



Added value to stress myocardial perfusion imaging studies with measurement of left ventricular mass

Anahita N. Tavoosi, MD,^a Yoshito Kadoya, MD,^a and Terrence D. Ruddy, MD, MASNC^{a,b}

^a Division of Cardiology, University of Ottawa Heart Institute, Ottawa, Canada

^b University of Ottawa Heart Institute, Ottawa, ON, Canada

Received Aug 6, 2021; accepted Aug 8, 2021

doi:10.1007/s12350-021-02802-8

See related article, pp. 2361–2373

IMPORTANCE OF INCREASED LEFT VENTRICULAR MASS (LVM)

Over 30 years ago, increased LVM on echocardiography was identified in the Framingham Heart Study as an important independent predictor for cardiovascular morbidity and mortality in patients without coronary artery disease (CAD).^{1,2} Subsequent studies have shown that increased LVM predicts mortality and sudden death in patients with stable CAD,³ future myocardial infarction and cardiac death in patients with and without inducible ischemia,⁴ cardiovascular events in patients with mild to moderate aortic valve stenosis⁵ and mortality and need for future revascularization in patients undergoing diagnostic coronary angiography.⁶

MEASURING LVM USING SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) MYOCARDIAL PERFUSION IMAGING (MPI)

Measurement of LVM using single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) has been validated using thallium-201 in a canine model with post-mortem weights with excellent correlation ($r = .91$) and reproducibility (coefficient of variation 24%).⁷ SPECT measurements using

conventional NaI gamma cameras and thallium-201, Tc-99m sestamibi or Tc-99m tetrofosmin correlate significantly and moderately with estimates from cardiac magnetic resonance imaging (CMR),⁸ echocardiography^{9,10} and cardiac computed tomography (CT).^{11,12} Interobserver and intraobserver variability was very good for SPECT measurements using commercially available software.^{10,12} LVM was underestimated with SPECT in patients with severe perfusion defects compared to echocardiography,¹⁰ probably related to SPECT imaging perfused tissue specifically and echocardiography identifying perfused and nonperfused tissue. Although mean values were similar with SPECT and CT, SPECT systematically overestimated low values and underestimated high values resulting in large limits of agreement.¹² SPECT values are not interchangeable for echocardiographic or CT measurements but can be used for LVM estimates in single patients and for serial evaluation (Figure 1).

Solid-state detector systems using cadmium-zinc-telluride (CZT) crystals have been recently introduced and have better resolution than conventional Anger cameras.¹³ A recent study compared LVM measurements with CZT SPECT using Tc-99m tetrofosmin and commercially available software versus CMR. Correlation was excellent between LVM estimates using SPECT and CMR with small limits of agreement.¹⁴ Diagnostic accuracy for detection of increased LVM by SPECT was high (84% to 88%) and minimally affected by perfusion abnormalities.

MEASURING LVM USING PET MPI

Although rubidium-82 chloride and nitrogen-13 ammonia are commonly used radiotracers for PET MPI, only a few centers a small number use oxygen-15 water due to its very short half-life and need for on-site cyclotron. Oxygen-15 water PET MPI is considered the

Funding None.

Reprint requests: Terrence D. Ruddy, MD, MASNC, University of Ottawa Heart Institute, 40 Ruskin Street, Room H-S407, Ottawa, ON K1Y 4W7, Canada; truddy@ottawaheart.ca

J Nucl Cardiol 2022;29:2374–7.

1071-3581/\$34.00

Copyright © 2021 American Society of Nuclear Cardiology.

