analyses were performed using Stata 13.1 (StataCorp, College Station, TX).

RESULTS

There were 6203 primary HF hospitalizations in 3745 individual patients. Data needed for ADHERE CART (5918 [95.4%] hospitalizations in 3628 patients) and GWTG (5794 [93.4%] hospitalizations in 3628 patients) risk score calculation were available in most hospitalizations.

Characteristics of Patients at Their First HF Hospitalization

Non-white patients made up 6% of our population, with 1.4% black. In patients with ADHERE data, overall, the mean age was 78 years, and 50% of patients were male (Table II in the Data Supplement). At least 1 echocardiogram was available in 3593 (99%) patients, with 48% classified as HF with preserved EF. Comorbidities included hypertension (95%), diabetes mellitus (50%), history of atrial fibrillation or flutter (69%), history of coronary artery bypass surgery (28%), and lung disease (24%). The mean Charlson Comorbidity Index was 9.2. On admission, use of standard HF medications was high, and 86% were on a loop diuretic. On average, patients were anemic, were overweight, and had stage 3 chronic kidney disease. When available, biomarker and echocardiographic variables indicated elevated left ventricular filling pressures and pulmonary hypertension. Overall characteristics of patients with

data for the GWTG score were similar (Table III in the Data Supplement).

By design, patients in the lower risk ADHERE CART groups had higher blood pressure and better renal function (Table 1). Stratifying risk by the ADHERE CART score variables (blood pressure, blood urea nitrogen, and creatinine) resulted in lower risk patients who were more likely to be female and have HF with preserved EF, less likely to have diabetes mellitus or atrial fibrillation, had lower Charlson Comorbidity Index, were more likely to be treated with angiotensin-converting enzyme inhibitors, had higher hemoglobin, had lower NT-proBNP (N-terminal pro-B-type natriuretic peptide), and had less severe diastolic dysfunction and pulmonary hypertension (Table 1).

Table 1. Characteristics of Patients at First Heart Failure Hospitalization According to ADHERE CART Risk Group

Characteristic	High 53 (1.5%)	Int-1 193 (5.3%)	Int-2 480 (13.2%)	Int-3 608 (16.8%)	Low 2294 (63.2%)	*P* Value
Demographic/clinical						
Age, y	74.7±16.0	80.1±12.1	78.4±12.5	75.0±14.3	78.3±12.2	0.59
Male, n (%)	35 (66)	118 (61)	260 (54)	343 (56)	1084 (47)	<0.001
Systolic BP, mm Hg*	98±11	99±11	145±24	103±9	145±22	<0.001
Diastolic BP, mm Hg	57±10	58±12	70±17	60±11	75±18	<0.001
Heart rate, beats per minute	77±21	76±18	75±18	80±18	80±19	<0.001
Body mass index, kg/m^2	32.3±7.6	30.8±9.0	31.6±8.2	31.2±10.8	31.7±11.3	0.49
HFpEF (3593 classifiable)	22 (42)	75 (40)	227 (48)	227 (38)	1187 (52)	<0.001
Medical history						
Hypertension	48 (91)	179 (93)	469 (98)	538 (89)	2210 (96)	0.009
Diabetes mellitus	31 (59)	95 (49)	292 (61)	269 (44)	1118 (49)	0.003
Atrial fibrillation or flutter	39 (74)	147 (76)	322 (67)	440 (72)	1547 (67)	0.034
Dementia	5 (9.4)	19 (9.8)	46 (9.6)	75 (12)	253 (11)	0.43
CABG	14 (26)	64 (33)	155 (32)	164 (27)	615 (27)	0.017
COPD	5 (9.4)	36 (19)	108 (23)	153 (25)	555 (24)	0.018
Charlson Comorbidity Index	9.7±3.7	10.1±3.5	10.8±3.1	8.5±3.4	9.0±3.5	<0.001
Medications						
β-Blocker	36 (68)	132 (68)	366 (76)	425 (70)	1670 (73)	0.64
ACE inhibitor	23 (43)	99 (51)	217 (45)	350 (58)	1342 (59)	<0.001
ARB	10 (19)	35 (18)	86 (18)	93 (15)	440 (19)	0.35
Aldosterone antagonist	3 (5.7)	39 (20)	38 (7.9)	122 (20)	223 (9.7)	0.009
Loop diuretic	42 (79)	180 (93)	411 (86)	524 (86)	1961 (86)	0.20
Statin	24 (45)	91 (47)	281 (59)	316 (52)	1208 (53)	0.96
NT-proBNP, pg/mL, n=1109	16 338 (11 399–35 000)	11 611 (5273–17 535)	10 930 (3989–23 206)	3869 (1940–8433)	3938 (2134–8410)	<0.001
Sodium, mEq/L, n=3628	136±5	137±5	138±5	137±5	138±5	0.30
Hemoglobin, g/dL, n=3603	10.4±1.7	11.2±2.0	10.9±1.8	12.1±1.9	12.1±1.9	<0.001
Blood urea nitrogen, mg/dL*	79±24	61±15	61±17	25±9	23±8	<0.001
Creatinine, mg/dL*	3.7±1.2	2.0±0.4	2.8±1.8	1.3±0.5	1.2±0.6	<0.001
GFR, mL/min/1.73 m^2	16.8±4.3	33.4±9.7	26.9±12.1	60.1±23.5	61.2±23.1	<0.001
Ejection fraction, %, n=3593	42±19	40±20	46±17	41±19	47±18	<0.001
E/*e*′ medial, n=2543	26.6±13.8	24.4±19.0	22.8±10.1	20.8±11.2	21.1±10.2	<0.001
Deceleration time, ms, n=2587	164±46	165±49	182±52	173±52	184±57	<0.001
PASP, mm Hg, n=3173	54.7±14.5	55.6±16.5	54.0±15.5	49.6±15.5	50.0±15.3	<0.001

Overall data in Table II in the Data Supplement. ACE indicates angiotensin-converting enzyme; ADHERE, Acute Decompensated Heart Failure National Registry; ARB, angiotensin receptor blocker; BP, blood pressure; CABG, coronary artery bypass graft; CART, Classification and Regression Tree; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; HFpEF, heart failure with preserved ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; and PASP, pulmonary artery systolic pressure.

*Variables included in the ADHERE-CART score. Variables are mean±SD, n (%), or median (interquartile range).

By design, patients in the lower risk GWTG quintiles were younger, were less likely to have chronic obstructive pulmonary disease or renal dysfunction, and had higher blood pressure and sodium and lower heart rate (Table 2). Trends in clinical, laboratory, and echocardiographic variables across the GWTG score quintiles were similar to those noted across the ADHERE CART risk groups.

