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The modified Rajan's heart failure risk score predicts all-cause mortality in patients hospitalized for heart failure with reduced ejection fraction: a retrospective cohort study

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Background: The dimensionless Rajan's heart failure (R-hf) risk score was proposed to predict all-cause mortality in patients hospitalized with chronic heart failure (HF) and reduced ejection fraction (EF) (HFrEF).

Purpose: To examine the association between the modified R-hf risk score and all-cause mortality in patients with HFrEF.

Methods: Retrospective cohort study included adults hospitalized with HFrEF, as defined by clinical symptoms of HF with biplane EF less than 40% on transthoracic echocardiography, at a tertiary centre in Dalian, China, between 1 November 2015, and 31 October 2019. All patients were followed up until 31 October 2020. A modified R-hf risk score was calculated by substituting brain natriuretic peptide (BNP) for N-terminal prohormone of BNP (NT-proBNP) using EF × estimated glomerular filtration rate (eGFR) × haemoglobin (Hb))/BNP. The patients were stratified into tertiles according to the R-hf risk score. The measured outcome was all-cause mortality. The score performance was assessed using C-statistics.

Results: A total of 840 patients were analyzed (70.2% males; mean age, 64 ± 14 years; median (interquartile range) follow-up 37.0 (27.8) months). A lower modified R-hf risk score predicted a higher risk of all-cause mortality, independent of sex and age [1st tertile vs. 3rd tertile: adjusted hazard ratio (aHR), 3.46; 95% CI: 2.11–5.67; $P < 0.001$]. Multivariate Cox regression analysis indicated that a lower modified R-hf risk score was associated with increased cumulative all-cause mortality [univariate: (1st tertile vs. 3rd tertile: aHR, 3.45; 95% CI: 2.11–5.65; $P < 0.001$) and multivariate: (1st tertile vs. 3rd tertile: aHR 2.21, 95% CI: 1.29–3.79; $P = 0.004$)]. The performance of the model, as reported by *C*-statistic was 0.67 (95% CI: 0.62–0.72).

Conclusion: The modified R-hf risk score predicted all-cause mortality in patients hospitalized with HFrEF. Further validation of the modified R-hf risk score in other cohorts of patients with HFrEF is needed before clinical application.

Keywords: Asia, chronic heart failure, heart failure reduced ejection fraction, mortality, R-hf risk score

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Introduction

Heart failure (HF) is associated with significant mortality and morbidity, affecting an estimated 64 million people worldwide[1]. Despite the wider use of guideline-directed medical therapy, morbidity and mortality remain high and difficult to predict[2–4]. The prognosis of patients with acute decompensated HF has been reported in previous studies; however, there are limited data regarding its applicability to chronic ambulatory HF[5]. Prognostic information and relevance also vary across studies because of the unpredictable pattern of disease progression[6,7]. Furthermore, patients with chronic HF frequently and significantly overestimate their survival when they are not informed of their actual prognosis[8]. Multivariate models are available to predict prognostic outcomes for patients with HF[9,10], but they are underutilized because of the complex mathematical calculations required[6]. In contrast, the Rajan's heart failure (R-hf) risk score is a simple prognostic tool that uses readily available clinical variables: estimated glomerular filtration rate (eGFR), ejection fraction (EF), haemoglobin (Hb), and N-terminal prohormone BNP (NT-proBNP))[11,12] which has been previously validated as a predictor of mortality in hospitalized patients with chronic HF

reduced EF (HFrEF)[13]. This study aimed to determine the prognostic value of the Rajan HF score in patients hospitalized for HFrEF.

HIGHLIGHTS

- The study examines the association between the modified Rajan's heart failure (R-hf) risk score and all-cause mortality in patients with heart failure with reduced ejection fraction (HFrEF).
- The modified R-hf risk score was calculated using easily accessible clinical variables: estimated glomerular filtration rate (eGFR), ejection fraction (EF), haemoglobin (Hb), and brain natriuretic peptide (BNP).
- The retrospective cohort study included 840 adult patients hospitalized with HFrEF at a tertiary centre in Dalian, China, with a follow-up median of 37 months.
- Patients with lower modified R-hf risk scores had a significantly higher risk of all-cause mortality, independently of sex and age, compared to those with higher risk scores.
- The performance of the model, as assessed by the C-statistic, was 0.67 (95% CI: 0.62–0.72).
- Comorbidities such as hypertension, coronary heart disease, and diabetes mellitus were prevalent among the patients in the study.
- BNP, creatinine, eGFR, and haemoglobin levels were significant predictors of risk scores, and their association with mortality was consistent with previous studies.
- The modified R-hf risk score offers a simple and practical tool for risk stratification in patients with HFrEF, potentially aiding in treatment management and improving patient outcomes.
- Further validation in larger and more diverse cohorts is recommended before clinical application of the modified R-hf risk score.

