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DECOMPENSATED HEART FAILURE (P BANERJEE, SECTION EDITOR)

Patient-Associated Predictors of 15- and 30-Day Readmission After Hospitalization for Acute Heart Failure

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Abstract

Background Identifying readmission predictors in heart failure (HF) patients may help guide preventative efforts and save costs. We aimed to identify 15- and 30-day readmission predictors due to cardiovascular reasons.

Methods and Results A total of 1831 patients with acute HF admission were prospectively followed during a year. Patient-associated variables were gathered at admission/discharge and events during follow-up. A multivariate Fine and Gray competing risk regression model and a cumulative incidence function were used to identify predictors and build a risk score model for 15- and 30-day readmission. The 15- and 30-day readmission rates due to cardiovascular reasons were 7.1% and 13.9%. Previous acute myocardial infarction, congestive signs at discharge, and length of stay > 9 days were predictors of 15- and 30-day readmission, while much weight loss and large NT-ProBNP reduction were protective factors. The NT-ProBNP reduction was larger at 30 days (> 55%) vs 15 days (> 40%) to protect from readmission. Glomerular filtration rate at discharge < 60 mL/min/1.73m^2 and > 1 previous admissions due to HF were predictors of 30-day readmission, while first post-discharge control at an HF unit was a protective factor.

Conclusions Previous identified factors for early readmission were confirmed. The NT-ProBNP reduction should be increased (> 55%) to protect from 30-day readmission.

Keywords Heart failure · Readmission · Predictive factors · NT-ProBNP

Abbreviations

HF	Heart failure
AMI	Acute myocardial infarction
CV	Cardiovascular
NT-proBNP	N-terminal proB-type natriuretic peptide
LVEF	Left ventricular ejection fraction
LOS	Hospital length of stay

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Introduction

Heart failure (HF) is the most frequent cause of hospitalization among adults 65 years of age or older [1], with more than 1 million HF-driven annual hospitalizations in the USA [1]. In Spain, the prevalence of HF has been estimated at ~ 5% [2], which seems higher than the estimated 1–2% in the western world [3]. However, and in addition to an aging Spanish population [2], the Spanish prevalence is probably overestimated, since most studies have been conducted in specific primary care centres. Heart failure is associated to a high death rate (~ 30/100,000 in Europe) [4], although it has progressively reduced in Europe since 1987, probably related to the implementation of evidence-based guidelines leading to better management of these patients [4].

Management of HF means a great deal of expenses in health-care resources and indirect costs [2, 5]. The mean per-patient cost of a HF-related hospitalization in the USA has

been estimated as $14,631, and it is compounded by a high rate of readmission [6], since the 30-day readmission rate is close to 25% in this country, and more than 50% of readmissions occur during the first 15 days [7••]. In Spain, although the cost of "informal" caregiving provided by non-healthcare professionals accounts for most (69.8%) of the total expenditure in HF patients (total €18,220 per patient/year), the average health-care expenditure (mostly due to hospitalizations) still accounts for more than a quarter of all costs at €4860 [5].

The identification of predictors of readmission may guide preventative efforts to save health-related costs and improve quality of care. Since excess HF readmission ratios translates into losing some of the Medicare reimbursement in the USA, according to the Patient Protection and Affordable Care Act, studies have been conducted to identify early readmission-related variables accessible for intervention to reduce readmissions. Some studies have considered predictors in particular HF cases or in specific putative variables [8, 9], but a well-rounded search for patient-associated readmission predictive factors is missing. Furthermore, almost exclusively, studies have considered readmission within 30 days from discharge, since the Centres for Medicare & Medicaid Services uses this period to report readmission rates for HF [10], while other periods have been hardly explored.

Therefore, a study was designed aiming to identify every predictive factor for 30-day, as well as for 15-day HF readmission. The ultimate objective is to enable preventive measures leading to a decrease in the need for readmission, to reduce costs and improve quality of care. The fact that these predictive factors are common for both 15- and 30-day HF readmissions should facilitate the implementation of these preventive measures. Furthermore, both European and American Guidelines recommend a very early follow-up visit after patient discharge (before 15 days) both in the primary care and cardiology specialist settings. This would justify the need for an early 15-day score, since it would allow healthcare professionals to prioritize the patients who are most at risk [11, 12].

