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The 24-Month Prognosis of Patients With Positive or Intermediate Results in the Intracoronary Ergonovine Provocation Test

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ABSTRACT

OBJECTIVES This study was an observational, multicenter registry to determine clinical characteristics and 24-month prognosis of patients who underwent intracoronary ergonovine provocation tests.

BACKGROUND The clinical characteristics and prognosis of patients who underwent the ergonovine provocation for vasospastic angina were not fully elucidated.

METHODS A total of 2,129 patients in the VA-KOREA (Vasospastic Angina in Korea) registry were classified into positive (n = 454), intermediate (n = 982), and negative (n = 693) groups by intracoronary ergonovine provocation tests. The 24-month incidences of cardiac death, new-onset arrhythmia, and acute coronary syndrome were determined (mean 26.7 ± 8.8 months).

RESULTS The number of smokers, frequency of angina before angiography, high-sensitivity C-reactive protein, and triglyceride were higher in the positive group than in other groups. The clinical characteristics of the intermediate and the negative groups were very similar. In the positive group, the incidences of diffuse, focal, and mixed spasm were 65.9%, 23.6%, and 10.6%. Coronary spasm was more frequently provoked on atherosclerotic segments. The 24-month incidences of cardiac death, arrhythmia, and acute coronary syndrome were low (0.9%, 1.6%, and 1.9%, respectively) in the positive group, and there was no cardiac death in the intermediate group (p = 0.02). In the positive group, frequent angina, current smoking, and multivessel spasm were independent predictors for adverse events.

CONCLUSIONS The 24-month prognosis of the positive group in the intracoronary ergonovine provocation test was relatively worse than that of the intermediate group. More intensive clinical attention should be paid to vasospastic angina patients with high-risk factors including frequent angina before angiography, current smoking, and multivessel spasm. (J Am Coll Cardiol Intv 2015;8:914–23) © 2015 by the American College of Cardiology Foundation.

Coronary spasm has been recognized as an important pathophysiology of myocardial ischemia in patients with or without coronary artery stenosis (1,2). Although vasospastic angina (VSA) has become less frequent, most likely due to the widespread use of calcium-channel blockers (CCBs), coronary spasm is still prevalent, and provocation tests for VSA are widely performed

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in Korea and Japan (1–4). Thus, VSA is regarded as one of the crucial functional coronary diseases, particularly in the East Asian countries (4,5).

In Japan, a number of studies have elucidated the pathogenesis, diagnosis, and characteristics of VSA (6,7). Moreover, the nationwide registry of the Japanese Coronary Spasm Association (JCSA) has established the clinical prognostic factors, such as out-of-hospital cardiac arrest and mixed-type spasm (8,9). Furthermore, the JCSA risk score was recently suggested for the comprehensive risk assessment and prognostic stratification of VSA patients (4).

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Many study groups in Korea have reported the clinical findings, prognostic factors, and possible new pharmacologic agents for Korean VSA patients with variable provocation methods (10–12). However, there have been few demographic reports so far from the large-scale analysis of Korean patients who underwent intracoronary ergonovine provocation tests. Moreover, most of the previous studies have not only included a small number of patients, but also applied different diagnostic methods and diverse criteria for the definition of VSA.

Consequently, we conducted a large-scale, multicenter registry for VSA patients who had been tested with the same provocation protocol using only intracoronary ergonovine. We also determined the clinical characteristics, prognosis, and associated risk factors in each of the groups of patients who were classified according to results of the ergonovine provocation.

METHODS

STUDY SUBJECTS. VA-KOREA (Vasospastic Angina in KOREA) is a prospective, observational, and web-based registry of clinical, angiographic, and prognostic data from patients who underwent intracoronary ergonovine provocation tests. Patients who had suspicious symptoms and underwent coronary angiography (CAG) with the ergonovine provocation test according to the clinician's decision were included. A total of 2,174 patients who underwent the ergonovine provocation test were consecutively entered into the registry from May 2010 to November 2013 in 11 cardiovascular centers and selected as the study subjects. All participated centers have performed high-volume CAG (>1,800 cases/year) and percutaneous coronary intervention (PCI) (>500 cases/year) and have used the same study protocol for the intracoronary ergonovine provocation test.

All of the registered patients had normal findings or minimal (<50% luminal diameter narrowing) atherosclerosis at the baseline CAG, whereas those with significant atherosclerosis (≥50% luminal diameter narrowing) were excluded. Patients with renal failure on continuous dialysis, known malignant or inflammatory diseases, and catheter-induced spasm at the baseline CAG were also excluded. All patients who showed positive results on their provocation tests or defined spontaneous spasm received medical treatments including CCBs and other vasodilators during the follow-up. Medications for nonpositive subjects were prescribed on the basis of the clinician's decision.

There was no industry involvement, and all patients gave their written informed consent. All of the surveys were approved by the institutional review board of each participating institution.

CAG AND PROVOCATION TEST FOR VSA. VSA was diagnosed on the basis of the criteria in the Guidelines for Diagnosis and Treatment of Patients with Vasospastic Angina of the Japanese Circulation Society (13). The baseline CAG was performed for the right coronary artery (RCA) and then the left coronary artery (LCA), respectively. Intracoronary infusion of ergonovine was used for the provocation test. Incremental doses of 20 (E1), 40 (E2), and 60 μg (E3) were injected into the LCA. If coronary spasm was not provoked on the LCA, incremental doses of 10 (E1), 20 (E2), and 40 μg (E3) were injected into the RCA (9). Once spasm was provoked, intracoronary nitrate was injected. The vasoactive drugs were discontinued at least 48 h before CAG.

The definition of a positive result was total or subtotal (>90% luminal diameter narrowing) occlusion accompanied by ischemic symptoms and/or electrocardiographic (ECG) changes (the positive group) (13). Patients who showed spontaneous total or subtotal coronary spasm on their baseline CAG resolved by nitrate were also included in the positive group. The definition of a negative result was <50% luminal narrowing without ischemic symptoms and ECG changes (the negative group). Additionally, we defined intermediate constriction as 50% to 90% luminal narrowing with or without ischemic symptoms and/or ECG changes (the intermediate group). All of the vascular responses to ergonovine in the provocation test and atherosclerosis on the baseline CAG were quantitatively analyzed for epicardial coronary artery diameters ≥2.5 mm by clinicians unaware of patient status at the core laboratory of Seoul St. Mary's Hospital, Seoul, South Korea.

ABBREVIATIONS AND ACRONYMS

CAG = coronary angiography
CCB = calcium-channel blocker
ECG = electrocardiography
JCSA = Japanese Coronary Spasm Association
LCA = left coronary artery
MI = myocardial infarction
RCA = right coronary artery
VSA = vasospastic angina