Distribution of All HF Hospitalizations Across the ADHERE CART or GWTG Risk Groups

As compared with the ADHERE registry cohort,[7] the distribution of hospitalizations across the risk groups suggested that the community cohort was at somewhat higher

Table 2. Characteristics of Patients at Their First Heart Failure Hospitalization According to GWTG Score Quintile

Characteristic	GWTG Q5 Score 51–77 (n=477; 13.5%)	GWTG Q4 Score 46–50 (n=641; 18.1%)	GWTG Q3 Score 42–45 (n=738; 20.8%)	GWTG Q2 Score 37–41 (n=827; 23.3%)	GWTG Q1 Score 14–36 (n=864; 24.4%)	*P* Value
Demographic/clinical						
Age, y*	83.7±9.7	82.0±9.3	80.2±10.4	77.0±12.5	70.3±14.7	<0.001
Male	259 (54)	320 (50)	380 (52)	390 (47)	451 (52)	0.41
Systolic BP, mm Hg*	107±18.4	120±17.4	129±18.9	140±20.2	162±25.3	<0.001
Diastolic BP, mm Hg	61.2±13.8	65.9±15.2	68.1±16.1	71.4±15.6	80.1±19.9	<0.001
Heart rate, beats per minute*	86±22	83±20	78±18	77±17	76±17	<0.001
Body mass index, kg/m^2	29.8±8.2	30.2±10.3	30.2±8.2	32.4±12.7	34.0±11.5	<0.001
HFpEF (3512 classifiable patients)	195 (42)	277 (43)	351 (48)	414 (51)	460 (54)	<0.001
Medical history						
Hypertension	449 (94)	605 (94)	694 (94)	787 (95)	833 (96)	0.031
Diabetes mellitus	212 (44)	284 (44)	335 (45)	430 (52)	497 (58)	<0.001
Atrial fibrillation or flutter	368 (77)	479 (75)	531 (72)	556 (67)	504 (58)	<0.001
Dementia	59 (12)	85 (13)	86 (12)	89 (11)	70 (8.1)	0.002
CABG	129 (27)	176 (28)	226 (31)	227 (28)	232 (27)	0.76
COPD*	124 (26)	179 (28)	198 (27)	203 (25)	135 (16)	<0.001
Charlson Comorbidity Index	10.2±3.3	9.8±3.0	9.7±3.5	9.1±3.5	8.1±3.8	<0.001
Medications						
β-Blocker	343 (72)	435 (68)	526 (71)	603 (73)	673 (78)	<0.001
ACE inhibitor	226 (47)	333 (52)	404 (55)	467 (57)	556 (64)	<0.001
ARB	75 (16)	111 (17)	142 (19)	146 (18)	176 (20)	0.052
Aldosterone antagonist	65 (14)	86 (13)	79 (11)	87 (11)	96 (11)	0.061
Loop diuretic	420 (88)	558 (87)	659 (89)	701 (85)	712 (82)	<0.001
Statin	227 (48)	314 (49)	381 (52)	462 (56)	498 (58)	<0.001
NT-proBNP, pg/mL, n=1095	8970 (4019–14438)	5303 (2725–11984)	5166 (2228–10861)	4213 (2322–8970)	3466 (1597–7616)	<0.001
Sodium, mEq/L, n=3547*	136±5.4	137±5.0	137±5.0	138±5.2	139±4.3	<0.001
Hemoglobin, g/dL, n=3523	11.2±1.9	11.7±1.9	11.8±2.0	12.0±1.9	12.2±2.0	<0.001
Blood urea nitrogen, mg/dL*	53±27	35±17	30±15	26±13	22±11	<0.001
Creatinine, mg/dL	2.0±1.2	1.5±0.8	1.4±0.9	1.5±1.2	1.4±1.1	<0.001
GFR, ml/min/1.73 m^2	38.3±19.7	50.3±23.6	54.7±22.2	57.7±25.5	63.1±26.5	<0.001
Ejection fraction, %, n=3512	43±19	43±18	45±18	47±17	48±18	<0.001
E/*e*′ medial, n=2485	22.9±14.5	21.4±11.0	21.4±10.5	21.5±10.6	21.1±9.7	0.061
Deceleration time, ms, n=2527	174±55	174±49	178±55	183±55	188±60	<0.001
PASP, mm Hg, n=3173	51.6±14.6	51.5±15.0	50.9±15.7	51.4±16.1	49.3±15.4	0.018

Overall data in Table III in the Data Supplement. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CABG, coronary artery bypass graft; CART, Classification and Regression Tree; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; GWTG, Get With The Guidelines; HFpEF, heart failure with preserved ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; and PASP, pulmonary artery systolic pressure.

*Variables included in the GWTG score. Variables are mean±SD, n (%), or median (interquartile range).

risk of inpatient mortality (Figure 1). Similarly, in the community cohort, more patients were in the higher risk categories than in the GWTG registry cohort[8] (Figure 2).

In-Hospital Mortality

In hospitalizations with ADHERE data, there were 176 (3.0%) in-hospital deaths. In-hospital mortality increased across ADHERE CART risk groups (Figure 3A and Table 3). While in-hospital mortality was similar to that observed in the ADHERE registry in the lower 2 risk groups, mortality was lower in the community setting for the 3 higher risk groups (Figure 3A). The odds ratio (OR) for in-hospital mortality per 1 U increase in the ADHERE CART risk group was 1.57 (P<0.001); the ORs for the 2 highest risk groups (high and intermediate-1) relative to the low-risk group were 4.8 and 5.5 (P<0.001 for both), and the C statistic for prediction of in-hospital mortality was 0.66 (Table 4).

In hospitalizations with GWTG risk score data, there were 170 (2.9%) in-hospital deaths. In-hospital mortality increased across 10 GWTG risk groups (deciles in the GWTG cohort), and the GWTG score was well-calibrated in our cohort (Figure 3B). The incremental risk of in-hospital mortality increased across quintiles of GWTG scores within the community sample (Table 3 and Figure 4B), with increases in the OR for in-hospital mortality per GWTG quintile of 1.98 (P<0.001), OR in the highest versus the lowest quintile of 12.4 (P<0.001), and a C statistic of 0.74 (Table 4).

Postdischarge Mortality

In hospitalizations with ADHERE data, there were 399 (6.7%), 869 (14.7%), and 1272 (21.5%) deaths within 30, 90, and 180 days of discharge respectively. The 30- to 180-day mortality increased with higher ADHERE CART risk group (Figure 4A and Table 3), with ≈50% mortality at 180 days in the 2 highest risk groups. Results were nearly identical with a per-patient analysis after the first hospitalization for each patient (data not shown). While age was not part of the ADHERE risk score, in multivariate analysis, age increased the C statistic for prediction of in-hospital and postdischarge mortality (Table IV in the Data Supplement), and the 180-day mortality far exceeded 50% in older patients (age >80 years) in the highest 2 ADHERE CART risk groups (Figure I in the Data Supplement). In contrast, neither serum sodium nor comorbidities (Charlson Comorbidity Index) meaningfully increased the predic-