Methods

An observational, multicentre, prospective study to identify predictors of readmission within the first 15 or 30 days after discharge from hospitalization for HF was conducted.

Study Population

This was a prospective, multicentre study which enrolled 1831 patients with acute HF admission through the Spanish Network for the Study of Heart Failure II (REDINSCOR II Registry) [13] with the objective of describing the clinical profile of patients with HF in Spain and assessing risk predictors of readmission. Patients were consecutively recruited between November 2013 and November 2014 in 18 hospitals. Inclusion criteria were age 18 years or older, hospitalization due to presentation of signs and/or symptoms compatible with HF, and a chest X-ray with pulmonary congestion, either "de novo" or decompensation of a chronic HF, in accordance with current guidelines at the time [11]. Exclusion criteria were HF due to ST-segment elevation acute coronary syndrome and concomitant terminal disease (life expectancy < 1 year).

Study Design

The main objective was to determine the predictive factors of hospital readmissions due to CV reasons that occurred (a) within the first 15 days and (b) within the first 30 days after discharge in patients included in the Spanish Network for the Study of Heart Failure II (REDINSCOR II Registry), who were hospitalized due to HF. The secondary objective was to elaborate a risk model.

Patient-associated variables were gathered at admission and at discharge and patients were followed during a year after registry inclusion. In addition to the clinical follow-up adjusted to the needs of the patient, the vital state and events were collected at 15 days, 1, 3, 6, and 12 months. If there was no visit in person at that time, the data was obtained by telephone interview. Only 30 patients (1.6%) were lost to follow-up.

Readmission was defined as any unplanned hospital readmission within the first 15 days or within the first 30 days after discharge due to CV causes, which included HF due to acute coronary syndrome (ACS) with or without ST-segment elevation, episode of ventricular tachycardia (VT)/atrial fibrillation (AF)/cardiorespiratory failure (CRF), implant of a pacemaker due to bradycardia, stroke, other CV diseases, pulmonary thromboembolism (PE), and syncope. This study also evaluated other causes for rehospitalization, as well as mortality during hospitalization and during follow-up.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee, and all patients gave written informed consent to participate in the study.

Study Variables

Data were collected using specifically designed web forms (http://www.redinscor2.org), and quality controls were undertaken periodically.

The following clinical variables, including variables known to be possible predictors of HF readmission [6], were gathered 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) pharmacological treatment.

Weight, ECG, echocardiography, laboratory blood tests, and pharmacological and non-pharmacological (devices) treatments were also gathered at discharge (see Supplemental data: Table 1 for full variable listing).

Patients who had left ventricular ejection fraction (LVEF) echocardiographically determined within 6 months prior to admission were included with their last available echocardiogram (i.e., they did not repeat echocardiography during admission). All patients were classified as HF with reduced (HFrEF; LVEF < 40%), with midrange (HFmrEF; LVEF 40–49%), and with preserved (HFpEF; LVEF ≥ 50%) ejection fraction.

Standard criteria were used to define each variable. The plasma levels of N-terminal proB-type natriuretic peptide (NT-proBNP) and their changes from admission to discharge [(Discharge-Admission)/Admission]×100, as well as the changes in weight coded as % changes from admission to discharge [(Discharge-Admission)/Admission]*100 were dichotomized for cutoff values according to the Youden criteria. The eGFR was calculated using the CKD-EPI (Chronic Kidney Disease-Epidemiology Collaboration) method.

Statistical Methods

Clinical characteristics of the study population at first admission (baseline) and at discharge were described using mean ± standard deviation (SD) or median (interquartile range), whenever appropriate, for continuous variables and frequencies and percentages for categorical variables. Differences between continuous variables and between categorical variables were tested by the Mann–Whitney *U* test and the Fisher's exact test, respectively.

A multivariate Fine and Gray competing risk regression model was built to assess the influence of the different risk predictors on readmission, with death or cardiac transplantation over the time period as competing events for readmission. The model reports subdistribution hazard ratios (SHRs) and models the covariate effect on a cumulative incidence function (CIF) to show the cumulative probability of hospital readmission within the time period of interest, due to specific risk predictors in presence of mortality and heart transplantation as competing events.[14]

There were two different endpoints for all regression analyses: The date of readmission due to CV reasons within the first 15 days of follow-up, and the day of readmission due to CV within the first 30 days of follow-up. Clinical meaningful variables showing a significant level of $P < 0.1$ in the univariate analysis were included in the multivariate model. A backward elimination method was used to identify independent risk predictors with $P < 0.05$ for the inclusion or deletion criterion.

