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ORIGINAL ARTICLE

Impact of Anaemia on Mortality and its Causes in Elderly Patients with Acute Coronary Syndromes

Albert Ariza-Solé, MD [a*], Francesc Formiga, PhD [b], Joel Salazar-Mendiguchía, MD [a], Alberto Garay, MD [a], Victòria Lorente, MD [a], José C. Sánchez-Salado, MD [a], Guillermo Sánchez-Elvira, MD [a], Josep Gómez-Lara, PhD [c], Joan A. Gómez-Hospital, PhD [c], Angel Cequier, PhD [c]

[a]Coronary Care Unit, Heart Diseases Institute, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Spain
[b]Geriatrics Unit, Internal Medicine Department, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Spain
[c]Interventional Cardiology Unit, Heart Diseases Institute, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Spain

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Background Prognostic impact of anaemia in the elderly with acute coronary syndromes has not been specifically analysed, and little information exists about causes of mortality in this setting.

Methods We prospectively included consecutive patients with acute coronary syndromes. Anaemia was defined as haemoglobin < 130 g/L in men, and < 120 g/L in women. Primary outcome was mid-term mortality and its causes. Analyses were performed by Cox regression method.

Results We included 2128 patients, of whom 394 (18.6%) were aged 75 years or older. Anaemia was more common in the elderly (40.4% vs 19.5%, p <0.001). Mean follow-up was 386 days. Anaemia independently predicted overall mortality (HR 1.47, 95% CI 1.05-2.06), cardiac mortality (HR 1.76, 95% CI 1.06-2.94) and non-cardiac mortality (HR 1.59, 95% CI 1.03-2.45) in the overall cohort. In young patients the association between anaemia and mortality was significant only for non-cardiac causes. The association between anaemia and mortality was not significant in the elderly (HR 1.08, 95% CI 0.71-1.63, p 0.736).

Conclusions The impact of anaemia on cause specific of mortality seem to be different according to age subgroup. The association between anaemia and mortality was not observed in elderly patients from our series.

Keywords Anaemia • Acute Coronary Syndrome • Prognosis • Frail elderly • Mortality

Introduction

Anaemia is a common comorbidity among patients with acute coronary syndromes (ACS) [1] and is associated with higher mortality in this clinical setting [2]. The exact mechanisms to explain this association remain unclear. Although anaemia may reduce oxygen delivery to the myocardium, thus increasing cardiovascular events, patients with anaemia are usually older, with more comorbidities that could also increase mortality due to non-cardiac diseases. Little information exists about cause specific mortality in ACS patients with anaemia.

On the other hand, frailty and comorbidities are common in elderly patients with ACS, making management and risk

*Corresponding author at: Coronary Care Unit, Cardiology Department. Bellvitge University Hospital, Feixa Llarga, sn. 08907. Hospitalet de Llobregat. Barcelona. Spain. Tel.: +34 932607924; fax: +34 932607541, Email: aariza@bellvitgehospital.cat

stratification difficult in this clinical scenario [3]. Information about the prognostic impact of anaemia in the elderly with ACS is scarce. The aim of the present study was to prospectively assess the impact of anaemia in overall mortality and its causes, in consecutive patients with ACS and also specifically in the elderly.

Patients and Methods

Study Design and Population

This is an observational single centre registry, which was conducted at a tertiary care Hospital in Spain (Hospital Universitari de Bellvitge, l'Hospitalet de Llobregat, Barcelona). All consecutive ACS patients admitted to the Coronary Care Unit between October 2009 and April 2014 were prospectively included. Informed consent was provided by all patients before their inclusion in the study. The confidential information of the patients was protected according to current national normative. This manuscript has been revised for its publication by the Clinical Research Ethics Committee of Bellvitge University Hospital (IRB00005523).

The primary outcome was mid-term mortality, its causes and its association with anaemia. Information on deaths was obtained from hospital records, death certificates, or telephone contact with relatives of the patients or referring physician. The assignment of the cause of death was based on clinical judgment of the physician taking care of the patient at the time of death. In cases of coexistence of two or more possible causes, the assignment was performed taking into account the clinical relevance of each of those conditions and their contribution at the time of death. Death was deemed cardiac when it was due to myocardial infarction, heart failure or sudden death.

Definitions, Data Collection and Management

ACS without ST segment elevation was defined as the presence of chest pain during the previous 48 hours with ST-segment changes on electrocardiography indicating ischaemia or a positive troponin test. ACS with ST segment elevation was defined as the presence of chest pain with persistent ST-segment elevation of at least 0.1 mV in at least two contiguous leads or a new left bundle-branch block. Patients were classified as anaemic using the definition of the World Health Organization: haemoglobin < 130 g/L in men, and < 120 g/L in women [4]. Patients aged 75 years or older were considered elderly for the purpose of this study.

Data were prospectively collected on site by trained physicians using a standardised case report form. Anthropometric measures, baseline characteristics, medical history, biochemical and electrocardiographic findings and in-hospital treatments were collected. Data about in-hospital clinical course was also collected, such as invasive procedures requirements (Swan Ganz catheter, intra-aortic counterpulsation, mechanical ventilation, renal replacement therapy) and in-hospital complications (bleeding, need for transfusion, infectious complications, reinfarction, mechanical and arrhythmic complications, in-hospital mortality). The quality of data collection was assessed by checking source documentation in random samples. Haemodynamic parameters (heart rate, systolic blood pressure) and Killip class were measured at admission. Creatinine clearance was calculated using the Cockcroft-Gault formula [5]. Body surface area was calculated using the Mosteller formula [6]. Patients were managed according to current clinical guidelines.

Statistical Analysis

Quantitative variables were expressed as mean and standard deviation. For baseline variables, Student t test was used for comparison of quantitative variables and chi-square test or Fisher's exact test, when appropriate, were used for categorical variables (PASW Statistics 18, Chicago, IL, USA). The analysis of normal distribution of variables was performed using the Kolmogorov-Smirnov test.

Association between Anaemia and Mortality

Patients with missing haemoglobin values and patients lost to follow-up were excluded from this analysis. Baseline characteristics of these patients were assessed in order to assess the impact of this exclusion. No significant differences were observed.

Survival curves were performed by the Kaplan-Meier method. The multivariate analysis of the association between anaemia and mortality was assessed by the Cox regression method. The proportionality assumption of the model was assessed by the Kalbfleisch and Prentice method [7]. Criteria for including [8] potential confounders in the multivariate analysis were: 1) a significant association (p<=0.2) both with exposition (anaemia) and effect (mortality); 2) a clinically reasonable potential confounding effect between anaemia and mortality; and 3) not being an intermediate variable in the association between exposition and effect. Confounders included in the final model are listed in Table 4. Unadjusted and adjusted hazard ratios of mid-term mortality were calculated for elderly patients (aged 75 tears or older), young patients and for the overall cohort.

The association between anaemia and mortality in the final model was considered significant when the Hazard ratio was p =<0,05 and its 95% confidence interval did not include value 1.

Association between Anaemia Severity and Mortality

For the purpose of this analysis, patients' haematocrit values were divided into seven categories (<24.0%, 24.1 to 27.0%, 27.1 to 30.0%, 30.1 to 33.0%, 33.1 to 36.0%, 36.1 to 39.0%, and 39.1% or higher). The analysis was performed by Cox regression method, calculating Hazard ratio for each haematocrit category, taking patients with haematocrit higher than 39.1% as reference group. Survival curves of each haematocrit category were performed by the Kaplan Meier method. These