

## Original article

## Prognostic Benefit of Beta-blockers After Acute Coronary Syndrome With Preserved Systolic Function. Still Relevant Today?



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## ABSTRACT

**Introduction and objectives:** The scientific evidence for using beta-blockers after acute coronary syndrome stems from studies conducted in the days before coronary revascularization and in patients with ventricular dysfunction. The aim of this study was to analyze the current long-term prognostic benefit of beta-blockers in patients with acute coronary syndrome and preserved left ventricular ejection fraction.

**Methods:** We conducted a retrospective cohort study of 3236 patients with acute coronary syndrome and left ventricular ejection fraction  $\geq 50\%$ . We performed a propensity-matched analysis to draw up two groups of 555 patients paired according to whether or not they had been treated with beta-blockers. The prognostic value of beta-blockers to predict mortality during follow-up was analyzed using Cox regression.

**Results:** During the follow-up (median, 5.2 years), 506 patients (15.6%) died. Patients treated with beta-blockers ( $n = 2277$  [70.4%]) had a lower mortality rate (11.6% vs 25.2%;  $P < .001$ ). After propensity score matching, we found that mortality during follow-up was still lower in the beta-blocker group (14.4% vs 18.9%;  $P = .020$ ). Therefore, this treatment was an independent protective factor after adjusting for confounding variables in the multivariate Cox regression analysis (hazard ratio = 0.64; 95% confidence interval, 0.48-0.87;  $P = .004$ ).

**Conclusions:** Beta-blocker treatment in patients with acute coronary syndrome and preserved left ventricular ejection fraction is associated with lower long-term mortality.

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### ¿En la era actual existe beneficio pronóstico del tratamiento con bloqueadores beta tras un síndrome coronario agudo con función sistólica conservada?

## RESUMEN

**Introducción y objetivos:** La evidencia científica para el uso de bloqueadores beta tras un síndrome coronario agudo radica en estudios previos a la era de la revascularización coronaria o en pacientes con disfunción ventricular. Con este trabajo se pretende analizar en la era actual el valor pronóstico a largo plazo de los bloqueadores beta en pacientes con síndrome coronario agudo y fracción de eyección del ventrículo izquierdo conservada.

**Métodos:** Estudio de cohortes retrospectivo que incluyó a 3.236 pacientes con síndrome coronario agudo y fracción de eyección del ventrículo izquierdo  $\geq 50\%$ . Se realizó un análisis mediante *propensity score* y después un emparejamiento basado en él, con lo que se obtuvieron dos grupos de 555 pacientes emparejados según fueran tratados con bloqueadores beta o no. El valor pronóstico de mortalidad durante el seguimiento con los bloqueadores beta se analizó mediante regresión de Cox.

**Resultados:** Durante el seguimiento (mediana, 5,2 años), murieron 506 pacientes (15,6%). Los pacientes tratados con bloqueadores beta ( $n = 2.277$  [70,4%]) tuvieron menos mortalidad (el 11,6 frente al 25,2%;  $p < 0,001$ ). Tras emparejar por *propensity score*, la mortalidad en el seguimiento continuó siendo más baja en el grupo de bloqueadores beta (el 14,4 frente al 18,9%;  $p = 0,020$ ), por lo que dicha terapia resulta un factor protector independiente tras ajustar por variables confusoras en el análisis multivariable de regresión de Cox (*hazard ratio* = 0,64; intervalo de confianza del 95%, 0,48-0,87;  $p = 0,004$ ).

## Palabras clave:

Bloqueadores beta

Síndrome coronario agudo

Mortalidad

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**Conclusiones:** Tratar con bloqueadores beta a pacientes con síndrome coronario agudo y fracción de eyección del ventrículo izquierdo preservada se asocia con menos mortalidad a largo plazo.  
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## Abbreviations

ACS: acute coronary syndrome  
LVEF: left ventricular ejection fraction  
PCI: percutaneous coronary intervention

## INTRODUCTION

The current American College of Cardiology and European Society of Cardiology guidelines recommend starting beta-blockers in all patients with acute coronary syndrome (ACS) within a few hours of onset and continuing indefinitely at discharge.<sup>1–4</sup> These recommendations are particularly strong for patients with reduced left ventricular ejection fraction (LVEF).