The model included only the main effects of the predictors, without any interaction term. The proportional hazard assumption was evaluated by the Schoenfeld residuals test. The discriminative ability of the models was assessed by the

Table 1 Risk scores

	β-coefficient	Adjustment factor × 10 points	Risk groups	Patients (n)	Cumulative incidence readmission risk (%)	Risk groups	Patients (n)	Cumulative incidence readmission risk (%)
15-day CV readmission risk								
Previous AMI	0.529	5						
Congestive signs at discharge	0.590	5	0–11 points	872	3.3%	0–6 points	545	2.8%
Mean LOS > 9 days	0.407	4				7–14 points	769	6.4%
Weight loss at discharge < 5.4%	0.664	6	12–25 points	959	10.5%	15–25 points	517	12.8%
NT-ProBNP reduction < 40%	0.543	5						
Total score		25						
30-day CV readmission risk								
Previous HF admissions > 1	0.42	4						
Previous AMI	0.35	3						
Congestive Signs at discharge	0.34	3	0–13 points	896	7.4%	0–11 points	598	6.7%
Unit of first control after discharge: NO HFU	0.38	3				12–15 points	630	12.2%
eGFR at discharge (CKD-EPI) < 60 mL/min/1.73m^2	0.35	3	14–29 points	935	20.2%	16–29 points	603	22.9%
NT-ProBNP reduction < 55%	0.46	4						
Weight loss at discharge < 5.6%	0.57	5						
Mean LOS > 9 days	0.41	4						
Total score		29						

AMI, Acute myocardial infarction; *LOS*, Length of Stay; *NT-proBNP*, N-terminal pro B-type natriuretic peptide; *HF*, Heart failure; *HFU*, Heart failure unit: *eGFR*: estimated Glomerular filtrate rate by Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI)

C-index. The internal validity of the final predictive models was tested for 500 bootstrap re-samples, using the "pec" package by Gerds in the R Project for Statistical Computing. The calibration of models was assessed by the corresponding plots using the same package.

Point-based risk scores were calculated for the variables identified by the multivariate analysis (Table 1). This way individual risks can be calculated by adding the scores of each risk predictor presented by the patient up to a total score. To calculate the risk score for 15-day or 30-day readmission, each final predictor was multiplied by its β-coefficient by 10, for the 15- and 30-day readmission models, respectively, and truncated to the integer number. Therefore, the score of a particular patient ranged from 0 to 25 and from 0 to 29 for 15- and for 30-day readmission, respectively. The cumulative incidence function (CIF) approach separated patients into two (low and high risk) or three (low, intermediate and high risk) risk categories, according to the total score, for 15-day and 30-day readmission (Fig. 1). Missing data were imputed using the "mice" package in R (Multivariate Imputation by Chained Equations) whenever necessary ($n = 5$).

A two-sided $P < 0.05$ was considered statistically significant. Data were analysed with the statistical packages SPSS 24 and R 3.2.

Results

A total 1831 patients with acute HF admission enrolled in the Spanish Network for the Study of Heart Failure II (REDINSCOR II Registry) participated in the study. Socio-demographic and clinical characteristics are shown in Table 2**.** Mean age was 72.4 (SD 12.1) years, 58.7% were male, 98.1% were Caucasian, and 58.5% had a history of chronic HF. Out of 1420 patients classified according to LVEF, 41% had HFrEF, 16% HFmrEF, and 43% HFpEF. The most frequent cause of HF was ischemic (37.5%), followed by valve disease (24.8%), and mean LVEF was 46.2%. The most frequent comorbidities were hypertension (77.8%) and diabetes mellitus (46.4%), and 85% of patients presented with congestive signs at admission.

Mortality was 3.9% during first hospitalization, 5.4% at 15 days, 6.4% at 30 days, and 20.5% at 1 year. Likewise, 2% of the cohort had received a heart transplant at the end of the first year.

Socio-demographic and clinical characteristics according to readmission groups are shown in Supplemental data: Table 2.

