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A simple validated method for predicting the risk of hospitalization for worsening of heart failure in ambulatory patients: the Redin-SCORE

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Aims Prevention of hospital readmissions is one of the main objectives in the management of patients with heart failure (HF). Most of the models predicting readmissions are based on data extracted from hospitalized patients rather than from outpatients. Our objective was to develop a validated score predicting 1-month and 1-year risk of readmission for worsening of HF in ambulatory patients.

Methods and results A cohort of 2507 ambulatory patients with chronic HF was prospectively followed for a median of 3.3 years. Clinical, echocardiographic, ECG, and biochemical variables were used in a competing risk regression analysis to construct a risk score for readmissions due to worsening of HF. Thereafter, the score was externally validated using a different cohort of 992 patients with chronic HF (MUSIC registry). Predictors of 1-month readmission were the presence of elevated natriuretic peptides, left ventricular (LV) HF signs, and estimated glomerular filtration rate (eGFR) <60 mL/min/m^2. Predictors of 1-year readmission were elevated natriuretic peptides, anaemia, left atrial size >26 mm/m^2, heart rate >70 b.p.m., LV HF signs, and eGFR <60 mL/min/m^2. The C-statistics for the models were 0.72 and 0.66, respectively. The cumulative incidence function distinguished low-risk (<1% event rate) and high-risk groups (>5% event rate) for 1-month HF readmission. Likewise, low-risk (7.8%), intermediate-risk (15.6%) and high-risk groups (26.1%) were identified for 1-year HF readmission risk. The C-statistics remained consistent after the external validation (<5% loss of discrimination).

Conclusion The Redin-SCORE predicts early and late readmission for worsening of HF using proven prognostic variables that are routinely collected in outpatient management of chronic HF.

Keywords Score • Readmission • Heart failure • Death • Competing risk

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†The list of the REDINSCOR investigators is given in the Supplementary material online, *Appendix 2*.

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Introduction

Hospital admissions for worsening of heart failure (HF) entail a huge amount of spending of medical care resources and are predictive of increased mortality risk.[1,2] Thus, health programmes addressing the management of chronic diseases pursue the prevention of hospital readmissions by establishing appropriate personalized measures for patients at risk.[3]

A large number of clinical studies predicting hospitalization for worsening of HF have been reviewed in detail.[4,5] However, these models have not yet been successfully implemented in current clinical practice. Most of the available models were constructed based on administrative and clinical data extracted from hospital records at patient discharge, thereby not fully reflecting the ambulatory clinical condition. On the other hand, many of these studies reported the overall cause of readmission rather than the specific cause of hospitalization and, quite often, they had a limited sample size and the reported study variables were not always routinely available. An ideal risk model should, among others, overcome the sample size limitations, use currently available clinical data, accommodate ongoing variations of the clinical status of outpatients with HF, be validated, and have the potential to discriminate the 'high-risk' patients who will benefit from more intensive therapies from the 'low-risk' patients who will be appropriately managed with less intensive protocols.

This study aimed to develop a validated risk score to predict short-term (1 month) and long-term (1 year) hospitalizations for worsening of HF in ambulatory patients using precise variables that are currently collected in primary care practice.

Methods

Study population

This study includes two cohorts of patients. The first one is a derivation cohort comprised of 2507 patients with chronic HF enrolled in the Spanish Network for the Study of Heart Failure (REDINSCOR registry). This is a prospective, longitudinal, multicentre study designed to assess risk predictors of cardiac mortality and readmissions in ambulatory patients with HF.[6,7] Patients were consecutively recruited between January 2007 and January 2011 at HF clinics in 18 hospitals. Inclusion criteria were: (i) age older than 18 years; (ii) prior hospitalization for HF (>24 h) during the previous year; and (iii) the presence of at least one echocardiographic abnormality (LVEF ≤40%, LV end-diastolic diameter ≥60 mm, altered LV relaxation indicating diastolic dysfunction, or thickness of interventricular septum/LV posterior wall ≥14 mm). All patients were symptomatic (functional NYHA class II–IV) and were treated according to the established clinical guidelines.[8] Exclusion criteria were: (i) reversible acute HF; (ii) severe valvular disease amenable to surgical repair; (iii) right HF secondary to chronic cor pulmonale; or (iv) concomitant terminal disease. The validation cohort was the MUSIC (MUerte Súbita en Insuficiencia Cardíaca) study population[9] that consisted of 992 ambulatory patients with chronic HF prospectively enrolled from the specialized HF clinics of eight Spanish University Hospitals between April 2003 and December 2004. All these patients had symptomatic chronic HF (NYHA class II–III) and were treated according to current guidelines. This study included patients with either depressed (<45%) or preserved (>45%) LVEF. The latter were included if they had HF symptoms and a prior hospitalization for HF or some objective signs of HF confirmed by chest X-ray (findings of pulmonary congestion) and/or echocardiography (abnormal LV filling pattern and LV hypertrophy). Patients were excluded if they had recent acute coronary syndrome or severe valvular disease amenable to surgical repair. Patients with other concomitant diseases expected to reduce life expectancy were also excluded. Both cohorts complied with the Declaration of Helsinki, and the protocol was approved by the ethics committees of each participating centre. All patients gave written informed consent.

