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Five-year clinical outcomes in patients with significant coronary artery spasm: A propensity score-matched analysis

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ABSTRACT

Background: Coronary artery spasm (CAS) is known to be a risk factor of acute coronary syndrome and angina pectoris. However, there is no currently available data with larger study population regarding long-term clinical outcomes of CAS in real world clinical practice.
Objectives: We evaluated the prevalence of CAS and the impact of CAS on 5-year clinical outcomes in a series of Asian CAS patients documented by intracoronary acetylcholine (Ach) provocation test.
Methods: A total of 1413 consecutive patients without significant coronary artery disease (CAD) who underwent Ach provocation test between Nov. 2004 and Oct. 2008 were enrolled. Significant CAS was defined as >70% of narrowing by incremental intracoronary injection of 20, 50 and 100 μg. Patients were divided into two groups based on the presence of significant CAS (the non-CAS group: n = 640, the CAS group; n = 773). To adjust potential confounders, a propensity score matched (PSM) analysis was performed using the logistic regression model.
Results: A total of 54.7% (773/1413) patients were diagnosed as CAS documented by Ach provocation test. After PSM analysis, 2 propensity-matched groups (451 pairs, n = 902, C-statistic = 0.677) were generated. Despite of similar incidence of individual hard endpoints including mortality, myocardial infarction and revascularization, the CAS group showed the higher trend of recurrent angina requiring follow up angiography than the non-CAS group up to 5 years (HR; 1.56, 95% C.I.; 0.99–2.46, p = 0.054).
Conclusions: The prevalence of CAS was 54.7%. Although the cumulative incidence of recurrent angina requiring follow up coronary angiography seems to be increased up to 5 years in CAS patients, CAS patients was not associated with major individual and composite clinical outcomes such as mortality, MI, PCI, CVA with optimal medical therapy as compared with patients without CAS.

1. Introduction

Coronary artery spasm (CAS) plays an important role in the pathogenesis of vasospastic angina and acute coronary syndrome and seems to be associated with adverse clinical outcomes [1–3]. However, there are limited data on the prevalence of CAS documented by intracoronary acetylcholine (Ach) provocation test in a series of large number of Asian population and the impact of CAS on long-term adverse clinical outcomes including death (cardiac and non-cardiac), non-fatal myocardial infarction and recurrent angina in real world clinical practice. Some of recent studies, Takagi et al. reported [4] that the 5-year survival free from MACEs and all cause death was 95 and 98% in patients with vasospastic angina, and Ong et al. reported [5] that the CAS patients without culprit lesion have an excellent prognosis for survival and coronary events after 3 years compared with patients with obstructive ACS. However, persistent angina represents a challenging problem in these patients, leading in some cases to repeated coronary angiography. Therefore, we evaluated the prevalence of CAS in consecutive Asian patients with typical or atypical chest pain and the impact of CAS on 5-year cumulative clinical outcomes.

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2. Methods

2.1. Study population

A total of 3178 consecutive patients presented with typical or atypical chest pain who underwent coronary angiography (CAG) from November 2004 to October 2008 at the Cardiovascular Center of Korea University Guro Hospital, Seoul, South Korea were enrolled for this study. Among these, 1827 patients [49.4% men; age (mean ± SD) 54.3 ± 12.1 years] presented with typical or atypical chest pain and without significant coronary artery disease (CAD) defined as the diameter stenosis less than 50% on quantitative coronary angiography (QCA) and underwent the Ach provocation test. Patients were excluded if they had any of the following conditions such as prior coronary artery bypass graft, prior percutaneous coronary intervention (PCI), prior cerebrovascular disease (CVD), advanced heart failure (New York Heart Association class III or IV) or serum creatinine ≥ 2 mg/dl because these conditions could be the major causes of adverse cardiovascular events and could be served as a bias in the result of the study. Finally, 1413 patients were enrolled and divided into two groups; the CAS group (n = 773) and the non-CAS group (n = 640) [Fig. 1].

