How Can the Assessment of Myocardial Flow Reserve by Nuclear Medicine Change the Interpretation of Myocardial Perfusion Scintigraphy?

Ronaldo de Souza Leão Lima
Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ – Brazil

Myocardial perfusion scintigraphy (MPS) with single-photon emission computed tomography (SPECT) is important for the diagnosis and prognostic evaluation in patients with coronary artery disease (CAD). MPS evaluates the presence, extent and degree of myocardial ischemia and/or infarction, usually through visual observation or semi-quantitative parameters. Despite its proven diagnostic and prognostic values, the relative nature of perfusion imaging may limit SPECT ability to identify patients with high-risk multivessel CAD. Limitations regarding visual or semi-quantitative assessment of regional myocardial perfusion defects may result in underestimation or misdiagnosis due to “balanced” ischemia.

This limitation can be addressed by quantifying myocardial blood flow (MBF) or myocardial flow reserve (MFR) using tracer kinetics in positron emission tomography (PET). PET is a well-validated non-invasive method for quantification of myocardial perfusion, demonstrating an incremental diagnostic and prognostic power compared to MPS in patients with suspected or known CAD. PET then is considered the gold standard for non-invasive quantification of MBF and MFR. However, the production of PET tracers is costly and the technology is not yet available in many countries.

The introduction of high-sensitivity cadmium-zinc-teluride (CZT) cameras for cardiology tests allows the dynamic acquisition of tomographic images to evaluate radiotracer kinetics, and opens a new era for measuring MBF and MFR.

Quantification of MBF and MFR using dynamic CZT-SPECT in list mode is technically feasible and clinically useful. The WATERDAY study compared MBF and MFR obtained with 99mTc-sestamibi in CZT-SPECT with those obtained in a 15O-water PET and fractional flow reserve (FFR). While stress and rest MBF were significantly overestimated with CZT-SPECT compared to PET, MFR was similar between the two techniques, which means that the quantification of MBF and MFR by dynamic 99mTc-sestamibi CZT-SPECT is clinically useful. Acampa et al. demonstrated that CZT-SPECT values are higher than those measured by 82Rb-PET imaging, with a moderate correlation between the two methods. CZT-SPECT showed good diagnostic accuracy for identifying obstructive CAD. Different studies have outlined the incremental value of MFR measurements in different categories of patients for diagnosis or prognosis. In patients with multivessel CAD, where normal myocardial perfusion imaging (MPI) may not necessarily identify truly low-risk subgroups among high-risk cohorts, they often show reduced MFR.

Despite the excellent diagnostic value of FFR, which quantifies pressure gradient through stenosis, it does not reflect microcirculation abnormalities. Unlike FFR, myocardial perfusion reserve (MPR) reflects flow in epicardial arteries and microvasculature. Therefore, FFR and MPR are not equivalent.

It should be noted that several factors can affect the hemodynamic flow response to luminal stenosis, including lesion geometry and location and the presence of collateral vessels, impacting overall regional flow. In a study by our group, De Souza et al. showed that both global MPR and MBF stress were reduced in patients with abnormal perfusion. In addition to assessing perfusion, this study demonstrated that overall MPR is inversely associated with CAD prognostic index (CADPI), a hierarchical index that includes the entire epicardial coronary tree and is related to overall cardiovascular risk.

In this scenario, Panjer et al. performed a systematic review and meta-analysis with the objective of evaluating the diagnostic accuracy of dynamic CZT-SPECT in coronary artery disease (CAD) compared to FFR and PET as a reference. To assess CZT-SPECT, the analysis yielded 0.79 sensitivity (95% CI 0.73–0.85) and 0.85 specificity (95% CI 0.74–0.92). Diagnostic odds ratio was 17.82 (95% CI 8.80–36.08, P < 0.001). Positive likelihood ratio and negative likelihood ratio were 3.86 (95% CI 2.76–5.38, P < 0.001) and 0.21 (95% CI 0.13–0.33, P < 0.001), respectively. The results of this systematic review and meta-analysis emphasize the role of dynamic CZT-SPECT MPI with good sensitivity and specificity for diagnosing CAD compared to gold standards. The use of CZT-SPECT systems for measuring MPR is very attractive considering that in just one scan it is possible to obtain perfusion and functional parameters with results comparable to PET. However, what emerges from this meta-analysis is that the protocol used in different centers should be better standardized. The included studies use different methodologies in terms of dose administration, acquisition protocol, CZT cameras, radiotracers and software package used. Furthermore, in each study a different cutoff value was defined for the dynamic SPECT MPI. Seven studies compared with FFR and two used PET. To measure acquisition, MPI was performed with different types of CZT-SPECT cameras. Six studies used Discovery NM 530c (GE Healthcare, Chicago, IL, USA), one study (11.1%) used Discovery NM/CT 570c.

Keywords
Coronary artery disease; Scintigraphy; Diagnosis.
Myocardial flow reserve and myocardial perfusion scintigraphy

Myocardial flow reserve assessment using CZT can be useful in many clinical situations, as shown by PET (Table 1).

One of the main uses was demonstrated in the extremely high sensitivity to detect multivascular disease, as in the study by DiCarli et al., where normal MFR on PET virtually excluded the possibility of this event. MFR evaluation by CZT-SPECT also allows for this increase in accuracy.

The possibility of identifying microvascular disease as the cause of angina is useful for reducing investigation costs but also very important as a determinant of prognosis. MFR, both on PET and on CZT-SPECT, is a non-invasive modality for confirming this phenomenon.

In preparation for pharmacological stress with dipyridamole or adenosine, abstinence from caffeine for at least 24 hours is recommended. However, when this preparation is not carried out properly, vasodilator response may be compromised and, consequently, induction of flow disparity. In traditional scintigraphy, this cannot be identified and may result in a “false-negative” result, but this inadequate response is detected by MFR evaluation.

As more studies are published, leading to better standardization of MBF and MFR quantification by CZT-SPECT, it will become an important tool in the clinical practice of ischemic cardiomyopathies, adding to our understanding of this disease.

Table 1 – In which situations can myocardial flow reserve make a difference?

<table>
<thead>
<tr>
<th>Situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Patients with little ischemia who may have multivessel CAD.</td>
</tr>
<tr>
<td>2) Perfusion defects, but with artifact.</td>
</tr>
<tr>
<td>3) Normal perfusion but at high risk for CAD.</td>
</tr>
<tr>
<td>4) Identification of microvascular disease.</td>
</tr>
<tr>
<td>5) Determine vaso-stressor effectiveness.</td>
</tr>
</tbody>
</table>


References


Author Contributions

Writing of the manuscript: Lima RSL.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.
Editorial