Readmission Rates and Predictors of Hospital Readmission

Readmission rates due to CV causes at 15- and at 30-day post-discharge were 7.1% and 13.9%, respectively. Also, readmission rates due to non-CV causes at 15- and 30-days were 3.9% and 6%, respectively.

Five parameters were independent predictors of 15-day readmission due to CV causes, and 8 of 30-day readmission in the multivariable analysis (Table 3). Competing risk regression analysis identified previous acute myocardial infarction (AMI), congestive signs at discharge, and mean hospital length of stay (LOS) > 9 days as predictors of 15-day readmission, while weight loss > 5.4% and a reduction in N-terminal ProB-type natriuretic peptide (NT-ProBNP) > 40% were protective factors (Table 3).

Likewise, more than 1 previous admissions due to HF, previous AMI, congestive signs at discharge, glomerular filtration rate (GFR) at discharge estimated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation < 60 mL/min/1.73 m^2, weight loss < 5.6% and mean LOS > 9 days were independent predictors of 30-day readmission, while NT-ProBNP reduction > 55% and first follow-up after discharge by a multidisciplinary heart failure team in a heart failure out-patient unit (HFU) were protective factors (Table 3). The discrimination C-index was 65% and 65.6% for the 15-and 30-day readmission model, respectively, and after internal validation with bootstrap sampling of 500, it was 63.3% and 63.7%. The calibration plots of the models, comparing expected and observed risks showed a fairly good calibration for 15-day and 30-day readmission (Supplemental data: Fig. 1 and Fig. 2).

Discussion

The data obtained in this study concerning 15- and 30-day readmission predictive factors in patients with HF may be highly valuable to help healthcare professionals prioritize at-risk patients, guide preventative efforts, and save on healthcare-related costs.

The present study shows that with few simple clinical variables obtained during a HF admission, a good estimation of the risk of re-admission at 15 and 30 days after discharge can be obtained. The identification of patients at greater early readmission risk can be helpful to reduce costs and health issues, since closer follow-up of such patients might facilitate preventive interventions to avoid the need for readmission. On the other hand, the identification of patients with a low readmission risk might avoid the implementation of unnecessary assessments.

Our findings also reinforce the relevant role of NT-proBNP monitoring during admission for predicting early re-admission, although the range of reduction that has a prognostic impact on 30-day readmission should be probably increased.

Readmission Rates

Our study showed a 30-day readmission rate (due to CV reasons) of 13.9%, consistent with that (13.4%) of a Spanish study conducted on 2110 consecutive patients discharged after

Risk score of readmission after hospitalization for acute heart failure			
15-day CV readmission risk		**30-day CV readmission risk**	
Variable	*Score*	*Variable*	*Score*
Previous AMI	5	Previous HF admissions >1	4
Congestive signs at discharge	5	Previous AMI	3
Mean LOS >9 days	4	Congestive Signs at discharge	3
Weight loss at discharge <5.4%	6	Unit of first control after discharge: NO HFU	3
NT-ProBNP reduction <40%	5	eGFR at discharge (CKD-EPI) <60 mL/min/1.73m^2	3
		NT-ProBNP reduction <55%	4
		Weight loss at discharge <5.6%	5
		Mean LOS >9 days	4
Total SCORE	25	**Total SCORE**	29

