Original article

Long-term Prognosis of Patients With Non—ST-segment Elevation Acute Myocardial Infarction and Coronary Arteries Without Significant Stenosis

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A B S T R A C T

Introduction and Objectives: There is debate regarding the prognostic significance of the absence of significant coronary lesions in patients with non—ST-segment elevation acute myocardial infarction. We investigated long-term prognosis in a contemporary cohort of these patients.
Methods: Retrospective observational study of 5203 patients with acute coronary syndrome. Propensity score matching was used to create 2 groups of 367 patients with non—ST-segment elevation acute myocardial infarction matched by the absence or presence of significant coronary lesions. In the matched cohort, we determined the impact of the absence of significant coronary lesions on mortality or readmission for acute coronary syndrome for 4.8 (2.6) years after discharge.
Results: Mortality or readmission for acute coronary syndrome was lower among patients without significant lesions (26.4% vs 32.7%; *P* = .09). Mortality in both groups was 19.1%. In contrast, patients without significant lesions had a lower incidence of readmission for acute coronary syndrome (2.0/100 vs 3.9/100 person-years; *P* = .003). The incidence of mortality or readmission for acute coronary syndrome was similar in patients without significant lesions and those with significant 1-vessel disease (26.4% vs 27.5%; *P* = .19), but lower than that in patients with 2-vessel disease (37.8%; *P* = .007) and 3-vessel disease or left main coronary artery disease (41.1%; *P* = .002).
Conclusions: Patients with non—ST-segment elevation acute myocardial infarction and coronary arteries without significant lesions have similar long-term mortality but lower readmission rates for acute coronary syndrome than patients with significant lesions. Mortality or readmission for acute coronary syndrome is similar in patients without significant lesions and patients with 1-vessel disease, but lower than in patients with disease in 2 or more vessels.

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Pronóstico a largo plazo de pacientes con infarto agudo de miocardio sin elevación del segmento ST y arterias coronarias sin estenosis significativa

R E S U M E N

Introducción y objetivos: El significado pronóstico de la ausencia de lesiones coronarias significativas en pacientes con infarto agudo de miocardio sin elevación del segmento ST es motivo de controversia. Se investigó en una cohorte contemporánea el pronóstico a largo plazo de esos pacientes.
Métodos: Estudio observacional retrospectivo de 5.203 pacientes con síndrome coronario agudo. Mediante *propensity score matching*, se obtuvieron dos grupos de 367 pacientes con infarto agudo de miocardio sin elevación del segmento ST apareados por la ausencia o presencia de lesiones coronarias significativas. En la cohorte apareada, se determinó el impacto de la ausencia de lesiones coronarias significativas en mortalidad o reingresos por síndrome coronario agudo durante 4,8 ± 2,6 años después del alta.
Resultados: La mortalidad o el reingreso por síndrome coronario agudo fueron menos entre los pacientes sin lesiones significativas (el 26,4 frente al 32,7%; p = 0,09). La mortalidad en ambos grupos fue del 19,1%. En cambio, los pacientes sin lesiones significativas presentaron menor incidencia de reingreso por síndrome coronario agudo: 2,0 frente a 3,9/100 personas-año; p = 0,003). La incidencia de muerte o

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reingreso por síndrome coronario agudo fue similar entre los pacientes sin lesiones y enfermedad significativa de un vaso (el 26,4 frente al 27,5%; p = 0,19), aunque más baja que la observada en pacientes con afección de dos vasos (37,8%; p = 0,007) y tres vasos/tronco común izquierdo (41,1%; p = 0,002).
Conclusiones: Los pacientes con infarto agudo de miocardio sin elevación del segmento ST y coronarias sin lesiones presentan similar mortalidad a largo plazo que el grupo con lesiones significativas, pero reingresan menos frecuentemente por síndrome coronario agudo. La mortalidad o reingreso por síndrome coronario agudo de pacientes sin lesiones es similar que con enfermedad de un vaso, pero menor que en la de dos o más vasos.

