

The undisputed principles of myocardial ischemia!

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Hot Topics

Advances in research have allowed for the construction of algorithms that assist physicians in the management of patients with suspected heart disease. Among heart problems, ischemic heart disease (IHD) represents the most frequent clinical presentation, and algorithms for patients presenting with chest pain are consequently those that have gained major attention [1]. Such algorithms are based on the pathophysiological principles that cardiac pain is an expression of myocardial ischemia, which becomes clinically manifest when the lumen of the coronary arteries is reduced beyond a critical level, a phenomenon mainly secondary to coronary atherosclerotic obstructions. Therefore, it is not surprising that ruling out obstructive coronary artery disease (CAD), the ultimate culprit element derived from this chain cause-effective relationship, is a fundamental step in the stepwise evaluation of patients with chest pain.

Identification of patients with obstructive CAD has encountered progressive evolution. The likelihood of obstructive CAD in the individual patient was initially estimated through the construction of models composed of a number of clinical risk factors [2]. More recently CAD has been non-invasively assessed by numerous methods, in this way promoting a new era in cardiovascular medicine.

However, contrary to expectations, the predictive ability for obstructive CAD still remains low [3]. Moreover, a mismatch between coronary physiology and anatomy has also been demonstrated. Nonetheless, the later phenomenon appears not to bother researchers, who continue undisturbed their search for the “best” technique. In line with these considerations, four recently published studies independently sought to demonstrate the ability of their tested methodology to identify mechanism(s) or prediction model(s) of CAD.

The study by Reszko et al [4], involving 14 048 consecutive patients with suspected CAD who underwent computed tomographic angiography (CTA), found that the traditional approach (age, sex and angina typicality based) greatly overestimates the prevalence of disease (coronary atherosclerosis). However, a significant number of patients with CAD had no symptoms of angina and, on the other hand, nearly as many patients with angina had no detectable CAD.

The discrepancy between anatomical severity and clinical findings has been related to the physiological effects that the individual CAD obstruction exerts on the myocardial perfusion territory. Naya et al [5] sought to determine the effects that the morphology and extent of coronary atherosclerosis (assessed by CTA) exert on myocardial flow reserve (MFR) (evaluated by positron emission tomography). The authors found that the description of atherosclerosis by CTA had only a modest effect on downstream MFR. Indeed, the severity of stenosis did not

reliably predict physiological myocardial blood flow effects. More specifically, while patients with 0% stenosis diameter or a zero summed stenosis score by CTA may have a MFR ranging from 1 to 5, on the other hand those patients with 70% or greater stenosis diameter or a higher summed stenosis score may present with normal MFR. Given that CTA has a very high negative predictive value for CAD, what is the cause of reduced MFR in patients with no documentable CAD? Moreover, in light of these findings, is there any reason to believe that the exclusion of visible CAD is a fundamental step in the stepwise evaluation of patients with suspected heart disease? On the other hand, does the documentation of obstructive CAD automatically authorize us to assume that this is the underlying cause of the symptoms?

To shed further light on this topic, Kang et al [6] assessed the value of intravascular ultrasound (IVUS) in predicting the functional significance of intermediate coronary lesions. In that study, 201 patients with 236 coronary lesions underwent IVUS and invasive physiological assessment with fractional flow reserve (FFR) before intervention. The authors identified an IVUS minimal lumen area (MLA) of 2.4 mm² or greater as a cutoff with a high predictive value for an FFR of 0.80 or greater. However, 63% of lesions with an MLA less than 2.4 mm² had an FFR of 0.80 or greater, and the results were similar when other IVUS measured parameters were related to FFR, in this way once again questioning the reliability of atherosclerotic obstructions as a cause of myocardial ischemia.

Similar results were also obtained in acute settings. Reynolds et al [7] studied the mechanism(s) of myocardial infarction (MI) in 50 women with no angiographically demonstrable obstructive CAD by using IVUS and cardiac magnetic resonance (CMR). Plaque disruption (rupture or ulceration) by IVUS was demonstrated in 38%, and abnormal CMR findings were documented in 59%. The authors concluded that plaque rupture and ulceration with CMR abnormalities are common in women with MI without angiographically demonstra-

ble obstructive CAD. Both IVUS and CMR play a significant role in the evaluation of this patient subset providing complementary mechanistic insights. However, if the results of that study are analyzed critically, the message emerging from adopting these high quality imaging modalities is that, currently, we are not able to detect the mechanism of MI in the vast majority of patients with no obstructive CAD (ie, 62% of patients). Moreover, plaque distribution was not related to the presence of left ventricular wall motion abnormalities or ECG changes. Given these observations, is there any evidence to suggest that a similar pattern does not affect vessels with angiographically significant obstructions?

The incremental value of the single technique tested is indubitable. However, at the moment, while the disease (ie, MI) can be diagnosed reliably, the underlying mechanism(s), the ones we thought we already knew, remain(s) unknown in the vast majority of patients.

Has the time for questioning fundamental pathophysiological postulations arrived yet? •

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