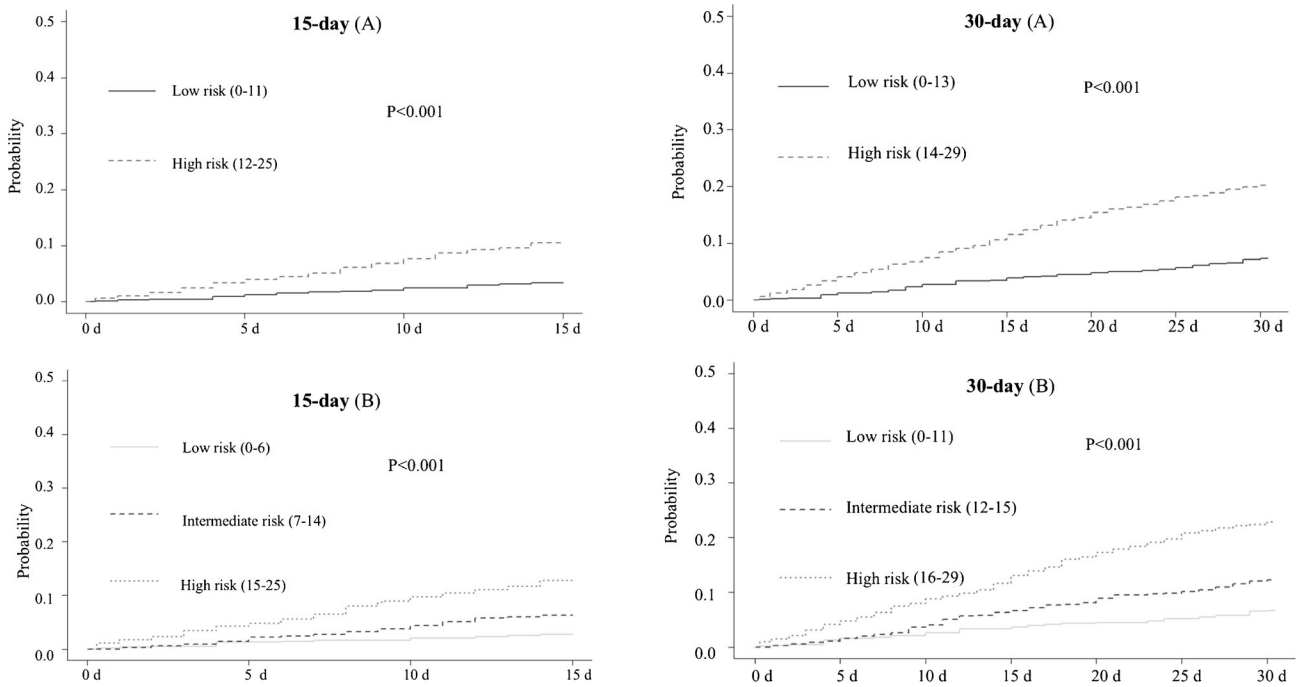

Fig. 1 Cumulative incidence function for 15- and 30-day readmission risk for (A) patients with low and high risk scores and for (B) patients with low, intermediate, and high risk scores. (A, 15-day) Low risk 0–11 points in the risk score; High risk 12–25 points; (30-day) Low risk 0–13 points in the risk score; High risk 14–29 points. (B, 15-day) Low risk 0–6 points in the risk score; Intermediate risk 7–14 points; High risk 15–25 points; (30-day) Low risk 0–11 points in the risk score; Intermediate risk 12–15 points; High risk 16–29 points. CV, Cardiovascular; AMI, Acute myocardial infarction; LOS, Length of Stay; NT-proBNP, N-terminal pro B-type natriuretic peptide; HF, Heart failure; HFU, Heart failure unit; eGFR, estimated Glomerular filtrate rate by Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI)

hospital admission for acute HF at a tertiary hospital [15•]; not only was the time period comparable but most readmissions (85.1%) were due to CV reasons. Two other previous Spanish studies showed readmission rates of ~ 35% [16, 17], but no 30-day readmission data were reported and were, thus, not comparable.

The American study conducted with data from over 1 million hospitalized Medicare beneficiaries for HF showed a 30-day readmission rate of 24.8%, even although readmissions were mainly due to HF and CV reasons.[7••] On one hand, the mortality risk due to HF has been decreasing in Spain thanks to the implementation of evidence-based guidelines, which have led to better patient management [4], and might have had a positive repercussion on readmission rates. On the other hand, and more importantly, there are profound differences in the health care systems of Spain and the USA that might account for our lower 30-day readmission rate. These differences reflect on the obvious larger median LOS for HF hospitalization in Spain (8.5 days in the current study) than in the USA (4 days) [18]. The longer LOS probably leads to more decongested patients at discharge as opposed to more congested patients when LOS is short, and it is known that congestion is the single most important contributor to readmission [18]. The association between short LOS and higher readmission rates has been previously observed. Some studies show higher readmission rates when LOS are shorter than 3–4 days [15•, 19•], and hospitals with lower than expected mean risk-adjusted LOS have higher readmission rates [20].

