

## Original article

## Efficacy of Bleeding Risk Scores in Elderly Patients with Acute Coronary Syndromes



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## ABSTRACT

**Introduction and objectives:** The incidence of acute coronary syndromes is high in the elderly population. Bleeding is associated with a poorer prognosis in this clinical setting. The available bleeding risk scores have not been validated specifically in the elderly. Our aim was to assess predictive ability of the most important bleeding risk scores in patients with acute coronary syndrome aged  $\geq 75$  years.

**Methods:** We prospectively included consecutive acute coronary syndromes patients. Baseline characteristics, laboratory findings, and hemodynamic data were collected. In-hospital bleeding was defined according to CRUSADE, Mehran, ACTION, and BARC definitions. CRUSADE, Mehran, and ACTION bleeding risk scores were calculated for each patient. The ability of these scores to predict major bleeding was assessed by binary logistic regression, receiver operating characteristic curves, and area under the curves.

**Results:** We included 2036 patients, with mean age of 62.1 years; 369 patients (18.1%) were  $\geq 75$  years. Older patients had higher bleeding risk (CRUSADE, 42 vs 22; Mehran, 25 vs 15; ACTION, 36 vs 28;  $P < .001$ ) and a slightly higher incidence of major bleeding events (CRUSADE bleeding, 5.1% vs 3.8%;  $P = .250$ ). The predictive ability of these 3 scores was lower in the elderly (area under the curve, CRUSADE: 0.63 in older patients, 0.81 in young patients;  $P = .027$ ; Mehran: 0.67 in older patients, 0.73 in younger patients;  $P = .340$ ; ACTION: 0.58 in older patients, 0.75 in younger patients;  $P = .041$ ).

**Conclusions:** Current bleeding risk scores showed poorer predictive performance in elderly patients with acute coronary syndromes than in younger patients.

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## Eficacia de los scores de riesgo hemorrágico en el paciente anciano con síndrome coronario agudo

## RESUMEN

**Introducción y objetivos:** La incidencia de síndrome coronario agudo en pacientes ancianos es elevada. Las complicaciones hemorrágicas empeoran el pronóstico en este escenario; a pesar de ello, los scores de riesgo hemorrágico disponibles no han sido validados específicamente en este subgrupo. Nuestro objetivo es analizar la capacidad predictiva de los principales scores de riesgo hemorrágico en pacientes de edad  $\geq 75$  años.

**Métodos:** Inclusión prospectiva de pacientes con síndrome coronario agudo consecutivos. Se registraron características basales, datos analíticos y hemodinámicos y la incidencia intrahospitalaria de hemorragias utilizando las definiciones CRUSADE, Mehran, ACTION y BARC. Se calcularon los scores CRUSADE, Mehran y ACTION de cada paciente y se analizó su capacidad predictiva de hemorragias mediante regresión logística binaria, cálculo de curvas *receiver operating characteristic* y áreas bajo la curva.

**Resultados:** Se incluyó a 2.036 pacientes con una media de edad de 62,1 años; el 18,1% (369 pacientes) era  $\geq 75$  o más años. Este subgrupo presentaba mayor riesgo hemorrágico (CRUSADE, 42 frente a 22; Mehran, 25 frente a 15; ACTION, 36 frente a 28;  $p < 0,001$ ) y una incidencia de hemorragias mayores ligeramente superior (CRUSADE, el 5,1 frente al 3,8%;  $p = 0,250$ ). La capacidad predictiva de los tres scores fue inferior en los ancianos (área bajo la curva, CRUSADE: ancianos, 0,63; jóvenes, 0,81;  $p = 0,027$ ; Mehran: ancianos, 0,67; jóvenes, 0,73;  $p = 0,340$ ; ACTION: ancianos, 0,58; jóvenes, 0,75;  $p = 0,041$ ).

**Conclusiones:** Los scores de riesgo hemorrágico actualmente disponibles mostraron en el paciente anciano con síndrome coronario agudo un rendimiento claramente inferior al observado en pacientes más jóvenes.

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## Palabras clave:

Riesgo hemorrágico

Síndrome coronario agudo

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## Abbreviations

ACS: acute coronary syndromes

## INTRODUCTION

Bleeding complications are associated with a less favorable prognosis in patients with an acute coronary syndrome (ACS).<sup>1-3</sup> Clinical practice guidelines<sup>4,5</sup> recommend basing therapy strategies for these patients on the risk of both ischemic and bleeding events. Hence, over the last few years, various risk scores have been designed to predict bleeding complications in this scenario.<sup>6-8</sup>

The incidence of acute myocardial infarction increases with age and is particularly elevated in the elderly population.<sup>9</sup> Comorbid conditions and frailty are common in older acute myocardial infarction patients and are associated with a higher incidence of complications, including bleeding complications, and with expenditure of health resources.<sup>10</sup> For this reason, health care for acute myocardial infarction in the elderly may become an important public health problem in the coming years. Nonetheless, patients of advanced age are usually underrepresented in clinical trials,<sup>11,12</sup> and clinical evidence on the management and risk stratification in elderly patients with an ACS is scarce. There is no information on the performance of bleeding risk scores in this age group.