Methods

Study population

We retrospectively analyzed a cohort of patients hospitalized for HFrEF at the First Affiliated Hospital of Dalian Medical University in Dalian, China. The subset of patients selected were adults ($\geq$18 years of age) who underwent echocardiography between 1 November 2015, and 31 October 2019, with a left ventricular ejection fraction (LVEF) less than 40%. The exclusion criteria were loss of patients to follow-up and missing echocardiographic, eGFR, and Hb data. Demographics, comorbidities, drug history, and clinical and laboratory data were collected from the hospital's database and used to calculate the modified R-hf risk score for each patient who was stratified into tertiles according to the risk score [Figure 1]. Patients were diagnosed with HF through LVEF and echocardiography using Simpson's biplane method[14]. This study was approved by the Institutional Review Board of the First Affiliated Hospital of Dalian Medical University 23-EB/DMU/2015. The study complied with the standards of the Declaration of Helsinki and, given the retrospective and observational nature of this study, informed consent was waived by Institutional Review Board of the First Affiliated Hospital of Dalian Medical University. The work has been reported in line with the STROCSS criteria[15] (Figure 2).

Definitions

HF is defined as a clinical syndrome arising from structural or functional impairment of ventricular filling or ejection of blood[16]. The definition of HFrEF was adapted by the 2021 European Society of Cardiology (ESC) guidelines as symptoms and/or signs of HF with LVEF less than 40%[17]. In this study, the R-hf risk score was modified using BNP instead of NT-proBNP. The modified R-hf risk score was calculated as the product of eGFR (ml/min), LVEF (%), and Hb level (g/dl) divided by BNP level (pg/ml). The patients were categorized into tertiles according to their respective R-hf risk scores. The R-hf risk score is available at https://www.hfriskcalc.in.

Follow-up and study endpoint

Follow-up was performed for a minimum of 1 year via outpatient hospital visits and/or telephone calls. The cutoff follow-up period was 31 October 2020. Clinical events were ascertained using information from the hospital's database and were based on a review of the primary diagnoses documented in each discharge summary during the follow-up period. The event included in this analysis was all-cause mortality. This study is registered with Research Registry UIN: researchregistry9793.

Statistical analysis

The subjects were categorized into tertiles according to their respective R-hf risk scores. The 1st tertile was R-hf risk score less than or equal to 22.51, 2nd tertile was R-hf risk score greater than 22.51-68.10 and 3rd tertile was R-hf risk score greater than 68.10[11,12]. Descriptive statistics were used to summarize the data. Qualitative variables were summarized by frequency and percentage, and Pearson's χ^2 test was employed to analyze group comparisons. Quantitative variables are outlined by means with standard deviation (SD), and analysis of variance (ANOVA) was used to assess differences between independent groups. Kaplan–Meier analysis was used to describe the cumulative incidence of adverse events. The impact of the R-hf risk score and HF on mortality was determined through multivariate Cox regression, which generated hazard ratios (HRs) and 95% CIs with the corresponding *P* value. All values were two-tailed, and a *P* value

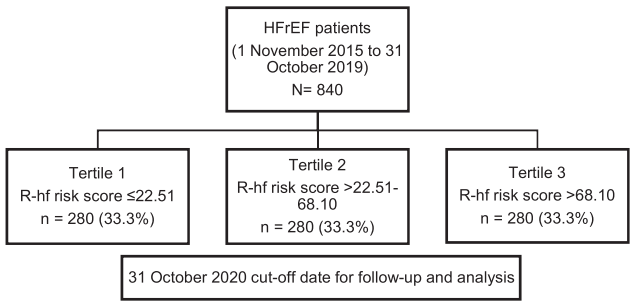

Figure 1. Flowchart demonstrating cohort selection and stratification. Percentages might not add up to 100% because of rounding. HFrEF, heart failure with reduced ejection fraction; R-hf, Rajan heart failure.