Study variables

Data were collected using specifically designed web forms (www.redinscor.org), and quality controls were undertaken every month. We recorded the following clinical variables at study inclusion: (i) demographic and previous clinical history; (ii) case history and physical examination; (iii) chest radiography; (iv) ECG; (v) echocardiography; (vi) laboratory blood tests; and (vii) medical treatment (*Appendix S1*). Standard criteria were used to define each variable. Anaemia was defined as haemoglobin <120 g/L for women and <130 g/L for men.[10] The plasma levels of NT-proBNP and BNP were dichotomized for cut-off values of BNP > 43 pmol/L (> 150 ng/L) or NT-proBNP > 118 pmol/L (> 1000 ng/L), respectively.[8] The eGFR was calculated using the CKD-EPI (Chronic Kidney Disease-Epidemiology Collaboration) method.[11] Left and right ventricular HF signs were defined according to the Framingham criteria.[12] Among them, we have included paroxysmal nocturnal dyspnoea, rales, orthopnoea, and third sound gallop as left HF signs, and neck vein distension, hepatojugular reflux, bilateral ankle oedema, ascitis, and hepatomegaly as right HF signs.

Follow-up

The follow-up data were obtained from the outpatient visits or from the event reports. Patients lost to follow-up (none at 1-month and 5 at 1-year) were censored in survival analysis. The reported events were reviewed by an ad hoc committee.[6]

Statistical analysis

Continuous variables were expressed as the mean ± standard deviation (SD) or as median (interquartile range) whenever appropriate. Differences in continuous variables were tested by analysis of variance (ANOVA) or Student's *t*-test for independent samples. Categorical variables are presented as frequency and percentage. Differences in the categorical variables were assessed by the χ^2 test or by Fisher's exact test. A multivariate analysis (Fine and Gray regression model) was built to assess the influence of the different risk predictors on survival.[13] The study endpoint for all regression analyses was the date of readmission due to HF at 1 month or at 1 year of follow-up. The competing event was death over the time period. Clinical meaningful variables showing a significant level in the univariate analysis ($P < 0.1$) were thereafter included in the multivariate model. A backward stepwise method was used to identify independent risk predictors with $P < 0.05$ for the inclusion or deletion criterion. We used competing risk methodology to estimate the probability of HF readmission or death over a time period of 1 month and 1 year using the cumulative incidence function (CIF) approach. To analyse the effect of baseline predictors on the CIF, we used the Fine–Gray regression model for

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Table 1 Baseline characteristics of 2507 outpatients with heart failure in the REDINSCOR registry (derivation cohort) and 992 outpatients in the MUSIC registry (validation cohort)