Therefore, the aims of this study were: *a*) analyze the incidence of bleeding complications and their characteristics in patients  $\geq 75$  years, and *b*) to evaluate the predictive ability of the main bleeding risk scores in this age group compared with that in the remaining patients in a consecutive cohort of ACS patients admitted to the coronary unit of a third-level hospital.

## METHODS

### Study Design

This is a prospective, observational study performed in a single referral hospital for ACS. We prospectively included all ACS patients admitted to the coronary unit of our center between October 2009 and June 2012. The diagnosis and therapeutic management of the patients was carried out in accordance with current recommendations.<sup>4,5</sup>

### Definitions and Data Collection

Trained staff prospectively compiled the study data using a standardized questionnaire. They recorded the patients' baseline characteristics, clinical history, biochemical and electrocardiographic findings, echocardiographic and angiographic parameters, procedures carried out, treatment administered during hospitalization, and in-hospital complications and deaths. The incidence and site of the in-hospital bleeding event was recorded, as well as the need for transfusion of blood products, the hemodynamic repercussions, and the intervention requirements.

### Bleeding Events

The CRUSADE,<sup>6</sup> Mehran,<sup>7</sup> ACTION,<sup>8</sup> and BARC<sup>13</sup> definitions were used to assign the bleeding events. All the elements comprising these definitions of bleeding were included in the data collection form. For each patient, the CRUSADE,<sup>6</sup> Mehran,<sup>7</sup> and ACTION<sup>8</sup> bleeding risk scores were calculated, as well as the GRACE<sup>14</sup> risk

score. In the analysis of the CRUSADE, Mehran and ACTION scores by risk group, the previously defined categories<sup>6-8</sup> for each of the scores were used.

The hemodynamic parameters (heart rate, systolic arterial pressure) and Killip grade were recorded at admission to the coronary unit. Creatinine clearance was calculated using the Cockcroft-Gault formula.<sup>15</sup>

Quantification of coronary disease was performed attending to the number of coronary arterial territories (left anterior descending, circumflex, right coronary) with stenosis of the arterial lumen  $\geq 70\%$  ( $\geq 50\%$  in the case of the left common trunk). The degree of stenosis was quantified by visual analysis.

### Statistical Analysis

Data analysis was performed using the PASW Statistics 18 statistical package (Chicago, Illinois, United States) and the R 3.0.1 software. Categorical values are expressed as number and percentage, and quantitative variables as mean (standard deviation). Variables with a nonnormal distribution are expressed as the median [interquartile range]. The Kolmogorov-Smirnoff test was used to analyze the normality of the distributions.

Comparisons between categorical variables were carried out with the chi-square test or Fisher's exact test, when appropriate. To analyze the incidence of bleeding events according to the various risk categories, the chi-square test was again used, together with the Mantel and Haenszel test for linear trends. Comparisons between quantitative variables were performed with the Student *t* test.

Binary logistic regression analysis was used to determine the predictive ability of the various bleeding risk scores, with calculation of the ROC (receiver operating characteristic) curves and the corresponding AUC (area under the ROC curve). Comparisons between AUCs were made with the nonparametric method of DeLong.<sup>16</sup> Two types of comparisons were performed: First, in patients  $\geq 75$  years, the ability of the CRUSADE, Mehran, and ACTION scores to predict bleeding according to the definitions used to design each score, was compared with the performance of the scores in younger patients. The comparison was made using the DeLong method with independent samples. Second, the capacity of the CRUSADE, Mehran, and ACTION bleeding risk scores and the GRACE score to predict major bleeding events was compared according to the recent BARC<sup>13</sup> bleeding definitions. For reasons of clinical relevance, BARC types 3 and 5 were considered for this purpose. This comparison was performed in both the group aged  $\geq 75$  years and in younger patients, using the DeLong method with paired samples. Patients with missing risk score data were excluded from the analysis.

## RESULTS

The study included 2036 patients (mean age, 62.1 years), 1570 (77.1%) of whom were men; 369 patients (18.1%) were aged  $\geq 75$  years. The characteristics of the study population according to age are shown in Table 1.

In general, elderly patients had a larger number of cardiovascular risk factors and other comorbidities, a greater incidence of signs of heart failure, and significantly lower glomerular filtration and hemoglobin values at admission than the remaining patients. In addition, coronary artery disease was more diffuse and left ventricular function was poorer in the older group. Furthermore, the overall bleeding risk was significantly higher in this group, as reflected by higher scores on each of the 3 bleeding risk scales compared with younger patients. The number of patients with missing data was 162 of 2036 (8%) for the CRUSADE score, 252 of

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