Cohort Study

Validation of R-hf risk score for risk stratification in ischemic heart failure patients: A prospective cohort study

Rajesh Rajan [a,c,*], Suman Omana Soman [b], Mohammed Al Jarallah [a], Zhanna Kobalava [c], Raja Dashti [a], Ibrahim Al Zakwani [d,e], Joud Al Balool [f], Gary Tse [g], Parul Setiya [h], Peter A. Brady [i], Ahmad Al-Saber [j], Govindan Vijayaraghavan [k]

[a] Department of Cardiology, Sabah Al Ahmed Cardiac Centre, Kuwait City, Kuwait
[b] Department of Cardiology, Badr Al Samaa Hospital, Ruwi, Muscat, Oman
[c] Department of Internal Diseases with Courses of Cardiology and Functional Diagnostics, Peoples' Friendship University of Russia (RUDN University), Moscow, Russia
[d] Department of Pharmacology & Clinical Pharmacy, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Oman
[e] Gulf Health Research, Muscat, Oman
[f] Faculty of Medicine, Kuwait University, Jabria, Kuwait
[g] Cardiovascular Analytics Group, Hong Kong, China, Tianjin Key Laboratory of Ionic-Molecular Function of Cardiovascular Disease, Department of Cardiology, Tianjin Institute of Cardiology, Second Hospital of Tianjin Medical University, Tianjin, 300211, China
[h] Department of Agrometeorology, College of Agriculture, G.B.Pant University of Agriculture & Technology, Pantnagar, Uttarakhand, India
[i] Department of Cardiology, Illinois Masonic Medical Center, Chicago, IL, USA
[j] Department of Mathematics and Statistics, University of Strathclyde, Glasgow, G1 1XH, UK
[k] Department of Cardiology, Kerala Institute of Medical Sciences, Kerala, India

A B S T R A C T

Background: The aim of this study was to validate R-heart failure (R-hf) risk score in ischemic heart failure patients.
Methods: We prospectively recruited a cohort of 179 ischemic and 107 non-ischemic heart failure patients. This study mainly focused on ischemic heart failure patients. Non-ischemic heart failure patients were included for the purpose of validation of the risk score in various heart failure groups. Patients were stratified in high risk, moderate risk and low risk groups according to R-hf risk score.
Results: A total of 179 participants with ischemic heart failure were included. Based on R-hf risk score, 82 had high risk, 50 had moderate risk and 47 had low risk heart failure scores. More than half of the patients having R-hf score of <5 had renal failure (n = 91, 50.8%) and anemia (n = 99, 55.3%). Notably, HFrEF was more prevalent in patients with high risk score (74, 90.2%). Patients with high risk score had significantly higher creatinine (2.63 ± 1.96, p < 0.001), Troponin-T HS (59.9 ± 38.0, p < 0.001) and PRO BNP (17842 ± 6684, p < 0.001) when compared to patients with low and moderate risk score. Patients with low risk score had significantly higher Hb (13.2 ± 1.85, p < 0.001), Albumin (3.69 ± 0.42, p < 0.001) and GFR (90.0 ± 8.04, p < 0.001). A R-hf score of <5 was a significant predictor of mortality in ischemic (OR = 50.34; 95% CI [16.94–194.00, p < 0.001]) and non-ischemic (OR = 46.34; 95% CI [12.97–225.39], p < 0.001) heart failure patients.
Conclusions: Lower R-hf risk score is a significant predictor of mortality in ischemic and non-ischemic heart failure patients. Risk score can be accessed at https://www.hfriskcalc.in.

1. Introduction

Heart failure (HF) is a clinical syndrome evident by structural or functional cardiac abnormalities, accompanied by elevated levels of natriuretic peptides [1]. With the advancement of therapeutic innovations in cardiac patients, an increasing prevalence of heart failure is marked in the growing aging population [2]. Despite significant improvements in the management of heart failure, the associated morbidity and mortality of heart failure remains to be high [3]. Previous studies have focused on determining the prognosis of patients with acute

---

decompensated HF, yet this data lack applicability to patients with chronic HF treated in an ambulatory setting [4]. Prognostication is specifically challenging in patients with chronic heart failure, as the clinical course varies at an individual level and at the spectrum of severity [5]. Due to the rapidly increasing prevalence of chronic HF, in part due to the ageing population, accurate assessment of prognosis is essential to drive clinical decision-making in terms of advanced therapies and end of life planning. Notably, chronic heart failure patients tend to overestimate their life expectancy when compared to model-based strategies, further delineating the necessity of an objective survival-predicting tool that can thereby guide shared-decision making [6]. Multivariate models have been established to predict mortality outcomes in heart failure patients [7,8]. However, these models generally incorporate complex mathematical formulas for risk assessment, requiring sophisticated techniques for calculation [6]. In contrast, the R-heart failure (R-hf) score is a unique risk-predicting tool that can be incorporated in risk assessment of patients with chronic heart failure with reduced ejection fraction (HFrEF) [9,10]. The purpose of this study is to validate the R–Hf risk score in patients with chronic ischemic heart failure.

2. Methods

We examined a subset of patients admitted with heart failure to the Kerala Institute of Medical Sciences, Trivandrum over a 2-year period from June 1, 2012. This study was a prospective descriptive design enrolling a cohort of 179 ischemic and 107 non-ischemic heart failure patients. This study mainly focused on ischemic heart failure patients. Non-ischemic heart failure patients were included for the purpose of validation of the risk score in various heart failure groups [11]. Patients were stratified in three group according to the R-hf risk score. Participants signed an informed consent prior to enrollment. A diagnosis of HF was made based upon Framingham criteria and by left ventricular ejection fraction (LVEF) with echocardiography using Simpson's biplane method. Patients were evaluated clinically and all underwent routine cardiac investigation, including cardiac biomarkers, renal function, full blood count and echocardiography. Follow-up was done at 90 days and at 2 years via hospital visits and/or telephone call. NT Pro BNP and high

sensitivity troponin T (trop T HS) levels were measured in all patients as a part of diagnostic purposes. R-hf score was calculated for all patients for risk stratification [Fig. 1]. This work has been reported in line with the STROCSS criteria [12].

