EDITORIAL COMMENT

Coronary Vasospasm and Coronary Atherosclerosis
Do We Have to Choose?

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In this issue of the Journal, Ong et al. (1) sought to determine the prevalence of coronary spasm in angina patients with angiographically normal coronary arteries. Of 304 patients with stable angina, 144 (47%) had normal coronary arteries or only minimal irregularities (<20% diameter reduction) at coronary angiography. Acetylcholine (ACH) testing was performed in 124 of the 144 patients and provoked coronary spasm in 77 (62%). Thirty-five patients (45%) with constrictor response presented with epicardial spasm (defined as a ≥75% diameter reduction with reproduction of the symptoms of the patient), and 42 patients (55%) presented with microvascular spasm (defined as ischemic electrocardiographic changes with symptom reproduction, but no epicardial spasm). Overall two-thirds of patients undergoing the ACH test presented with abnormal coronary artery vasomotion, a finding that also confirmed the presence of the ischemic syndrome.

The authors are to be congratulated for attempting to determine pathophysiological mechanisms underlying symptoms and evidence of myocardial ischemia in this patient population. Indeed, in the absence of obstructive coronary artery disease (CAD), management of patients with angina represents an unsolved challenge. Such patients are often labeled as either patients with “atypical angina” or patients with “false positive results” at noninvasive evaluation. However, long-term follow-up studies suggest that patients with angina and ischemia, who do not display obstructive CAD, have increased coronary event rates and adverse quality of life as compared with those with no evidence of ischemia (2), underscoring the relevance of proper identification and treatment.

Acetylcholine, an endogenous neurotransmitter, is adopted to invasively assess the coronary endothelial function. In normal conditions, ACH causes vasodilation by releasing nitric oxide or closely related substances via endothelial receptors (3). However, in the presence of endothelial dysfunction, an early marker of coronary atherosclerosis (4–6), ACH induces coronary vasoconstriction via receptors localized into the smooth muscle cells (7,8). The degree of coronary constriction in response to ACH administration can vary considerably, ranging from mild to complete or near-complete coronary flow obstruction, as typically observed in patients with variant angina (9) who present with localized hyper-responsiveness (10). Indeed, as documented from the first angiography studies (11,12), the “state of the art” patient with variant angina was the patient with: 1) rest angina; 2) normal or near coronary artery tree; and 3) complete or near-complete dynamic focal obstruction at provocative test.

However, the concept of coronary spasm has evolved since then. The relevance of coronary spasm has been demonstrated in clinical scenarios other than variant angina (i.e., stable angina) (13,14), in which involvement of the coronary microcirculation has been suggested as well (15). Moreover, it is now accepted that the degree of spasm can be affected by a number of factors, including resting vasmotor tone, segmental epicardial coronary artery hyperactivity, and organic stenosis (16,17).

Ong et al. (1) administered intracoronary ACH in patients with exertional angina. The test was considered positive for spasm when either an epicardial coronary flow reduction of ≥75% at angiography or ischemic electrocardiographic changes occurred during symptom reproduction. They excluded per-protocol patients with significant coronary atherosclerosis, adhering to the dogma for searching coronary artery spasm only in patients with normal and near-normal coronary arteries.

Actually, there is no reason to believe that abnormal coronary vasomotion and endothelial dysfunction are exclusive to coronary vessels with no or minimal atherosclerosis. By limiting investigations to this subset of patients, the relevance of functional factors in precipitating myocardial ischemia might be underestimated.

Coronary spasm, which was initially demonstrated in patients with normal or near-normal coronary arteries (11,12), frequently occurs at sites of significant atherosclerosis, both in acute and chronic settings (18–21). Spasm of atherosclerotic lesions is often associated with myocardial ischemia (16,22,23), with coronary vasomotor response closely related to plaque burden (24). Moreover, normal or near-normal coronary arteries of patients with focal vaso- spasms show angiographically insignificant atherosclerosis (25), suggesting that paradoxical constriction can occur both during the early as well as advanced stages of disease (26). In addition, the presence of obstructive CAD does not preclude spasm of adjacent, nonobstructive coronary segments (27,28), which can actually be responsible for ischemia.
Finally, the contribution of coronary vasomotion to precipitation of myocardial ischemia has been recently demonstrated in patients with acute coronary syndrome and significant atherosclerotic lesions who were administered intracoronary nitroglycerin (29).

In conclusion, Ong et al. (1) must be congratulated for stressing the role functional factors in precipitating myocardial ischemia. However, to achieve a more comprehensive approach to ischemic heart disease, such factors should be considered also in patients with obvious coronary atherosclerosis.

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REFERENCES


