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Original Article

A one-year mortality clinical prediction rule for patients with heart failure

Antonio Escobar [a,b,c,*], Lidia García-Pérez [b,d], Gemma Navarro [e], Amaia Bilbao [b,f], Raul Quiros [b,g], On behalf of the CACE-HF Score group

[a] Research Unit, Hospital Universitario Basurto, Avda. Montevideo 18, 48013 Bilbao, Spain
[b] Red de Investigación en Servicios de Salud en Enfermedades Crónicas (REDISSEC), Spain
[c] Kronikgune, Spain
[d] Planning and Evaluation Service, Canary Islands Health Service, Camino Candelaria, 44. C.S. San Isidro-El Chorrillo, 38109 El Rosario, Tenerife, Spain
[e] Epidemiology Unit, Hospital Universitari, Parc Taulí, 1, 08208 Sabadell, Barcelona, Spain
[f] Research Unit, Hospital Universitario Basurto, Avda. Montevideo 18, 48013 Bilbao, Spain
[g] Hospital Costa del Sol, Carretera Nacional 340, km 186, Marbella, Málaga, Spain

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ABSTRACT

Aims: To create and validate a clinical prediction rule which is easy to manage, reproducible and that allows classifying patients admitted for heart failure according to their one-year mortality risk.
Methods: A prospective cohort study carried out with 2565 consecutive patients admitted with heart failure in 13 hospitals in Spain. The derivation cohort was made up of 1283 patients and 1282 formed the validation cohort. In the derivation cohort, we carried out a multivariate logistic model to predict one-year mortality. The performance of the derived predictive risk score was externally validated in the validation cohort, and internally validated by K-fold cross-validation. The risk score was categorized into four risk levels.
Results: The mean age was 77.2 years, 49.7% were female and there were 611 (23.8%) deaths in the follow-up period. The variables included in the predictive model were: age ≥ 75, systolic blood pressure < 135, New York Heart Association class III–IV, heart valve disease, dementia, prior hospitalization, haemoglobin < 13, sodium < 136, urea ≥ 86, length of stay ≥ 14 and Physical dimension of Minnesota Living with Heart Failure questionnaire. The AUC for the risk score were 0.73 and 0.70 in the derivation and validation cohorts, respectively, and 0.73 in the K-fold cross-validation. The percentage of mortality ranged from 8.08% in the low-risk to 58.20% in the high-risk groups ($p < 0.0001$; AUC, 0.72).
Conclusions: This model based on routinely available data, for admitted patients and with a follow-up at one year is a simple and easy-to-use tool for improving management of patients with heart failure.

1. Introduction

Heart failure (HF) is called the great chronic illness of the 21st century. Due to its growing incidence and prevalence, as well as to the high complexity of the patients, HF has an important influence on associated costs and the quality of life of the patients.

Although survival has improved, the prognosis continues to be negative; after the diagnosis, the estimated survival rate is 50% and 10% at five and ten years respectively [1].

We have evidence that we can reduce the re-admittances with individualized attention, reinforcing self-care, and guiding the treatment according to the patient's characteristics through multidisciplinary teams; but the outcomes on survival are still to be determined [2].

Although we have greater diagnostic and therapeutic capacity, the care needs have increased in parallel with the age and the level of complexity of the patients. The stratification in prognostic levels improves their care, according to their needs, and increases the effectiveness of the healthcare system. One of the ways of stratifying patients is through the elaboration of clinical prediction rules (CPR), which inform on the probabilities of different outcomes such as re-admittance or death and which can lead to decreasing the uncertainty with which one works in clinical practice.

Different papers have developed CPR which stratify the patients and which can be applied at different stages of the illness. Among them, there are studies in outpatients [3] and hospitalized patients which try to predict the intrahospital mortality [4,5] or mortality in longer [6,7] or much longer periods [8].

Nonetheless, the applicability of these models in clinical practice is uncertain, the majority were created from cohorts of clinical trials in

* Corresponding author at: Unidad de Investigación, Hospital Universitario Basurto, OSI Bilbao-Basurto, Avda. Montevideo 18, 48013 Bilbao, Bizkaia, Spain.
E-mail addresses: antonio.escobarmartinez@osakidetza.eus (A. Escobar), lidia.garciaperez@sescs.es (L. García-Pérez), gnavarro@tauli.cat (G. Navarro), Amaia.bilbaogonzalez@osakidetza.eus (A. Bilbao).

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which HF with reduced Ejection Fraction (HFrEF) and young patients in early stages of the illness are predominant. Another limitation is that some models are based on a retrospective evaluation or come from small series [7–9]. Finally, these models do not include Health Related Quality of Life (HRQoL) questionnaires, despite being an independent predictor of survival adjusted for different sociodemographic, clinical or laboratory variables. We have found only one CPR that includes this variable [9].

Our objective was to create and validate CPR that are easy to manage, reproducible and that allow classifying the patients admitted for HF according to their one-year mortality risk, the CACE-HF Score (Canary Islands, Andalusia, Catalonia and Euskadi).

2. Methods

2.1. Patients

A prospective, multicentre cohort study, conducted in Spain, in 13 hospitals: 3 in the Canary Islands, 4 in Andalusia, 1 in Catalonia, and 5 in the Basque Country (Euskadi). The cohort was formed by patients admitted consecutively between January 2009 and May 2013 in the cardiology or internal medicine departments. The first admission within the study period was the index admission, and the subsequent ones were considered re-admissions.