2.2. Study definition

The significant CAS was defined as luminal narrowing of more than 70% during Ach provocation test with or without ischemic ECG change or chest pain. Deaths were regarded as cardiac death unless non-cardiac death could be confirmed. Repeat CAG (mostly due to the recurrent angina) was performed in the patients who complained of recurrent angina despite of adequate antianginal medication at least for 6 months since 1st CAG. In this case, the physician assumed that CAS may be progressed or there may be newly developing atherosclerotic CAD. Major adverse cardiovascular events (MACEs) were defined as the composite of total death, de novo myocardial infarction (MI), and revascularization including PCI and coronary artery bypass graft (CABG).

2.3. Acetylcholine provocation test

The design of the Ach provocation test has been introduced before [6]. The initial investigation for CAG included clinical history taking and non-invasive stress tests such as treadmill test, stress echocardiography, and radionuclide study. And then the CAG was performed to confirm the presence of significant CAD. However, CAG was immediately done without functional studies in case of typical resting ischemic chest pain to confirm vasospastic angina. The vasodilators or vasoconstrictors such as nitrates, calcium channel blockers, beta blockers, nicorandil, molsidomine and so on were discontinued at least 72 h before CAG. CAS induction was tested by intracoronary injection of Ach immediately after the diagnostic angiography by either trans-radial or trans-femoral approach. Ach was injected by incremental doses of 20 (A1), 50 (A2) and 100 (A3) μg/min into the left coronary artery over a 1-minute period with 5-minute intervals up to the maximal tolerated dose under continuous monitoring of electrocardiogram and blood pressure. Routine provocation test of the right coronary artery was not done due to safety issues by higher prevalence of advanced

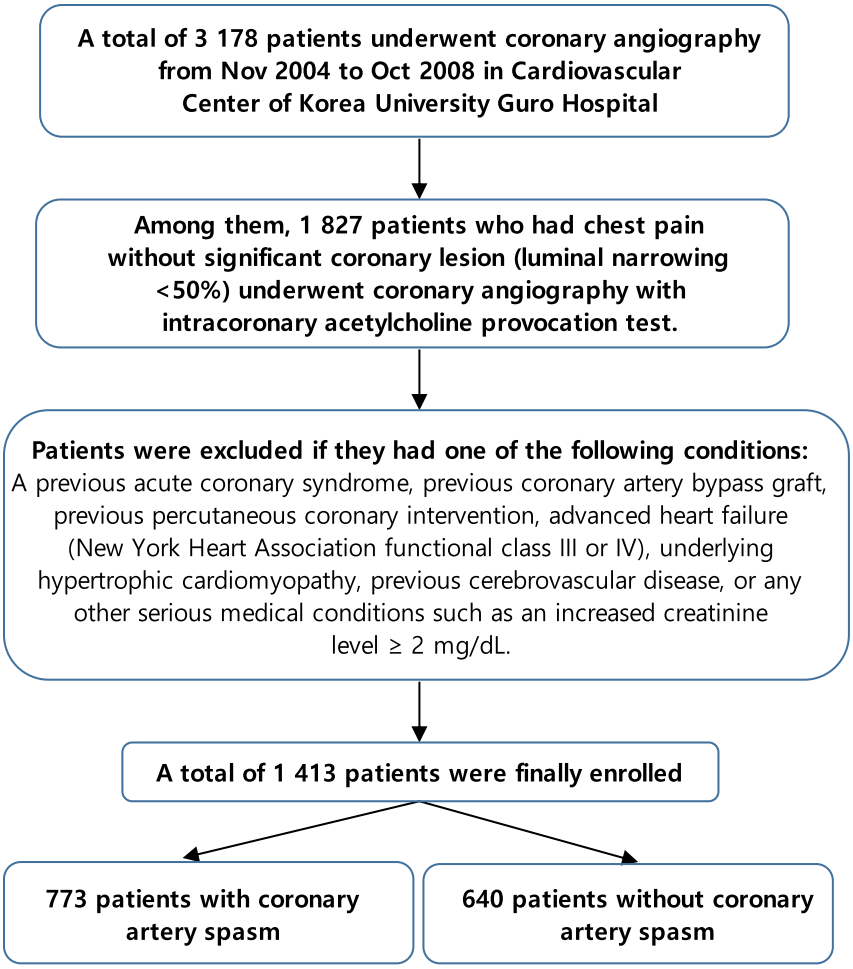

Fig. 1. Flow chart of study population.