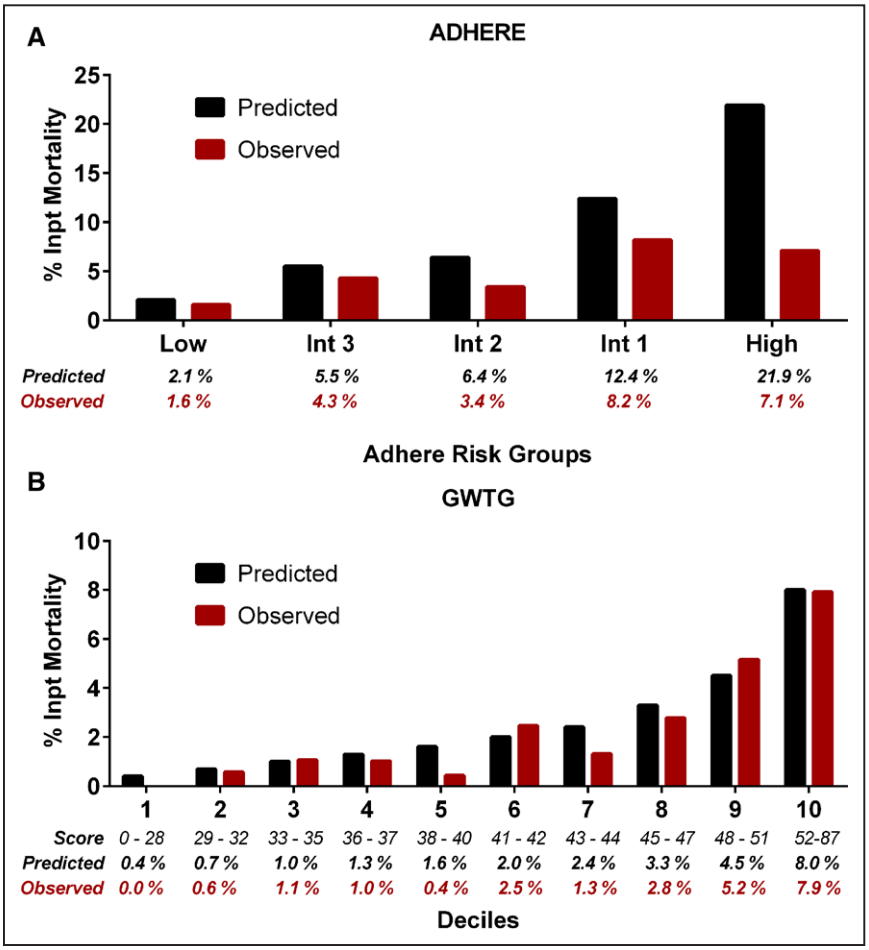

Figure 3. In-hospital mortality in community and derivation cohort patients by Acute Decompensated Heart Failure National Registry (ADHERE) Classification and Regression Tree (CART) and Get With The Guidelines (GWTG) risk groups.
Observed in-hospital mortality rates in the community population are shown compared with the respective predicted in-hospital mortality as reported for the ADHERE (**A**) or GWTG (**B**) scores.

Table 3. In-Hospital and Postdischarge Mortality According to ADHERE CART Risk Group and GWTG HF Risk Score Quintiles

	Risk Grp 1 (highest)	Risk Grp 2	Risk Grp 3	Risk Grp 4	Risk Grp 5 (lowest)	*P* value
Study Risk Group	ADHERE High	ADHERE Int 1	ADHERE Int 2	ADHERE Int 3	ADHERE Low	
N	141	465	993	962	3357	
In-hospital mortality, n (%)	10 (7.1)	38 (8.2)	34 (3.4)	41 (4.3)	53 (1.6)	<0.001
30-day mortality, n (%)	33 (26)	75 (18)	104 (11)	53 (5.9)	134 (4.1)	<0.001
90-day mortality, n (%)	51 (41)	152 (37)	197 (21)	134 (15)	335 (11)	<0.001
180-day mortality, n (%)	67 (54)	194 (47)	295 (32)	210 (24)	506 (16)	<0.001
Study Risk Group	GWTG > 50	GWTG 46–50	GWTG 42–45	GWTG 37–41	GWTG < 37	
N	1029	1156	1192	1246	1171	
In-hospital mortality, n (%)	81 (7.9)	47 (4.1)	20 (1.7)	14 (1.1)	8 (0.7)	<0.001
30-day mortality, n (%)	168 (18)	91 (8.4)	67 (5.8)	50 (4.1)	14 (1.2)	<0.001
90-day mortality, n (%)	315 (34)	213 (20)	155 (14)	127 (11)	45 (4.1)	<0.001
180-day mortality, n (%)	439 (49)	298 (28)	227 (20)	203 (17)	86 (8.0)	<0.001

The denominator for event frequency is less than the group n due to censoring of patients with readmissions (for mortality outcomes) or insufficient follow-up during the specified interval. ADHERE indicates Acute Decompensated Heart Failure National Registry; CART, Classification and Regression Tree; GWTG, Get With The Guidelines; HF, heart failure; and Int, intermediate.

tive characteristics of the ADHERE CART score (Table IV in the Data Supplement).

For 30- to 180-day mortality, the OR per 1 U increase in the ADHERE CART risk group ranged from 1.61 to 1.72 (P<0.001 for all), the OR for the highest 2 versus the low-risk group ranged from 5.9 to 8.3 (P<0.001 for all), and the C statistics ranged from 0.64 to 0.67 (Table 4).

In hospitalizations with GWTG data, there were 390 (6.7%), 855 (14.8%), and 1253 (21.6%) deaths within 30, 90, and 180 days of discharge, respectively. The rate of postdischarge mortality increased across the GWTG score quintiles observed in our cohort (Figure 4B and Table 3), with ≈50% mortality at 180 days in the highest quintile. For 30- to 180-day mortality, the OR per increase in GWTG score quintile ranged from 1.71 to 1.85 (P<0.001 for all), the OR for the highest versus lowest quintile ranged from 10.8 to 17.6 (P<0.001 for all), and the C statistics ranged from 0.70 to 0.73 (Table 4).

Performance of Risk Scores According to HF Type

The increase in in-hospital mortality per ADHERE CART risk group or GWTG score quintile did not vary by HF

