International Journal of Cardiology 203 (2016) 708–713

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Frequency, clinical and angiographic characteristics, and outcomes of high-risk non-ST-segment elevation acute coronary syndromes patients with left circumflex culprit lesions☆

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ARTICLE INFO

Article history:
Received 23 February 2015
Received in revised form 21 May 2015
Accepted 4 November 2015
Available online 10 November 2015

Keywords:
Left circumflex artery
Acute coronary syndromes
Infarct size

ABSTRACT

Background: The relationship between culprit vessel, infarct size, and outcomes in non-ST-segment elevation acute coronary syndromes (NSTE ACS) is unclear. In some reports, the left circumflex artery (LCX) was more often the culprit at angiography than the right coronary artery (RCA) or left anterior descending artery (LAD), and infarcts were larger with LCX culprits.

Methods: We determined culprit vessel frequency and initial patency (TIMI flow grade), median fold elevation of peak troponin above the upper limit of normal, and outcomes (30-day death or myocardial infarction [MI] and 1-year mortality) by culprit vessel in high-risk NSTE ACS patients in the EARLY ACS trial.

Results: Of 9406 patients, 2066 (22.0%) had angiographic core laboratory data. We evaluated 1774 patients for whom the culprit artery was not the left main, a bypass graft, or branch vessel. The culprit was the LCX in 560 (31.6%), LAD in 653 (36.8%), and RCA in 561 (31.6%) patients. There were fewer women (24.1%) and more prior MI (25.5%) among patients with a culprit LCX compared with those with a culprit LAD or RCA. Patients with LCX (21.2%) and RCA (27.5%) culprits more often had an occluded artery (TIMI 0/1) than did those with LAD (11.3%). Peak troponin elevation was significantly higher for LCX than RCA or LAD culprits. LCX culprit vessels were not associated with worse 30-day or 1-year outcomes in adjusted models.

Conclusions: Among patients with NSTE ACS, the frequencies of LCX, LAD, and RCA culprits were similar. Although LCX lesions were associated with higher peak troponin levels, there was no difference in short- or intermediate-term outcomes by culprit artery.

1. Introduction

Among patients with non-ST-segment elevation acute coronary syndromes (NSTE ACS), complete occlusion of the culprit artery is infrequent and patients often have multi-vessel coronary disease. Moreover, unlike complete occlusion of the right coronary (RCA) and left anterior descending (LAD) arteries, ST-segment elevation is present on the initial electrocardiogram (ECG) of left circumflex (LCX) occlusions less than 50% of the time [1], raising the possibility that some NSTE myocardial infarctions (MIs) are in fact due to LCX occlusion that is not electrocardiographically apparent. Despite many patients with NSTE ACS having better short-term outcomes compared with ST-segment elevation myocardial infarction (STEMI) due to smaller infarcts, patients with LCX occlusions may be considered "STEMI-equivalent" and may

☆ Author statement: All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation. Please see the corresponding sections below for funding information and potential conflicts of interest.

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http://dx.doi.org/10.1016/j.ijcard.2015.11.036
0167-5273/

have worse short-term outcomes due to larger infarcts and delayed reperfusion. Therefore, knowledge of the frequency, characteristics, and outcomes of LCX culprit infarcts among patients with NSTE ACS may have important clinical implications. The EARLY ACS (Early glycoprotein IIb/IIIa inhibition in non-ST-segment elevation acute coronary syndrome) trial randomized 9406 patients with high-risk NSTE ACS undergoing an early invasive strategy [2]. The goal of this analysis was to examine the incidence, clinical and angiographic characteristics, and outcomes of patients with NSTE ACS with LCX culprit lesions.

2. Methods

2.1. Patient population

The EARLY ACS trial enrolled high-risk NSTE ACS patients intended to undergo an early invasive treatment strategy. The patient population has been described previously [2,3]. Briefly, patients at least 18 years of age were eligible if they had cardiac ischemia lasting for at least 10 min occurring within 24 h prior to presentation with a planned invasive strategy no sooner than the next calendar day after randomization. Patients had to be randomized within 12 h of presentation. Patients were considered high-risk if they met two or more of the following criteria: ischemic changes on electrocardiography (ST-segment depression of ≥0.1 mV or transient [<30 min] ST-segment elevation of ≥0.1 mV in two or more contiguous leads), troponin or creatine kinase-MB (CK-MB) level above the upper limit of the normal (ULN) range for the local assay, and age ≥ 60 years. Informed consent was obtained from each patient, and the study protocol conformed to the Declaration of Helsinki, as reflected by approval by necessary institutional review boards and ethics committees.