2.1. Definitions

Ischemic heart failure (IHD-HF) was defined as a history of chronic stable angina or acute coronary syndrome or with evidence of significant coronary artery disease by coronary angiogram. Optimal medical management was defined as prescribed a combination of angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), beta-blockers, and aldosterone receptor blockers in patients with left ventricular systolic dysfunction (LVSD, EF <45%).

Based upon the 2021 ESC guidelines [13], heart failure with reduced ejection fraction (HFrEF) was defined as:

1. Symptoms ± signs of heart failure
2. Left ventricular ejection fraction ($\leq$40%)

Heart failure with mildly reduced ejection fraction (HFmrEF) was defined as:

1. Symptoms ± signs of heart failure
2. Left ventricular ejection fraction (41–49%)

The R-hf risk score (https://www.hfriskcalc.in.) is derived from the product of estimated glomerular filtration rate [eGFR (mL/min)], left ventricular ejection fraction [LVEF (%)], and haemoglobin levels [Hb (g/dL)] divided by *N*-terminal pro-brain natriuretic peptide [NT proBNP (pg/mL)]. A R-hf score of <5 indicates high risk, 5-<10 moderate risk, 10-<50 low risk [9,10]. The study was registered (KIMS1306/12), the ethical committee for health coordination and medical research at the Kerala Institute of Medical Sciences approved the study protocol and accepted. This study is registered with Research Registry UIN: researchregistry8148.
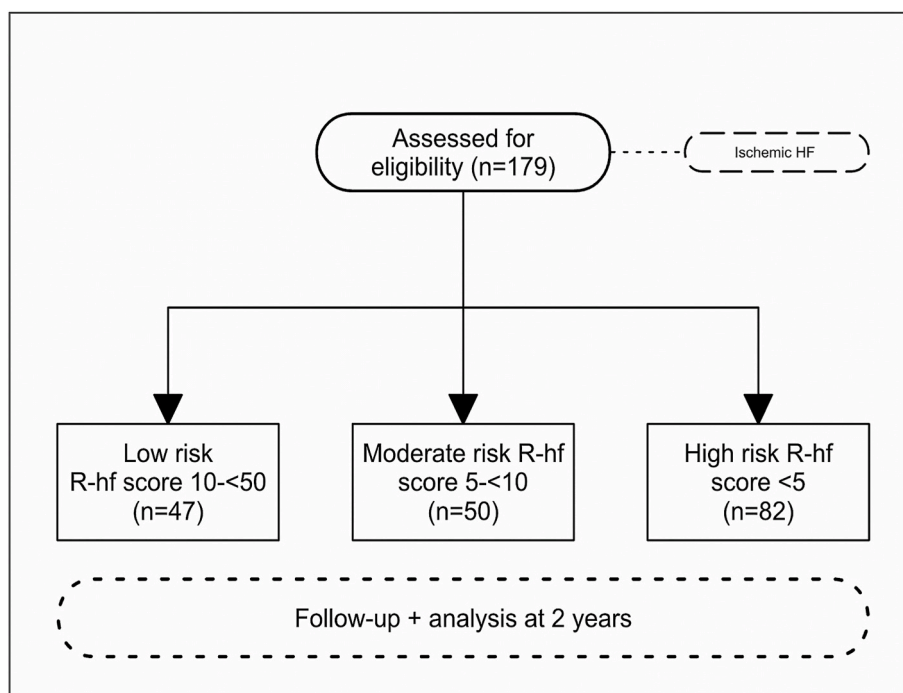

Fig. 1. Flowchart demonstrates population enrollment.

3. Statistical analysis

Based on risk assessment, patients were classified into the categories of high risk, moderate risk and low risk. Qualitative and quantitative variables were summarized by frequency with percentage and mean with Standard Deviation (SD), respectively. Chi-square test was used to determine the association amongst qualitative variables and ANOVA was employed to check the differences between quantitative variables in the independent groups. Logistic regression was used to determine the impact of Rhf-Risk Score and HF on mortality. The logistic regression analysis produced the odds ratios (OR) and corresponding 95% confidence intervals with p value. Finally, Walch test with post hoc Bonferroni test was conducted to examine the association between Rhf-score and Ejection fraction (EF) and Rhf-score with PRO-BNP, grouped by alive versus dead. A 5% significance level was used to determine the significance of the results. R and SPSS software version 27 (SPSS Inc., Chicago, IL, USA) was used for the analysis of the dataset.

4. Results

A total of 179 patients with ischemic heart failure were analyzed. Of these, 78% were males and 22% were females. The mean age of the patients with high (68.8 ± 10.4) and moderate (67.9 ± 8.92) risk was greater than the mean age of patients deemed low (61.3 ± 10.2) risk. Approximately 17% of patients with high risk, 22% of the patients with moderate risk and 4% of the patients with low risk were hypothyroid. More patients in high risk (76%) group had renal failure when compared to moderate (38%) and low risk (21%) patients. More patients in the high risk (74%) group had anemia compared to patients with moderate (54%) and low risk (23%) groups. HFrEF was more prevalent in patients with high (90%) and moderate (98%) risk as compared to patients deemed low risk (81%). HFmrEF was more prevalent in patients with low risk (19%) and high risk (10%) as compared to the patients having moderate risk score (2%) [Table 1].

Laboratory parameters amongst patients having high, moderate and low risk were compared. Patients in high risk cohort had significantly higher creatinine (2.63 ± 1.96, p < 0.001), TROP-T HS (59.9 ± 38.0, p < 0.001) and PRO BNP (17842 ± 6684, p < 0.001) as compared to the patients in low and moderate risk cohort. In comparison, patients in the low risk cohort had significantly higher Hb (13.2 ± 1.85, p < 0.001), ALBUMIN (3.69 ± 0.42, p < 0.001) and GFR (90.0 ± 8.04, p < 0.001). [Table 2].