Table 4. ADHERE CART Risk Group and GWTG HF Risk Score: Predictive Characteristics for In-Hospital and Postdischarge Mortality

	c-statistic	OR (95% CI) per Risk Group*	OR (95% CI) versus the Low ADHERE CART Group† or the GWTG < 37 Group‡				
Study Risk Group	ADHERE	ADHERE	ADHERE High	ADHERE Int 1	ADHERE Int 2	ADHERE Int 3	ADHERE Low
N			141	465	993	962	3357
In-hospital mortality	0.66	1.57 (1.41–1.75)	4.76 (2.39–9.46)	5.55 (3.62–8.51)	2.21 (1.43–3.43)	2.78 (1.84–4.19)	referent
30-day mortality	0.67	1.72 (1.58–1.87)	8.26 (5.19–13.16)	5.06 (3.68–6.95)	2.89 (2.19–3.81)	1.45 (1.03–2.04)	referent
90-day mortality	0.64	1.61 (1.51–1.72)	5.86 (3.93–8.75)	4.92 (3.81–6.34)	2.28 (1.85–2.81)	1.51 (1.2–1.89)	referent
180-day mortality	0.64	1.61 (1.51–1.71)	6.07 (4.05–9.1)	4.57 (3.56–5.87)	2.45 (2.04–2.96)	1.63 (1.33–1.99)	referent
Study Risk Group	GWTG	GWTG	GWTG > 50	GWTG 46–50	GWTG 42–45	GWTG 37–41	GWTG < 37
N			1029	1156	1192	1246	1171
In-hospital mortality	0.74	1.98 (1.72–2.28)	12.42 (5.98–25.81)	6.16 (2.90–13.09)	2.48 (1.09–5.66)	1.65 (0.69–3.95)	referent
30-day mortality	0.73	1.85 (1.69–2.03)	17.61 (10.13–30.64)	7.31 (4.13–12.92)	4.91 (2.73–8.83)	3.42 (1.88–6.23)	referent
90-day mortality	0.71	1.74 (1.63–1.85)	12.22 (8.70–17.16)	5.82 (4.13–8.19)	3.68 (2.60–5.21)	2.78 (1.96–3.94)	referent
180-day mortality	0.70	1.71 (1.61–1.81)	10.80 (8.20–14.22)	4.52 (3.45–5.92)	2.92 (2.22–3.84)	2.38 (1.81–3.12)	referent

Sample sizes include multiple heart failure hospitalizations for each patient. ADHERE indicates Acute Decompensated Heart Failure National Registry; CART, Classification and Regression Tree; CI, confidence interval; GWTG, Get With The Guidelines; Int, intermediate; and OR, odds ratio.

*P<0.001 for all mortality endpoints for ADHERE and GWTG risk scores.

†P<0.001 versus referrant for all.

‡P<0.001 versus referent for all except inpatient mortality in the GWTG 37–41 Group.

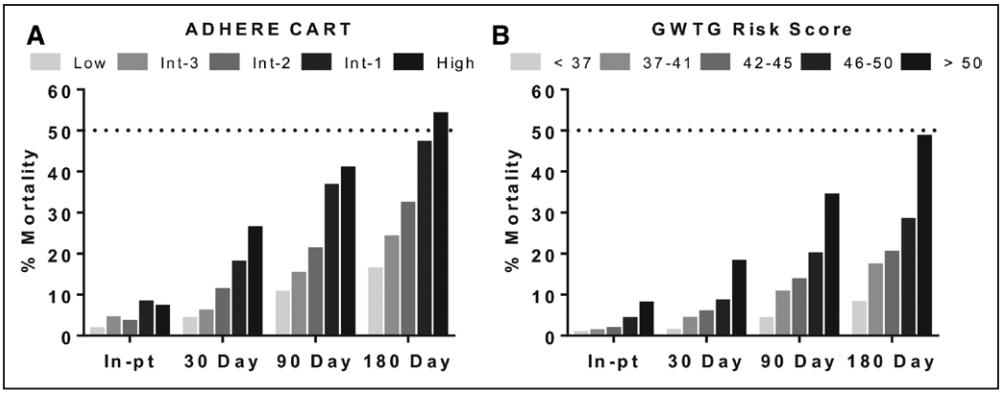

Figure 4. In-hospital and postdischarge mortality in community patients by Acute Decompensated Heart Failure National Registry (ADHERE) Classification and Regression Tree (CART) risk group and Get With The Guidelines (GWTG) score quintile.

In-hospital, 30-, 90-, and 180-day mortality in the community sample according to the ADHERE CART risk groups (**A**) or GWTG score quintiles (**B**) are shown. Patients at risk and numeric data are provided in Table 3.

type (Table V in the Data Supplement), with C statistics of 0.649 (reduced) and 0.656 (preserved) for ADHERE and 0.731 (reduced) and 0.753 (preserved) for GWTG (interaction *P*>0.6 for both). For both scores, increments in 30- to 180-day mortality per risk group and C statistics were or tended to be higher in HF with reduced EF than in HF with preserved EF, although for the GWTG quintiles, interactions between incremental risk per quintile and HF type were of marginal significance (Table V in the Data Supplement).

Association of Readmission Rates With Risk Scores

All-cause and HF-specific readmission rates at 30, 90, and 180 days increased significantly across the ADHERE CART risk score groups and the GWTG score quintiles (Figure II and Table VI in the Data Supplement), but neither risk score had robust predictive characteristics for readmission rates, with C statistics from 0.57 to 0.64 (Table VII in the Data Supplement).

Comparison of the Two Scores

Formal comparison of the 2 scores was not an objective of the current study because both identify high- and low-risk groups of different sizes and differ in the ease of calculation, factors which may influence their use guiding care strategies in clinical practice. However, for all mortality end points (in-hospital, 30, 90, and 180 days), the C statistics was higher for the GWTG than for the ADHERE scores (Table 4), suggesting that the additional variables included in the GWTG score (beyond the shared blood urea nitrogen and systolic blood pressure variables) add predictive value. For in-hospital mortality, based on observed risk in the ADHERE score groups, there was good concordance between risk allocation (68%), with few patients (1%) being reclassified by the GWTG score from high to low or low to high risk. More patients (31%) were reclassified by 1 risk grade (high or low to intermediate or intermediate to high or low; Table VIII in the Data Supplement).

DISCUSSION

Here we examine 2 validated acute HF in-hospital mortality risk scores for risk stratification of postdischarge events in a single-center community setting, as well as confirm their predictive ability for in-hospital mortality. The community cohort was older and more likely white than the registry cohorts in which the risk scores were developed. Based on the distribution of hospitalizations across ADHERE CART or GWTG risk groups, our community cohort was at higher risk for inpatient mortality than either registry cohort. For inpatient mortality, compared with the derivation cohorts, the GWTG risk score but not the ADHERE CART score was well calibrated in our setting. Both scores performed similarly for prediction of early (30–180 days) postdischarge mortality as for prediction of in-hospital mortality. Importantly, the ADHERE CART algorithm identified 10% of hospitalizations and the GWTG risk score identified 20% of hospitalizations in which the 180-day mortality was 50%, a prognostic benchmark relevant to consideration of advanced HF therapies, palliative care consultation, or hospice referral. These simple, universally available, and potentially electronically generated risk scores have only modest (ADHERE) to moderate (GWTG) discrimination. However, they provide a means to simultaneously assess risk of inpatient and postdischarge mortality at the time of admission, identify groups that differ dramatically in their risk of adverse outcomes, and inform timely consideration and allocation of scarce inpatient and postdischarge resources to those at highest risk. The GWTG score, in particular, may provide the critical

balance between predictive characteristics and simplicity needed to engender widespread clinical use.

