How viable is SPECT for viability assessment in the PET era?

Pavithra S. Jayadeva, MBBS,^a and Nathan Better, MBBS, FRACP, FASNC^{a,b,c}

^a Department of Cardiology, Royal Melbourne Hospital, Parkville, VIC, Australia

^b Department of Nuclear Medicine, Royal Melbourne Hospital, Parkville, VIC, Australia

^c Department of Medicine, University of Melbourne, Parkville, VIC, Australia

Received Feb 19, 2020; accepted Feb 19, 2020

doi:10.1007/s12350-020-02084-6

See related article, pp. 2545–2556

The article published by Zhang et al has entertained a novel assessment of myocardial viability with the integration of myocardial perfusion, wall motion and thickening with SPECT as a valid alternative to conventional PET imaging. In patients with ischemic heart failure, the ability to assess viable myocardium has been a cornerstone to assess cardiac status and potentially alter outcomes in patients with reduced left ventricular function. Patients with dysfunctional but viable myocardium have historically benefited from revascularization.¹ Hibernation is a phase best described as viable myocardium existing in a transitional state with recurrent ischemic triggers rendering the myocardium dysfunctional, but still in possession of the metabolic capacity to contribute to contractile reserve following revascularization.²

Hence, the ability to accurately predict viable myocardium and refer for revascularization remains a hinge point in the management of ischemic heart disease. One current definition of viability remains the presence of > 50% uptake of a perfusion tracer by the myocardium.³ The ability to accurately predict viable myocardium in abnormally contracting segments with < 50% uptake remains limited.

Zhang et al. explored the utility of adding information gained by review of myocardial wall motion and thickening to the results of myocardial perfusion

utilizing gated SPECT. Eighty-three patients with severe ischemic heart failure undergoing ⁹⁹Tc-MIBI gated SPECT myocardial perfusion imaging (MPI) and ¹⁸F-FDG positron emission tomography (PET) were enrolled. They questioned whether the addition of a thickening score provided a means to distinguish between hibernating and scarred myocardium in myocardial segments exhibiting decreased perfusion. The study group was divided into three groups: (1) normal perfusion, (2) SPECT/PET mismatch (segments with decreased perfusion but relatively preserved or increased glucose metabolism, suggestive of hibernating myocardium), and (3) SPECT/PET match: segments with decreased perfusion and decreased metabolism (suggestive of scar). Myocardial thickening was measured using a semi-quantitative approach with gated SPECT MPI. Both wall motion and wall thickening were graded from normal to akinesis or no thickening, with analysis performed by two independent, experienced operators. When compared to FDG PET, the addition of wall motion and wall thickening had the ability to help discriminate hibernating myocardium from scar in segments with reduced perfusion. The combination of these factors improved diagnostic accuracy from 64.2% to 73.2% ($P < 0.001$) in identifying hibernating myocardium.

Whilst the authors should be commended on their novel approach to improving viability assessment, the study is not without limitations. Firstly, the sample size is small and secondly, the study is retrospective in nature. However, compared to previous trials on viability assessment, this patient number is within similar size cohorts. A significant proportion of patients (72/83) were male, 80% of patients were also significantly symptomatic with NYHA class III or IV symptoms. Furthermore, given the semi-quantitative approach to myocardial thickening assessment, there becomes a need to standardize reporting and allow all laboratories to

Reprint requests: Nathan Better, MBBS, FRACP, FASNC, Department of Cardiology, Royal Melbourne Hospital, Grattan St, Parkville, VIC, Australia; nathan.better@mh.org.au

J Nucl Cardiol 2021;28:2557–9.

1071-3581/\$34.00

Copyright © 2020 American Society of Nuclear Cardiology.

Table 1. Summary of specificity and sensitivity of viability studies⁸⁻¹³

Method of assessment	PET-FDG (%)	Contrast enhanced-MRI (%)	99mTc-labeled tracers (%)	Dobutamine stress echo (%)	Thallium-201 (%)
Sensitivity	93	85-88	81	75-80	80-85
Specificity	58	71-80	66	80-85	60
Negative predictive value	85	90	77	81	75-80
Positive predictive value	77	55-60	71	64	60-65

gain experience before incorporating this component into their usual practice. This would help to allow the method to be adopted on a wider scale. The key unanswered point still remains the assessment of prognosis and outcomes with this added viability tool. This is food for thought and larger multi-center and potentially prospective studies are needed to confirm the author's findings and find the right niche for this technique.

The major impact of this trial is the current “real world” feasibility of this viability assessment tool and its easy accessibility. The availability of PET worldwide, especially for the assessment of myocardial viability, remains severely limited, partly related to cost and training, but particularly as most PET centers are increasingly being used to answer the demands of our oncology colleagues. This issue is relevant to both the developed and the developing world; the ability to answer the question of viability without a PET center would seem particularly attractive to a busy PET facility and administrators alike.

Currently, a gold standard for myocardial viability assessment is still yet to exist; however, different modalities offer functional and anatomical assessment of varying specificity and sensitivity. Current methods include dobutamine stress echocardiography (DSE), cardiac magnetic resonance (CMR) imaging, position emission tomography (PET) and SPECT with 99 m technetium and thallium-201 based imaging. At a cellular and metabolic level it is still the mandate of a test to try and accurately predict and identify viability by distinguishing myocardial stunning or hibernating from scarred myocardium.⁴

Maruyama et al. observed the value of SPECT Tc-99 m-tetrofosmin wall thickening in addition to exercise/rest myocardial SPECT compared to FDG PET. This study enrolled 33 patients with 689 PET viable segments identified; 37/689 segments with irreversible defects had apparent wall thickening, improving sensitivity from 79% to 85% but reducing specificity from 70% to 56%.⁵ Overall, similar to Zhang et al., it was felt

that wall thickening evaluation enhanced myocardial viability assessment.