Medications prescribed amongst high, moderate and low risk cohort were also compared with the only significant difference being the frequency of Warfarin, prescribed to 24% of the patients in high risk cohort, 22% of the patients in the moderate risk cohort and 45% in the low risk cohort [Table 3]. Multinominal logistic regression analysis was conducted to determine the impact of Rhf-Risk Score on all-cause mortality in ischemic heart failure patients. This revealed that high risk Rhf-score (OR = 50.34; 95% CI [16.94–194.00], p < 0.001) was associated with cumulative all-cause mortality [Table 4]. Multinominal logistic regression analysis performed on non-ischemic heart failure patients also shown statistically significant results (OR = 46.34; 95% CI [12.97–225.39], p < 0.001) in terms of cumulative all-cause mortality associated with high risk Rhf score [Table 5].

Fig. 2 illustrates the association between Rhf-score and ejection fraction for the group of alive and dead patients. The result of Welch test ($F_{welch}(2,39.04) = 5.55$, p = 0.008, $E(\omega_p^2) = 0.18$, C.I. [2.11e-03, 0.37]) indicated a significant association between Rhf-score and ejection fraction. Further, Bonferroni test was conducted for the pair wise comparison of Rhf-score with ejection fraction. The finding shows significant difference in mean ejection fraction amongst the pairs low risk-moderate risk (p = 0.026) for alive patients only.

Fig. 3 illustrates the association between Rhf-score and PRO BNP for the group of alive and dead patients. The result of Welch test indicated

significant association between Rhf-score and PRO BNP for the group of alive ($F_{welch}(2,32.01) = 51.19$, p < 0.001, $E(\omega_p^2) = 0.74$, C.I. [0.56, 0.83]) and deceased ($F_{welch}(2,7.32) = 104.51$, p < 0.001, $E(\omega_p^2) = 0.95$, C.I. [0.81, 0.98]) patients. Further, Bonferroni test of pair wise comparison revealed a significant difference in the mean value of PRO BNP amongst the pairs low risk-moderate risk (p = 0.000), low risk-high risk (p = 0.000) and moderate risk-high risk (p = 0.005) for alive patients. Whereas, for deceased patients a significant difference in the mean value of PRO BNP was observed amongst the pairs low risk-high risk (p = 2.37e-06) and moderate risk-high risk (p = 0.000).

Table 1

Demographic and clinical characteristics of patients of the Ischemic Heart Failure cohort stratified by R-hf risk score.

	[ALL]	High Risk	Moderate Risk	Low Risk	p-value
	N = 179	N = 82	N = 50	N = 47	
AGE, mean ± SD, years	66.6 (10.4)	68.8 (10.4)	67.9 (8.92)	61.3 (10.2)	<0.001
Male, gender	139 (77.7%)	59 (72.0%)	39 (78.0%)	41 (87.2%)	0.134
TOTAL HF RE ADMISSION	49 (27.4%)	24 (29.3%)	14 (28.0%)	11 (23.4%)	0.767
STEMI	116 (64.8%)	48 (58.5%)	33 (66.0%)	35 (74.5%)	0.186
NSTEMI	64 (35.8%)	32 (39.0%)	18 (36.0%)	14 (29.8%)	0.574
CABG	38 (21.2%)	20 (24.4%)	10 (20.0%)	8 (17.0%)	0.597
CVA	27 (15.1%)	14 (17.1%)	8 (16.0%)	5 (10.6%)	0.603
T2DM	132 (73.7%)	62 (75.6%)	37 (74.0%)	33 (70.2%)	0.798
HTN	116 (64.8%)	55 (67.1%)	35 (70.0%)	26 (55.3%)	0.268
HYPOTHYROID	27 (15.1%)	14 (17.1%)	11 (22.0%)	2 (4.26%)	0.040
HYPERURICEMIA	46 (25.7%)	21 (25.6%)	17 (34.0%)	8 (17.0%)	0.161
COPD	34 (19.0%)	14 (17.1%)	8 (16.0%)	12 (25.5%)	0.408
SMOKER	80 (44.7%)	32 (39.0%)	25 (50.0%)	23 (48.9%)	0.372
DLP	130 (72.6%)	60 (73.2%)	33 (66.0%)	37 (78.7%)	0.369
RENAL FAILURE	91 (50.8%)	62 (75.6%)	19 (38.0%)	10 (21.3%)	<0.001
ANEMIA	99 (55.3%)	61 (74.4%)	27 (54.0%)	11 (23.4%)	<0.001
AFib	18 (10.1%)	11 (13.4%)	4 (8.00%)	3 (6.38%)	0.410
CRT	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (2.13%)	0.263
ICD	6 (3.35%)	2 (2.44%)	2 (4.00%)	2 (4.26%)	0.765
Heart Failure Classification:					0.018
HFrEF	161 (89.9%)	74 (90.2%)	49 (98.0%)	38 (80.9%)	
HFmrEF	18 (10.1%)	8 (9.76%)	1 (2.00%)	9 (19.1%)	

Percentages might not add up to 100% due to rounding off. Analyses were performed using Student's t-test or Pearson's $\chi 2$ test, whenever appropriate. STEMI, ST-segment elevation myocardial infarction; NSTEMI, non ST-segment elevation myocardial infarction; CABG, coronary artery bypass graft; CVA, cerebrovascular accident; T2DM, Type 2 Diabetes Mellitus; HTN, hypertension; COPD, chronic obstructive pulmonary disease; DLP, dyslipidemia; Afib, atrial fibrillation; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; HFrEF, heart failure (HF) with reduced ejection fraction (EF) (≤40%); HFmrEF, HF with mildly reduced EF (41–49%).
Data were given as n (%) unless specified otherwise. SD, standard deviation.

Table 2
Laboratory findings of the Ischemic Heart Failure cohort stratified by R-hf risk score.