Although most studies have been conducted focusing on 30-day readmission, since that is the period not covered by Medicare, a high percentage of those readmissions occur during the first 15 days from discharge. The study mentioned above

Table 2 Patients' characteristics

	N = 1831
At admission	
Male	1075 (58.7%)
Ethnicity: Caucasian	1797 (98.1%)
Age (years)	72.4 ± 12.1
Chronic/de novo HF	1072 (58.5%)/759 (41.5%)
Classification by LVEF*	1420 (77.5%)
HFrEF (LVEF < 40%)	583 (31.8%)
HFmrEF (LVEF 40–49%)	227 (12.4%)
HFpEF (LVEF ≥ 50%)	610 (33.3%)
HF evolution (years)	1.0 [0.0; 4.0]
HF aetiology	
Ischemic	687 (37.5%)
Valve	455 (24.8%)
Hypertensive	306 (16.7%)
Idiopathic dilated	231 (12.6%)
Hypertrophic	65 (3.5%)
Infiltrative	19 (1.0%)
Extracardiac	68 (3.7%)
Previous HF diagnosis	993 (58.4%)
Congestive signs	1559 (85.1%)
Hypertension	1424 (77.8%)
Dyslipidaemia	1016 (55.5%)
Diabetes mellitus	849 (46.4%)
Chronic renal failure	625 (34.1%)
eGFR < 30/ dialysis	111 (6.1%)
eGFR 30–59	407 (22.2%)
eGFR ≥ 60	107 (5.8%)
COPD	293 (16.0%)
OSAHS	193 (10.5%)
Stroke	191 (10.4%)
Peripheral vascular disease	213 (11.6%)
NYHA class at admission	
I	37 (2.0%)
II	276 (15.1%)
III	894 (48.8%)
IV	473 (25.8%)
eGFR CKD-EPI (mL/min/1.73m^2)	59.7 ± 24.9
NT-proBNP (ng/ml)	3972 [1904; 8291]
At discharge	
NT-proBNP (ng/ml)	2213 [1019; 5124]
Charlson index	3.37 ± 2.61
Barthel index	89.2 ± 21.3
Pfeiffer index	0.94 ± 1.71
LOS (days)	8.5 [5.5; 12.5]
ACEIs	948 (51.8%)
ARBs	336 (18.4%)
Beta-blockers	1285 (70.2%)
MRAs	815 (44.5%)

HF, Heart Failure; *LVEF*, Left Vevntricular Ejection Fraction; *HFrEF*, HF with reduced ejection fraction; *HFmrEF*, HF with midrange ejection fraction; *HFpEF*, HF with preserved ejection fraction; *eGFR*, estimated Glomerular Filtration Rate; *COPD*, Chronic Obstructive Pulmonary Disease; *OSAHS*, Obstructive Sleep Apnoea Hypopnea Syndrome; *NYHA*, New York Heart Association; *NT-proBNP*, N-terminal proB-type natriuretic peptide; *LOS*, Length of stay; *ACEIs*, Angiotensin converting enzyme inhibitors; *ARBs*, Angiotensin II receptor blockers; *MRAs*, Mineralocorticoid receptor antagonists

*LVEF was determined echocardiographically in 1420 patients during admission (1084) or within 6 months prior to admission (336), while in 411 patients cardiac ultrasounds were not considered necessary

Categorical variables expressed as *n* (%) and continuous variables expressed as mean ± SD or median [1st quartile; 3rd quartile]

with Medicare beneficiaries showed that 61% of readmissions during the first 30 days post-discharge occurred within the first 15 days [7••] (i.e., 15-day readmission rate 15.1%). Thus, that very early period post-discharge was worth assessing. Our 15-day readmission rate at 7.1% was much lower than the American rate but similar to the 8.6% 15-day readmission rate of the mentioned study conducted at a Spanish tertiary hospital [15•].

Readmission Risk Factors

Previous AMI, congestive signs at discharge, long LOS, more than 1 previous admission due to HF, and eGFR at discharge < 60 mL/min/1.73 m2 were predictors of 15-day and/or 30-day readmission, while relevant weight loss, large NT-ProBNP reduction, and first control after discharge at an HFU were protective factors. These factors have been previously reported as readmission risk and protective factors, respectively, along with some others [6, 15•, 19•].