Abbreviations

ACS: acute coronary syndrome
LCA: left main coronary artery
nSCL: no significant coronary lesions
NSTEMI: non—ST-segment elevation acute myocardial infarction
reACS: readmission for acute coronary syndrome

INTRODUCTION

Complex coronary atherosclerosis is the common pathological substrate of acute coronary syndrome (ACS). However, angiographic studies have shown that a considerable number of patients with non—ST-segment elevation acute coronary syndrome lack significant obstructive coronary lesions.[1–3]

Several pathophysiological theories have been advanced to explain this phenomenon, including abnormal coronary flow reserve due to macrovascular or microvascular dysfunction, rupture or erosion of atherosclerotic plaques with spontaneous lysis of the thrombus, and other noncoronary causes of myocardial damage.[4–8]

Non—ST-segment elevation acute coronary syndrome is often a diagnostic and therapeutic challenge to the clinician. Furthermore, there is no consensus on whether coronary angiography alone is an effective tool to define risk in this group of patients, regardless of clinical stratification.[3,9–12]

The aim of this study was to investigate the long-term outcome of a cohort of patients with non—ST-segment elevation acute myocardial infarction (NSTEMI) and with no significant coronary lesions (nSCL) by angiography.

METHODS

Study Population

A retrospective cohort study based on the CardioCHUS registry, which included all consecutive patients admitted with a diagnosis of ACS to the *Servicio de Cardiología* of the *Complejo Hospitalario Universitario de Santiago de Compostela* (coronary care unit, intermediate care unit, and hospitalization ward) from December 2003 to September 2012 (n = 5532).

Figure 1 shows the patient selection flowchart. Firstly, patients with an incorrect diagnosis of ACS were excluded as well as those with ACS precipitated by a secondary cause: severe anemia (hemoglobin < 7 g/dL), recent surgery, sepsis, substance abuse, or CO poisoning. Subsequently, patients with ST-segment elevation acute myocardial infarction were excluded because its prognosis differs from that of NSTEMI.

Given that the aim was to study long-term prognosis, patients who did not survive the hospital phase were also excluded.

Patients who die at this stage have different characteristics and their inclusion would alter the analysis of results of follow-up after hospital discharge. In addition, patients who did not undergo coronary angiography during admission were excluded as well as patients with a history of coronary artery bypass surgery or percutaneous coronary intervention due to the difficulty involved in establishing the presence and severity of coronary lesions in these patients. Patients with a diagnosis of unstable angina were also excluded to minimize sample heterogeneity. Finally, 43 patients were excluded due to the lack of follow-up data following discharge.

Thus, the final cohort consisted of 1883 patients with a definite diagnosis of NSTEMI.

Non—ST-segment elevation acute myocardial infarction was defined by symptoms consistent with myocardial ischemia, the absence of persistent ST-segment elevation on the initial electrocardiogram, and cardiac troponin I above the upper boundary of the normal reference range (Flex® reagent cartridges, Dimension® system, Siemens®, Inc.; United States).

The patients were classified into 2 groups based on the presence or absence of stenotic lesions $\geq$ 70% visually assessed at the discretion of the attending cardiologist. This percentage is equivalent to 50% stenosis as assessed using quantitative analysis.[13] Lesions of the left main coronary artery (LCA) were considered significant if they were $\geq$ 50%.

The study was conducted according to the principles of the Declaration of Helsinki.

Objective and Follow-up

The primary aim was to evaluate the prognostic effect of the absence of significant coronary lesions on the composite event of death and readmission for ACS (reACS).

The secondary objective was to determine mortality and reACS. After discharge, patients were followed up in a specialized ischemic heart disease clinic and primary care center. Structured follow-up was conducted by using electronic records (exclusively in the autonomous community of Galicia, IANUS program), reviewing medical care reports and hospital records, and contacting the patient by phone if needed. Mean follow-up was 4.8 (2.6) years.

Statistical Analysis

Quantitative variables are expressed as mean (standard deviation) and categorical variables as number (percentage). Prior to propensity score matching, the chi-square test or Fisher exact test were used to compare qualitative variables in the pre-matching cohort.

Given the nonrandomized nature of the study and the multiple biases that could have influenced the prognosis of patients with nSCL, propensity score matching was performed to minimize the bias inherent to observational studies. Firstly, the propensity score