As recently reviewed,[4] over 60 risk scores have been developed to assess risk of adverse outcomes in HF, including multiple studies restricted to hospitalized HF patients. A minority have been validated and calibrated in study settings or databases other than those in which they were derived. The models identify similar predictive variables, with age, renal function, and blood pressure being the top 3 variables and serum sodium being the fourth variable most commonly found predictive of outcomes. The models examined here use such data and are endorsed by HF guidelines.[1] The GWTG inpatient risk model[8] has been cited as particularly useful given its discriminative value and relative simplicity.[4] Using a multihospital, electronic health record–derived data set, Lagu et al[15] reported the inpatient mortality predictive characteristics for the ADHERE and GWTG scores. However, to our knowledge, these risk scores have not been evaluated for postdischarge risk stratification. As observed here, scores that include more variables generally perform better,[4,6] and clinical use must strike a balance between complexity and clinically meaningful versus statistically significant differences in information. Addition of more variables provides most value in identifying a small segment of patients with particularly high or low risk and may improve discrimination without substantially altering clinical utility.[7,8] In general, models perform better for prediction of mortality than readmission,[4] as also demonstrated here.

Despite the wealth of HF risk models, clinical use is perceived as low[4] as is use of cardiovascular disease risk prediction models.[16,17] An exception may be the use of simple stroke risk scores for atrial fibrillation patients, which are more widely used,[18] despite modest to moderate and highly variable discriminative power demonstrated in different validation studies.[19] Model complexity and skepticism regarding the accuracy of the models in providers' unique practice settings are believed to limit use of risk scores.[4] To address these barriers to implementation, here we assessed simple models in a single-center, community setting. This is relevant as both the ADHERE and GWTG risk scores were generated from voluntary registries, which included a wide range of hospital types and settings, used different means to identify HF hospitalizations, did not restrict entry to patients with a primary diagnosis of HF, and did not mandate inclusion of all HF hospitalizations, which may introduce a sampling bias if not performed randomly. Indeed, our cohort differed from the registry studies because patients were older (77.8 years) than either registry study (72.5 years for both) and included fewer blacks (1.4%) as compared with 20% in ADHERE and 17.6% in the GWTG study. Despite these differences, the discrimination (C statistics) for in-hospital mortality here (0.66 and 0.74) were nearly identical to those observed in the ADHERE CART (0.668) and GWTG HF risk score (0.75) derivation studies. Thus, our findings may engender increased confidence in the utility of these risk scores.

With both scores, higher risk patients had higher NT-proBNP levels and more severe diastolic dysfunction and pulmonary hypertension, although there was significant overlap in the values of these parameters between risk score groups. For both scores, incremental risk for postdischarge but not in-hospital mortality varied by HF type (preserved or reduced EF HF). Notably, the interaction between HF type and the predictive value of the GWTG score for postdischarge mortality was of marginal statistical significance (interaction *P* of 0.01–0.03).

The clinical utility of knowledge concerning risk of adverse outcomes in patients hospitalized with acute HF has been emphasized in HF guidelines, where use of multivariable risk scores is a class IIa recommendation.[1] While knowledge of mortality risk informs decisions regarding referral for advanced HF therapies, other implications deserve mention. The observed to expected in-hospital and 30-day postdischarge mortality are publicly reported HF quality measures. Awareness of a patients risk for death on admission can influence choices concerning the intensity of the care environment, engender adequate documentation of factors indicating expected risk, aid in counseling patients and families regarding the severity of the patient's condition, and influence treatment decisions. Both palliative care services and hospice referral are underutilized in hospitalized HF patients. Fewer than 10% of patients ultimately dying within 6 months of discharge received a hospice referral, in part because of lack of recognition of limited prognosis by both providers and patients.[3,20] Length of stay for HF hospitalizations is an important metric for healthcare systems because it adversely affects access to inpatient care and fiscal performance. Data regarding pre- and postdischarge risk should be available on admission where it can inform decisions and facilitate discharge planning. Many healthcare systems have developed care transition programs for HF patients as such programs may improve outcomes, but such programs are resource-intensive and most cost-efficient when allocated to those at highest risk.[5]

Several features of our study are potential strengths but also potential limitations, including its retrospective design and use of *International Classification of Disease* codes to identify HF hospitalizations. While lack of ethnic diversity and rural community setting may be limitations for studies striving to derive a risk score, the ability to validate published scores in a sample with characteristics differing from the derivation cohort is a strength. We restricted the

sample to patients living within a radius of 40 miles of the hospital. In this region, ≈95% of hospital admissions occur at Mayo Clinic, therefore, improving follow-up and capture of readmission data. We did not endeavor to devise yet another risk score but did explore the impact of additional variables on the simple ADHERE CART algorithm where age did improve discrimination and impact absolute event rates across the risk groups. Patients missing data needed to calculate the risk scores were excluded from the analysis, and this may potentially introduce bias. However, the number of patients with missing data was small. Because of the small number of variables in the models, imputation may also produce misleading information. As the 2 scores share 2 variables, most patients excluded from ADHERE analysis would be excluded from GWTG analysis scores. These 2 scores only have modest (ADHERE) to moderate (GWTG) predictive characteristics. Future development of machine learning derived risk scores from the electronic medical record may provide enhanced accuracy with similar simplicity.

In summary, the simple ADHERE and GWTG scores stratify hospitalized HF patients for both in-hospital and early postdischarge mortality and readmission risk, allowing comprehensive risk assessment on admission. The GWTG score showed good calibration for in-hospital mortality and significant differences in risk between groups, suggesting that it may provide a reasonable balance between performance and simplicity needed to engender widespread clinical use. Future studies are needed to evaluate the impact of risk score use on clinical management and outcomes in hospitalized HF patients.

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DISCLOSURES

None.

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FOOTNOTES

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Inpatient Mortality Risk Scores and Postdischarge Events in Hospitalized Heart Failure Patients: A Community-Based Study

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SUPPLEMENTARY MATERIALS

Manuscript: Inpatient Mortality Risk Scores and Post-Discharge Events in Hospitalized Heart Failure Patients: A Community-Based Study

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CONTENTS

SUPPLEMENTAL METHODS:

DATA DISCOVERY AND QUERY BUILDER (DDQB)

Inpatient care for residents of Rochester MN and the surrounding area is provided by the Mayo affiliated hospitals in Rochester, MN and a single other provider.

As previously described[1], Mayo Clinic has established a sophisticated data warehouse (Mayo Clinic Life Sciences [MCLSS]), which contains a near real-time normalized replicate of Mayo Clinic's electronic medical record (EMR). This warehouse is developed from multiple original clinical data sources, including highly annotated, full-text clinical notes, laboratory tests, diagnostic findings, demographics, and related clinical data from the year 2000 onward. Mayo Clinic's EMR data are extracted, transformed, and loaded into MCLSS using IBM's WebSphere Commerce Analyzer, creating DB/2 Universal Database structures of Mayo Clinic's normalized clinical data. Clinical patient data are mapped to standard medical terminologies using LexGrid (Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN) natural language processing technology. The MCLSS provides approved users with a query-building tool called the *Data Discovery and Query Builder* (DDQB). The DDQB is a Web-based application configured for query building that is intended to help investigators interrogate data files contained in the MCLSS. The DDQB allows users to build queries without requiring programming knowledge.