	REDINSCOR ($n = 2507$)	MUSIC ($n = 992$)	*P*-value
Demographic and clinical variables			
Male, *n*	1731 (69.0%)	718 (72.4%)	0.053
Age, years	66.7 (12.9)	64.6 (11.6)	<0.0001
Current smoker, *n*	399 (16.1%)	108 (10.9%)	<0.0001
History of dyslipidemia, *n*	1324 (53.3%)	494 (49.8%)	0.064
Diabetes mellitus, *n*	1058 (42.4%)	356 (35.9%)	<0.001
History of hypertension, *n*	1700 (68.2%)	565 (57.0%)	<0.0001
Prior AMI, *n*	934 (37.6%)	418 (42.1%)	0.013
Prior CABG or PTCA, *n*	817 (32.6%)	256 (25.8%)	<0.0001
Ischaemic aetiology, *n*	1192 (47.5%)	453 (45.7%)	0.315
Idiopathic dilated myocardiopathy, *n*	482 (19.2%)	226 (22.8%)	0.018
Atrial fibrillation/flutter, *n*	628 (25.1%)	191 (19.2%)	<0.001
Prior pacemaker, *n*	194 (7.7%)	83 (8.4%)	0.537
Prior cardiac resynchronization therapy, *n*	146 (5.8%)	37 (3.7%)	0.012
Prior implantable cardioverter defibrillator, *n*	370 (14.8%)	11 (1.1%)	<0.001
NYHA class III–IV, *n*	983 (39.2%)	214 (21.6%)	<0.0001
Heart rate, b.p.m.	76.4 (16.5)	71.4 (15.4)	<0.0001
Systolic blood pressure, mmHg	121.4 (20.9)	127.0 (21.7)	<0.0001
BMI, kg/m^2	28.7 (5.1)	28.5 (4.5)	0.255
Framingham left HF signs, *n*	1387 (56.3%)	336 (33.9%)	<0.0001
Framingham right HF signs, *n*	1077 (44.3%)	223 (23.5%)	<0.0001
Radiographic variables			
Signs of pulmonary venous hypertension	1053 (52.2%)	169 (17.0%)	<0.0001
Cardiothoracic ratio	0.59 (0.08)	0.55 (0.07)	<0.0001
Laboratory variables			
Haemoglobin, g/L	130.9 (19.9)	137.2 (16.0)	<0.0001
Natraemia, mEq/L	139.1 (4.2)	139.2 (3.2)	0.449
eGFR, mL/min/1.73 m^2	64.3 (24.0)	62.8 (20.4)	0.063
BNP > 43 pmol/L (> 150 ng/L) or NT-proBNP > 118 pmol/L (> 1000 ng/L)	1320 (67.4%)	379 (43.6%)	<0.0001
12-lead ECG variables			
QRS duration, ms	123.6 (36.1)	125.5 (35.1)	0.158
LBBB	573 (23.2%)	290 (29.2%)	<0.001
RBBB	152 (6.2%)	48 (4.8%)	0.130
Echocardiographic variables			
LVEF, %	35.7 (14.6)	36.9 (14.1)	0.028
LV end-diastolic diameter, mm	60.7 (10.7)	61.0 (10.2)	0.453
LA size, mm/m^2	25.2 (5.4)	24.6 (4.8)	0.002
Mitral regurgitation III/IV, *n*	453 (18.5%)	116 (11.7%)	<0.0001
Pharmacological treatment			
Beta-blocker	1997 (79.8%)	675 (68.0%)	<0.0001
Loop diuretics	2119 (84.7%)	698(70.4%)	<0.0001
ACE inhibitor or ARB	2124 (84.9%)	861 (86.8%)	0.151
Spironolactone	1108 (44.3%)	372 (37.5%)	<0.001
Eplerenone	279 (11.2%)	–	
Aspirin or clopidogrel	654 (26.1%)	391 (39.4%)	<0.0001
Acenocumarol or warfarin	795 (31.8%)	339 (34.2%)	0.172
Statins	1483 (59.2%)	489 (49.3%)	<0.0001
Digoxin	572 (22.9%)	298 (30.0%)	<0.0001
Amidarone	276 (11.0%)	105 (10.6%)	0.703
Ivabradine	42 (1.7%)	–	

Qualitative data are presented as absolute frequencies and percentages, and quantitative data as mean ± standard deviation.
AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; HF, heart failure; LA, left atrial; PTCA, percutaneous transluminal coronary angioplasty RBBB, right bundle branch block.

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Table 2 Univariable and multivariable predictors of 1-month readmission for worsening of heart failure

	Univariable HR (95% CI)	t	*P*-value	Multivariable HR (95% CI)	β-coefficient	t	*P*-value
Clinical variables							
History of dyslipidemia	0.65 (0.42–1.03)	1.84	0.066				
NYHA class III–IV	2.00 (1.21–3.31)	2.72	0.007				
Heart rate >70 b.p.m.	2.03 (1.17–3.51)	2.52	0.012				
Systolic blood pressure	0.98 (0.97–1.00)	2.17	0.030				
BMI	0.95 (0.90–1.00)	1.98	0.048				
Framingham left HF signs	4.01 (2.21–7.28)	4.58	<0.001	2.79 (1.46–5.33)	1.02	3.09	0.002
Framingham right HF signs	2.49 (1.56–3.96)	3.83	<0.001				
Laboratory variables							
Anaemia	2.13 (1.36–3.34)	3.30	0.001				
Natraemia (>138 mEq/L)	0.69 (0.44–1.08)	1.64	0.102				
eGFR <60 mL/min/1.73 m^2	2.20 (1.39–3.50)	3.34	0.001	1.87 (1.06–3.30)	0.63	2.16	0.031
BNP > 43 pmol/L (> 150 ng/L) or NT-proBNP > 118 pmol/L (> 1000 ng/L)	5.61 (2.25–14.0)	3.70	<0.001	3.95 (1.56–10.03)	1.37	2.89	0.004
Echocardiographic variables							
LA size >26 mm/m^2	1.54 (0.97–2.46)	1.82	0.069				
Mitral regurgitation III/IV	1.62 (0.98–2.66)	1.88	0.060				
Pharmacological treatment							
ACE inhibitor or ARB	0.43 (0.26–0.70)	3.35	0.001				
Statins	0.62 (0.40–0.96)	2.12	0.034				

BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; LA, left atrial.

the subdistribution hazard. The model included only the main effects of the predictors, without any interaction term. The proportionality assumption of the models was verified using time-dependent variables. The discriminative ability of the models was assessed by the C-statistic. The internal validity of the final predictive models was tested for 500 bootstrap re-samples, using the 'pec' package by Thomas A. Gerds[14] in the R Project for Statistical Computing. The calibration of models was assessed by the corresponding plots using the same package. To calculate the risk score for 1-month or 1-year readmission, each final predictor was multiplied by its β-coefficient (by 10 for 1-month follow-up and by 13 for 1-year follow-up and rounded to the nearest integer number). Therefore, the predictors of a particular patient ranged from 0 to 30. The CIF approach was used to separate populations of patients into different risk groups. Variables with >10% of missing data were not included in the models, except for BNP and NT-proBNP due to clinical relevance. A regression multiple imputation ($n = 5$) was applied whenever necessary.[15–17] A two-sided $P < 0.05$ was considered statistically significant. All analyses were performed using SPSS (v. 21.0) and STATA (v. 13.1) software.

External validation cohort

As the MUSIC registry did not have a 1-month follow-up visit, we used a logistic regression analysis with the prognostic variables of the Redin-SCORE model at 6-month and 1-year follow-up. Accordingly, using the fitted model, predictions for each subject were used to calculate the area under the receiver operating characteristic curve (AUC), which has been considered equivalent to the C-statistic.[18] A loss of <10% of the discriminative ability was accepted. In addition, the AUCs for both models were compared with the DeLong method[19] using the EPIDAT (v. 3.1) software. The calibration of the model and its ability to allocate patients into the different risk groups were evaluated by assessing the calibration plot and Hosmer–Lemeshow test for goodness of fit.

Results

Characteristics of the study population

The REDINSCOR registry included 2507 consecutive outpatients with chronic HF followed during a median period of 3.3 years. The clinical characteristics of these patients are summarized in *Table 1*. There was a predominance of males (69%), with a mean age of 66.7 years. In nearly half of the cases, the aetiology of HF was ischaemic heart disease. The mean LVEF was 35.7%, and 39.2% were in NYHA class III–IV. Preserved LVEF (≥50%) was observed in 433 patients (17.3%).

The MUSIC registry (external validation cohort) included 992 ambulatory patients with chronic HF followed during a median period of 3.6 years. As compared with the REDINSCOR cohort, patients in the MUSIC registry were younger, had fewer cardiovascular risk factors, lower incidence of coronary artery bypass (CABG) surgery, fewer right or left HF signs, and less pulmonary hypertension and mitral valve regurgitation. They also had better renal function and lower plasma levels of NT-proBNP.

Hospitalization for worsening of heart failure

Hospital readmissions for worsening of HF occurred in 78 cases (3.1%) at 1 month after inclusion and in 424 (16.9%) patients after 1 year of follow-up. The univariable and multivariable predictors of 1-month and 1-year readmission are summarized in *Tables 2* and *3*.

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Table 3 Univariable and multivariable predictors of 1-year readmission for worsening of heart failure

	Univariable HR (95% CI)	t	*P*-value	Multivariable HR (95% CI)	β-coefficient	t	*P*-value
Clinical variables							
Male	0.76 (0.62–0.92)	2.79	0.005				
Age	1.01 (1.01–1.02)	3.53	<0.001				
Current smoker	0.75 (0.57–1.00)	1.95	0.051				
Diabetes mellitus	1.37 (1.13–1.66)	3.24	0.001				
History of hypertension	1.26 (1.02–1.56)	2.13	0.033				
NYHA class III–IV	1.73 (1.41–2.13)	5.24	<0.001				
Heart rate >70 b.p.m.	1.42 (1.15–1.76)	3.26	0.001	1.37 (1.07–1.75)	0.32	2.52	0.012
Systolic blood pressure	0.99 (0.99–1.00)	2.14	0.032				
Framingham left HF signs	2.08 (1.69–2.57)	6.83	<0.001	1.50 (1.18–1.92)	0.41	3.27	0.001
Framingham right HF signs	1.85 (1.53–2.24)	6.26	<0.001				
Radiographic variables							
Cardiothoracic ratio	10.9 (2.9–40.7)	3.55	<0.001				
Signs of pulmonary venous hypertension	1.02 (0.97–1.08)	0.79	0.427				
Laboratory variables							
Anaemia	1.72 (1.42–2.08)	5.58	<0.001	1.38 (1.10–1.73)	0.32	2.77	0.006
eGFR <60 mL/min/1.73 m^2	1.68 (1.39–2.04)	5.31	<0.001	1.29 (1.03–1.62)	0.25	2.18	0.029
BNP > 43 pmol/L (> 150 ng/L) or NT-proBNP > 118 pmol/L (> 1000 ng/L)	2.61 (1.96–3.47)	6.59	<0.001	1.88 (1.39–2.56)	0.63	4.07	<0.001
Echocardiographic variables							
LA size >26 mm/m^2	1.70 (1.40–2.06)	5.39	<0.001	1.42 (1.13–1.78)	0.35	3.02	0.003
Mitral regurgitation III/IV	1.30 (1.03–1.64)	2.21	0.027				
Pharmacological treatment							
ACE inhibitor or ARB	0.66 (0.52–0.84)	3.43	0.001				
Beta-blocker	0.66 (0.53–0.82)	3.75	<0.001				
Loop diuretics	2.15 (1.47–3.15)	3.96	<0.001				
Eplerenone	0.65 (0.46–0.93)	2.34	0.019				
Digoxin	1.30 (1.05–1.61)	2.42	0.015				