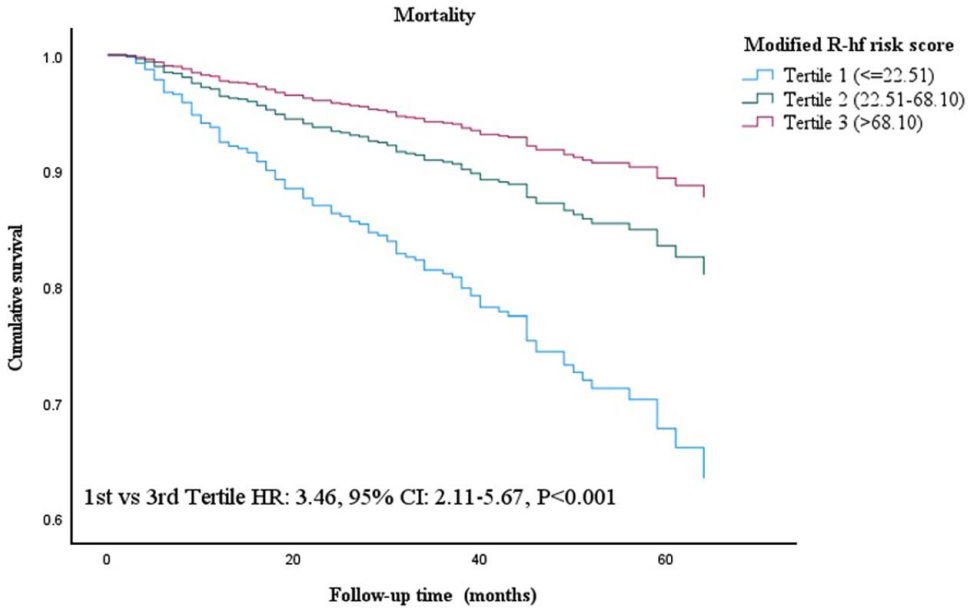

Figure 2. Illustrates the Kaplan–Meier survival curve of all-cause mortality stratified by tertiles of the R-hf risk score during the 3-year follow-up period. Independent of sex and age, a lower modified R-hf risk score predicted a higher risk of all-cause mortality (1st tertile vs. 3rd tertile: aHR, 3.46; 95% CI: 2.11–5.67; $P < 0.001$). aHR, adjusted hazard ratio; R-hf, Rajan heart failure.

Table 1

Demographic and clinical characteristics of patients of the heart failure with reduced ejection fraction cohort stratified by R-hf risk score

Characteristics, *n* (%) unless specified otherwise	Total (*N* = 840)	Tertile 1 (≤ 22.51) (*n* = 280)	Tertile 2 (> 22.51-68.10) (*n* = 280)	Tertile 3 (> 68.10) (*n* = 280)	*P*
Age, mean ± SD, years	64.1 (13.6)	66.0 (13.8)	63.2 (13.9)	63.1 (12.8)	0.015
Male sex	590 (70.2)	189 (67.5)	201 (71.8%	200 (71.4)	0.469
BSA, mean ± SD, kg/m^2	1.48 (0.64)	1.35 (0.69)	1.52 (0.59)	1.56 (0.62)	< 0.001
Cerebrovascular disease	92 (11.0)	39 (13.9)	31 (11.1)	22 (7.9)	0.071
Diabetes mellitus	289 (34.4)	96 (34.3)	98 (35.0)	95 (33.9)	0.964
Hypertension	526 (62.6)	182 (65.0)	172 (61.4)	172 (61.4)	0.601
Atrial fibrillation	207 (24.6)	74 (26.4)	66 (23.6)	67 (23.9)	0.694
Coronary heart disease	351 (41.8)	111 (39.6)	114 (40.7)	126 (45.0)	0.397
Cancer	164 (19.5)	50 (17.9)	53 (18.9)	61 (21.8)	0.480
CRT	42 (5.0)	14 (5.0)	13 (4.6)	15 (5.4)	0.928
ICD	19 (2.3)	4 (1.4)	5 (1.8)	10 (3.6)	0.188
Pacemaker	40 (4.8)	14 (5.0)	12 (4.3)	14 (5.0)	0.900
NYHA class III/IV	206 (24.5)	74 (26.4)	72 (25.7)	60 (21.4)	0.331

Percentages might not add up to 100% due to rounding off. Analyses were performed using χ^2 test or ANOVA, whenever appropriate.
BSA, body surface area; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; R-hf, Rajan heart failure.