	[ALL]	High Risk	Moderate Risk	Low Risk	p-value
	N = 179	N = 82	N = 50	N = 47	
HBA1C (%)	8.68 (5.60)	8.52 (2.04)	8.17 (1.98)	9.51 (10.4)	0.472
Hb (gm/dl)	11.9 (2.06)	11.3 (1.95)	11.7 (1.93)	13.2 (1.85)	<0.001
T.CHOLESTEROL (mg/dl)	157 (42.4)	156 (40.4)	156 (47.0)	159 (41.3)	0.938
TG (mg/dl)	104 (36.9)	106 (38.7)	102 (37.6)	103 (33.4)	0.839
HDL (mg/dl)	38.5 (9.50)	39.0 (9.09)	38.7 (10.1)	37.4 (9.61)	0.638
LDL (mg/dl)	96.1 (35.6)	94.9 (33.0)	95.2 (40.7)	99.0 (34.7)	0.805
VLDL (mg/dl)	19.3 (7.03)	19.3 (6.86)	19.0 (7.58)	19.7 (6.86)	0.893
CREATNINE (mg/dl)	1.89 (1.52)	2.63 (1.96)	1.33 (0.46)	1.19 (0.47)	<0.001
ALBUMIN (g/dl)	3.51 (0.46)	3.32 (0.46)	3.65 (0.39)	3.69 (0.42)	<0.001
TROPT HS (ng/L)	49.0 (35.2)	59.9 (38.0)	40.5 (29.3)	39.0 (30.8)	0.001
PRO BNP (pg/ml)	10464 (8241)	17842 (6684)	5231 (1385)	3161 (906)	<0.001
CRP (mg/L)	23.3 (33.7)	23.2 (23.7)	23.0 (47.2)	23.8 (34.9)	0.994
GFR (ml/min)	81.0 (19.6)	71.1 (24.5)	88.9 (6.44)	90.0 (8.04)	<0.001

Data were given as n (%) unless specified otherwise.
HbA1c, hemoglobin A1C; Hb, hemoglobin; T cholesterol, total cholesterol; TG, triglycerides; HDL, high density lipoprotein; LDL, low density lipoprotein; VLDL, very-low-density lipoprotein; TROPT HS, high sensitivity troponin T; PRO BNP, prohormone of brain natriuretic peptide; CRP, *C*-reactive protein; GFR, glomerular filtration rate.

5. Discussion

This study is the first to use R-hf risk score comparison (a derivative of e-GFR, EF, Hb, and NT proBNP) to predict mortality outcomes in a cohort of patients with ischemic and non-ischemic heart failure. Using this risk score, patients deemed high-risk had significantly increased rate of all cause mortality compared to low- and moderate-risk cohorts. The application of such model into prognostication will aid in risk stratification, potentially identifying patients at the end of the spectrum requiring advanced medical therapies. The low R-hf score clearly reflects the risk associated with myocardial damage and the score is not influenced by the etiology of heart failure.

Previous risk prediction models that do not include EF or renal parameters predict a lower mean death rate than expected. The R-hf risk score model was successful in predicting the prognosis and mortality of HFrEF patients. Specifically, a R-hf score <5 is considered poor prognosis and this has been demonstrated in the current study. However, given our population, this score is exclusively applied to the ischemic heart failure cohort, which is largely a South-Indian population. By integrating only four variables in the risk score (ejection fraction (EF,%), estimated glomerular filtration rate (e-GFR, mL/min), hemoglobin levels (Hb, g/dL), and *N*-terminal prohormone of brain natriuretic peptide (NT-proBNP, pg/mL) this offers a simple yet robust tool. For physicians, the application and the calculator is available online and is easily accessible at https://www.hfriskcalc.in [9,10].

Previous risk models have established risk factors and prognosis in a variety of heart failure settings including acute heart failure, heart failure with preserved ejection fraction along with heart failure with reduced ejection fraction. These models include a variety of parameters that aid in predicting the morbidity and mortality in heart failure. For example, the Meta-Analysis Global Group in Chronic Heart Failure Risk

Table 3
Discharge medications of the Ischemic Heart Failure cohort stratified by R-hf risk score.

	[ALL]	High Risk	Moderate Risk	Low Risk	p-value
	N = 179	N = 82	N = 50	N = 47	
ACE	44 (24.6%)	18 (22.0%)	11 (22.0%)	15 (31.9%)	0.397
ARB	18 (10.1%)	6 (7.32%)	4 (8.00%)	8 (17.0%)	0.194
BETA BLOCKERS	90 (50.3%)	46 (56.1%)	23 (46.0%)	21 (44.7%)	0.356
ZYTZNIX	32 (17.9%)	16 (19.5%)	9 (18.0%)	7 (14.9%)	0.805
LASIX	82 (45.8%)	34 (41.5%)	27 (54.0%)	21 (44.7%)	0.368
DYTOR	78 (43.6%)	35 (42.7%)	18 (36.0%)	25 (53.2%)	0.228
ALDACTONE	72 (40.2%)	37 (45.1%)	15 (30.0%)	20 (42.6%)	0.212
EPILERINONE	20 (11.2%)	9 (11.0%)	4 (8.00%)	7 (14.9%)	0.558
NITRATES	44 (24.6%)	19 (23.2%)	16 (32.0%)	9 (19.1%)	0.313
RANOLAZINE	17 (9.50%)	7 (8.54%)	5 (10.0%)	5 (10.6%)	0.898
IVABRADINE	16 (8.94%)	10 (12.2%)	2 (4.00%)	4 (8.51%)	0.275
CCB	29 (16.2%)	14 (17.1%)	8 (16.0%)	7 (14.9%)	0.948
MINIPRESS	14 (7.82%)	5 (6.10%)	3 (6.00%)	6 (12.8%)	0.351
WARF	52 (29.1%)	20 (24.4%)	11 (22.0%)	21 (44.7%)	0.022
ECOSPIRIN	150 (83.8%)	67 (81.7%)	42 (84.0%)	41 (87.2%)	0.714
CLOPIDOGREL	137 (76.5%)	61 (74.4%)	37 (74.0%)	39 (83.0%)	0.478
STATINS	131 (73.2%)	61 (74.4%)	40 (80.0%)	30 (63.8%)	0.188
AMIODARONE	35 (19.6%)	16 (19.5%)	11 (22.0%)	8 (17.0%)	0.826
FEBU/ ALLOPURINOL	20 (11.2%)	11 (13.4%)	6 (12.0%)	3 (6.38%)	0.464
PPI	13 (7.26%)	6 (7.32%)	2 (4.00%)	5 (10.6%)	0.431

Notes: ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; IV, intravenous; WARF, warfarin; PPI, proton-pump inhibitors.
Data were given as n (%) unless specified otherwise.

Table 4
Impact of R–Hf risk score on mortality in ischemic heart failure patients.