CHARLSON COMORBIDITY INDEX

The age and disease severity weighted Charlson Comorbidity Index incorporates several comorbidities (myocardial infarction, heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic pulmonary disease, connective tissue disease, ulcer, mild liver disease, hemiplegia, chronic kidney disease, diabetes, cancer, leukemia, lymphoma, moderate-severe liver disease, metastatic cancer) in an age and severity adjusted model. The maximal score possible is 26. Given that all patients in this study had heart failure, the minimal score was 1.

Table S1. Heart Failure International Classification of Disease Codes

	ICD-9 Diagnostic Codes
Heart failure	402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.93, 428-xx

Abbreviations: ICD, International Classification of Disease

Table S2. Overall characteristics of patients with ADHERE CART data at their first HF hospitalization

Characteristic	Overall N=3628
Demographic/Clinical	
Age, years*	77.8 ± 12.7
Male	1840 (50.1)
Systolic, mmHg*	135 ± 27.6
Diastolic, mmHg	70.5 ± 17.7
Heart rate, bpm	79.2 ± 18.7
Body mass index, kg/m2	31.6 ± 10.6
HFpEF (3593 classifiable)	1738 (48.4)
Medical History	
Hypertension	3444 (94.9)
Diabetes	1805 (49.8)
Atrial fibrillation or flutter	2495 (68.8)
Dementia	398 (11)
CABG	1012 (27.9)
COPD	857 (23.6)
CCI	9.2 ± 3.5
Medications	
Beta-blocker	2629 (72.5)
ACE inhibitor	2031 (56)
ARB	664 (18.3)
Aldosterone antagonist	425 (11.7)
Loop diuretic	3118 (85.9)
Statin	1920 (52.9)
Laboratory/Echocardiographic	
NT-proBNP, pg/mL, n=1109	4816 (2295-10983)
Sodium, mEq/L, n=3628	137.5 ± 5.1
Hemoglobin, g/dL, n=3603	11.8 ± 2
Blood urea nitrogen, mg/dL*	31.2 ± 18.9
Creatinine, mg/dL*	1.5 ± 1.1
GFR, ml/min/1.73m^2	54.4 ± 25.2
Ejection fraction, %, n=3593	45.4 ± 18.1
E/e' medial, n=2543	21.5 ± 11.0
Deceleration time, ms, n=2587	180.7 ± 55.4
PASP, mmHg, n=3173	50.8 ± 15.5

* Variables included in the ADHERE-CART score. Variables are mean ± SD, n (%), or median (interquartile range). P values are from linear regression for continuous variables and logistic regression for categorical variables. Abbreviations: HFpEF, heart failure with preserved ejection fraction defined as left ventricular ejection fraction ≥ 50%; CABG, coronary artery bypass graft; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; GFR, glomerular filtration rate; COPD, chronic obstructive pulmonary disease; PASP, pulmonary artery systolic pressure.

Table S3. Overall characteristics of patients with GWTG score data at their first HF hospitalization

Characteristic	Overall N=3547
Demographic/Clinical	
Age, years*	77.8 ± 12.7
Male	1800 (50.8)
Systolic, mmHg*	134.9 ± 27.6
Diastolic, mmHg	70.5 ± 17.7
Heart rate, bpm*	79.2 ± 18.7
Body mass index, kg/m2	31.6 ± 10.7
HFpEF (3512 classifiable patients)	1697 (48.3)
Medical History	
Hypertension	3368 (95.0)
Diabetes	1758 (49.6)
Atrial fibrillation or flutter	2438 (68.7)
Dementia	389 (11.0)
CABG	990 (27.9)
COPD*	839 (23.7)
Charlson Comorbidity index	9.2 ± 3.5
Medications	
Beta-blocker	2580 (72.7)
ACE inhibitor	1986 (56.0)
ARB	650 (18.3)
Aldosterone antagonist	413 (11.6)
Loop diuretic	3050 (86.0)
Statin	1882 (53.1)
Laboratory/Echocardiographic	
NT-proBNP, pg/mL, n=1095	4748 (2284-10887)
Sodium, mEq/L, n=3547*	137.4 ± 5.1
Hemoglobin, g/dL, n=3523	11.8 ± 2.0
Blood urea nitrogen, mg/dL*	31.3 ± 19.0
Creatinine, mg/dL	1.5 ± 1.1
GFR, ml/min/1.73m^2	54.5 ± 25.2
Ejection fraction, %, n=3512	45.4 ± 18.0
E/e' medial, n=2485	21.5 ± 11.0
Deceleration time, ms, n=2527	180.8 ± 55.5
PASP, mmHg, n=3173	50.8 ± 15.5

* Variables included in the GWTG score. Variables are mean ± SD, n (%), or median (interquartile range). P values are from linear regression for continuous variables and logistic regression for categorical variables. Abbreviations: HFpEF, heart failure with preserved ejection fraction defined as left ventricular ejection fraction ≥ 50%; CABG, coronary artery bypass graft; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; GFR, glomerular filtration rate; COPD, chronic obstructive pulmonary disease; PASP, pulmonary artery systolic pressure

Table S4. Impact of age, heart rate and Charlson Comorbidity Index (CCI) on predictive characteristics of the ADHERE CART risk algorithm

	In-Patient Mortality	30-Day Mortality	90-Day Mortality	180-Day Mortality
ADHERE-CART Group	0.66	0.67	0.64	0.64
+ Age	0.68	0.72	0.69	0.69
+ Age and heart rate	0.71	0.72	0.70	0.70
+ Age, heart rate and CCI	0.71	0.73	0.70	0.71

Table S5. ADHERE CART Risk Groups and GWTG HF Risk Scores According to Heart Failure Type

Mortality	ADHERE_CART c-statistic	OR (95% CI) per ADHERE-CART Group	Interaction p	GWTG c-statistic	OR (95% CI) per GWTG quintile	Interaction p
In-hospital						
HFrEF	0.649	1.53 (1.31-1.77)	0.744	0.731	1.91 (1.55-2.34)	0.610
HFpEF	0.656	1.58 (1.35-1.85)		0.753	1.58 (1.35-1.86)	
30 day						
HFrEF	0.699	1.82 (1.63-2.03)	0.076	0.753	2.08 (1.81-2.39)	0.012
HFpEF	0.618	1.55 (1.36-1.77)		0.695	1.55 (1.36-1.77)	
90 day						
HFrEF	0.675	1.74 (1.59-1.90)	0.004	0.726	1.86 (1.69-2.04)	0.031
HFpEF	0.593	1.42 (1.28-1.58)		0.684	1.42 (1.28-1.58)	
180 day						
HFrEF	0.670	1.73 (1.59-1.88)	0.009	0.724	1.82 (1.68-1.98)	0.032
HFpEF	0.600	1.46 (1.33-1.60)		0.679	1.46 (1.33-1.60)	

Table S6. Readmissions according to ADHERE-CART risk group or GWTG HF score Quintiles.