The inclusion criteria were: primary diagnosis of HF (International Classification of Diseases (ICD), 9th Revision, Clinical Modification code 428), being over 18 years of age, and acceptance of participating in the study. We excluded the patients who developed the HF episode during hospital stay, transfers from other healthcare centres or those that died during the stay. The follow-up period of all the patients was for one year. The study complies with the Helsinki Declaration and all the patients signed the informed consent.

2.2. Variables

Variables were arranged in demographic, clinical, laboratory and comorbidity groups according to the Charlson Index [10]. In addition, the patients filled out three HRQoL questionnaires: two generic questionnaires, Short Form-12 (SF-12) [11] and the Euro-Qol-5D (EQ-5D-3L) [12] and the third is a specific HF questionnaire, the Minnesota Living with Heart Failure Questionnaire (MLHFQ) [13].

SF-12 provides two summary measures, the mental (MCS) and physical (PCS) component summaries. It is scored from 0 (worst status) to 100 (best status). It has been validated in Spanish [14].

EQ-5D-3L consists of two components: the descriptive system and a visual analogue scale (EQ-VAS). The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, and for each dimension there are three response levels: no problems, some problems, and extreme problems. The EQ-VAS records the respondent's self-rated health on a vertical VAS, where the endpoints are 'best imaginable health state' and 'worst imaginable health state'. It has been validated in Spanish [15].

The MLHFQ is a 21-item scale scored from 0 (best) to 105 (worst). It has two dimensions: physical with eight items (range 0–40), emotional with five items (range 0–25) and a total score (range 0–105). The questionnaire has been validated in Spanish [16].

2.3. Outcomes

The variable was mortality due to any cause at one year from hospital discharge. It was collected by means of clinical records and access to the National Death Index (registry in the Ministry of Health which includes 100% of the deaths registered in Spain). The follow-up, at one year, was completed in all the patients.

2.4. Statistical analysis

The sample was randomly divided into two subsamples, derivation and validation subsamples, each with half of the total population. Descriptive statistics included frequency tables, means and standard deviation (SD). Patient characteristics were compared between two subsamples. Chi-square or Fisher's exact test was performed for the comparison of categorical variables, and the Student's *t*-test or nonparametric Wilcoxon tests for continuous variables.

Univariate logistic regression models were performed in the derivation sample to identify the statistical significance of each prognostic factor. The continuous independent variables were also considered as categorical. For the categorization, the Receiver Operating Characteristics (ROC) curve approach was used, considering as optimal cut-off value the one which maximized the sum of sensitivity and specificity. Variables with a significance of $p < 0.15$ were considered potential independent variables in the multivariate logistic regression model. In the final model, only factors with $p < 0.05$ were retained. The odds ratio (OR) and the 95% confidence interval (CI) were calculated. The possible interaction between variables was also examined. The predictive accuracy of the model was determined by the area under the ROC curve (AUC) for discrimination [17], and by comparing predicted and observed one-year mortality using the Hosmer–Lemeshow test for calibration [18].

To develop the predictive risk score, we first assigned a weight to each prognostic factor in relation to each β parameter. Next, we added the weights of each of the prognostic factors, with a higher score corresponding to a higher likelihood of one-year mortality. The predictive accuracy of the mortality risk score was determined by means of the AUC [17] and the Hosmer–Lemeshow test [18], in both derivation and validation samples (external validation). In addition, we attempted to validate the risk score by K-fold cross-validation [19] (internal validation).

Once the one-year mortality risk score was developed, we divided the score into four categories (low, medium, high, and very high risk) by means of the CatPredi function of the R package [20] using the genetic algorithm. The performance of the risk categories was studied by comparing the mortality rate and using the logistic regression model with the AUC, in both derivation and validation samples. Finally, Kaplan-Meier curves were constructed for each risk category, and comparisons were performed by the log-rank test.

All effects were considered significant at $p < 0.05$, unless otherwise stated. All statistical analyses were performed using SAS for Windows statistical software, version 9.2 (SAS Institute, Inc., Carey, NC), R© software version 3.0.0.

3. Results

A total of 2565 patients were recruited, 54.4% admitted in Cardiology Services ($n = 1.369$) and 45.6% in Internal Medicine Services ($n = 1.169$). The mean age was 77.2 years (SD: 10.2), and 49.7% were women. The mean length of stay was 9.9 days (SD: 8.5). The Left Ventricle Ejection Fraction (LVEF) was obtained in 2268 (88.4%) patients by echocardiography (98.5%).

During the follow-up, 611 (23.8%) deaths occurred in the cohort. The derivation and validation cohorts are formed by 1283 and 1282 patients respectively. The main data are in Table 1.

Based on the logistic models in the derivation cohort, we developed two predictive models (Table 2): the first one included the HRQoL measured by the MLHFQ (Model I), and the second one did not (Model II). In the multivariate logistic regression analysis, eleven factors were independently associated with one-year mortality (Model I): age, Systolic Blood Pressure, NYHA, aetiology of HF (valvular), dementia, previous admissions, haemoglobin, sodium, urea, length of stay, and the physical factor of the MLHFQ. The model showed good discrimination, with AUC of 0.734, and was well calibrated (Hosmer–Lemeshow, $p = 0.9611$). In relation to each β parameter, a weight was assigned to each risk factor.

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