Table 2

Laboratory findings of the heart failure with reduced ejection fraction cohort stratified by R-hf risk score

Characteristics, *n* (mean with SD) unless specified otherwise	Total (*N* = 840)	Tertile 1 (≤ 22.51) (*n* = 280)	Tertile 2 (> 22.51-68.10) (*n* = 280)	Tertile 3 (> 68.10) (*n* = 280)	*P*
Hb, mean ± SD, gm/dl	13.6 (2.14)	12.9 (2.38)	13.8 (1.88)	14.6 (6.30)	< 0.001
BNP, mean ± SD, pg/ml	1230 (1660)	2578 (2294)	822 (334)	290 (174)	< 0.001
Creatinine, mean ± SD, umol/l	98.7 (59.4)	128 (88.9)	89.9 (29.4)	77.9 (21.3)	< 0.001
eGFR, mean ± SD, ml/min	73.4 (25.4)	58.3 (24.3)	75.2 (21.5)	86.6 (21.9)	< 0.001
Urea, mean ± SD, mmol/l	8.73 (4.30)	10.9 (5.50)	8.02 (2.95)	7.25 (3.00)	< 0.001
K, mean ± SD, mmol/l	4.00 (0.49)	4.04 (0.55)	3.93 (0.47)	4.02 (0.42)	0.015
Na, mean ± SD, mmol/l	142 (36.7)	141 (21.5)	144 (59.8)	141 (3.42)	0.481

BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; Hb, haemoglobin; K, potassium; Na, sodium; R-hf, Rajan heart failure.

Table 3

Echocardiography findings of the heart failure with reduced ejection fraction cohort stratified by R-hf risk score

Characteristics, *n* (mean with SD) unless specified otherwise	Total (*N* = 840)	Tertile 1 (≤22.51) (*n* = 280)	Tertile 2 (>22.51-68.10) (*n* = 280)	Tertile 3 (>68.10) (*n* = 280)	*P*
LVEF, mean ± SD, %	31.3 (6.48)	28.4 (6.81)	31.3 (6.06)	34.3 (5.02)	<0.001
LAV, mean ± SD, ml	73.3 (37.4)	76.2 (29.8)	74.2 (30.9)	69.5 (48.4)	0.093
LAVI, mean ± SD, ml/m^2	– 326 (1687)	– 648 (2360)	– 64.2 (914)	– 267 (1405)	<0.001

LAV, left atrial volume; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; R-hf, Rajan heart failure.

less than 0.05 was considered statistically significant. The score performance was assessed using C-statistics. Analyses were performed using Stata software version 13 (StataCorp LLC) and SPSS software version 27 (SPSS Inc.).

Results

A total of 840 patients hospitalized for HFrEF were included in the study. The median (interquartile range) follow-up was 37.0 (27.8) months, and the cohort comprised 70.2% males. There was an equal distribution of 280 patients among the three tertiles. The mean age of patients in the 1st tertile (66.0 ± 13.8) was greater than that in the 2nd tertile (63.2 ± 13.9) and 3rd tertile (63.1 ± 12.8). There were significant differences in the body surface area of patients in the 1st tertile (1.35 ± 0.69) compared to those in the 2nd tertile (1.52 ± 0.59) and 3rd tertile (1.56 ± 0.62) patients ($P < 0.001$). A total of 24.5% of patients were classified as New York Heart Association (NYHA) class III or IV, of which 26.4% were in the 1st tertile, 25.7% in the 2nd tertile and 21.4% in the 3rd tertile [Table 1].

Table 2 summarizes the laboratory parameters. Patients in the 1st tertile had significantly higher BNP ($P < 0.001$), creatinine ($P < 0.001$), and urea ($P < 0.001$) levels than those in the 2nd tertile and 3rd tertile. However, patients in the 3rd tertile had higher Hb levels ($P < 0.001$) and eGFR ($P < 0.001$) than those in the other tertiles.

Table 3 presents the echocardiographic data of the cohort. Patients in the 1st tertile had a lower LVEF ($P < 0.001$) and left atrial volume index (LAVI) ($P < 0.001$) than those in the 2nd and 3rd tertiles.

Table 4 details the medications prescribed to the cohort at discharge. There were no significant differences between the tertiles regarding the medications prescribed.