CI, confidence interval; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; LA, left atrial.

The presence of Framingham left HF signs, eGFR <60 mL/min/m^2, and BNP > 43 pmol/L (> 150 ng/L) or NT-proBNP > 118 pmol/L (> 1000 ng/L) were independent predictors for 1-month hospitalization in the multivariable analysis. In addition to these variables, a heart rate >70 b.p.m., the presence of anaemia, and a left atrial (LA) size >26 mm/m^2 were independent predictors for 1-year hospitalization.

In order to build a score able to predict the risk of HF admission for a given patient, we assigned a scale of 30 points for both a 1-month and a 1-year hospitalization based on the β-coefficient of each variable (*Table 4*). This score allowed the estimation of the risk of hospitalization for worsening HF, as illustrated in *Figure 1*. Indeed, the cumulative incidence function curves distinguished a low-risk and a high-risk group (<1% and >5% event rate, respectively) for 1-month HF readmission risk, and low-risk (7.8% event rate), intermediate-risk (15.6% event rate), and high-risk groups (26.1% event rate) for 1-year HF readmission.

The C-statistics for the two models were 0.72 and 0.66, respectively. In the preserved LVEF group, the C-statistics were 0.71 and 0.72. After the bootstrap sampling, these indexes were 0.71 and 0.65. The calibration plots of the Fine and Gray models showed a fairly good calibration for 1-month and 1-year HF readmission (*Figure 2*).

External validation

The AUC of the model fitted on the REDINSCOR derivation sample for 1-month and 1-year HF readmission was 0.73 and 0.67, respectively. The external validation in the MUSIC cohort showed an AUC of 0.71 and 0.69 for 6-month and 1-year readmission models, respectively. Moreover, after comparing the AUCs of both models, no significant statistical differences were found ($P = 0.727$ for short-term risk, and $P = 0.708$ for long-term risk). External validation of the calibration ability of the 1-year HF readmission model is illustrated in *Figure 3* as a calibration plot, where the Hosmer–Lemeshow test gave a non-significant *P*-value.

Discussion

Main findings

This study provides a validated new score that predicts 1-month and 1-year hospitalization for worsening of HF in ambulatory patients based on precise variables that are currently assessed in clinical practice. Moreover, the score allows discrimination between low- and high-risk patients based on a competing risk analysis.

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Table 4 The Redin-SCORE

1 month-HF readmission risk	β-coefficient	Adjustment factor × 10 points	Risk groups	Patients (*n*)	Cumulative incidence readmission risk (%)
Framingham left HF signs	1.02	10			
eGFR <60 mL/min/1.73 m^2	0.63	6	0–19 points	906	0.9%
BNP>43 pmol/L (>150 ng/L) or NT-proBNP>118 pmol/L (>1000 ng/L)	1.37	14	20–30 points	1053	5.1%
Total score		30 points			
1 year-HF readmission risk	**β-coefficient**	**Adjustment factor × 13 points**	**Risk groups**	**Patients (n)**	**Cumulative incidence readmission risk (%)**
Framingham left HF signs	0.41	5			
Heart rate >70 b.p.m.	0.32	4			
Anemia	0.32	4	0–12 points	641	7.8%
BNP > 43 pmol/L (> 150 ng/L) or NT-proBNP > 118 pmol/L (> 1000 ng/L)	0.63	8	13–20 points	562	15.6%
eGFR <60 mL/min/1.73 m^2	0.25	4	21–30 points	756	26.1%
LA size >26 mm/m^2	0.35	5			
Total score		30 points			

eGFR, estimated glomerular filtration rate; HF, heart failure; LA, left atrial.