The decrease in NT-proBNP from discharge is one of the risk factors common to 15-day and 30-day readmissions, and it is easily quantifiable. NT-proBNP has been used as a biomarker for HF diagnosis and prognosis [21] and can be used to guide treatment [22]. Notably, our results suggest that the change in NT-proBNP levels is more predictive than the absolute values of NT-proBNP at admission or discharge. This is in accord with a previous studies by Bettencourt et al., which showed that a decrease of 30% or more in NT-proBNP from admission levels was a protective factor for readmission and death, while a decrease smaller than 30% (or worse, an increase) was associated to shorter time of readmission and death [23]. It seems that week-to-week biological variability of NT-proBNP is approximately 30% in HF patients, and thus, only changes greater than this amount should be considered as reflecting a significant change in the abnormal physiology triggering NT-proBNP release [24]. Thus, the standard therapeutic objective in HF has been to decrease NT-proBNP by more than 30%. However, our study shows that to protect HF patients from 15-day readmission, the decrease should be greater than 40% and that to increase the time of protection to 30 days, we should aim for yet a further decrease (> 55%). It seems that with longer LOS and more decongested patients (suggested by the lower readmission rates), we require a greater reduction of the biomarker to be a readmission predictor, and the larger the reduction, the longer time for readmission prediction. This finding might lead to a stricter therapeutic objective with respect to NT-proBNP decrease, especially in men, since the NT-proBNP level seems to be a more valuable marker in the prediction of long-term mortality and HF readmission in men than in women [25].

Regarding LOS, stays greater than 9 days were associated with both, 15-day and 30-day readmission, consistent with data from previous studies. A study showed a higher rate of 30-day

Table 3 Univariable and multivariable predictors of 15- and 30-day readmission due to CV reasons

	15-day readmission				30-day readmission			
	Univariable SHR (95% CI)	*P* value	Multivariable SHR (95% CI)	*P* value	Univariable SHR (95% CI)	*P* value	Multivariable SHR (95% CI)	*P* value
*Age (years)	1.009 (0.994–1.025)	0.228			_	_	_	_
HF aetiology: ischaemic	1.561 (1.096–2.224)	0.014			1.507 (1.155–1.966)	0.003		
Previous HF admissions >1	1.418 (0.9453–2.129)	0.091			1.718 (1.307–2.258)	< 0.001	1.523 (1.137–2.039)	0.005
Previous AMI	1.728 (1.213–2.462)	0.002	1.697 (1.186–2.430)	0.004	1.536 (1.187- 1.987)	0.001	1.418 (1.088–1.849)	0.010
Diabetes Mellitus	1.361 (0.964–1.922)	0.080			1.483 (1.159–1.898)	0.002		
Baseline NYHA class III/IV	1.163 (0.702–1.924)	0.557			1.593 (1.153–2.202)	0.005		
Congestive Signs at discharge	1.901 (1.259–2.872)	0.002	1.805 (1.196–2.724)	0.005	1.613 (1.189–2.188)	0.002	1.401 (1.018–1.928)	0.039
Mitral regurgitation ≥ Moderate at discharge	0.993 (0.681–1.449)	0.972			1.234 (0.9421–1.616)	0.126		
†Weight loss > 5.4% (< 5.6%)	0.585 (0.335–1.023)	0.060	0.515 (0.289–0.916)	0.025	1.556 (1.034–2.344)	0.035	1.767 (1.154–2.706)	0.011
Anaemia at discharge	1.408 (0.979–2.025)	0.065			1.547 (1.18–2.028)	0.002		
eGFR < 60 mL/min/1.73m^2 at discharge	1.430 (0.997–2.051)	0.052			1.593 (1.224–2.072)	< 0.001	1.422 (1.081–1.872)	0.012
‡NT-ProBNP reduction > 40% (> 55%)	0.556 (0.367–0.841)	0.006	0.581 (0.383–0.881)	0.011	0.588 (0.409–0.845)	0.005	0.634 (0.442–0.910)	0.015
NYHA class at discharge III/IV	1.656 (1.049–2.614)	0.030			1.644 (1.184–2.284)	0.003		
Unit of first control after discharge: HFU	0.665 (0.436–1.015)	0.059			0.718 (0.531–0.971)	0.031	0.683 (0.506–0.923)	0.013
§Unit of long-term control after discharge: HFU	_	_	_	_	0.786 (0.581–1.062)	0.117		
LOS >9 days	1.478 (1.049–2.083)	0.026	1.502 (1.059–2.130)	0.023	1.492 (1.168–1.907)	0.001	1.501 (1.166–1.932)	0.002
Charlson index	1.050 (0.996–1.108)	0.072			1.068 (1.026–1.111)	0.001		

