Myocardial blood flow reserve and absolute myocardial blood flow for the assessment of patients with coronary artery disease with or without microvascular dysfunction

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Received Jun 16, 2020; accepted Jun 16, 2020
doi:10.1007/s12350-020-02297-9

See related article, pp. 2992–3003

The introduction of SPECT with CZT technology (solid-state detectors by Cadmium Zinc Telluride compounds) allows the dynamic acquisition of SPECT after tracer infusion. The input function and myocardial uptake can be easily measured. Algorithms for analysis of absolute myocardial blood flow (MBF) and myocardial blood flow reserve ratio (MFR, stress/rest MBF ratio) are currently provided by the principal Cardiac CZT vendors.

Several studies have recently documented the feasibility of MBF/MFR measurements by CZT technology in comparison to different reference standards, including positron emission tomography (PET) with $N^{13}H_3$ or H_2O^{15} ,^{1–4} invasive coronary angiography,^{5–8} magnetic resonance imaging,⁹ flow fractional reserve,^{5,10} and semiquantitative analysis of MPI.¹¹ Several of the previously cited papers were accompanied by editorial comments^{12–15} which emphasized critical methodological limitations such as most clinical studies have been single site and enrolled a limited number of patients and

the methodology is not standardized and varied from center to center.

Standardization of protocols requires addressing several aspects including (a) choice of the radiotracers, (b) tracer injection method (bolus vs. pump), (c) injected activity, (d) acquisition protocols (dual day vs single day, stress-rest vs. rest/stress), (e) kinetic models, (f) processing algorithms, (g) use of attenuation correction, scatter correction, spillover correction, partial volume correction, and motion correction, and (h) imaging systems.¹⁶

The group of the University of Ottawa Heart Institute has recently proposed a methodologic approach¹⁷ that is the first step for a multicenter validation study (NCT03427749) aimed to evaluate diagnostic accuracy, intra- and inter-observer variabilities, and incremental prognostic value of SPECT MBF over semiquantitative approaches. This study will provide an answer to many of the critical issues outlined above.

In this issue of the Journal of Nuclear Cardiology, Bailly et al proposed evaluation of the impact of attenuation correction (AC) of CZT-SPECT measurement of MBF. They applied a fast imaging protocol with 6-min dynamic acquisition after both stress and rest followed by a 5-min acquisition for static MPI imaging. They concluded that AC does not significantly affect MFR measurements in both regional and global LV analyses.

However, reading carefully the well-detailed and written paper the reader could conclude that AC strongly affects measurements of absolute MBF both at rest and after vasodilation stress test. Furthermore, the absolute MBF was lower after stress and rest than those obtained by PET with $N^{13}H_3$, or H_2O^{15} ,^{18,19} especially for AC studies (values which are incompatible with life!).

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J Nucl Cardiol 2021;28:3007–9.

1071-3581/\$34.00

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This underestimation could be related to suboptimal tuning of the adopted kinetic model. The strength of the study of Bailly et al is that the MFR is a parameter that is less affected by technological and methodological issues, being a ratio between two measures and, therefore, partially independent of the absolute values at rest and during hyperemia. However, it is mandatory to raise the question whether the measurement of MFR alone is enough to characterize macro- and micro-vascular dysfunction and myocardial ischemia.

In the study by Johnson and Gould²⁰ it was clearly shown that an integration of MBF, MFR, and ischemic thresholds is needed for the assessment of the ischemic burden of coronary artery disease (CAD) and microvascular dysfunction.

MFR or stress flow alone failed to reflect ischemic burden in some patients. The MFR could be normal despite a low absolute stress MBF if the resting MBF is low and vice versa. We recognize that the above conditions affect only a minority of CAD patients, but at the same time the absence of a reliable measure of MBF at rest and during hyperemia limits the possibility of a correct classification of these patients. Gupta et al²¹ in 4029 consecutive patients studied by rest/stress PET-MPI showed that both maximal MBF and MFR were strong predictors of major cardiac events and that the integrated assessment of the two indexes identified unique phenotypes of patients with known or suspected CAD who are at different risk for events. At least two studies with gamma-emitting perfusion tracers by CZT or traditional Anger cameras^{3,22} have shown the superiority of reconstruction algorithms which included motion and attenuation correction. Measuring MFR by CZT cameras requires additional time, due to the need of early dynamic acquisition for both stress and rest studies. The additional time to acquire a low-dose CT of the cardiac region by a stand-alone equipment is limited to few minutes, which compensates for the time needed to perform prone imaging.

In conclusion, the availability of a low-cost non-invasive technology for a reliable measure of MFR and MBF with a potential widespread distribution could open a new era in the evaluation of coronary microvascular disease with or without obstructive or non-obstructive atherosclerosis and may have important prognostic and therapeutic implications.²³ MFR is a cornerstone in this process but an additional, reliable measure of MBF at rest and during hyperemia would be advisable. The results of a multicenter trial will define and standardize the methodology for the best approach to the measure of MBF and MFR by CZT technology with ^{99m}Tc-labeled perfusion tracers.

Disclosures

The authors declare that they have no conflict of interest.

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