Mortality:		Alive	Dead	Univariate aOR (95% CI, aP-value)	Multivariate logistic regression aOR (95% CI, aP-value)
Rhf-Risk Score	1-Low Risk	43 (91.5)	4 (8.5)	–	–
	2-Moderate Risk	46 (92.0)	4 (8.0)	0.93 (0.21–4.18, p = 0.927)	1.00 (0.22–4.69, P = 0.996)
	3-High Risk	15 (18.3)	67 (81.7)	48.02 (16.51–178.73, p < 0.001)	50.34 (16.94–194.00, **P < 0.001**)
HF	HFrEF	94 (58.4)	67 (41.6)	0.89 (0.33–2.45, p = 0.818)	0.69 (0.14–3.06, P = 0.638)

Notes: Multivariable analyses were conducted using logistic regression models utilizing the simultaneous method. The models were adjusted for R-hf risk score and HF. Percents are row percentages. Abbreviations: aOR, adjusted odds ratio; aP-value, adjusted p-value; CI, confidence interval.

Table 5

Impact of R–Hf risk score on mortality in Non-ischemic heart failure patients.

Mortality:		Alive	Dead	Univariate aOR (95% CI, aP-value)	Multivariate logistic regression aOR (95% CI, aP-value)
Rhf-Risk Score	1-Low Risk	44 (91.7)	4 (8.3)	–	–
	2-Moderate Risk	18 (85.7)	3 (14.3)	1.83 (0.33–9.14, p = 0.456)	2.20 (0.39–11.97, p = 0.349)
	3-High Risk	9 (23.7)	29 (76.3)	35.44 (10.97–144.21, p < 0.001)	46.34 (12.97–225.39, p < **0.001**)
HF	HFrEF	61 (66.3)	31 (33.7)	1.02 (0.33–3.50, p = 0.978)	0.32 (0.06–1.69, p = 0.173)

Notes: Multivariable analyses were conducted using logistic regression models utilizing the simultaneous method. The models were adjusted for R-hf risk score and HF. Percents are row percentages. Abbreviations: aOR, adjusted odds ratio; aP-value, adjusted p-value; CI, confidence interval.

Score (MAGGIC) has been validated to predict outcomes like heart failure and cardiovascular hospitalizations along with all cause mortality in heart failure with preserved ejection fraction (HFpEF). This scoring system incorporates 13 clinical variables, and has been validated in 407 patients with HFpEF [14]. Using the R-hf risk score, however, the prognosis of patients with heart failure has been validated exclusively in ischemic heart failure, using four simple variables.

The Get With the Guidelines–Heart Failure (GWTG-HF) risk score is used to predict in-hospital mortality in patients with heart failure. This risk score has been validated in heart failure patients with reduced and preserved ejection fraction [15–17]. The increase in plasma B-type natriuretic peptide level is directly proportional to the severity and grade of the GWTG-HF risk score. This correlation was also found in the present study, since bNP levels were a significant contributor to mortality in our cohort. Other scoring systems have been validated in patients with acute heart failure, which usually lack applicability in chronic heart failure patients. The AHEAD score by Chen et al. has been related to an increased risk of all cause mortality in an Asian population of acute heart failure with either reduced or preserved ejection fraction [18]. Along with an increasing AHEAD score, patients had lower

hemoglobin and estimated GFR and subsequently an increased risk of mortality. Similarly, the R-hf risk score includes those variables when assessing prognosis in ischemic heart failure patients. Another simple tool is the ADHERE score, which includes blood urea nitrogen, systolic blood pressure, and creatinine and has been validated in hospitalized HF patients to predict in-hospital and early post discharge mortality [19]. When we compare R-hf risk score with ADHERE CART, the pattern of readmission and mortality was similar. The ESCAPE risk model uses a set of variables to identify high-risk patients at discharge. This allows identification of patients at high risk that would benefit from intensive strategies and advanced medical techniques including implantable cardioverter-defibrillators, LV assist devices, and cardiac transplantation [20]. Other prognostic models have additionally been identified to predict all cause mortality, including HF-action model and CORONA model. These models are yet to be validated, in an attempt to contribute in risk stratification of patients admitted with heart failure [21,22]. Furthermore, the Seattle heart failure model is a complex tool, which includes 24 variables, used to predict 1-, 2-, and 3- year survival in heart failure patients [23].

As previously mentioned, the r-HF risk score, which incorporates eGFR, LVEF, hemoglobin, and NT proBNP levels, is a practical tool used in prognosis of patients with ischemic heart failure. Multiple studies have demonstrated the prognostic role of the latter variables in different cohorts. BNP and NT-pro BNP were found to be the most predictive measure for the diagnosis and prognosis of patients with heart failure in the Acute Decompensated Heart Failure National Registry [24]. Furthermore, in a prospective study of patients admitted with severe congestive heart failure, a higher level of NT-proBNP was significantly associated with mortality [25]. The role of NT-proBNP in prognosis was additionally supported by the ACC/AHA guidelines on heart failure, which recommend measuring its levels at admission and during discharge to allow predicting mortality and rehospitilization [26].

The prognostic significance of a lower hemoglobin level was additionally determined to increase mortality in patients with heart failure with reduced and preserved ejection fraction [27]. The pathophysiology behind this involves adverse myocardial remodeling secondary to reduced oxygen delivery to metabolizing tissues [28]. The recent ESC guidelines (2021) recommend periodic screening for iron deficiency anemia, along with ferric carboxymaltose supplementation in patients with low hemoglobin and LVEF $\leq$45 [29]. Moreover, the prognostic impact of impaired renal function have additionally been validated in
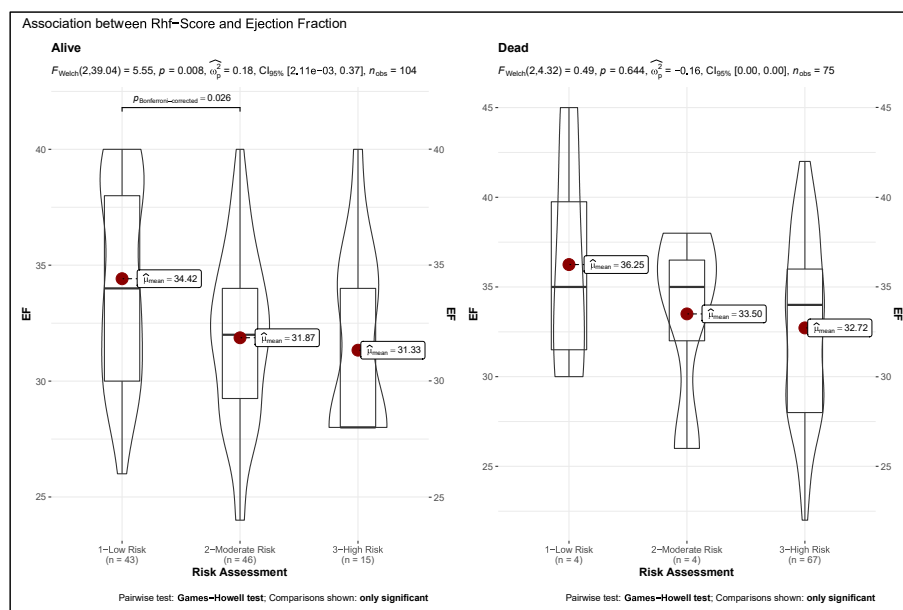