2.2. Study procedures

Patients in EARLY ACS were randomized to either double-bolus eptifibatide plus infusion or matching placebo, in addition to standard antithrombotic therapy including aspirin, clopidogrel, and anticoagulant. After coronary angiography but before percutaneous coronary intervention (PCI), investigators could request a PCI study drug kit for patients who they deemed would benefit from eptifibatide administration based on clinical and angiographic findings. During PCI, if a thrombotic complication occurred, investigators could request a "bailout" kit that contained bolus therapy opposite to the initial study group assignment.

2.3. Angiographic cohort

For the EARLY ACS angiographic substudy, copies of patient angiograms were sent to the PERFUSE Angiographic Core Laboratory at Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts. All sites were encouraged to submit angiograms, with a goal of obtaining 2000 angiograms for the substudy. For the current analysis, of 2066 patients with available angiographic core laboratory data, those whose culprit artery was not the left main, a coronary bypass graft, or branch vessel were included (N = 1774).

2.4. Endpoints

We describe the frequency of LCX, RCA, and LAD culprit arteries among patients in the EARLY ACS angiographic substudy cohort. The primary clinical endpoint for this analysis was death or MI at 30 days stratified by culprit artery. Secondary endpoints according to culprit artery included 30-day death/MI/recurrent ischemia requiring urgent revascularization (RIUR), 1-year death, and peak troponin elevation (fold elevation above the local laboratory ULN) prior to coronary angiography. We also assessed the in-hospital occurrence of cardiogenic shock, arrhythmias, and congestive heart failure by culprit artery. In a sensitivity analysis, we also limited 30-day MI to spontaneous MI to assess the contribution of periprocedural MI to the results.

2.5. Statistical methods

Baseline clinical and angiographic characteristics were summarized according to culprit vessel (LCX, RCA, LAD) as identified in the angiographic substudy core laboratory. Continuous variables were summarized as medians (1st, 3rd quartiles), and categorical variables were summarized as counts and proportions. Baseline clinical and angiographic characteristics are presented for descriptive purposes only, and no formal statistical comparisons were made between groups.

Clinical endpoints were compared using analysis of variance (ANOVA) for continuous outcomes and chi-square or Fisher exact tests for dichotomous outcomes ($\alpha = 0.05$). Peak troponin elevation (fold-elevation above the ULN) measured prior to coronary angiography was compared across culprit arteries using nonparametric tests due to the skewed distribution of this variable. Multivariable logistic regression was used to model 30-day outcomes, and Cox proportional hazard regression was used to model 1-year mortality as a function of culprit coronary vessel. Adjusted models included variables predictive of the outcomes of interest in previous clinical modeling in the EARLY ACS cohort. The adjusted death/MI model included age, body weight, baseline estimated creatinine clearance, Killip class >1, qualifying event electrocardiogram, baseline troponin elevation, and history of peripheral vascular disease. The adjusted death/MI/RIUR model included the same variables with the exception of body weight. The Cox model for 1-year mortality included the same variables as the death/MI model plus white blood cell count, history of MI, diabetes, heart failure, sex, smoking status, prior revascularization, heart rate, and systolic blood pressure. In a sensitivity analysis, the 30-day death/MI model was repeated using only spontaneous MI for the MI component of the composite.

Similar analyses were conducted for patients without angiographic core laboratory data; however, culprit artery data were only available for patients undergoing PCI in this cohort. Accordingly, there were no patients receiving medical management or surgical coronary revascularization in this analysis. The culprit artery was identified as recorded on the case-report form (CRF) by the investigator as the target artery for PCI.

3. Results

3.1. Patient population and baseline characteristics

Of 9406 patients enrolled in EARLY ACS, 2066 had angiographic core laboratory data. We evaluated 1774 patients from the angiographic cohort for whom the culprit artery was the LAD, RCA, or LCX coronary artery. Baseline characteristics stratified by culprit artery are shown in Table 1. The culprit artery was the LCX in 560 (31.6%), LAD in 653 (36.8%), and RCA in 561 (31.6%) patients. Patients with an LCX culprit artery were younger, more frequently men, and more likely to have had a prior MI and prior coronary revascularization than patients with other culprit vessels. Myocardial necrosis biomarkers were more frequently elevated above the local ULN at baseline among patients with LCX culprits, despite similar median time to catheterization compared with patients with non-LCX culprit arteries. Table 2 displays baseline characteristics for the angiographic core laboratory cohort and the cohort without angiographic core laboratory data (non-angiographic cohort). Baseline demographics and comorbidities were similar between groups.

3.2. Angiographic findings

Table 3 summarizes angiographic findings and procedural data for patients stratified by culprit artery. Three-vessel coronary disease was