Additionally, Cox regression analysis was conducted and adjusted for all the variables listed in the four preceding tables with the exception of LVEF, eGFR, Hb and BNP. A lower modified R-hf risk score predicted a higher risk of all-cause mortality in univariate analysis (1st tertile vs. 3rd tertile: aHR, 3.45; 95% CI: 2.11–5.65; P <0.001) and multivariate analysis (1st tertile vs. 3rd tertile: aHR, 2.21; 95% CI: 1.29–3.79; $P = 0.004$) [Table 5]. The area under the curve C-statistic of the model was 0.67 (95% CI: 0.62–0.72).

Discussion

The major finding of this study was that the modified R-Hf risk score predicts all-cause mortality in patients hospitalized with chronic HFrEF.

Several prognostic models have been established to assess the mortality and morbidity outcomes in a range of HF settings [Table 6]. The Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) risk model is a reliable predictor of cardiovascular and HF hospitalization and all-cause mortality in HF preserved EF (HFpEF) patients. Researchers examined the correlation between BNP and MAGGIC scores and found that the addition of BNP to the MAGGIC risk score significantly improved prognostication ($P < 0.01$ by likelihood ratio test for the combination of BNP + MAGGIC vs. MAGGIC alone)[18]. Similarly, with the incorporation of BNP into the modified R-hf risk score, the model successfully predicted the prognosis of patients with HFrEF. Notably, with the exception of LVEF, the MAGGIC model accounted for 12 other predictor models that we excluded[18].

The Get With the Guidelines Heart Failure (GWTG-HF) risk score has been validated as a predictor of in-hospital mortality in patients with HFrEF and HFpEF. While the model's seven risk parameters differed from ours, akin to our data, high BNP and creatinine levels were associated with higher risk scores. Furthermore, high Hb levels were associated with lower risk scores ($P < 0.001$)[19–21]. The AHEAD score is designed to predict all-cause mortality or cardiovascular death in acute HF with HFrEF and HFpEF. They also showed a pattern comparable to that of our data. High Hb and eGFR levels were correlated with low-risk scores, and high creatinine and Uric Acid levels were associated with high-risk scores ($P < 0.001$)[22]. The Acute Decompensated Heart Failure National Registry (ADHERE) classification and regression tree (CART) algorithm utilizes blood urea nitrogen, systolic blood pressure, and creatinine for risk

Table 4

Discharge medications of the heart failure with reduced ejection fraction cohort stratified by R-hf risk score

Characteristics, *n* (%) unless specified otherwise	Total (*N* = 840)	Tertile 1 (≤22.51) (*n* = 280)	Tertile 2 (>22.51-68.10) (*n* = 280)	Tertile 3 (>68.10) (*n* = 280)	*P*
ACE/ARB	653 (77.7)	209 (74.6)	223 (79.6)	221 (78.9)	0.306
Beta blockers	801 (95.4)	265 (94.6)	265 (94.6)	271 (96.8)	0.380
Spironolactone	571 (68.0)	183 (65.4)	186 (66.4)	202 (72.1)	0.181
Digoxin	241 (28.7)	71 (25.4)	81 (28.9)	89 (31.8)	0.242
Loop diuretics	371 (44.2)	112 (40.0)	128 (45.7)	131 (46.8)	0.221
Aspirin	361 (43.0)	116 (41.4)	124 (44.3)	121 (43.2)	0.788
Nitrates	291 (34.6)	96 (34.3)	97 (34.6)	98 (35.0)	0.984
Warfarin	242 (28.8)	80 (28.6)	79 (28.2)	83 (29.6)	0.927
Statins	450 (53.6)	151 (53.9)	143 (51.1)	156 (55.7)	0.539

ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; R-hf, Rajan heart failure.

Table 5

Impact of R-hf risk score on mortality in heart failure with reduced ejection fraction patients

Mortality	Alive	Dead	Univariate aHR (95% CI, *P*)	Multivariate Cox regression aHR (95% CI, *P*)
R-hf Risk Score				
Tertile 1 (≤22.51)	212 (75.7)	68 (24.3)	3.45 (2.11–5.65, $P<0.001$)	2.21 (1.29–3.79, $P=0.004$)
Tertile 2 (>22.51-68.10)	248 (88.6)	32 (11.4)	1.59 (0.92–2.77, $P=0.097$)	1.37 (0.77–2.44, $P=0.278$)
Tertile 3 (>68.10)	259 (92.5)	21 (7.50)	—	—

Multivariable analyses were conducted using Cox regression models. The models were adjusted for R-hf risk score. Percents are row percentages.
aHR, adjusted hazard ratio; R-hf, Rajan heart failure.

stratification of in-hospital mortality. Similar to our study, the ADHERE scores were positively correlated between Hb and eGFR levels and low-risk scores, and creatinine with high-risk scores[23].