Fig. 2. Illustrates the results of association of Rhf-score with ejection fraction for the group of alive and dead patients.
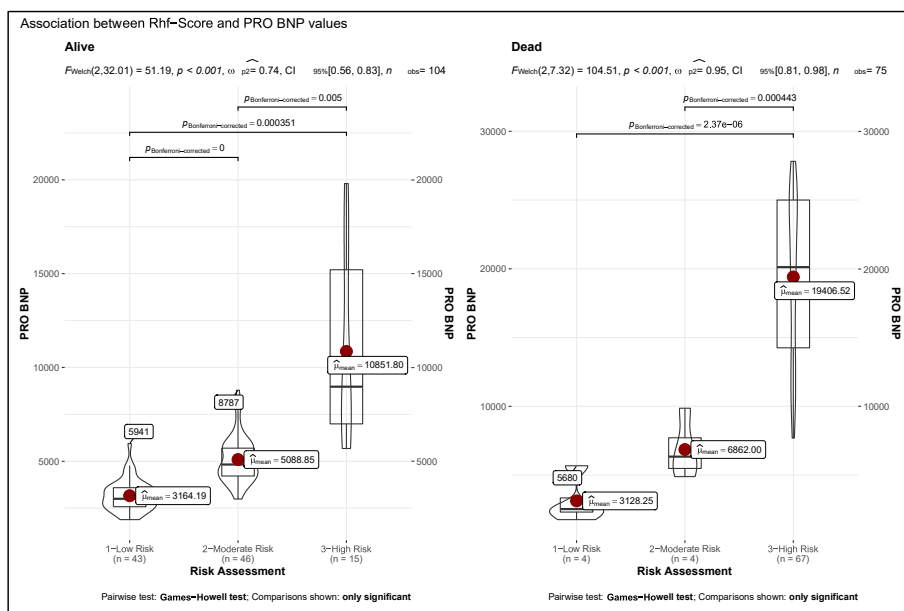
Fig. 3. Illustrates the results of association of Rhf-score with PRO BNP for the group of alive and dead patients.

patients with acute heart failure, where lower eGFR levels demonstrate an independent increase in mortality rates [30]. These results emphasize that important prognostic clinical parameters are taken into account in the R-hf score, allowing an easily accessible scoring tool that calculates mortality risk using well proven prognostic variables [Table 6].

This study has a few limitations. First, this is a validation study on patients admitted to a tertiary centre with established diagnosis of ischemic heart failure. Hence, clinical inferences and implications may not be applicable to other general populations where other factors could modify the results. In addition, only patients above the age of 40 were applicable for enrollment, further limiting the sample size of the study population.

6. Conclusions

In patients with Ischemic and non-ischemic heart failure the R-hf risk score is a useful and simple tool to predict all-cause mortality. Low R-hf risk score demonstrates the risk associated with myocardial damage and the score is not influenced by the etiology of heart failure. Further large cohort study is needed to substantiate these findings and to determine the impact of the R-hf score on HF treatment strategies and outcomes in other more diverse populations. Rajan's-hf risk score calculator is easily accessible at https://www.hfriskcalc.in.

Table 6
Selected prognostic models in heart failure *versus* R-hf risk score.

Prognostic model	Key covariates	Outcome
Meta-Analysis Global Group in Chronic Heart Failure Risk Score (MAGGIC) [13]	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) [14–16]	Age, systolic blood pressure, heart rate, blood urea nitrogen, sodium, chronic obstructive pulmonary disease, race	Predictor of in hospital mortality
AHEAD Score [17]	A: atrial fibrillation, H: hemoglobin <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 & preserved EF
ADHERE Score [18]	Blood urea nitrogen, systolic blood pressure, creatinine	Predictor of In hospital and 30–180 day mortality in hospitalized HF patients
ESCAPE risk model and discharge score [19]	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 [20]	Exercise duration on CPX test, serum urea nitrogen, female sex, BMI	All-cause mortality
CORONA Model [21]	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) [22]	Age, ejection fraction, systolic blood pressure, weight, gender, NYHA class, etiology, furesomide (mg), torsemide (mg), bumetidine (mg), metolazone (mg), hydrochlorothiazide (mg), allopurinol, statin, ACE inhibitor, beta blocker, K sparing diuretic, devices, sodium, total cholesterol, hemoglobin, lymphocytes, uric acid	Estimates 1-, 2-, 3- year survival in heart failure patients
R-hf score	eGFR, left ventricular ejection fraction, hemoglobin, *N*-terminal BNP	Identifies high-risk heart failure patients

ADHERE: Registry for Acute Decompensated Heart Failure Patients; ACE: angiotensin converting enzyme; apoA-1: apolipoprotein A1; BMI: body mass index; BNP: *N*-terminal pro-B-type 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; K: potassium; LVEF: left ventricular ejection fraction; NT-proBNP: *N*-terminal pro-hormone brain natriuretic peptide; NYHA: New York heart association.

Ethics approval and consent to participate

This study was approved by the ethics committee and Ministry of Health Kuwait.

Funding statement

No funding available for this article.