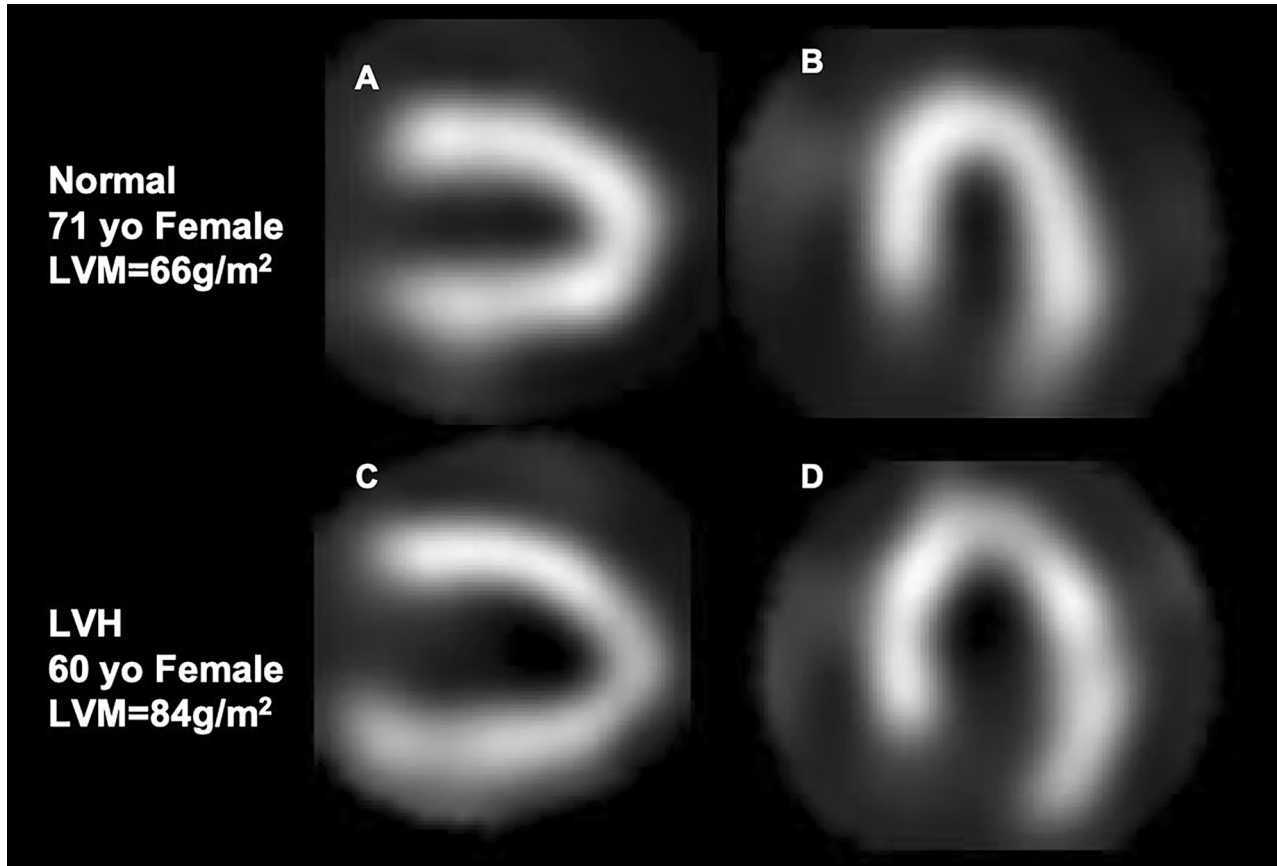


Figure 1. Left ventricular mass estimates. SPECT images were acquired (Discovery NM530c, GE Healthcare) 30 minutes after rest injection with Tc-99m tetrofosmin (~ 150 MBq, 4 mCi). Display zoom 1.3 for all images. **A** and **B** Normal patient. LVEF 74%, LVEDV 65 mL, LVESV 17 mL. **C** and **D** Patient with LVH. LVEF 50%, LVEDV 119 mL, LVESV 59 mL.

