Med Clin (Barc). 2017;149(4):147–152

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Original article

Influence of blood pressure at the beginning of decompensations in the prognosis of patients with heart failure☆

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ARTICLE INFO

Article history:
Received 28 September 2016
Accepted 19 January 2017
Available online 12 August 2017

Keywords:
Blood pressure
Heart failure
Reverse epidemiology

ABSTRACT

Background and objective: An inverse relationship has been described between blood pressure and the prognosis in heart failure (HF). The characteristics of this relationship are not well unknown. The objective of this study was to determine if this relationship is maintained in a non-selected cohort of patients with HF and if it can be modified by treatment.
Material and methods: Prospective study of cohorts including patients hospitalised for decompensated HF in Internal Medicine departments and followed as outpatients in a monographic consultation. Patients were classified according to their levels of systolic (SBP) and diastolic blood pressure (DBP). Clinical characteristics, all-cause mortality and readmissions after the first, third and sixth month of follow-up were analysed.
Results: Two hundred and twenty-one patients were included after their admission to the hospital for acute HF. Mean patient age was 79.5 years (SD 8.09); 115 patients were male. No significant differences between SBP quartiles and basal characteristics were found. Patients with lower SBP (Q1) had higher mortality rates (20%, $p < 0.05$). No significant differences between mortality/readmissions and DBP were found. However, the Kaplan–Meier analysis showed higher all-cause mortality rates for the group of patients with lower SBP and DBP (log-rank = 0.011 and 0.041, respectively). The pharmacological treatment did not differ significantly between both study groups.
Conclusion: For non-selected patients suffering HF, higher SBP upon the admission is associated with significantly lower all-cause mortality rates during follow-up. Pharmacological treatment of HF does not seem to influence this inverse relationship between SBP at admission and patient mortality.

Influencia de la presión arterial al inicio de las descompensaciones en el pronóstico de pacientes con insuficiencia cardiaca

Palabras clave:
Presión arterial
Insuficiencia cardiaca
Epidemiología reversa

RESUMEN

Fundamento y objetivo: Existe una relación inversa entre las cifras de presión arterial en las descompensaciones y el pronóstico de la insuficiencia cardiaca (IC). Las características de esta relación no son bien conocidas. El objetivo del estudio fue analizar si esta relación se mantiene en una cohorte no seleccionada de pacientes con IC y si el tratamiento la modifica.
Material y métodos: Estudio prospectivo de cohortes de pacientes ingresados por IC descompensada en un servicio de Medicina Interna y seguidos ambulatoriamente en una consulta monográfica. Los pacientes fueron agrupados en función de la presión arterial sistólica (PAS) y diastólica (PAD); se analizaron las características clínicas, la mortalidad global y los reingresos al primer, tercer y sexto mes de seguimiento.
Resultados: Se incluyeron 221 pacientes tras un ingreso índice por IC. Media de edad: 79,5 años (DE 8,09); varones: 115. No hubo diferencias significativas en las características basales de los pacientes en función de los cuartiles de PAS. Los pacientes con menor PAS (Q1) tenían mayor mortalidad (20%, p < 0,05).

☆ Please cite this article as: Torrente Iranzo S, Garcés Horna V, Josa Laorden C, Rubio Gracia J, Ruiz Laiglesia FJ, Sánchez Marteles M, et al. Influencia de la presión arterial al inicio de las descompensaciones en el pronóstico de pacientes con insuficiencia cardiaca. Med Clin (Barc). 2017;149:147–152.
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No se encontraron diferencias para la PAD. Sin embargo, el análisis de Kaplan-Meier mostró una mayor mortalidad global en los pacientes con menor PAS y PAD (log-rank = 0,011 y 0,041, respectivamente). Las características del tratamiento farmacológico no diferían entre los grupos del estudio.
Conclusión: En pacientes con IC no seleccionados, las cifras elevadas de PAS al ingreso se asocian con una menor mortalidad durante el seguimiento. El tratamiento farmacológico de la IC no parece influir en la relación inversa entre la PAS al ingreso y la mortalidad.

