Atherosclerotic disease of the vascular system is a continuum. Disease may begin early in life, but it does not become clinically overt until atherosclerotic plaques reach a critical stage. The clinical manifestations of the disease are related to the impairment of tissue perfusion caused by the growth of the plaque inside the lumen of the vessel, causing impairment of blood flow and symptoms such as angina pectoris.

Positron emission tomography (PET) has been shown to allow noninvasive, accurate, and reproducible quantification of regional myocardial blood flow if suitable tracers are used and appropriate mathematical models are applied. These PET measurements of myocardial blood flow have units of volume per time per unit weight of myocardium (i.e., ml/min/g). PET has been used to study the relationship between stenosis severity and impairment of myocardial blood flow and flow reserve in patients with CAD. Furthermore, measurement of absolute myocardial blood flow with PET in subjects with risk factors for CAD or with cardiomyopathies and normal coronary angiogram has highlighted the role of the microcirculation as an additional cause of myocardial ischemia, leading to the new concept of coronary microvascular dysfunction (2).

In this issue of *iJACC*, Hajjiri et al. (3) provide further evidence showing how absolute myocardial blood flow measured with $^{13}$N-ammonia and PET is superior to measurement of relative tracer content for identification of CAD. Another important finding of this study is that maximum myocardial blood flow (i.e., the flow measured during adenosine stress) is superior not only to the semiquantitative measurement of myocardial tracer retention, but also to coronary flow reserve (i.e., the ratio of maximum myocardial blood flow to resting flow). The data of Hajjiri et al. (3) are consistent with previous reports indicating that the degree of impairment of maximum myocardial blood flow bears important prognostic information. In fact, it has been shown that in both hypertrophic (4) and dilated (5) cardiomyopathies, the severity of impairment of myocardial blood flow measured during dipyridamole stress is predictive of major adverse cardiac events at follow-up. In these patients, who have no evidence of CAD, the curtailment of myocardial
blood flow is caused by dysfunction of the coronary microcirculation.

But why is measurement of maximum flow superior to coronary flow reserve? Because coronary flow reserve is a ratio, factors that influence either the numerator or the denominator may affect its calculation. Therefore, a low coronary flow reserve does not necessarily reflect a reduction of maximum flow, but it can be caused by an abnormally elevated resting flow in face of a normal hyperemic flow. This problem can be overcome, at least in part, by normalizing resting flow for the external cardiac workload that is generally assessed using the rate-pressure product (6).

Potentially, the results of the study by Hajjiri et al. (3) also have important practical implications. Recently, new PET perfusion tracers have been produced that have the potential to allow measurement of absolute myocardial blood flow and do not require a cyclotron on site for their production. The 18F-BMS747158-02 is an example of such new tracers that has several promising features: 1) a relatively long t1/2 (110 min), allowing distribution from a central cyclotron facility, similar to 18F-2-fluoro-2-deoxy-D-glucose; 2) good image quality, because it emits a low-energy positron that travels a short distance in tissue before annihilation, providing a good contrast between the heart and the surrounding tissues that remains stable over time; and 3) high extraction at first pass that is not affected at higher flow rates, hinting at linearity between tracer uptake and perfusion (7,8). The latter feature should enable accurate quantification of myocardial blood flow.

In summary, the data of Hajjiri et al. (3) show that absolute myocardial blood flow measured with PET is superior to measurement of relative tracer content for identification of CAD, and that a single measurement during vasodilator stress might be sufficient to identify myocardium subtended by hemodynamically significant stenoses.

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