Previous studies

Several studies have reported predictive models of hospitalization in HF patients.[20] The benefits of identifying HF patients needing a more personalized care are fully recognized, but predictive models of HF hospitalization are far from being implemented in current clinical practice. Factors limiting the predictive power of the available studies have been recently reviewed in detail.[4,5] Chief among the limitations are their lower C-statistic values as compared with those found in mortality models,[21,22] and, on the other hand, hospitalization may greatly depend on quality of care and health system characteristics rather than on the patient's clinical condition itself. Moreover, the analysed variables were largely heterogeneous among the studies and were not always validated. Quite often data were extracted from retrospective administrative data[21] or from inpatient clinical registries,[22–25] and were rarely obtained from ambulatory HF patients. Therefore, the validation and performance of these tools have not been established in outpatients. In several instances, the scores have been developed based on data from clinical trials,[26–28] and this scenario might be far removed from real-life daily practice.

Recently, investigators from the University of Michigan have proposed the HFPSI score (Heart Failure Patient Severity Index) to predict the 6-month risk of death and/or all-cause medical hospitalization in HF outpatients.[29] Using multivariable Cox modelling in a cohort of 1536 patients, the HFPSI included blood urea nitrogen (BUN), BNP, diabetes, history of atrial fibrillation/flutter, NYHA class, and all-cause hospitalization within the 6 months. Kaplan–Meier curves distinguished between a low-risk group (8% even rate) and a high-risk group (57%). The C-statistics were 0.71 and 0.68 in the validated Ann Arbor Veterans' Affairs cohort. Of note, this study only reported all-cause hospitalization, but not specific causes of HF admissions.

Two of the former clinical prediction tools were derived from the trial Candesartan in Heart Failure: Assessment of Reduction in Mortality and morbidity (CHARM)[28] and the Seattle Heart Failure Model.[30] The CHARM trial evaluated all-cause mortality and the combined outcome of cardiovascular death and HF hospitalization over a 2-year period, leading to a C-statistic of 0.75. The way to calculate the CHARM score is complex because it requires fulfilling up to 24 variables. On the other hand, the model does not include data on blood laboratory tests, and the study was conducted as a clinical trial with a selected non-real-life population of HF patients. Finally, the CHARM model predicts a combined event that has different clinical implications. The widely validated Seattle Heart Failure Model looked at mortality risk in ambulatory HF patients with LVEF <30%.

Likewise, investigators of the HF-ACTION trial have developed a multivariable model predicting a combined endpoint (death and all-cause admission) with a C-index of 0.63 in outpatients with chronic HF and LVEF <35%, using patient data at the time of initial presentation from this trial.[31] As potential limitations, these authors indicated: exclusion of preserved LVEF, lack of natriuretic peptide data, and no external validation. Investigators of the CORONA trial built a series of models for several outcomes, including admission for worsening of HF. They proved the incremental prognostic value of adding biomarkers such as high-sensitivity C-reactive peptide and NT-proBNP.[32] All ambulatory patients from the CORONA trial had an ischaemic aetiology, and several biochemical parameters such as sodium or haemoglobin were not available. Moreover, these data were not validated in an external cohort.

Thus, nowadays there is a lack of available scores allowing the prediction of which ambulatory patients are at risk of hospitalization for worsening of HF in our current clinical practice.

