Transient dilation of the left ventricular cavity observed during myocardial perfusion imaging: What is its incremental diagnostic value

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Transient ischemic dilation (TID) of the left ventricle (LV), defined as the apparent significant enlargement in the LV size on post-stress images in comparison to the rest images on SPECT radionuclide myocardial perfusion imaging (MPI), has been recognized as an important marker of severe and extensive coronary artery disease (CAD) and indicative of high risk of cardiac events as well, even when MPI studies appear to be normal.[1-10] TID is predictive of proximal left anterior descending arteries or triple vessels with greater than 90% stenosis. This has been shown with various MPI protocols and radionuclides, with both treadmill stress test and vasodilators (dipyridamole and adenosine). The frequency of TID on radionuclide MPI has been reported to range from 3% to 37%[8,9,11,12] depending on several factors such as the type of patients population (with or without previously known CAD, previous myocardial infarction, advanced age, diabetes mellitus, LV hypertrophy, elevated LV end-diastolic pressure, etc.), the gender (difference between male and female patients), the method used to define TID (visual analysis versus the use of automatic quantitative assessment of TID), the quantitative upper limits to define TID, the stress modalities (exercise vs pharmacologic stress MPI), the radioisotopes used (^{201}thallium vs 99mTc-labeled MPI agents), and the imaging protocols (single radiotracers, dual radiotracers ^{201}Tl-99mTc-MPI, same-day rest-stress, same-day stress-rest imaging sequences, 2-day protocols, etc.).

The exact underlying pathophysiologic mechanisms of TID remain unclear. The involved mechanisms are likely to be varied, either related to pathologic or physiologic changes. The TID ratio measured from SPECT MPI may reflect true stress-induced stunning of the LV, extensive subendocardial ischemia, or a combination of the two mechanisms. There is still no definite conclusion about the underlying mechanisms of TID. The presence of severe stress-induced diffuse subendocardial hypoperfusion resulting in the non-visualization of extensive amount of the subendocardial myocardium (producing a visually larger LV cavity on SPECT images), following stress in comparison to the rest normal study, is probably the most common pathologic mechanism causing an apparent TID (or ''pseudo-dilation,'' as opposed to true dilation),[1,8,13] although some studies have shown data supporting the concept that TID represented true LV dilation.[14-16] In 1987, Weiss et al[16] postulated that the finding of TID was likely to represent extensive myocardial ischemia because it is reversible; the amount of ischemia has to be significant enough to cause sometimes true transient ventricular enlargement as detected on planar ^{201}thallium studies; and the ischemia is likely to be quite severe because it lasts for at least 30 minutes after the stress, a time at which ''usual'' stress-induced myocardial ischemia would be expected to have been resolved. They found that LV volumes calculated from the epicardial borders were also enlarged, indicating that if TID was due to diffuse subendocardial ischemia alone, it would have been expected that TID would be observed with the use of

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endocardial but not epicardial boundaries for the TID ratio calculation. Using gated ^{201}thallium dipyridamole stress and redistribution MPI, Hung et al[14] found a greater enlargement of post-stress end-systolic volume than of end-diastolic volume in the group of patients with TID compared to those without TID, suggesting that there should be explanations other than apparent LV dilation to explain the occurrence of TID, since subendocardial hypoperfusion in patients with TID should give the same degree of enlargement for both end-diastolic and end-systolic volumes. Other studies with 99mTc-tetrofosmin[17] showed that patients with ischemic myocardial stunning had a significant increase in end-systolic volume post-stress but not in end-diastolic volumes. These findings suggest that TID represents true ventricular dilation rather than just an apparent LV dilation, related to myocardial ischemic stunning manifested by stress-induced decrease of the LV ejection fraction and worsening of wall motion. This finding has been described on both exercise and pharmacologic MPI stress tests.[18,19] It is also very likely that if SPECT MPI is performed very early after the radiotracer injection at stress, the likelihood that post-stress myocardial stunning and TID will be observed is higher. No matter the exact mechanism of TID, both true dilation and extensive subendocardial ischemia play a significant role in TID, and both are caused by extensive stress-induced abnormality. Microvascular disease and/or impaired coronary flow reserve have also been postulated as potential mechanisms.[20]

