



Usefulness of scoring system for diagnosis of vasospastic angina – Is spasm provocation test no longer needed?

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ARTICLE INFO

Article history:

Received 11 April 2019

Received in revised form 14 April 2019

Accepted 15 April 2019

Available online 28 April 2019

Vasospastic angina (VSA) is one of the important functional cardiac disorders characterized by myocardial ischemia due to epicardial coronary artery spasm. The clinical manifestations are various such as stable angina, acute coronary syndrome, and life-threatening arrhythmic events. It has been believed that there is an ethnic difference in the incidence of VSA, because it has been reported mainly from Asian countries. A previous study revealed that the incidence of VSA is similar between Asian and White [1]. Another study indicated that coronary vasospasm is inducible in approximately one-quarter of myocardial infarction patients without non-obstructive coronary arteries [2]. A recent study also indicated that acute coronary syndrome (ACS) due to epicardial VSA is associated with a high incidence of MACE [3]. Therefore, diagnosis of VSA is important to assess the risk of MACE in patients with ACS but without organic stenosis. According to the guidelines, VSA was defined as a total or subtotal (>90%) coronary artery narrowing induced by ergonovine or acetylcholine during coronary angiography, accompanied by chest pain and/or ischemic electrocardiography (ECG) changes [4,5]. This diagnostic assessment is established and safe [6], but invasive, in the present study, Lin Y et al. examined usefulness of the scoring system to diagnose VSA non-invasively in patients with chest pain [7] (the present manuscript). The score consisted of chest pain at rest, a positive result of hyperventilation test, history of allergy, history of bronchial asthma, ST-segment elevation at chest pain attack and presence of myocardial bridge. The sensitivity and specificity of the scoring system are >90%, suggesting that it could be useful epicardial VSA in patients without obstructive coronary artery disease. However, we need to note that this score applies to patients who have no organic stenosis angiographically, because only the patients who had no organic stenosis in coronary arteries were enrolled in the present study.

1. Clinical implications of coronary vasospasm provocation test

Although this score might be useful to diagnose epicardial VSA without provocation tests, several studies recently demonstrate the importance of the spasm provocation tests not only for the diagnosis but also risk assessment and stratification of medical therapy in patients with coronary vasospasm.

First, Takagi Y et al. reported a score for comprehensive risk assessment and prognostic stratification in epicardial VSA patients, in which multi-vessel spasm induced by the provocation test is one of the predictors for major adverse cardiac events (MACE) [6]. The incidence of MACE in patients with multi-vessel spasm is 1.7 times greater than in those without it. Also, another Japanese study indicated that coronary vasospasm at the site of significant organic stenosis is a significant predictor of MACE [8]. Thus, the provocation test might be useful for risk stratification in patients with epicardial VSA.

Second, the provocation test might enable to diagnose microvascular vasospasm (MVA). A previous study from Germany revealed that 24% of patients who underwent diagnostic angiography for suspected myocardial ischemia and were found to have unobstructed coronary arteries (no stenosis $\geq 50\%$) was diagnosed as MVA which is defined as showing angina and ischemic ECG shifts without epicardial spasm [1]. MVA has never been diagnosed appropriately, because of difficulty of diagnosis and lacking established criteria [9]. Recently, diagnostic criteria of microvascular angina have been proposed by the Coronary Vasomotion Disorders International Study Group (COVADIS) [10], in which one of the 4 criteria is an impaired coronary microvascular function evaluated by invasive coronary vasoreactivity tests including coronary flow reserve, coronary microvascular resistance, and coronary microvascular spasm, defined as reproduction of symptoms, ischemic ECG shifts but no epicardial spasm during acetylcholine testing. Therefore, invasive coronary vasoreactivity tests are essential to diagnose MVA, and the accurate diagnosis of MVA could result in the appropriate choice of medical therapy.

Finally, a more recent study, CorMicA trial, indicates that stratification of medical therapy based on results of the spasm provocation test leads to favorable outcomes in patients with myocardial ischemia but no obstructive coronary artery disease [11]. In an intervention group, according to the results of provocation test, calcium channel blocker and beta-blocker are used for patients with epicardial VSA and those with MVA, respectively. Whereas, in a control group, the results were blinded to clinicians, and guideline-directed medical therapy and antianginal therapies were selected according to the preference of the

DOI of original article: <https://doi.org/10.1016/j.ijcha.2019.02.001>

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<https://doi.org/10.1016/j.ijcha.2019.100364>

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patients' usual cardiologists. In the interventional group, less severity of angina and better quality of life were observed compared with the control group.

Thus, the spasm provocation test enables individualized management of this undifferentiated population (epicardial VSA, microvascular angina and both).

2. Clinical implications of the diagnostic scoring system

As mentioned above, the spasm provocation test is an invasive procedure, but still useful for risk assessment and optimization of medical therapy with acceptable complication risk [1,6]. The scoring system for diagnosis of VSA is suitable to diagnose epicardial VSA, however, it is difficult to diagnose MVA and assess the prognosis of patients with epicardial VSA and/or MVA by the score. In the future, it would be better to examine the validity of a scoring system including patients with microvascular angina, and optimization of medical therapy based on diagnosis by the scoring system.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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