Introduction

Heart failure (HF) is the main cause of hospitalisation in Internal Medicine services, and involves a high rate of morbidity and mortality. The prevalence of HF in Europe is 1–2% of the population, and its survival rates are lower than those of prostate, intestine, and breast cancer.[1]

Obesity and high blood pressure are known risk factors for the development of cardiovascular diseases, including HF, among others. However, recent studies show that once HF is established, both appear to behave as predictive factors for greater prognosis, associated with reduced mortality during monitoring. These still poorly characterised phenomena have been called the "hypertension and obesity paradox" respectively, which encompasses the somewhat generic concept of reverse epidemiology.[2,3] Pharmacological treatment for HF with reduced ejection fraction (HFrEF) has demonstrated its efficacy in reducing morbidity and mortality.[4] There is no treatment for HF with preserved ejection fraction (HFpEF) that has demonstrated a clear benefit, however the same pharmaceuticals used for HFrEF are regularly administered, and the mortality rates for both are similar or slightly higher for HFrEF.[5,6] It is possible that the inverse relationship observed between the blood pressure (BP) taken at the onset of the decompensations and the HF prognosis may change during monitoring in order to optimise pharmacological treatment according to the clinical practice guidelines.[7]

The primary objective of this study was to analyse if there was a relationship between systolic blood pressure (SBP) and diastolic blood pressure (DBP), and readmissions or mortality during the monitoring of patients previously admitted for decompensated HF that were monitored in a specialised unit, and if this relationship persisted regardless of the treatment administered.

Patients and methods

This is a prospective observational cohort study.

All patients were included who were discharged consecutively following an HF hospitalisation episode between June 2010 and October 2014, and who were to be monitored by the specialised HF unit. A routine visit was carried out during the first, third, and sixth month. The referral criteria were clinical, with such determination being left to the general practitioner responsible for the patient, without any restrictions to this regard. The decision to refer the patient to the specialised unit was followed by biomarkers and clinical criteria, selecting *a priori* those patients that may have the worst prognosis, and who would therefore benefit from treatment that is more suitable. The patients gave their written consent to have their data collected and used for the research purposes of the study.

The inclusion criteria were: patients over the age of 18 with a clinical diagnosis of acute HF (*de novo* or acute chronic HF) and concentrations of N-terminal pro-B-type natriuretic peptide (NT-proBNP) > 1000 pg/ml when hospitalised. Excluded were those patients with cognitive impairment, a life expectancy of less than 6 months, active neoplasm, advanced kidney failure (glomerular filtration < 30 ml/min/1.73 m^2 according to the *Modification of Diet of Renal Disease 4* formula), inotropic treatment when hospitalised, or an allergy to diuretic treatment.

Following the index hospitalisation, patients continued with outpatient monitoring in the HF unit at the one month, three month, and six month mark after discharge, as a minimum.

In order to analyse the relationship between BP and episodes during monitoring, the first BP reading was taken as a reference, which was recorded when the patient arrived at the hospital's Emergency Room.

Mortality due to HF and the combined variable of mortality and readmissions due to HF at 180 days were considered as primary episodes. Overall mortality was also analysed. Test, ultrasound, and demographic data were collected during the medical record review.

In the first 24–48 h following hospital admission, kidney function was determined through urea, creatinine, and serum cystatin concentrations; ion, haemoglobin, hematocrit, total proteins, albumin, total cholesterol, and NT-proBNP were measured.

Patients with a left ventricular ejection fraction (LVEF) of ≥50% were considered HFpEF.

Statistical analysis

Quantitative variables are described by the average and standard deviation (SD), while qualitative variables are done with frequency distribution. The quantitative variables are compared with the with the Student's *t*-test (2 groups), ANOVA (more than 2 groups), or nonparametric tests from Mann–Whitney or Kruskal–Wallis, while qualitative tests are done with the χ test.[2]

The result's primary variable was the total mortality, carrying out patient monitoring from the time of their inclusion until they completed the study, either due to the study's finalisation date being reached, or because of death or loss. The mortality study between SBP and DBP quartiles were carried out through Kaplan–Meier analysis and the log-rank test.

Lastly, a Cox regression analysis was carried out, estimating the hazard ratios and their 95% confidence intervals (95% HF), in order to evaluate the mortality risk of the various factors, with a multivariable sequential exclusion analysis being carried out later to determine independent predictive factors for mortality. In order to facilitate understanding of the multi-variable study, normalised BP values were used.

Significant values were considered to be $p < 0.05$. The *Statistical Package for the Social Sciences* 15.0 (SPSS Inc., Chicago, IL, USA) statistical programme was used.

Results

Included were 221 patients (115 male and 106 female) with an average age of 79.51 years (SD 8.09). The average SD of our patients was 138.92 mmHg (SD 29.46), and the average DBP was 73.57 (SD 14.67). Smokers make up 26% of the group, and the average LVEF was 52.80%; 56% of patients had a LVEF ≥ 50%. The NT-proBNP average was 5339.58 pg/ml.

In Tables 1 and 2, the test and clinical characteristics for patients are presented, distributed according to the SD and DBP quartiles, respectively. Patients in the SBP Q4 (SBP > 157.5 mmHg) had a