The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) trial analyzed discharge HF risk factors and 6-month mortality following in-hospital therapy in patients with advanced HF. The model underscores important discharge variables to screen inpatients at risk for recurrent events[24]. Other models, including the CORONA and HF-action models, have yet to be externally validated[25,26]. The Seattle Heart Failure Model yields estimates of 1-year, 2-year, and 3-year survival using 24 variables[27]. Finally, the initial R-hf risk score model predicted prognosis and mortality in patients with HFrEF. Corresponding to the initial R-hf risk score, a modified R-hf risk score of less than 5 exhibited a poor prognosis in the cohort. Thus, substitution of NT-proBNP for BNP conserves the prognostic ability of the risk model. However, the applicable population varied between the two studies. The cohort of the initial R-hf risk model was predominantly comprised of South Indian patients, whereas the modified R-hf risk model is primarily of the Chinese population[13].

The three most prevalent comorbidities were hypertension (62.6%), coronary heart disease (41.8%), and diabetes mellitus (34.4%). Patients in the 1st tertile had higher BNP ($P<0.001$), creatinine ($P<0.001$), and urea ($P<0.001$) levels and lower BSA ($P<0.001$), LVEF ($P<0.001$), and LAVI ($P<0.001$) than those in the other tertiles. Furthermore, patients in the 3rd tertile had higher Hb levels ($P<0.001$) and eGFR ($P<0.001$) than those in the 1st tertile and 2nd tertile. Independent of sex and age, a lower modified R-hf risk score predicted a higher risk of all-cause mortality (1st tertile vs. 3rd tertile: aHR, 3.46; 95% CI: 2.11–5.67; $P<0.001$). Additionally, a lower modified R-hf risk

Table 6

Selected prognostic models in heart failure versus modified R-hf risk score

Prognostic model	Key covariates	Outcome
Meta-Analysis Global Group in Chronic Heart Failure Risk Score (MAGGIC)[18]	Age, sex, body mass index, systolic blood pressure, EF, creatinine, current smoker, diabetes mellitus, chronic obstructive pulmonary disease, NYHA class, HF duration >18 months Beta-blocker use, ACE inhibitor use	Predictor of all-cause mortality and HF hospitalizations in HF with preserved EF
Get With The Guidelines Heart Failure Risk Score (GWTG-HF)[19–21]	Age, systolic blood pressure, heart rate, blood urea nitrogen, sodium, chronic obstructive pulmonary disease, race	Predictor of in-hospital mortality in HF with reduced and preserved EF
AHEAD Score[22]	A: atrial fibrillation, H: haemoglobin <130 g/l (M) < 120 g/l (F), E: elderly >70 years, A: abnormal renal parameters (creatinine >130), D: diabetes mellitus	Predictor of all-cause mortality or cardiovascular death in acute heart failure with reduced and preserved EF
ADHERE Score[23]	Blood urea nitrogen, systolic blood pressure, creatinine	Predictor of in-hospital and 30–180 days mortality in hospitalized HF patients
ESCAPE risk model and discharge score[24]	BNP, cardiopulmonary resuscitation or mechanical ventilation, BUN, sodium, age >70, daily loop diuretic dose, lack of beta blocker, 6-min walk distance	Identifies high-risk heart failure patients at hospital discharge
HF-ACTION Model[25]	Exercise duration on CPX test, serum urea nitrogen, female sex, BMI	All-cause mortality
CORONA Model[26]	NT-proBNP, age, diabetes mellitus, LVEF, BMI, CABG, Female, atrial fibrillation, NYHA class ApoA-1, serum creatinine, intermittent claudication, heart rate, myocardial infarction	All-cause mortality
Seattle heart failure Model (SHFM)[27]	Age, ejection fraction, systolic blood pressure, weight, sex, NYHA class, aetiology, furesomide (mg), torsemide (mg), bumetidine (mg), metolazone (mg), hydrochlorothiazide (mg), allopurinol, statin, ACE inhibitor, beta blocker, K sparing diuretic, devices, sodium, total cholesterol, haemoglobin, lymphocytes, uric acid	Estimates 1-year, 2-year, 3-year survival in heart failure patients
R-hf risk score[13]	eGFR, left ventricular ejection fraction, haemoglobin, N-terminal BNP	Identifies high-risk heart failure patients
Modified R-hf risk score	eGFR, left ventricular ejection fraction, haemoglobin, BNP	Predicts all-cause mortality in hospitalized patients with HF with reduced EF