Outcome	ADHERE High N=141	ADHERE Int 1 N=465	ADHERE Int 2 N=993	ADHERE Int 3 N=962	ADHERE Low N=3357	P value
All HF hospitalizations						
30-day readmission	38 (38.0)	144 (38.7)	266 (31.0)	210 (24.6)	661 (21.6)	<0.001
30-day HF readmission	19 (19.0)	87 (23.4)	101 (11.8)	74 (8.7)	200 (6.5)	<0.001
90-day readmission	63 (65.6)	207 (59.3)	455 (55.0)	382 (46.5)	1205 (40.7)	<0.001
90-day HF readmission	30 (31.3)	109 (31.2)	159 (19.2)	129 (15.7)	344 (11.6)	<0.001
180-day readmission	72 (77.4)	244 (71.8)	565 (70.5)	489 (61.0)	1538 (53.0)	<0.001
180-day HF readmission	32 (34.4)	122 (35.9)	189 (23.6)	153 (19.1)	438 (15.1)	<0.001
	GWTG Score Q-5 (> 50) N=1029	**GWTG Score Q-4 (46-50) N=1156**	**GWTG Score Q-3 (42-45) N=1192**	**GWTG Score Q-2 (37-41) N=1246**	**GWTG Score Q-1 (< 37) N=1171**	
All HF hospitalizations						
30-day readmission	272 (33.8)	310 (30.5)	230 (21.1)	248 (21.5)	223 (20.9)	<0.001
90-day readmission	423 (56.3)	506 (51.5)	436 (41.8)	492 (43.6)	402 (38.6)	<0.001
180-day readmission	520 (72.5)	612 (63.5)	552 (54.4)	626 (56.2)	526 (51.6)	<0.001
30-day HF readmission	136 (16.9)	131 (12.9)	73 (6.7)	67 (5.8)	59 (5.5)	<0.001
90-day HF readmission	189 (25.1)	194 (19.7)	134 (12.9)	128 (11.4)	103 (9.9)	<0.001
180-day HF readmission	214 (29.9)	225 (23.3)	162 (16.0)	168 (15.1)	138 (13.5)	<0.001

The numeric values for event rates shown in Figure 4 in the primary manuscript are presented. Data are median (interquartile range) or n (%). The denominator for event frequency is less than the group n due to censoring of patients with death or insufficient follow-up during the specified interval. Abbreviations: Int, intermediate; HF, heart failure; Q, Quinitle

Table S7: Predictive characteristics of ADHERE CART Risk Group and GWTG HF Risk Score for Readmissions

	c-statistic	OR (95% CI) per ADHERE CART Group	OR (95% CI) versus the Low ADHERE CART Group				
			High N=141	Int 1 N=465	Int 2 N=993	Int 3 N=962	Low N=3357
30-day readmission	0.57	1.28 (1.21-1.36)	2.22 (1.49-3.32)	2.29 (1.81-2.91)	1.63 (1.37-1.95)	1.18 (0.98-1.43)	referent
30-day HF readmission	0.62	1.49 (1.38-1.62)	3.35 (1.95-5.76)	4.36 (3.24-5.88)	1.91 (1.47-2.49)	1.36 (0.99-1.86)	referent
90-day readmission	0.57	1.30 (1.23-1.38)	2.79 (1.75-4.42)	2.13 (1.67-2.7)	1.78 (1.52-2.09)	1.27 (1.08-1.49)	referent
90-day HF readmission	0.60	1.42 (1.33-1.53)	3.46 (2.21-5.42)	3.46 (2.65-4.51)	1.81 (1.45-2.26)	1.42 (1.11-1.82)	referent
180-day readmission	0.58	1.37 (1.29-1.46)	3.04 (1.85-5.01)	2.25 (1.74-2.93)	2.12 (1.79-2.52)	1.39 (1.17-1.64)	referent
180-day HF readmission	0.59	1.38 (1.29-1.47)	2.95 (1.88-4.63)	3.15 (2.42-4.09)	1.74 (1.42-2.13)	1.33 (1.05-1.67)	referent

	c-statistic	OR (95% CI) per GWTG Quintile	OR (95% CI) versus the lowest GWTG Quintile				
			GWTG Score Q-5 (> 50) N=1029	GWTG Score Q-4 (46-50) N=1156	GWTG Score Q-3 (42-45) N=1192	GWTG Score Q-2 (37-41) N=1246	GWTG Score Q-1 (< 37) N=1171
30-day readmission	0.57	1.20 (1.14-1.26)	1.93 (1.56-2.40)	1.66 (1.35-2.05)	1.01 (0.82-1.26)	1.03 (0.85-1.27)	referent
30-day HF readmission	0.64	1.19 (1.14-1.24)	2.04 (1.68-2.49)	1.69 (1.40-2.03)	1.14 (0.95-1.37)	1.23 (1.03-1.47)	referent
90-day readmission	0.57	1.22 (1.16-1.27)	2.48 (2.00-3.07)	1.63 (1.35-1.97)	1.12 (0.93-1.35)	1.20 (1.01-1.44)	referent
90-day HF readmission	0.62	1.43 (1.32-1.55)	3.47 (2.50-4.83)	2.53 (1.81-3.54)	1.23 (0.86-1.76)	1.05 (0.74-1.50)	referent
180-day readmission	0.58	1.35 (1.26-1.44)	3.06 (2.31-4.05)	2.24 (1.69-2.97)	1.34 (1.00-1.80)	1.17 (0.88-1.54)	referent
180-day HF readmission	0.60	1.30 (1.22-1.38)	2.72 (2.09-3.54)	1.95 (1.50-2.52)	1.21 (0.93-1.59)	1.14 (0.89-1.46)	referent

Sample sizes include multiple heart failure hospitalizations for each patient.
Abbreviations: HF, heart failure; EF, ejection fraction; HF, heart failure; OR, odds ratio; Int, intermediate; GWTG, Get with the Guidelines risk score; Q, Quintile

Table S8. Concordance between in-hospital risk stratification by ADHERE-CART and GWTG risk scores: For in-hospital mortality, using the score groups from the derivation cohorts (5 ADHERE Groups and 10 GWTG Groups), the observed event rates in our population for both scores was used to define the relationship between the GWTG and ADHERE scores in our cohort. In our cohort, the ADHERE score actually identified three groups (rather than five) with different observed in-hospital mortality; the original ADHERE "Low Risk" group (mortality 1.6%); an "Intermediate" Group (original ADHERE Int-3 and Int-2 groups; mortality 4.3 and 3.4% respectively) and a "High Risk" group (original ADHERE Int-1 and High risk groups; mortality 8.2 and 7.1% respectively). We enumerated the concordance and discordance between the observed mortality in the GWTG groups and these three ADHERE risk groups. Among patients who were low or high risk by ADHERE, few patients were re-classified to a markedly different risk strata (high or low respectively)by the GWTG score; overall, only 1% of the total population had a marked difference in risk by the two scores. Predictably, there were higher rates of moving from low to intermediate, high to intermediate or intermediate to low or high; overall, 31% of the total population had such a moderate reclassification of patients (to or out of the intermediate range).

