Quantitative PET Myocardial Blood Flow

“Trust, But Verify”

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Noninvasive quantification of absolute hyperemic myocardial blood flow and flow reserve with positron emission tomography (PET) imaging is an elite tool for coronary artery disease (CAD) detection and could offer a paradigm shift in CAD management. It extends the scope of conventional single-photon emission computed tomography myocardial perfusion imaging from primarily qualitative or semiquantitative assessment of regional perfusion in terms of relative radiotracer content in left ventricular myocardial regions and vascular territories to absolute quantitative measures in terms of milliliters per minute per gram of tissue (1). Refining the tools of regional and global myocardial blood flow measures extends our clinical determination from detection of advanced flow-limiting epicardial CAD to earlier stages of atherosclerosis or microvascular dysfunction (2). Such PET-derived regional and global absolute myocardial blood flow assessments have ascertained incremental coronary event risk to that provided by severity of coronary artery stenosis alone. However, to integrate and rely on these quantitative blood flow measures in the clinical setting, it is critical that the boundaries of variability of the quantitative absolute blood flow measure be established, as has been done with other absolute values of key parameters such as electrolytes, blood acid-base balance, and serum lipoprotein and glucose levels.

In this issue of JACC, Kitkungwan et al. (3) report test-retest reliability of rubidium PET absolute myocardial blood flow measurement performed the same day (with a 5- to 20-min time interval) or 1 to 3 weeks apart. Such test-retest agreement and reliability are routinely evaluated during the validation phase for many measurement tools and require that there be no confounding factor during the intervening time interval of retesting. To avoid the inherent biological variability of reimaging a subject twice, U.S. Food and Drug Administration (FDA) clinical trials usually keep the minimal time interval between serial studies and maintain the same medical regimen and image acquisition parameters. Agreement requires a measurement tool to produce the same exact values on both test occasions. In contrast, reliability requires a measurement tool to produce the same classification on both occasions, such as normal or abnormal in the case of PET myocardial blood flow, when the test is applied twice. Even if a test-retest reliability process is applied with no sign of intervening factors, there will always be some degree of error, known as error of measurement.

In the present study, the investigators inform us that when PET imaging was retested the same day, the error of measurement was 10%, and when PET imaging was performed 1 to 3 weeks apart, the coefficient of variance was nearly 20%, reflecting added biological variability. These reasonable test-retest values underscore the importance and the clinical utility of quantitative PET absolute myocardial blood flow as an adjunct to visual interpretation of relative radiotracer distribution and content in the left ventricular myocardium. It is important to point out, however, that test-retest reliability of the particular software used in the present study is not necessarily interchangeable with other FDA-approved PET absolute myocardial blood flow software packages that are used in clinical practice.
Kitkungvan et al. (3) also inform us that global myocardial perfusion at 8 min after 4-min dipyridamole infusion was 10% higher than at the conventional 3 to 5 min after the completion of dipyridamole infusion. These data suggest that accurate quantification of myocardial blood flow is critically dependent on the interplay between the vasodilator applied and the timing of the radiotracer injection in relation to the peak coronary vasodilation achieved by that particular vasodilator. The latter highlights the critical nature of the timing with which a radiotracer is injected in relation to peak coronary vasodilation and its ultimate impact on the quantitative blood flow measure and its reproducibility for clinical decision making (4).

The clinical objective of quantitative myocardial blood flow with PET imaging is to provide physiological, mechanistic, and prognostic information to guide and tailor therapeutic and invasive therapy to the individual needs of patients. It is important to recognize, however, that myocardial blood flow and flow reserve could be decreased secondary to epicardial coronary artery narrowing or microvascular disease due to abnormal neurohormonal tone, small vessel disease, or biochemical disorders. Myocardial flow reserve can also be spuriously lowered by elevated resting blood flow in the denominator, as seen in patients with hypertension or prominent left ventricular hypertrophy. However, as aggressive medical therapy and prevention become effective alternative treatment options for CAD, computer-assisted quantification of myocardial blood flow makes it very attractive to study longitudinal changes in regional and global myocardial blood flow and coronary artery remodeling. Good test-retest reliability is particularly important when evaluating the natural time course of coronary atherosclerosis and for monitoring therapeutic effects of novel drugs designed to reduce atherosclerosis in the coronary arteries. Reliable quantitative comparison between baseline and follow-up PET myocardial blood flow studies brings us 1 step closer to personalized medicine.

Accurate quantitative description of an index or disease is a requisite for effective communication and for clinical investigation. However, the FDA currently favors visual interpretation of images by expert readers rather than semiquantitative or fully automated quantitative analysis (5). Most clinical single-photon emission computed tomography and PET myocardial perfusion studies are reviewed in a visual, artisan approach, which entail reviewing the reconstructed and normalized paired stress and rest tomographic images to identify all sorts of extracardiac and patient motion artifacts. Similarly, although it is well known that visual interpretation of coronary artery narrowing is not reproducible or accurate, it remains the standard for the interpretation of coronary angiograms and the delivery of care. Despite the prognostic importance of left ventricular ejection fraction, many laboratories still visually estimate this parameter, even though it is incredibly simple to measure. Is it possible that the human visual cortex, with its remarkable capacity to resolve and integrate a multitude of imaging findings, whether in grayscale or in color, remains the most sophisticated gold standard for image interpretation? Until quantitative absolute myocardial blood flow measurements become as reliable and reproducible as other absolute values of key parameters in medicine, such as electrolytes and serum glucose levels, perhaps the best approach to interpreting PET myocardial perfusion studies at the present time is to “trust” the quantitative values but “verify” them visually.

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**REFERENCES**