Discrimination C index = 65% (Internal validation B = 500: 63.3%) for 15-day readmission

Discrimination C index = 65.6% (Internal validation B = 500: 63.7%) for 30-day readmission

*Univariable predictor for 15-day readmission only

† Weight loss > 5.4% for 15-day readmission and < 5.6% for 30-day readmission

‡ NT-ProBNP reduction > 40% for 15-day readmission and > 55% for 30-day readmission

§ Univariable predictor for 30-day readmission only

Schoenfeld residuals to test the proportionality of subdistribution hazards for the Fine and Gray model: $p > 0.05$

SHR, subdistribution hazard ratio; *CI*, Confidence interval; *AMI*, Acute myocardial infarction; *LOS*, Length of Stay; *NT-proBNP*, N-terminal pro B-type natriuretic peptide; *CHF*, Congestive heart failure; *HFU*, Heart failure unit: *eGFR*, estimated Glomerular filtrate rate

CV readmission for long LOS starting at 9 days (9–14 days) as compared with intermediate LOS (3–8 days) [19•]; however, that study also showed higher readmission rates when LOS was short (1–2 days). Another study conducted in Spain, showed a long LOS (8 to more than 10 days) association with 30-day readmission and long (> 10 days), as well as short, LOS (≤ 4 days) associations with 15-day readmission (and with 7-day readmission) [15•]. We did not find that *U*-shaped curve regarding LOS association to readmission. However, it seems likely that a longer LOS may be pointing towards patients with more severe HF and/or comorbidities. This, in turn, may be related to a higher risk of readmission.

The first follow-up after discharge by a multidisciplinary heart failure team in a heart failure out-patient unit (HFU) was a protective factor of 30-day readmission. In fact, strategies that incorporate follow-up by a specialized multidisciplinary team (either in a clinic or a non-clinic setting) and programs that focus on enhancing patient self-care activities reduce HF hospitalizations and all-cause hospitalizations in HF patients [26]. In Spain, 41% of hospitals have HFUs that provide specialized care with multidisciplinary teams, including nurses, whose main task is patient education [27]. Thus, our data suggest that these specialized units are effective in managing HF patients.

Risk Score Model

The risk model presented could be used in clinical practice to predict individual risk. The C-index for the 15-day and 30-day readmission models was modest at 65% and 65.6%, respectively. However, most readmission predictive models show a C-index of about 60–65% [10, 28, 29], and only a few reach higher C-values [30, 31]. The model was built with a large Spanish hospitalized HF population, making it the best model to be applied in these patients. In addition, the model is easy to use in the clinical practice, since a simple addition of the scores corresponding to the predictors presented by the patient can identify those patients at the highest risk. Thus, it would be worthy to treat all patients identified by the model as having high readmission risk as such. These patients could be followed-up closer and be included into disease management programs, which have been efficient in reducing hospital readmissions [32]. Additionally, and in view of the overload of the health care system in Spain, using the model might save costs and resources, since it also identifies patients with the lowest readmission risk, for whom an early post-discharge visit will not be necessary.

Study Limitations

One major limitation of this study is the lack of a validation cohort to test the validity of the risk score. However, this limitation is mitigated by the fact that the internal validity of the final predictive models was tested for 500 bootstrap resamples, using the "pec" package by Gerds in the R Project for Statistical Computing. It should also be noted that the conclusions from this paper can only be applied to Caucasian populations.

Conclusions

Several predictors have been identified to determine the risk of HF patients to be readmitted at the hospital within the first 15 or 30 days after discharge, and a score has been developed to guide preventative efforts. Thus, the follow-up after discharge of patients at greater risk could be maximized, and the follow-up of those at lower risk could be adjusted.

The current study reinforces the relevant role of monitoring the NT-proBNP decrease during admission for predicting early readmission; however, our findings suggest that the range of reduction that has a prognostic impact on 30-day readmission should be reviewed and increased to > 55%.

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Authors' Contribution Juan F. Delgado takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Compliance with Ethical Standards

Conflicts of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors

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- • Of importance
- •• Of major importance

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