Klein et al. studied 31 patients in ischemic heart failure imaged with both PET and MRI. MRI hyperenhancement not only correlated well with PET, but also had a greater propensity to identify scar than PET. Wall thickening in end diastole and end systole were also derived from MRI techniques. Although regional wall thickness or thickening was significantly reduced with increasing myocardial damage, the wall thickness parameters had only limited diagnostic value to differentiate between viable and scar tissue. This may be related to alteration in left ventricular geometry which could potentially mask the detection of viable myocardium.¹

The key clinical question of the impact of viability on clinical outcomes was explored in the PARR-2 trial. Patients with severe left ventricular dysfunction and suspected coronary artery disease were randomized to F-18-FDG PET assisted management or standard care with the results not demonstrating a significant reduction in cardiac events when patients were managed with a PET-assisted clinical decision pathway.⁶ At the 5 year follow-up, PET-assisted management did not significantly change clinical outcomes compared to standard care in patients with ischemic cardiomyopathy being considered for revascularization or transplantation.⁷ The long-term follow-up data for PARR-2 (at 5 years) only demonstrated improved outcomes in a post hoc analysis related to improvements in cardiovascular outcomes when PET recommendations are adhered to. The “real-world” utility of PET-FDG in improving outcomes in this cohort remains unanswered. If any conclusions are to be drawn from PARR-2, it is that the greatest utility of FDG PET imaging may lie in patients in whom the clinical decision to revascularize is complex. The ability of SPECT to reproduce this benefit remains to be determined.

The sensitivity and specificity of the various forms of myocardial viability assessment are summarized in Table 1.

In summary, the authors should be congratulated for their work. This multi-level approach with SPECT of adding assessment of wall thickening to myocardial perfusion and wall motion potentially increases the accuracy of viability assessment to make it even more comparable to PET imaging. Future trials will hopefully answer whether this translates to improved patient outcomes, while freeing up the more expensive technology of PET for other uses. While we continue to “watch this space”, all nuclear cardiology facilities have the ability to assess wall thickening in some way, with no added cost. While it still does not provide the complete answer, a review of wall thickening can already become a part of a standard study. Currently, using SPECT remains a very viable option.

References

1. Klein C, Nekolla SG, Bengel FM, et al. Assessment of myocardial viability with contrast-enhanced magnetic resonance imaging: comparison with positron emission tomography. *Circulation* 2002;105:162-7.
2. Braunwald E, Kloner R. The stunned myocardium: prolonged, postischemic ventricular dysfunction. *Circulation* 1982;66:1146-9.
3. Pagley P, Beller G, Watson D, Gimple L, Ragosta M. Improved outcome after coronary bypass surgery in patients with ischemic cardiomyopathy and residual myocardial viability. *Circulation* 1997;96.
4. Gewirtz H, Dilsizian V. Myocardial viability: survival mechanisms and molecular imaging targets in acute and chronic ischemia. *Circ Res* 2017;120:1197-212.
5. Maruyama A, Hasegawa S, Paul AK, et al. Myocardial viability assessment with gated SPECT Tc-99m tetrofosmin % wall thickening: comparison with F-18 FDG-PET. *Ann Nucl Med* 2002;16:25-32.
6. Beanlands RS, Nichol G, Huszti E, et al. F-18-fluorodeoxyglucose positron emission tomography imaging-assisted management of patients with severe left ventricular dysfunction and suspected coronary disease: a randomized, controlled trial (PARR-2). *J Am Coll Cardiol* 2007;50:2002-12.
7. Mc Ardle B, Shukla T, Nichol G, et al. Long-term follow-up of outcomes with F-18-fluorodeoxyglucose positron emission tomography imaging-assisted management of patients with severe left ventricular dysfunction secondary to coronary disease. *Circ Cardiovasc Imaging* 2016;9.
8. Afridi I, Quinones MA, Zoghbi WA, Cheirif J. Dobutamine stress echocardiography: sensitivity, specificity, and predictive value for future cardiac events. *Am Heart J* 1994;127:1510-5.
9. Bax JJ, Poldermans D, Elhendy A, Boersma E, Rahimtoola SH. Sensitivity, specificity, and predictive accuracies of various non-invasive techniques for detecting hibernating myocardium. *Curr Probl Cardiol* 2001;26:147-86.
10. Bax JJ, Delgado V. Myocardial viability as integral part of the diagnostic and therapeutic approach to ischemic heart failure. *J Nucl Cardiol* 2015;22:229-45.
11. Morton G, Schuster A, Perera D, Nagel E. Cardiac magnetic resonance imaging to guide complex revascularization in stable coronary artery disease. *Eur Heart J* 2010;31:2209-15.
12. Sciagra R, Santoro GM, Bisi G, Pedenovi P, Fazzini PF, Pupi A. Rest-redistribution thallium-201 SPECT to detect myocardial viability. *J Nucl Med* 1998;39:384-90.
13. Hunold P, Jakob H, Erbel R, Barkhausen J, Heilmair C. Accuracy of myocardial viability imaging by cardiac MRI and PET depending on left ventricular function. *World J Cardiol* 2018;10:110-8.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.