Although TID is not always necessarily associated with obstructive CAD as it has been described in patients with diabetes mellitus, LV hypertrophy, and patients with a hypertensive blood pressure response to exercise,[20,21] it is widely accepted that the principal added value of TID in MPI is that it is a marker of severe and extensive CAD. This parameter is also an independent adverse prognostic predictor. Patients with an entirely normal exercise or vasodilator MPI study but with TID have been shown to have a significantly increase in follow-up cardiac events in comparison to patients with no TID and normal MPI study. Implementation of non-perfusion imaging parameters such as increased radiotracer lung uptake on post-stress images or TID also improves the diagnostic accuracy of MPI. In this regard, this issue of the Journal of Nuclear Cardiology includes an interesting study by Gultekin et al[22] on the value of TID for detecting restenosis after coronary artery revascularization using either a same-day or a 2-day 99mTc-sestamibi SPECT MPI protocol in 104 patients who had recent coronary revascularization and recurrent symptoms with a repeat coronary angiography. Both treadmill exercise and dipyridamole vasodilator stress were used. The sensitivity of SPECT MPI alone for detecting significant obstructive disease was 61% while this number significantly increased to 93% ($P < .0001$) by adding TID as a diagnostic criterion to MPI. The relatively low sensitivity of 61% of MPI defects for detecting significant CAD is probably related to the referral bias since all the patients in their cohort had known severe CAD with many patients having multivessel disease, and they all had previous revascularization of at least one vessel. Although it was a highly selective patient cohort, it is interesting to note that TID remains a robust marker for the presence and absence of severe CAD but also provided incremental value over myocardial perfusion markers alone. Therefore, the method used for the quantitative assessment and the definition of TID used in the study are of great importance if this criteria is applied on all patients having a MPI study. In their study, Gultekin et al[22] have found that the optimal cut-off value for detecting significant obstructive CAD for the stress-rest LV volume ratio was 1.20 with the imaging protocol used in their patient population, for both exercise stress and vasodilator SPECT MPI. This finding raises the question of the reliability of the TID ratio measurement and its definition.

Different studies have shown that reported TID ratio or index can vary according to the radiotracer used, the MPI data acquisition protocol, the use of attenuation correction or not, the gender, the type of stress modality, and the threshold used to define TID. It is therefore mandatory to establish the normal values according to the above-mentioned variables in order to make TID a reproducible and useful index for CAD diagnosis and prognosis. The upper normal limit of TID for dual radioisotope exercise rest ^{201}thallium/stress 99mTc-labeled MPI radiotracer has been defined at 1.22, while other upper normal limits for TID with rest ^{201}thallium and same-day pharmacologic stress were 1.27 for dipyridamole, 1.40 for dobutamine, and 1.35 for adenosine.[23] Xu et al[24] also reported the upper normal limit of TID using same-day rest-exercise stress 99mTc-sestamibi injection sequence. Their TID ratios were automatically derived using QPS/QGS software from static stress/rest MPI study (TID) and from gated stress/rest MPI study from the end-diastolic phase (TID_{ed}) and end-systolic phase (TID_{es}). In a relatively large database obtained from low likelihood CAD patients, the upper limits were 1.19 for TID, 1.23 for TID_{ed}, and 1.46 for TID_{es}. The use of TID ratios derived from the gated SPECT end-diastolic and end-systolic phases can be very useful in order to avoid averaging errors seen from the static MPI studies. Although previous studies have demonstrated that variations in gender or heart size may result in different TID thresholds (related to smaller absolute LV volumes in female patients), Xu et al[24] did

not find any statistically significant difference between TID ratios observed in patients with small hearts versus those with regular hearts.

As with any quantitative imaging parameter derived from radionuclide procedures, it is mandatory to obtain normal upper limit values of a given parameter derived from a large normal data base in order to define with more precision the standard deviation. Furthermore, all the technical and/or clinical variables which can potentially modify the normal values must be taken into consideration in establishing the clinical application of the given parameter. Numerous studies have now demonstrated the incremental diagnostic and prognostic values of the finding of TID during both treadmill exercise and vasodilator SPECT MPI. Measurement of TID should be an integral part of both SPECT MPI analysis and report on a routine basis with specification of the upper limit value used considering the above-mentioned criteria. The values used to define TID should be adapted to the specific imaging protocol and stress modality used in a given laboratory in order to obtain an optimal diagnostic accuracy.

Disclosure

The authors declare that they have no conflict of interest.

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