However, clinical practice guidelines that recommend the use of beta-blockers after ACS are based on scientific evidence from studies conducted in the pre-percutaneous revascularization era.<sup>5–13</sup> Since the introduction of percutaneous coronary intervention (PCI), the protective role of beta-blockers is less clear, and appears to apply more to high-risk patients<sup>14</sup> such as those with multivessel disease,<sup>15</sup> previous myocardial infarction<sup>16</sup>, and reduced LVEF.<sup>17</sup> There is little evidence supporting the benefit of beta-blockers after an ACS in patients with preserved LVEF function in the current era.

To investigate this issue, we conducted a study based on propensity score matching to assess the prognostic benefit of beta-blockers on mortality in a contemporary cohort of patients with ACS and preserved left ventricular systolic function.

## METHODS

### Study Population

We based our retrospective cohort study on all patients entered in the CardioCHUS registry who were consecutively admitted with a diagnosis of ACS to the Cardiology Department of Hospital Clínico de Santiago de Compostela (consisting of the coronary unit, intermediate care, and wards) between December 2003 and September 2012 (n = 5203). We selected patients surviving the hospital stay (n = 4904) and then filtered for those who had an LVEF  $\geq 50$  at discharge, calculated using Simpson's rule (n = 3355) (Figure 1). Follow-up data were available for 96.5% of these patients, and therefore the study cohort consisted of 3236 patients. Cardiologists from our department prospectively collected patients' demographic, clinical, and angiographic data as well as details on treatment and follow-up. The study was conducted in accordance with the principles of the Declaration of Helsinki.

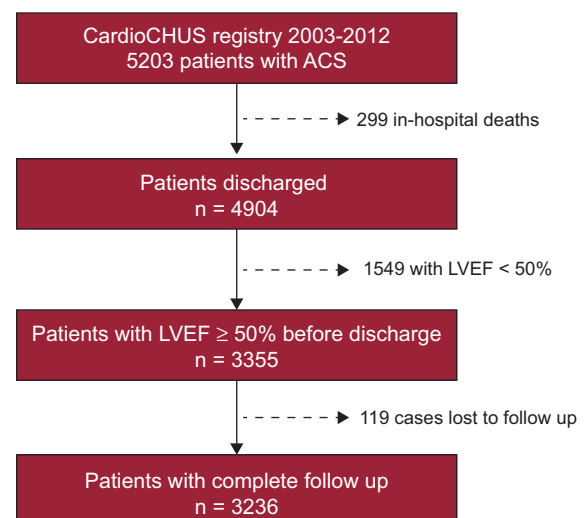
### Study Objective and Follow-up

We divided patients into two groups, according to whether they were receiving beta-blocker treatment at discharge

(n = 2277 [70.4%]) or not (n = 959 [19.6%]). The clinical cardiologist in charge of each patient decided whether to use beta-blocker treatment. The primary study endpoint was the effect of beta-blocker treatment on overall mortality during follow-up (median, 5.2 years [interquartile range, 2.0–7.2 years]). After discharge, patients were followed up at an ischemic heart disease clinic and by their general physicians. Our structured follow-up was based on each patient's unique electronic health record (IANUS program, Galicia autonomous community), reviewing all medical contacts and hospital notes. We followed up by telephone in some cases.

### Statistical analysis

Quantitative variables were expressed as mean (standard deviation) and we used Student *t* test for between-group comparisons. Categorical variables were expressed as a percentage and we compared them using chi-square. Since this study had a nonrandomized design and multiple factors affect the decision to start beta-blocker treatment, we performed a propensity-matched analysis to reduce the bias from studying treatment effect in an observational context. We used the propensity score to assess the probability of a patient receiving beta-blocker treatment according to his or her baseline characteristics. We then matched the propensity scores, a statistical technique that equates group characteristics using defined variables to analyze the effect of a single variable. In our case, this variable was nonrandomized beta-blocker treatment at discharge. We applied a greedy 1:1 matching algorithm without replacement and defined optimal matching as a standard deviation of 0.2. Binary logistic regression was used for the analysis, where the dependent variable was beta-blocker treatment (yes/no) and explanatory variables were age (continuous variable), female sex, diabetes mellitus, smoker, peripheral



**Figure 1.** Flow chart of patients enrolled in the study. LVEF, left ventricular ejection fraction; ACS, acute coronary syndrome.

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