	Current Cohort ADHERE Group	Low	Intermediate		High	
	Original ADHERE Group	Low	Int-3	Int-2	Int-1	High
	Total n	3284	945	969	455	141
GWTG Score	Observed Risk	1.6	4.3	3.4	8.2	7.1
0-28	0	159	0	7	0	0
29-32	0.6	324	12	17	0	0
33-35	1.1	412	14	46	0	0
36-37	1	341	12	40	0	0
38-40	0.4	550	59	85	4	1
41-42	2.5	459	69	74	6	1
43-44	1.3	375	101	128	4	1
45-47	2.8	400	223	166	32	5
48-51	5.2	203	262	223	89	18
52-87	7.9	61	193	183	320	115

Effect of GWTG N (%)	ADHERE Low	ADHERE Intermediate	ADHERE High
Reclassified Low	NA	664 (35%)	17 (3%)
Reclassified Intermediate	603 (18%)	NA	144 (24%)
Reclassified High	61 (2%)	376 (20%)	NA

Figure S1. Impact of age on 180 day post-discharge mortality by ADHERE CART risk group

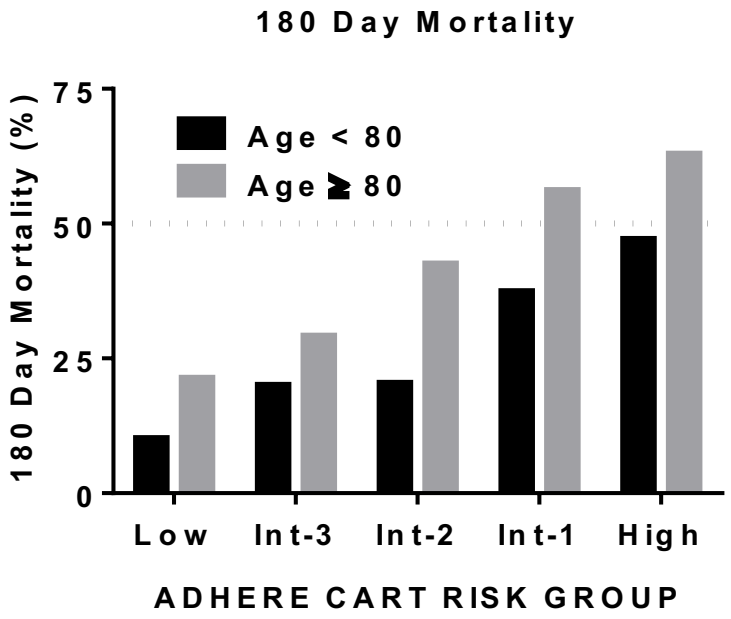
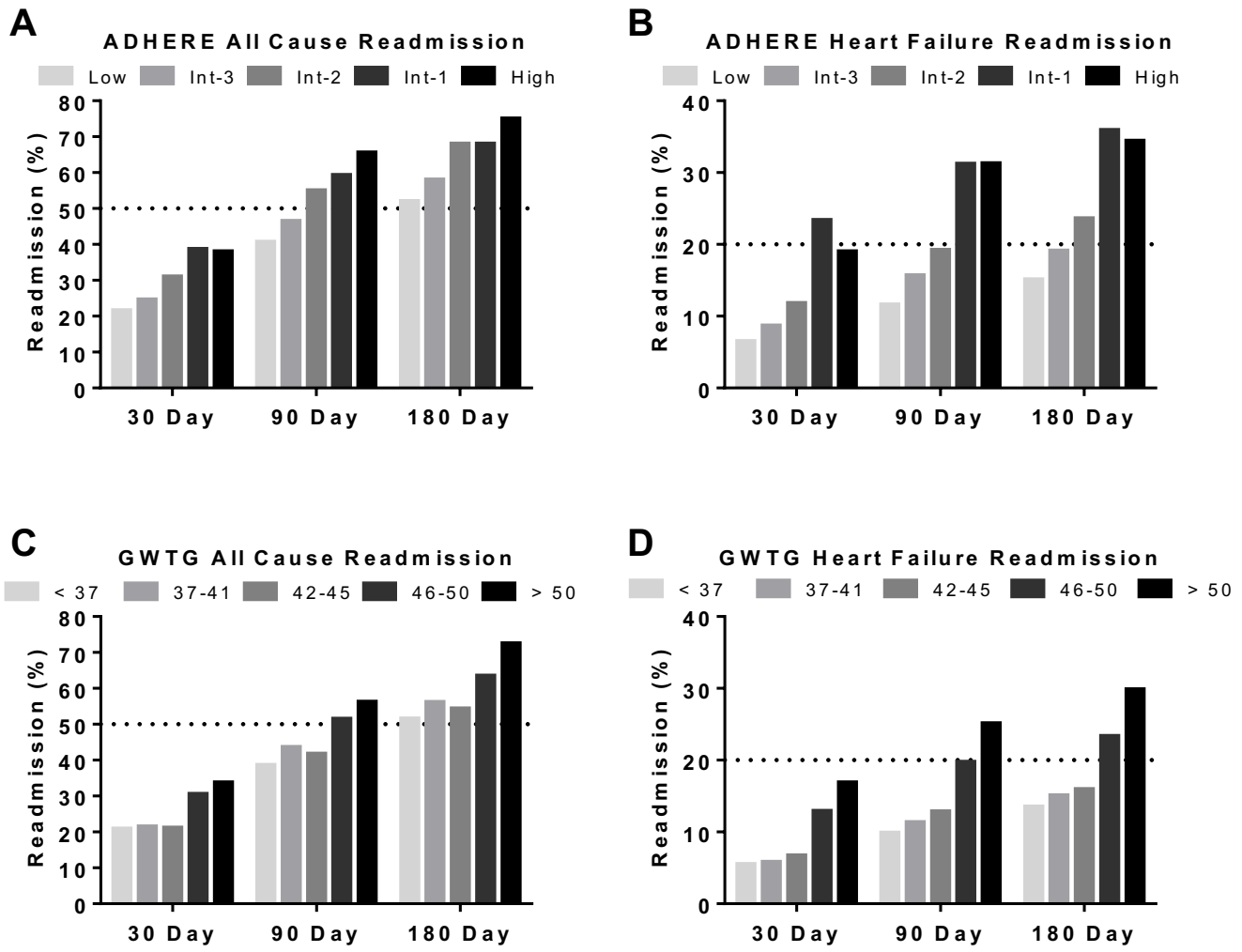


Figure S2. All-cause and heart failure readmissions according to ADHERE CART risk groups or GWTG risk score quintiles.



Supplemental Appendix References

1. Alsara A, Warner DO, Li G, Herasevich V, Gajic O, Kor DJ. Derivation and validation of automated electronic search strategies to identify pertinent risk factors for postoperative acute lung injury. Mayo Clin Proc 2011;86:382-8.