Author's contributions

RR, SOS and MAJ participated with both the analysis and writing of the article. KZD & RD supported with data analysis and manuscript drafting. AAS & IAZ was in charge of both statistical analysis and manuscript review. RD was involved in the data analysis and manuscript writing.

Consent for publication

Patient consented was not mandated for this retrospective observational study. Permission to reproduce material from other sources: No material from other sources is included in this study.

Availability of data and materials

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.

Declaration of competing interest

The authors declare that they have no competing interests.

List of Abbreviations

ACC	American College of Cardiology
ACEIs	Angiotensin-converting enzyme inhibitors
ARB	Angiotensin receptor blocker
ADCHF	Acute decompensated chronic heart failure
AHF	Acute heart failure
AHA	American Heart Association
aOR	Adjusted Odds ratio
ARBs	Angiotensin II receptor blockers
BMI	body mass index
CABG	coronary artery bypass graft procedure
CCBs	calcium channel blockers
CRF	Case-record form
CAD	Coronary artery disease
DM	Diabetes mellitus
EF	Ejection fraction
eGFR	Estimated glomerular filtration rate
ESC	European Society of Cardiology
GDMT	guideline directed medical therapy
GWTG-HF	Get With The Guidelines Heart Failure Risk Score
Hb	haemoglobin
HF	heart failure
HF*mr*EF	Heart failure with *mid-range*
HF*p*EF	Heart failure with *preserved*
HF*r*EF	Heart failure with *reduced*
IHD	ischemic heart disease
LVEF	Left ventricular ejection fraction
LVSD	left ventricular systolic dysfunction

NT-proBNP	*N*-terminal pro-B-type natriuretic peptide
MACE	Major adverse cardiovascular events
OR	odds ratio
OLS	Ordinary least squares
PCI	percutaneous coronary intervention
PVD	peripheral vascular disease
ROC	Receiver operating characteristics
R-hf	R-heart failure
SD	standard deviation
TROPT HS	high sensitivity troponin T

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104333.

References

[1] B. Bozkurt, A. Coats, H. Tsutsui, et al., Universal definition and classification of heart failure: a report of the heart failure society of America, heart failure association of the European society of Cardiology, Japanese heart failure society and writing committee of the universal definition of heart failure, Eur. J. Heart Fail. 23 (2021) 352–380.

[2] N. Conrad, A. Judge, J. Tran, H. Mohseni, D. Hedgecott, A.P. Crespillo, M. Allison, H. Hemingway, J.G. Cleland, J.J. McMurray, K. Rahimi, Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals, Lancet 391 (2018) 572–580.

[3] C.J. Taylor, J.M. Ordóñez-Mena, A.K. Roalfe, S. Lay-Flurrie, N.R. Jones, T. Marshall, F. Hobbs, Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population based cohort study, BMJ (Clin. Res. ed.) 364 (2019) l223.

[4] P. Ponikowski, A.A. Voors, S.D. Anker, H. Bueno, J.G. Cleland, A.J. Coats, V. Falk, J.R. González-Juanatey, V.P. Harjola, E.A. Jankowska, M. Jessup, C. Linde, P. Nihoyannopoulos, J.T. Parissis, B. Pieske, J.P. Riley, G.M. Rosano, L.M. Ruilope, F. Ruschitzka, F.H. Rutten, P. van der Meer, 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC, Eur. J. Heart Fail. 18 (2016) 891–975.

[5] M. Metra, P. Ponikowski, K. Dickstein, J.J. McMurray, A. Gavazzi, C.H. Bergh, A. G. Fraser, T. Jaarsma, A. Pitsis, P. Mohacsi, M. Böhm, S. Anker, H. Dargie, D. Brutsaert, M. Komajda, & Heart Failure Association of the European Society of Cardiology, Advanced chronic heart failure: a position statement from the study group on advanced heart failure of the heart failure association of the European society of Cardiology, Eur. J. Heart Fail. 9 (6–7) (2007) 684–694.

[6] L. Allen, L. Stevenson, K. Grady, et al., Decision making in advanced heart failure, Circulation 125 (2012) 1928–1952.

[7] Seattle heart failure model, university of Washington. http://depts.washington.edu/shfm/. (Accessed 30 December 2020).

[8] K.D. Aaronson, J.S. Schwartz, T.M. Chen, K.L. Wong, J.E. Goin, D.M. Mancini, Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation, Circulation 95 (1997) 2660–2667.

[9] R. Rajan, M. Al Jarallah, Prognostic risk calculator for heart failure, Oman Med. J. 33 (2018) 266–267.

[10] Rajesh Rajan, Mohammed Al Jarallah, Ibrahim Al Zakwani, Raja Dashti, Bassam Bulbanat, Mustafa Ridha, Kadhim F. Sulaiman, Impact of R-hf risk score on all-cause mortality in acute heart failure patients in the Middle East, J. Card. Fail. 25 (8) (2019) S97.

[11] O.S. Suman, G. Vijayaraghavan, A.R. Muneer, N. Ramesh, S. Harikrishnan, N. KalyaginA, Long-term outcomes of patients admitted with heart failure in a tertiary care center in India, Indian Heart J. 70 (Suppl 1) (2018 Jul) S85–S89. Suppl 1.

[12] G. Mathew, R. Agha, for the STROCSS Group, STROCSS 2021: strengthening the Reporting of cohort, cross-sectional and case-control studies in Surgery, Int. J. Surg. 96 (2021), 106165.

[13] T.A. McDonagh, M. Metra, M. Adamo, R.S. Gardner, A. Baumbach, M. Böhm, H. Burri, J. Butler, J. Čelutkienė, O. Chioncel, J. Cleland, A. Coats, M.G. Crespo-Leiro, D. Farmakis, M. Gilard, S. Heymans, A.W. Hoes, T. Jaarsma, E.A. Jankowska, M. Lainscak, ESC Scientific Document Group, 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, Eur. Heart J. 42 (36) (2021) 3599–3726, https://doi.org/10.1093/eurheartj/ehab368.