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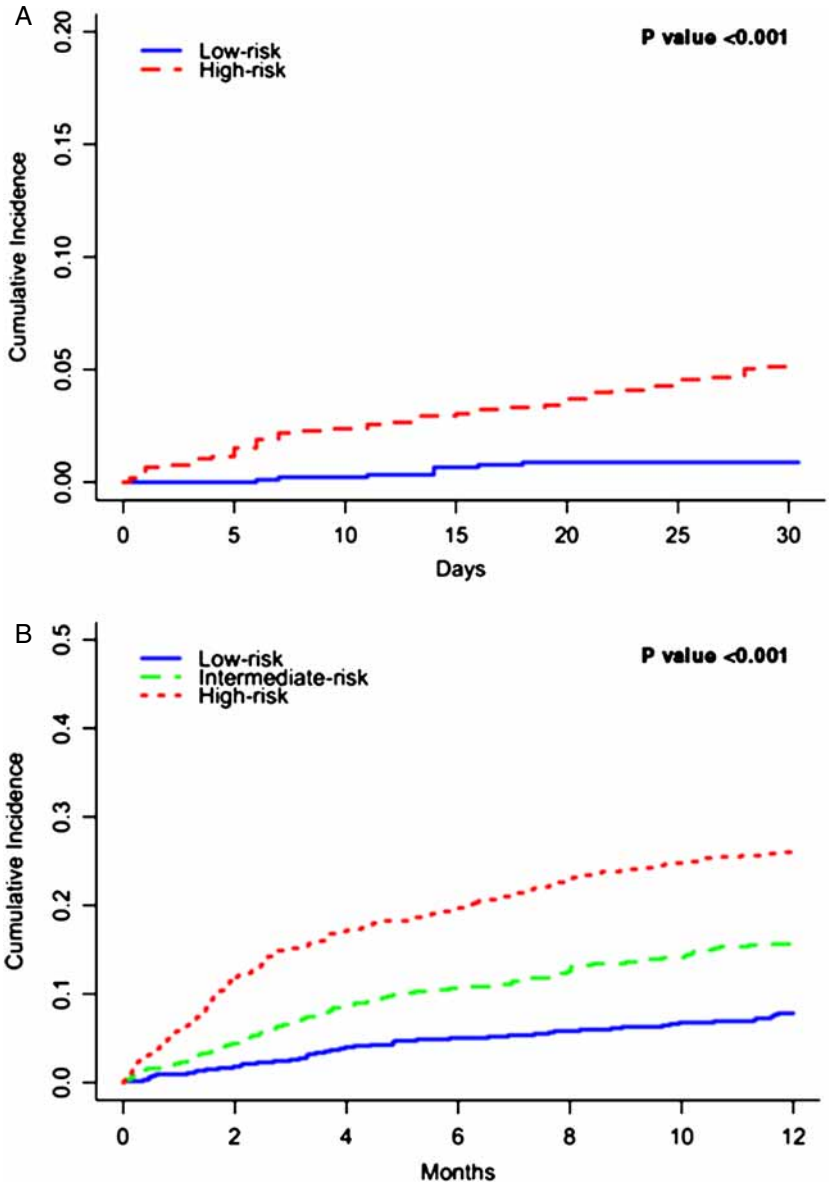


Figure 1 Cumulative incidence curves of hospitalizations risk for worsening of heart failure in the REDINSCOR cohort after 1-month (upper panel) and 1-year (lower panel) follow-up.

Considerations on the Redin-SCORE

The Redin-SCORE is an easy, simple tool able to stratify the short- and long-term risk of admission for worsening of HF. It only requires from three to six clinically precise variables. This score has been constructed from a large multicentre registry, with a broad spectrum of integrative information (clinical history, physical exam, ECG, blood test, echo data, treatment) that is easily available in daily clinical practice. The variables conforming the Redin-SCORE model were not chosen by chance because they share pathophysiology plausibility. Indeed, our risk predictors are indicators of some of the pathophysiological derangements present in HF syndrome: volume overload (Framingham left HF signs, BNP, or NT-proBNP), deleterious compensatory mechanisms (heart rate), target organ damage (anaemia, eGFR), and cardiac remodelling (LA size). Moreover, the predictors found in our study have been previously reported as prognostic markers of HF outcome.

The Redin-SCORE identifies high-risk groups of HF patients prone to be admitted within the short term (>5% rate) or long term (nearly 30% rate) and has been validated in a different population of HF patients (MUSIC cohort) with a robust result. In the outpatient environment, this score should provide the opportunity to identify those patients requiring care management programmes at specific HF clinics. Home visiting programmes and

