Left ventricular function during hyperemia: A dive into the unknown

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The relationship between myocardial ischemia and left ventricular (LV) dysfunction was described almost 30 years ago by Hauser et al[1] who observed the appearance of regional myocardial dysfunction during coronary angioplasty by two-dimensional echocardiography. Following these observations, the theory of the ischemic cascade was developed, and abnormal myocardial perfusion was recognized as an early manifestation of ischemia. Myocardial ischemia is the mismatch between oxygen/metabolites supply and metabolic needs of myocardial cells. An inadequate blood flow causes an impairment in venous return and, consequently, accumulation of catabolites and tissutal acidosis that further contributes to the deterioration of LV function. In the ischemic cascade, there is a clear association between blood flow, oxygen supply, development of ischemia, and diastolic/systolic functional impairment. It is now clear that ischemia is the trigger for LV dysfunction, and it can be observed both after exercise and pharmacological stress test by dobutamine, which can activate the ischemic process increasing the oxygen demand. Maldistribution of flow itself, which can be observed during hyperemia induced by vasodilators, not necessarily induces ischemia unless horizontal and/or vertical coronary steal, affecting the regional blood flow, occur.

Coronary steal is not a frequent phenomenon; in a recent paper, Stuijfzand et al[2] observed that in the presence of angiographically well-developed collateral arteries, patients with total occlusion of a coronary artery and preserved LV ejection fraction showed significantly impaired perfusion by PET as only 9% of patients displayed a preserved coronary flow reserve of $\geq$2.50; however, coronary steal (coronary flow reserve $<$1.0) was observed in only 13% of patients.

Nussbacher et al demonstrated that continuous intravenous administration of adenosine to humans often results in a paradoxical rise in pulmonary capillary wedge pressure, primarily resulting from changes in vascular loading rather than from direct effects on cardiac diastolic or systolic function.[3]

In this issue of the Journal of Nuclear Cardiology, Juarez-Orozco et al[4] in a study with PET/CT with N13-ammonia have found that stress myocardial blood flow correlates with ventricular function and synchronizes better than myocardial perfusion reserve. They have evaluated a retrospectively enrolled group of patients, which represents a typical population with appropriate indications to stress imaging by PET.[5] They have found that absolute global myocardial blood flow during adenosine infusion, but not the coronary blood reserve, is correlated to LV function. This is not surprising as the coronary flow reserve is a ratio between myocardial blood flow during vasodilator-induced hyperemia and myocardial blood flow at rest. Normal values (>2) can be observed due to either a physiologic increase during stress or to a low myocardial blood flow at rest as observed in infarcted territories.

Little is known about the relationship between myocardial blood flow and LV function during vasodilation. A correlation was found in the study by Juarez-Orozco et al who have integrated in a complex statistical analysis several functional measures (LVEF, LV filling rate, and entropy) which are continuous variables, not independent from each other. Stress myocardial blood flow is lower in patient with previous MI in comparison to the normal patient subgroup and correlates with LV function better that rest myocardial blood flow and coronary flow reserve. Presumably, the same happens in patients with reversible LV dysfunction due to coronary steal during hyperemia.

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Different from SPECT, gated PET offers the possibility of evaluation of LV function from data acquired during stress and not post stress as in traditional SPECT MPI. Juarez-Orozco et al have applied a standard acquisition protocol that contemplates a 6-minute adenosine infusion through a peripheral vein (140 μg/kg/min) and injection of Nitrogen-13 ammonia at the third minute of the adenosine administration with image acquisition lasting for 10 min. Since the adenosine infusion was stopped at the third minute of PET acquisition and that the pharmacological activity persists for more 1–2 minutes, that means that half acquisition was registered during the peak stress and half acquisition as a post stress. It would be therefore interesting to reproduce the same study after regadenoson infusion whose hyperemic effect reached peak values within 0.5 to 2.3 minutes, and the mean duration of the increase in flow velocity of twofold or greater was 8.5 minutes in the study by Lieu et al.[6]

As stressed in the discussion, the possibility of performing stress-only protocols by PET measuring peak stress myocardial blood flow and peak stress LV function will simplify a complicate study protocol, saving time, costs, and limiting the radiation exposure. A threshold value of stress myocardial blood flow able to identify abnormal perfusion and to predict left ventricular dysfunction should be defined. Juarez-Orozco et al have opened a new window on PET with perfusion tracers. New branches of research aimed to define the diagnostic, functional, and prognostic values of their findings will certainly follow after this pioneering study.

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