

Editorial



Ergonovine Provocation Echocardiography for Detection and Prognostication in Patients with Vasospastic Angina

Jae-Hyeong Park , MD, PhD

Division of Cardiology, Department of Internal Medicine, Chungnam National University Hospital, Chungnam National University School of Medicine, Daejeon, Korea

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Correspondence to

Jae-Hyeong Park, MD, PhD

Division of Cardiology, Department of Internal Medicine, Chungnam National University Hospital, Chungnam National University School of Medicine, 282, Munhwa-ro, Jung-gu, Daejeon 35015, Korea.
E-mail: jaehpark@cnu.ac.kr

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ORCID iDs

Jae-Hyeong Park 
<https://orcid.org/0000-0001-7035-286X>

Conflict of Interest

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► See the article "Ergonovine Stress Echocardiography for the Diagnosis of Vasospastic Angina and Its Prognostic Implications in 3,094 Consecutive Patients" in volume 48 on page 906.

Vasospastic angina (VSA) is caused by total or subtotal occlusion of coronary arteries due to intense vasoconstriction and can lead to unstable angina, acute myocardial infarction, and sudden cardiac death. VSA is more prevalent in East Asian countries, including Korea and Japan, than in Western countries.¹⁾ Although the mechanisms underlying VSA are unknown, inflammation, endothelial dysfunction, oxidative stress, and smoking are proposed to contribute.²⁾ The diagnosis of VSA is based on clinical history and transient electrocardiographic changes or inducible coronary artery spasm.³⁾ Nitrate-responsive angina, defined as resting angina that promptly responds to ingestion of nitrates, is suggestive of VSA. Electrocardiographic changes suggesting ischemia during angina attacks can be diagnostic clues, especially if the electrocardiographic findings disappear with nitrate ingestion or symptom resolution. However, if electrocardiographic findings are insufficient to diagnose VSA, then a provocation test is required to confirm the diagnosis of VSA. Strong indications for provocation tests include a clinical history of VSA without documented spontaneous episodes, presentation of acute coronary syndrome without a culprit coronary artery lesion, unexplained cardiac arrest, unexplained syncope with precedent angina, and recurrent resting angina after angiographically successful coronary intervention.³⁾ The primary confirmatory diagnostic method for VSA is coronary angiography alongside provocative testing with acetylcholine or ergonovine.⁴⁾ Positive results are defined as reduction of coronary artery diameter with accompanying symptoms and/or ischemic ST-segment changes that are resolved by intracoronary injection of nitroglycerin. Although the detection of coronary vasospasm and exclusion of obstructive coronary artery diseases are the main advantages of using coronary angiography with provocation, this is an invasive test and usually requires hospital admission.

Echocardiographic examinations can detect coronary artery disease through the presence of regional wall motion abnormalities and are facilitated by newer strain analysis methods.⁵⁾ Since ergonovine provocation echocardiography was first introduced in 1994 by Song et al.,⁶⁾ it has been validated and regarded as a useful noninvasive method to diagnose VSA. Compared to invasive coronary angiography with provocation tests, ergonovine provocation echocardiography is both reliable for the diagnosis of VSA and offers advantages such as safety and feasibility. Song et al.⁷⁾ found that ergonovine provocation echocardiography was safe for the diagnosis of VSA in a large sample of patients (n=3,094). Most ergonovine

provocation echocardiography (85%) was performed in an outpatient context. Song et al.⁷⁾ reported an overall positive rate of ergonovine provocation test was 8.6% in their sample and an increased positive rate of 21% in patients with clinical suspicion of VSA. Interestingly, they reported an increased rate of major adverse cardiac events (MACEs) in patients with positive ergonovine echocardiographic tests (14.0% vs. 5.1%, $p<0.001$). The hazard ratio (HR) was greater in patients with positive results (1.77, $p=0.003$) than those with negative results for ergonovine echocardiography.

These results suggest several clinical implications. First, ergonovine provocation echocardiography is a safe diagnostic method that can be performed in outpatient contexts. Second, VSA patients confirmed by ergonovine echocardiography have a higher incidence of MACE over the long-term follow-up. The conventional management of VSA involves lifestyle modification, avoidance of aggravating factors, and use of pharmacologic therapies. Although many patients with VSA can be controlled with these treatments, about 20% have drug-refractory symptoms. Percutaneous coronary intervention is an option for patients with recurrent or drug-refractory symptoms and fixed obstructive coronary lesions.

In the current study, there were 23 cardiac deaths in the positive ergonovine provocation echocardiography group, and the incidence of cardiac death was greater than that in the negative ergonovine echocardiography group (8.7% vs. 3.5%, $p<0.001$). With appropriate treatment, some of these cardiac deaths might have been prevented. Survivors who avoid sudden cardiac death due to VSA have poorer clinical outcomes than other VSA patients.⁸⁾ Thus, other preventive treatments, including insertion of implantable cardioverters and defibrillators, should be considered in these patients.

There are several gaps in knowledge in the field of VSA. In the present study, data regarding differences in prevalence between Asian and Western countries remained insufficient. The pathophysiology of VSA needs to be evaluated in greater depth. There are unsolved issues regarding the treatment of drug-refractory angina and prevention of sudden cardiac death in VSA patients. Further studies will be needed to address these knowledge gaps and improve the clinical outcomes of patients with VSA.

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