Table is adapted from Validation of R-hf risk score for risk stratification in ischaemic heart failure patients: A prospective cohort study[13].
ACE, angiotensin-converting enzyme; ADHERE, Registry for Acute Decompensated Heart Failure Patients; apoA-1, apolipoprotein A1; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CABG, coronary artery bypass graft; CPX, cardiopulmonary exercise; EF, ejection fraction; eGFR:estimated glomerular filtration rate; ESCAPE, Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness; HF, heart failure; HF-ACTION, Heart Failure: A Controlled Trial Investigating Outcomes of Exercise TraiNing; K, potassium; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal prohormone brain natriuretic peptide; NYHA, New York heart association; R-hf, Rajan heart failure.

score was associated with increased cumulative all-cause mortality [univariate (1st tertile vs. 3rd tertile: aHR, 3.45; 95% CI: 2.11–5.65; P <0.001) and multivariate (1st tertile vs. 3rd tertile: aHR 2.21, 95% CI: 1.29–3.79; P =0.004]). These findings demonstrate the application of the R-hf model in the risk stratification of patients with chronic HFrEF in ambulatory settings, and thus guide treatment management. By design, a low R-hf risk score indicates that the risk associated with myocardial damage is not governed by HF aetiology. Previous studies have demonstrated the importance of eGFR, ejection fraction, and BNP or NT-proBNP in prognosis in diverse populations. The ADHERE study established BNP and NT-proBNP as predictive markers in patients with acute decompensated HF[28], while the ESCAPE trial reported that higher discharge BNP levels were the strongest predictors of mortality[24]. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines state that high levels of BNP and NT-proBNP are positively correlated with a greater risk of short-term and long-term all-cause mortality in ambulatory settings[29,30]. The mean death rate in prognostic risk models that exclude LVEF or renal variables is lower than anticipated[13]. A study by Juntendo University Hospital validated eGFR as a prognostic variable for acute HF and demonstrated that lower eGFR at admission was an independent predictor of death[31]. In a study by Hein *et al.*[32], eGFR was significantly associated with mortality in patients with HF. Hb is another independent marker of long-term mortality in patients[33,34]. Moreover, the European Society of Cardiology (ESC) guidelines emphasize its importance and recommend that all HF patients be periodically screened for iron deficiency and anaemia[14].

This study had some limitations. First, observational studies may introduce bias through confounding variables that are not controlled or measured. Second, our study is a single-centre study and may not be generalizable to a large population. Third, the cohort was almost exclusively Chinese and racial differences could not be determined. A multicenter study with a more diverse cohort is required to overcome these limitations.

Conclusion

The modified TR-hf risk score is a simple, easy-to-calculate tool that can be used to predict the prognosis of patients hospitalized with HFrEF. A lower modified R-hf risk score was associated with an increased cumulative all-cause mortality.

Ethical approval

This study was approved by the Institutional Review Board of the First Affiliated Hospital of Dalian Medical University 23-EB/DMU/2015.

Patient consent statement

Patient consented was not mandated for this retrospective observational study.

Sources of funding

Not applicable.

Author contribution

R.R. participated in analysis and manuscript preparation. J.M.H.H. and M.A.J. participated in data analysis and manuscript preparation. G.T. and J.M.H.H. conducted the statistical analysis and reviewed the manuscript. All authors had access to the data and take responsibility for the integrity of data and the accuracy of data analysis. All authors have read and approved the manuscript.

Conflicts of interest disclosure

The author declares no conflict of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: researchregistry9793.
2. Unique Identifying number or registration ID: researchregistry 9793.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-the-registry#home/ Clinical trial registration Researchregistry9793.

Guarantor

Rajesh Rajan.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Permission to reproduce material from other sources

No material from other sources is included in this study.

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