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ORIGINAL ARTICLE

# Effect of beta-blocker dose on mortality after acute coronary syndrome

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**KEYWORDS**
Beta-blocker;
Dose;
Acute coronary syndrome;
Mortality

**Abstract**
*Introduction:* Beta-blocker doses that have been shown to be effective in randomized clinical trials are not commonly used in daily clinical practice. The aim of this study was to analyze whether there is a prognostic benefit of high rather than low doses of beta-blockers after an acute coronary syndrome (ACS).
*Methods:* In this retrospective cohort study, 2092 ACS patients discharged from hospital between June 2013 and January 2016 were classified according to the beta-blocker dose prescribed: high dose (≥50% of the target dose tested in clinical trials) and low dose (<50%). Two groups of 501 matched patients were obtained through propensity score matching according to treatment with high or low doses of beta-blockers. The prognostic impact (mortality) during follow-up of high vs. low dose was analyzed by Cox regression and represented by Kaplan-Meier curves.
*Results:* Of the 2092 patients, 80.5% were discharged under beta-blockers, with lower mortality during follow-up (18.6±9.7 months). Of the 1685 patients discharged under beta-blockers, only 31.4% received high doses. There were no differences in mortality during follow-up between patients under high-dose vs. low-dose beta-blockers (HR 0.935, 95% CI 0.628-1.392, p=0.740), and the equivalence between the two doses remained after propensity score matching (HR 1.183, 95% CI 0.715-1.958, p=0.513).
*Conclusion:* No prognostic benefit was found in terms of mortality for high-dose vs. low-dose beta-blockers after an ACS.


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**PALAVRAS-CHAVE**
Betabloqueador;
Dose;
Síndrome coronária aguda;
Mortalidade

**Efeito da dose de betabloqueador na mortalidade após síndrome coronária aguda**

**Resumo**
*Introdução:* A dose de betabloqueador que demonstrou ser efetiva em ensaios clínicos aleatorizados não é a comummente usada na prática clínica diária. O objetivo deste estudo foi analisar se existe um benefício prognóstico da dose alta *versus* baixa dose de betabloqueador após uma síndrome coronária aguda (SCA).
*Métodos:* Estudo de coorte retrospetivo, envolveu 2092 doentes com alta após SCA, entre junho de 2013 e janeiro de 2016. Os doentes foram classificados de acordo com a dose de betabloqueador prescrita: alta (≥50% da dose-alvo testada em ensaios clínicos) e baixa (<50%). Foram obtidos dois grupos de 501 doentes emparelhados, por meio de *propensity score matching*, de acordo com terem sido tratados com alta ou baixa dose de betabloqueadores. O impacto prognóstico (mortalidade) durante o seguimento da dose elevada *versus* baixa foi analisado pela regressão de Cox e representado pelas *curvas* de Kaplan-Meier.
*Resultados:* Dos 2092 doentes, 80,5% tiveram alta com betabloqueadores, com uma menor mortalidade durante o seguimento (18,6±9,7 meses). Dos 1685 doentes com betabloqueadores na alta, apenas 31,4% receberam altas doses de betabloqueadores. Não houve diferenças na taxa de mortalidade durante o seguimento entre os doentes com doses altas *versus* doses baixas de betabloqueadores (HR 0,935, IC 95% 0,628-1,392, p=0,740), manteve-se a equidade entre as duas doses após o *propensity score matching* (HR 1,183, IC 95% 0,715-1,958, p=0,513).
*Conclusão:* Não foi encontrado qualquer benefício prognóstico em termos de mortalidade entre doses elevadas e doses baixas de betabloqueadores após uma SCA.


## Key points

Therapy with beta-blockers is recommended for patients after an acute coronary syndrome, but the most commonly prescribed doses are less than half those evaluated in the randomized clinical trials that demonstrated efficacy, and optimum doses have not been validated. The data of our study do not demonstrate increased survival in patients treated with beta-blocker doses approximating those used in previous randomized clinical trials compared with lower doses. These findings provide the rationale to investigate the appropriate beta-blocker dosage after acute coronary syndrome to derive optimal benefit from this therapy.

## Introduction

Beta-blocker treatment is part of the therapeutic arsenal commonly used after an acute coronary syndrome (ACS). The prognostic benefit of these drugs after an ACS was established by studies carried out in the era prior to percutaneous revascularization[1,2] as well as by studies on patients with left ventricular systolic dysfunction.[3] However, based on data from multiple contemporary non-randomized studies,[4–6] clinical practice guidelines consider it reasonable to extrapolate their prognostic benefit to the full spectrum of ACS patients, unless there is an established contraindication.[7–10]

While the recommendation for beta-blockers after an ACS is based on solid scientific evidence, the type and dosage are not consensual. Clinical trials used high doses of beta-blockers to establish the efficacy of this medication,[1,2,11] however such high doses are often not tolerated and are not used in daily clinical practice.[12] Based on available clinical trials and extrapolation of existing evidence in the field of heart failure,[13] it seems reasonable to prescribe the beta-blocker doses used in these studies, or at least titrate to the highest dose tolerated by the patient. However, there is little evidence on this question, and the available data are controversial.[14,15]

This study aims to analyze whether there are prognostic differences between high and low doses of beta-blockers in terms of long-term survival after an ACS.

## Methods

### Study population

This retrospective cohort study included all consecutive patients admitted to the cardiology department of the Álvaro Cunqueiro University Hospital of Vigo between June 2013 and January 2016 with a diagnosis of ACS and who underwent coronary angiography (n=2702). Patients with no evidence of angiographically significant coronary lesions (n=432) were excluded from the original registry, as were those who died during hospital stay (n=102). Follow-up data were obtained in 96.6% of these 2168 patients (74 patients without follow-up data), so the study cohort comprised 2092 patients. Demographic, clinical and angiographic data, as well as information on treatment and follow-up, were collected and reviewed prospectively by cardiologists of this department. The study was carried

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