How to Evaluate Microvascular Function and Angina?

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There are 10-30% of patients undergoing cardiac catheterization to evaluate angina-like chest pain have normal coronary angiograms and patients with angina pectoris with documented myocardial ischemia in the absence of coronary artery disease are often labeled as having cardiac syndrome X(CSX). CSX is classically acknowledged as a female-predominent disorder and nearly 70% patients of CSX are women. Coronary microvascilar dysfunction (CMD) is a main etiologic mechanism of a subset of patients with CSX. CMD refers to abnormalities in the vasomotor, metabolic regulators, or structural abnormalities of vessel wall of the small coronary arterioles (<500μm). Therefore, it is not possible to allow the direct visualization of coronary microvasculature in human. Coronary microvasculature can be assessed by TIMI myocardial perfusion grade (myocardial blush score) during coronary angiography. Following contrast injection into the coronary arteries, there is late filling of the distal capillaries, which appears as a blushing of contrast in the myocardium. In order to visualize myocardial blush, it is important to remain on the cine pedal for an extended period –longer than is customary for routine coronary angiography. Myocardial blush score is simple to assess microvasculatue, however, it is semiqantitative and subjective. Many parameters for evaluation of microvascular function rely on the quantification of coronary blood flow. Coronary blood flow reserve (CFR) is the magnitude of the increase in coronary flow that can be measured the ratio of coronary flow during maximal microvascular dilation and basal coronary flow. CFR can be measured by intracoronary Doppler wire. CFR is calculated as the ratio of hyperemic averaged peak velocity (hAPV) during maximal hyperemia induced by adenosine or others and baseline averaged peak velocity (bAPV). And it is possible to measure pressure and to estimate coronary artery flow simultaneously with a single pressure-temperature sensor-tipped coronary wire. By the thermodilution technique, the mean transit time (Tmn) of room-temperature saline injected down a coronary artery can be determined and has been shown to correlate inversely with absolute flow. From this technique, a thermodilution-based CFR can be derived that has been shown to correlate well with Doppler velocity wire-derived CFR both in their experimental model and in humans. Reduced CFR (<2.5) appears to be a common underlying factor noted in many patients exploring the pathogenesis of patients with chest pain and normal coronary angiograms. It is not clear whether myocardial ischemia in these patients due to abnormal production or destruction of NO, receptor abnormalities, reduced sensitivity of vascular smooth muscle cell to relax. Previous study demonstrated half of women with chest pain and normal or minimal coronary artery had reported a reduced CFR in response to adenosine, suggesting an endothelial-independent mechanism of microvascular dysfunction. Hyperemic microvascular resistance index was calculated from Pd, which was assessed using a pressure wire, divided by hAPV, which was assessed using a Doppler wire. More recently, this index can be measured simultaneously by Combo wire which has dual

sensor with pressure sensor and pressure sensor. Theoretically, this index may be independent to resting hemodynamic condition unlike CFR and has an advantage in the viewpoint of accounting coronary pressure and coronary blood flow simultaneously. However, lack of many clinical studies about this index and lack of normal value are limitations to solve following future studies. Index of microvascular resistance index (IMR) defined as Pd divided by the inverse of the hyperemic mean transit time (a correlate to absolute flow, hTmn), measured simultaneously with the coronary pressure wire. The IMR measured acutely was higher in patients with microvascular obstruction on ce-CMR, and IMR independently predicted LV function and infarct volume. Compared with CFR, IMR provides a more reproducible assessment of the microcirculation, which is independent of hemodynamic perturbations. IMR was studied in acute myocardial infarction and patients with an IMR >40 had a higher rate of the primary end point at 1 year than patients with an IMR ≤40. CMD caused by traditional coronary risk factors or by yet unknown mechanisms is enough to cause myocardial ischemia and is associated with worse clinical outcomes. Therefore, the exact evaluation of coronary microvascular function by appropriate parameters should be needed for understand pathogenic mechanisms and treatment strategies.