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ORIGINAL INVESTIGATIONS

Prognosis of Variant Angina Manifesting as Aborted Sudden Cardiac Death

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ABSTRACT

BACKGROUND The long-term prognosis of patients with variant angina presenting with aborted sudden cardiac death (ASCD) is unknown.

OBJECTIVES The purpose of this study was to evaluate the long-term mortality and ventricular tachyarrhythmic events of variant angina with and without ASCD.

METHODS Between March 1996 and September 2014, 188 patients with variant angina with ASCD and 1,844 patients with variant angina without ASCD were retrospectively enrolled from 13 heart centers in South Korea. The primary endpoint was cardiac death.

RESULTS Predictors of ASCD manifestation included age (odd ratio [OR]: 0.980 by 1 year increase; 95% confidence interval [CI]: 0.96 to 1.00; $p = 0.013$), hypertension (OR: 0.51; 95% CI: 0.37 to 0.70; $p < 0.001$), hyperlipidemia (OR: 0.38; 95% CI: 0.25 to 0.58; $p < 0.001$), family history of sudden cardiac death (OR: 3.67; 95% CI: 1.27 to 10.6; $p = 0.016$), multivessel spasm (OR: 2.06; 95% CI: 1.33 to 3.19; $p = 0.001$), and left anterior descending artery spasm (OR: 1.40; 95% CI: 1.02 to 1.92; $p = 0.04$). Over a median follow-up of 7.5 years, the incidence of cardiac death was significantly higher in ASCD patients (24.1 per 1,000 patient-years vs. 2.7 per 1,000 patient-years; adjusted hazard ratio [HR]: 7.26; 95% CI: 4.21 to 12.5; $p < 0.001$). Death from any cause also occurred more frequently in ASCD patients (27.5 per 1,000 patient-years vs. 9.6 per 1,000 patient-years; adjusted HR: 3.00; 95% CI: 1.92 to 4.67; $p < 0.001$). The incidence rate of recurrent ventricular tachyarrhythmia in ASCD patients was 32.4 per 1,000 patient-years, and the composite of cardiac death and ventricular tachyarrhythmia was 44.9 per 1,000 patient-years. A total of 24 ASCD patients received implantable cardioverter-defibrillators (ICDs). There was a nonsignificant trend of a lower rate of cardiac death in patients with ICDs than those without ICDs ($p = 0.15$).

CONCLUSIONS The prognosis of patients with variant angina with ASCD was worse than other patients with variant angina. In addition, our findings supported ICDs in these high-risk patients as a secondary prevention because current multiple vasodilator therapy appeared to be less optimal. (J Am Coll Cardiol 2016;68:137–45) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ASCD = aborted sudden cardiac arrest

CI = confidence interval

HR = hazard ratio

ICD = implantable cardioverter-defibrillator

IPTW = inverse-probability-of-treatment weighting

OR = odds ratio

Variant angina is characterized by chest pain at rest and transient ST-segment elevation on an electrocardiogram caused by dynamic coronary artery spasm (1). It usually has a favorable long-term prognosis because coronary artery spasms respond well to vasodilator therapy (2). However, coronary artery spasms might also have an important role in the pathogenesis of ventricular arrhythmia and subsequent cardiac arrest (3). The long-term prognosis of patients with variant angina who present with aborted sudden cardiac death (ASCD) is controversial. Previous studies have demonstrated a recurrence of lethal arrhythmic events and poor clinical outcomes (4–6). Other studies have reported favorable long-term outcomes (7–9). This uncertainty has led to variations in treatment, with some cardiologists favoring implantable cardioverter-defibrillators (ICDs) (10) and others believing that coronary spasms are reversible and can be controlled by intensive vasodilator treatment (11).

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Therefore, to overcome mixed evidence from anecdotal reports hampered by the limited number of patients and short follow-up periods, and to provide clinically relevant information in long-term appropriate management for this high-risk subset, a large multicenter cohort study with long-term follow-up was of paramount importance. In this study, we hypothesized that patients presenting with ASCD would have worse long-term prognosis, which would be irreversible to optimal vasodilator therapy only. To test our hypothesis, we first evaluated the long-term risk of mortality and ventricular tachyarrhythmic events in patients with variant angina with ASCD compared with those without ASCD. Second, we compared cardiac mortality between patients who received ICDs or did not in ASCD patients.

METHODS

STUDY DESIGN AND PATIENTS. This is a retrospective observational cohort study that discusses the characteristics of patients with variant angina with ASCD or without ASCD from 13 major heart centers in South Korea. The diagnosis of variant angina was made based on the Guidelines for Diagnosis and Treatment of Patients with Vasospastic Angina of the Japanese Circulation Society (12). In addition, all patients with variant angina with ASCD who met the following criteria were included: (1) patients who experienced out-of-hospital cardiac arrest due to documented ventricular fibrillation, sustained rapid ventricular tachycardia, or pulseless electrical activity; (2) patients who were successfully resuscitated from cardiac arrest; (3) patients who had variant angina, which was defined by spontaneous coronary spasm with ST-segment elevation (≥0.1 mV) on the coronary angiogram and/or documented coronary spasm on an ergonovine provocation coronary angiogram; and (4) patients who did not have organic heart disease, including significant coronary artery stenosis or any other condition known to be associated with sudden cardiac arrest. To definitely rule out significant coronary artery disease, all ASCD patients underwent coronary angiography, and when the coronary angiogram showed a normal coronary artery, patients underwent an ergonovine provocation test. In addition, we excluded patients (n = 3) with poor neurological outcomes (defined as cerebral performance category scale ≥3) (13).

The non-ASCD group consisted of patients who had positive coronary artery spasm provocation tests due to typical or atypical angina-like chest pain suspected of being variant angina. In general, angina at rest in the early morning or at night was the hallmark feature that prompted the provocation test. Ergonovine provocation coronary angiography or echocardiography were used as provocation tests and were performed according to standard methods, which are described in the Online Appendix (12,14). The definitions of positive results were total or subtotal (>90% luminal diameter narrowing) occlusion in ergonovine provocation coronary angiography and new development of regional wall motion abnormalities on the ergonovine provocation echocardiogram. The local ethics committee at each hospital approved the use of the clinical data for this study.

TREATMENT. All patients who were enrolled in the present study received medical treatment, including calcium-channel blockers, long-acting nitrates, or

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