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Original article

Benefit of statin therapy in patients with coronary spasm-induced acute myocardial infarction

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ABSTRACT

Background: Coronary artery spasm is associated with vascular smooth muscle hyper-reactivity. Statins suppress coronary spasm by inhibiting the vascular smooth muscle contraction. However, it is unclear whether statin therapy benefits patients with coronary spasm-induced acute myocardial infarction (AMI).

Methods and results: We analyzed 501 (median age 57 years; male/female, 346/155) patients with coronary spasm-induced AMI with nonobstructive coronary arteries (stenosis severity <50%) from the Korea AMI Registry between November 2005 and October 2013. They were divided into two groups according to statin prescription at discharge (statin group $n = 292$; nonstatin group $n = 209$). The primary endpoint was the composite of 12-month major adverse cardiac events, including all causes of death, non-fatal myocardial infarction, and target vessel revascularization. The primary endpoint occurred in 17 patients during 12 months of follow-up. Statin therapy significantly reduced the risk of the composite primary endpoint [adjusted hazard ratio (HR): 0.30; 95% confidence interval (CI): 0.09–0.97; $p = 0.045$]. Statin therapy reduced the risk of myocardial infarction (HR: 0.19; 95% CI: 0.04–0.93; $p = 0.040$). However, we found no significant difference in the risk of the composite of all-cause death.

Conclusion: Statin therapy in patients with coronary spasm-induced AMI with nonobstructive coronary arteries was associated with improved clinical outcome, which was predominantly accounted for by reducing the incidence of myocardial infarction.

Introduction

Although acute myocardial infarction (AMI) is generally associated with obstructive coronary artery disease [1], the prevalence of AMI with nonobstructive coronary arteries (stenosis severity <50%) was 6% [2]. A previous Asian study reported that the prevalence of coronary artery spasm (CAS) is around 38% in patients with AMI with nonobstructive coronary arteries [3].

CAS is caused by abnormal hypercontraction of coronary vascular smooth muscle [4,5], and plays an important role in the pathogenesis of a wide variety of acute coronary syndrome (ACS), particularly among Asians [6,7]. Coronary spasm can be suppressed effectively with calcium channel blockers (CCBs) or nitrates [8]. However, a large number (20%) of patients with CAS are resistant to high doses of CCBs and nitrates [9], some of whom develop myocardial infaction [10,11].

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Although guidelines recommend statins for secondary prevention for patients with AMI [12], it is unclear whether statin therapy also benefits patients with coronary spasm-induced AMI. Statins have been shown to be effective in suppressing coronary spasm by inhibiting the vascular smooth muscle contraction [13]. However, a recent study reported that the long-term administration of statins may not improve prognosis in patients with CAS [14]. Given these uncertainties, based on the data in the Korea AMI Registry (KAMIR), we decided to determine whether statin therapy is beneficial in patients with coronary spasm-induced AMI with nonobstructive coronary arteries.

Methods

Study population

This study was based on a database collected by the KAMIR. The KAMIR is a prospective, multicenter online registry designed to describe characteristics and clinical outcomes of patients with AMI and it reflects current management of patients with AMI in Korea. The registry included 53 community and university hospitals with capability of primary percutaneous coronary intervention (PCI). Data were collected retrospectively at each site by a trained study coordinator based on a standardized protocol.

A total of 37 617 consecutive patients were enrolled in the KAMIR from November 2005 to May 2013. Of these, 1593 patients underwent coronary angiography (CAG) with nonobstructive coronary arteries (stenosis severity <50%). We analyzed 501 consecutive patients with coronary spasm-induced AMI from the KAMIR. They were divided into 2 groups according to statin prescription at discharge (statin group $n = 292$, 58.3%; nonstatin group $n = 209$, 41.7%) (Fig. 1).

Medical treatment

Loading doses of aspirin and clopidogrel were administered immediately after the patients agreed to receive CAG. Statin, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, nitrate, nicorandil, and beta-blocker were administered according to the attending doctor's decision. Statins included atorvastatin, rosuvastatin, simvastatin, pitavastatin, and fluvastatin. Beta-blockers included carvedilol, bisoprolol, and nebivolol. More than 80% of the patients were treated with CCBs.