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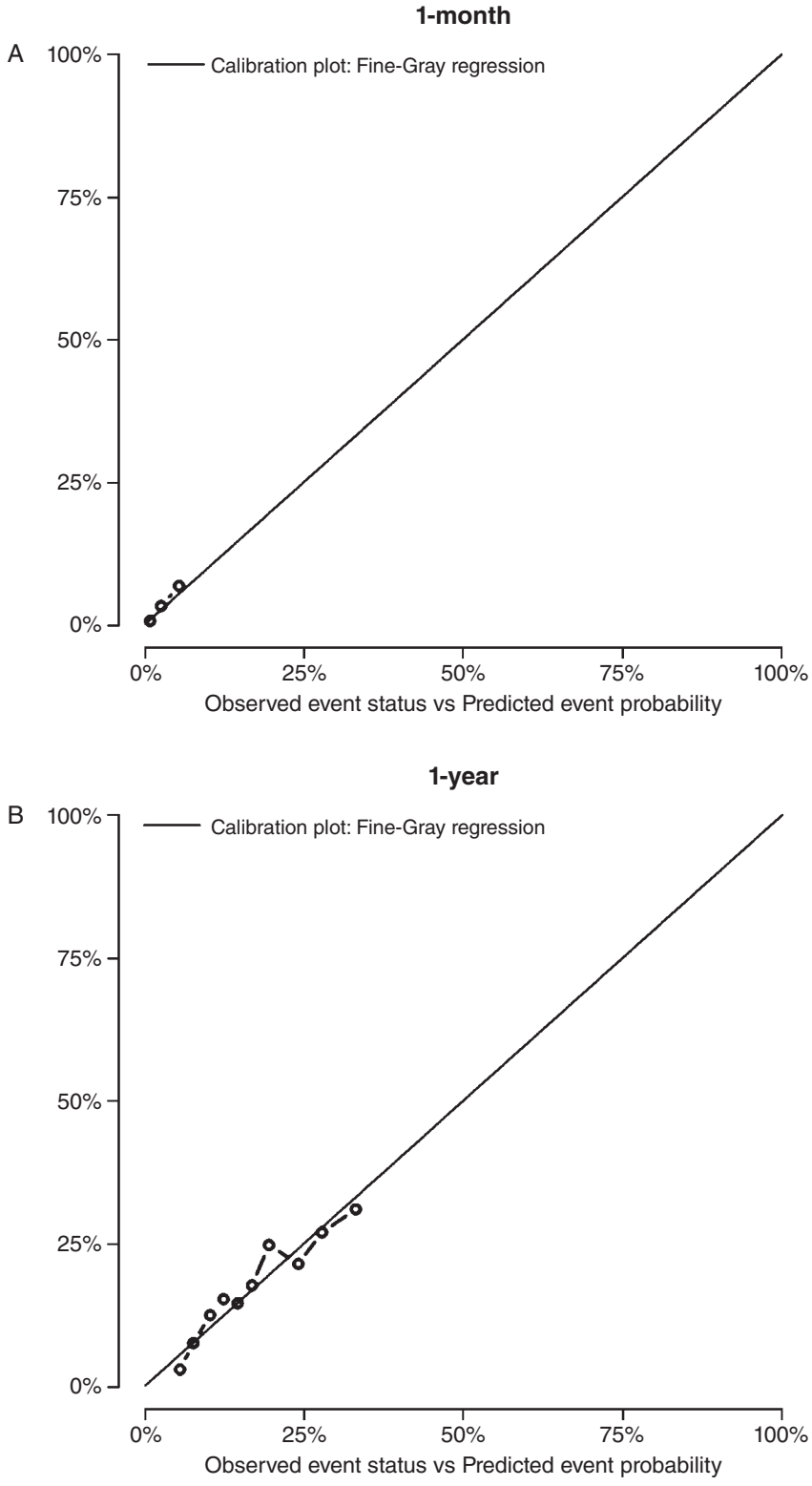


Figure 2 Calibration plot of the 1-month (upper panel) and 1-year (lower panel) hospitalization Fine–Gray regression models for worsening of heart failure.

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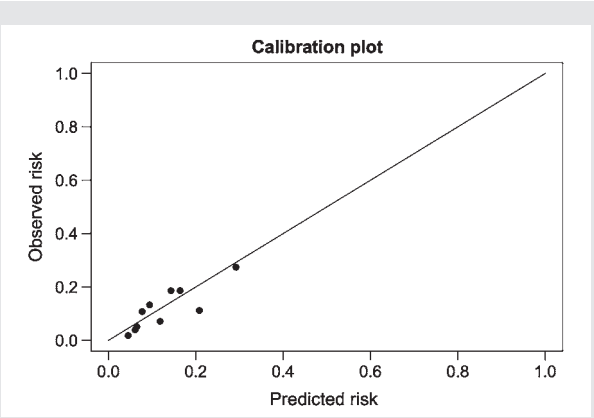


Figure 3 Calibration plot of the 1-year hospitalization model for worsening of heart failure (external validation).

specialized HF units are nowadays the most efficient means of reducing all-cause admissions (and even mortality) for chronic HF patients.[33]

Although the Redin-SCORE includes a wide range of relevant variables of HF, the REDINSCOR registry did not collect specific information about co-morbidities or psychosocial factors. As mentioned in the Methods section, the MUSIC registry did not have a 1-month follow-up visit, and therefore we used a logistic regression analysis with the prognostic variables at 6-month and 1-year follow-up. Both the study and validation cohorts comprised patients from the same geographic area, and thus our model would need further validation in other countries. Finally, some admissions may be missing if they occurred in non-REDINSCOR centres. However, the Spanish Health System assigns a geographic distribution of medical resources for each patient, and thus losses will not be significant. The incidence of hospitalization for worsening of HF of ∼17% in our study was apparently low in comparison with those reported in previous publications.[4,5] However, studies reporting higher hospitalization rates include all-cause hospitalization and often they included patients with acute rather than ambulatory chronic HF. Lastly, the percentages of second-line therapies such as CRT and defibrillators were low, so we have not been able to analyse their probable prognostic role.

Supplementary Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. List of REDINSCOR variables.

Appendix S2. The investigators of the Spanish Heart Failure Network (REDINSCOR).

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