
We thank Dr Mohri for his insightful comments. We completely agree with Dr Mohri that standardization of intracoronary provocation testing for coronary spasm with respect to dosage, infusion time, and a route of administration is urgently needed, as mentioned in our article.1 As highlighted in the Methods section of our article, the maximum dosage of 200 μg acetylcholine for the left coronary artery was derived from the Evaluation of Nifedipine on Coronary Endothelial Function (ENCORE) study. In this trial, the dose for the left anterior descending artery and for the left circumflex artery was 100 μg in each vessel injected via a selective catheter in a coronary segment without significant coronary artery disease. In the most constraining context, this dose of acetylcholine reduced the coronary diameter by ≈ 25%.2 For practical reasons, the acetylcholine injection in the present study was performed unselectively via the diagnostic catheter in the left coronary artery with a maximum dose of 200 μg. Furthermore, as previously reported by our group, a substantial proportion of patients will only respond at the maximum dose of 200 μg.1 Despite the higher dose, specificity of the test is preserved as >40% of patients suspected to abnormal coronary vasomotion show an abnormal response at this dose. The high dose approach is further corroborated by a Japanese study that recently reported the usefulness of applying the 200-μg dose in Japanese patients undergoing intracoronary provocation testing in search of coronary artery spasm.4 An interesting aspect brought up by Dr Mohri is the role of microvascular spasm in patients with effort angina, positive exercise stress test, and unobstructed coronary arteries. Although it is difficult to prove what mechanism may be responsible for the symptoms of a patient with these characteristics in daily life, microvascular spasm certainly represents a possible and plausible cause.1

We are grateful for Dr Yasue et al’s comments. As nicely highlighted by Dr Yasue and colleagues, there may be important differences between patients with epicardial compared with those with microvascular spasm. Nevertheless, we believe that the term vasospastic angina or coronary spasm is justified for patients with resting angina and epicardial or microvascular spasm as it describes the common pathogenic mechanism (ie, hyperreactivity of the vascular smooth muscle layer). The reason why we have speculated that diffuse and distal epicardial spasm may be a sign of concomitant microvascular disease lies in the fact that ischemic ECG changes and reproduction of the patient’s symptoms are often seen at lower acetylcholine doses before distal and diffuse epicardial spasm can be observed.1,5 Nevertheless, as pointed out in the Discussion of our article, more studies are needed to elucidate the relationship between epicardial and microvascular spasm. We agree with Dr Yasue et al’s comment that ECG changes and the degree of vasoconstriction may vary in the same patient because there is a large spectrum of coronary artery spasm ranging from subtle ST-segment depression and diffuse vasoconstriction to ST-segment elevation with focal occlusive spasm.6 In addition, we also agree with the statement that coronary artery spasm can often coexist in patients with obstructive coronary artery disease, which becomes obvious after myocardial revascularization. We have recently reported a similar frequency of epicardial spasm in white patients with previous stent implantation compared with Asian patients.1

Disclosures

None.

References


Response to Letters Regarding Article, "Clinical Usefulness, Angiographic Characteristics, and Safety Evaluation of Intracoronary Acetylcholine Provocation Testing Among 921 Consecutive White Patients With Unobstructed Coronary Arteries"

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