Study definitions and endpoint

In this study, spasm-induced AMI was identified by the patients with coronary organic stenosis <50% and the detection of "rise and/or fall" of troponin was associated with at least one of the following: (1) positive acetylcholine (ACh) or ergonovine (ER) test; (2) verified spontaneous spasm (spontaneous and transient ST elevation on electrocardiography [ECG] that was quickly relieved by one tablet of sublingual nitroglycerin or spontaneous spasm during CAG) without a spasm provocation test. The ACh spasm provocation test was performed using the following procedure: incremental doses of ACh were injected into the left coronary artery (20, 50, and 100 μg) and right coronary artery (20 and 50 μg) until the elicitation of coronary spasm. The ER spasm provocation test was performed using the following procedure: incremental doses of ER were injected into the left coronary artery (20, 40, and 80 μg) and right coronary artery (10, 20, and 40 μg) until the elicitation of coronary spasm [8,15]. Positive findings of coronary spasm were defined as a transient, total, or subtotal occlusion (≥90% stenosis) of a coronary artery associated with both chest pain and myocardial ischemic ST segment changes on ECG.

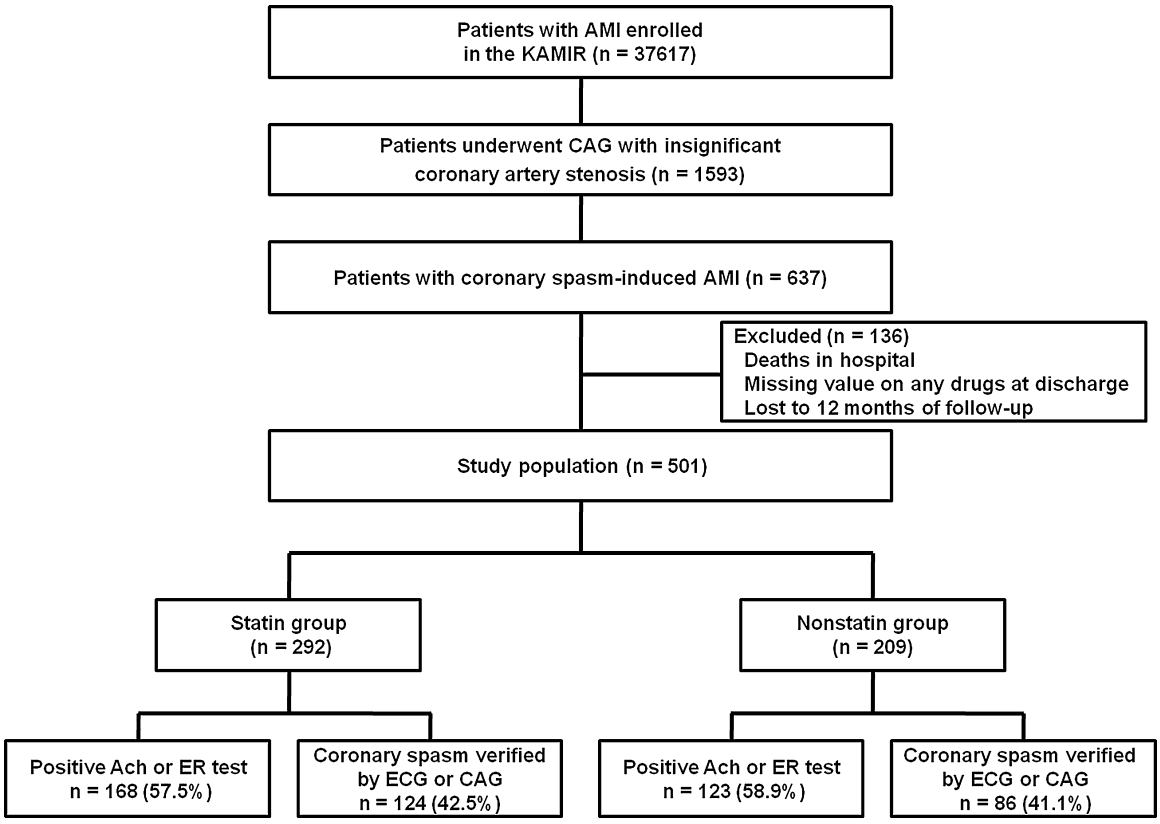

Fig. 1. Study flowchart. KAMIR, Korean Acute Myocardial Infarction Registry; AMI, acute myocardial infarction; CAG, coronary angiography; ECG, electrocardiogram; Ach, acetylcholine; ER, ergonovine.