[14] D. Jonathan, Rich 1, Jacob Burns 1, H. Benjamin, Freed 1, S. Mathew, Maurer 1, Daniel Burkhoff 1, J. Sanjiv, Shah 1, Meta-analysis global group in chronic (MAGGIC) heart failure risk score: validation of a simple tool for the prediction of morbidity and mortality in heart failure with preserved ejection fraction, J. Am. Heart Assoc. 7 (20) (2018 Oct 16), e009594, https://doi.org/10.1161/JAHA.118.009594.

[15] Lyle Melissa, Wan Siu-Hin, Murphree Dennis, Bennett Courtney, M Wiley Brandon, Barsness Gregory, Redfield Margaret, Jentzer Jacob, Predictive value of the get

with the guidelines heart failure risk score in unselected cardiac intensive care unit patients, J. Am. Heart Assoc. 9 (3) (2020 Feb 4), e012439.

[16] P.N. Peterson, J.S. Rumsfeld, L. Liang, N.M. Albert, A.F. Hernandez, E.D. Peterson, G.C. Fonarow, F.A. Masoudi, American Heart Association Get with the Guidelines-Heart Failure Program. A validated risk score for in-hospital mortality in patients with heart failure from the American Heart Association get with the guidelines program, Circ. Cardiovasc. Qual. Outcomes 3 (1) (2010 Jan) 25–32.

[17] Satoshi Suzuki, Akiomi Yoshihisa, Yu Sato, Yuki Kanno, Shunsuke Watanabe, Satoshi abe clinical significance of get with the guidelines–heart failure risk score in patients with chronic heart failure after hospitalization, J. Am. Heart Assoc. 7 (2018), e008316.

[18] Y.J. Chen, S.H. Sung, H.M. Cheng, W.M. Huang, C.L. Wu, C.J. Huang, P.F. Hsu, J. S. Yeh, C.Y. Guo, W.C. Yu, C.H. Chen, Performance of AHEAD score in an Asian cohort of acute heart failure with either preserved or reduced left ventricular systolic function, J. Am. Heart Assoc. 6 (2017), e004297.

[19] Sithu Win, Imad Hussain, B. Virginia, M. Shannon, Dunlay, M. Margaret, M. D. Redfield, Inpatient mortality risk scores and post-discharge events in hospitalized heart failure patients: a community-based study, Circ. Heart Fail 10 (7) (2017 Jul), e003926.

[20] M. Christopher, O'Connor, Vic Hasselblad, Rajendra H.Mehta, Gudaye Tasissa, Califf Robert M, Fiuzat Mona, Rogers Joseph G, Leier Carl V, Stevenson Lynne W, Triage after hospitalization with advanced heart failure: the ESCAPE risk model and discharge score, J. Am. Coll. Cardiol. (9) (2010 Mar 2) 55, https://doi.org/10.1016/j.jacc.2009.08.083.

[21] M. Christopher, O'Connor, David J. Whellan, Wojdyla Daniel, Eric Leifer, M. Robert, M.S. Clare, J. Stephen, Ellis, Lawrence J. Fine, L. Jerome, Fleg, Faiez Zannad, J. Steven, Keteyian, Dalane W. Kitzman, William E. Kraus, David Rendall, Pa-C, L. Ileana, M.D. Piña, S. Lawton, M.D. Cooper, Mona Fiuzat, PharmD, L. Kerry, PhD. Lee, Factors related to morbidity and mortality in patients with chronic heart failure with systolic dysfunction: the HF-ACTION predictive risk score model, Circ. Heart Fail 5 (1) (2012 Jan) 63–71.

[22] Wedel H, McMurray JJ, Lindberg M, Wikstrand J, Cleland JG, Cornel JH, Dunselman P, Hjalmarson A, Kjekshus J, Komajda M, Kuusi T, Vanhaecke J, Waagstein F; CORONA Study Group. Predictors of fatal and non-fatal outcomes in the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA): incremental value of apolipoprotein A-1, high-sensitivity C-reactive peptide and N-terminal pro B-type natriuretic peptide. Eur. J. Heart Fail., 11(3), 281–291.

[23] W.C. Levy, D. Mozaffarian, D.T. Linker, et al., The Seattle Heart Failure Model: prediction of survival in heart failure, Circulation 113 (11) (2006) 1424–1433.

[24] G.C. Fonarow, W.F. Peacock, C.O. Phillips, et al., Admission B-type natriuretic peptide levels and in-hospital mortality in acute decompensated heart failure, J. Am. Coll. Cardiol. 49 (2007) 1943–1950.

[25] F. Hartmann, M. Packer, A.J. Coats, M.B. Fowler, H. Krum, P. Mohacsi, J. L. Rouleau, M. Tendera, A. Castaigne, S.D. Anker, I. Amann-Zalan, S. Hoersch, H. A. Katus, Prognostic impact of plasma N-terminal pro-brain natriuretic peptide in severe chronic congestive heart failure: a substudy of the Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS) trial, Circulation 110 (13) (2004) 1780–1786.

[26] C.W. Yancy, M. Jessup, B. Bozkurt, J. Butler, D.E. Casey Jr., M.M. Colvin, et al., 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American heart association task force on clinical practice guidelines and the heart failure society of America, Circulation 136 (2017) e137–e161.

[27] I.S. Anand, Anemia and chronic heart failure implications and treatment options, J. Am. Coll. Cardiol. 52 (2008) 501–511, https://doi.org/10.1016/j.jacc.2008.04.044.

[28] B.N. Datta, M.D. Silver, Cardiomegaly in chronic anaemia in rats; gross and histologic features, Indian J. Med. Res. 64 (1976) 447–458.

[29] T.A. McDonagh, M. Metra, M. Adamo, R.S. Gardner, A. Baumbach, M. Böhm, H. Burri, J. Butler, J. Čelutkienė, O. Chioncel, J. Cleland, A. Coats, M.G. Crespo-Leiro, D. Farmakis, M. Gilard, S. Heymans, A.W. Hoes, T. Jaarsma, E.A. Jankowska, M. Lainscak, ESC Scientific Document Group, 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, Eur. Heart J. 42 (36) (2021) 3599–3726.

[30] A. Takagi, Y. Iwama, A. Yamada, K. Aihara, H. Daida, Estimated glomerular filtration rate is an independent predictor for mortality of patients with acute heart failure, J. Cardiol. 55 (2010) 317–321.