gold standard for measurement of global and regional myocardial blood flow (MBF) and has excellent diagnostic accuracy for detecting obstructive CAD.¹⁵ Oxygen-15 water is freely diffusible and equilibrates rapidly with the large endogenous water pool. Static myocardial images acquired more than 1 minute after injection have minimal contrast with no specific myocardial uptake. Kinetic analysis of nongated dynamic oxygen-15 water data can be used to generate parametric images of MBF¹⁶ and perfusable tissue fraction (PTF), used for partial volume correction.¹⁷ This approach of generating parametric images was applied to nongated dynamic carbon-11 acetate imaging and permitted measurements of LVM and volumes that correlated well with CMR.¹⁸

In this issue of the *Journal of Nuclear Cardiology*®, Jens Sørensen and team describe the feasibility of measuring LVM and wall thickness from parametric PTF images derived from nongated dynamic oxygen-15 water PET MPI studies, which is an extension of their

previous work using nongated dynamic carbon-11 acetate imaging.¹⁸ The study was a retrospective analysis of 139 patients (197 oxygen-15 water PET MPI studies) with varying degrees of hypertrophy and remodeling from 4 previous research studies. The method was developed using 66 scans and then evaluated using the remaining scans with a blinded comparison to CMR (n = 47) and echocardiography (n = 36). High correlations with minimal bias were found for PET measurements of LVM and wall thickness compared to CMR and echocardiography. Using ROC analysis, diagnostic accuracy of PET for LVH and increased wall thickness was high in both the CMR and echocardiography groups. Reproducibility of the PET measurements was very good for interobserver variability and rest-stress repeatability. As noted by the authors, this single-center study needs external validation in a larger and more diverse group of patients and with more scanner types.

Measurement of LVM with rubidium-82 chloride PET MPI was compared with CMR in a retrospective

analysis of 105 patients having both studies in a 1-year period.¹⁹ PET images were processed with commercially available software. Correlations for LVM were good with moderate limits of agreement. As with SPECT, PET underestimated LVM at high values compared to CMR. Interobserver variability and stress-rest repeatability were excellent.

Reproducibility of measurements of LV mass between two rubidium-82 chloride PET MPI scans using two commercially available software packages has been assessed in 40 healthy young volunteers.²⁰ Reproducibility between scans was high but concordance was poor between the two software packages. Thus, each software package should have its own normal reference range and the same software package should be used for serial studies.

ADDED VALUE FOR REPORTING LVM IN MPI REPORTS

Stress MPI detects ischemia due to obstructive CAD and has been used for many years to guide therapy and predict short-term prognosis. However, there are many concerns expressed for the continued viability of stress MPI imaging and particularly SPECT. The frequency and severity of abnormal and ischemic SPECT MPI studies has decreased over the last 2 to 3 decades²¹ and this suggests a need for alternative risk stratification approaches, such as coronary artery calcium scanning with or without treadmill ECG testing. Recent randomized trials in patients with ischemia and stable CAD have found little benefit of revascularization added to optimal medical therapy for reducing cardiovascular events^{22,23} suggesting less need for identification of ischemia to direct revascularization therapy. However, stress MPI is very useful for evaluating the probability of ischemia due to obstructive CAD as a cause of symptoms and often redirecting subsequent diagnostic testing. Depending on the technology, stress MPI can provide data about left ventricular function (volumes, ejection fraction, mass, transient ischemic dilation, dyssynchrony), coronary artery calcium and MBF for determining short and long term for determining prognosis in patients with and without obstructive CAD. We can increase the clinical value of our MPI reports by adding prognostic information.

Increased LVM predicts cardiovascular events and can be calculated using commercially available software at the same time as LV volumes and ejection fraction without additional image acquisition or processing time. The American Society of Nuclear Cardiology imaging guidelines for nuclear cardiology procedures encourage structured and standardized MPI reports and require LV myocardial wall thickness to be reported as text with the

response of normal or increased.²⁴ In the sample template for pharmacologic-based stress MPI (Appendix 5), LV mass (g) is included. Since the accuracy of SPECT and PET estimates of LVM has been validated and very good observer variability demonstrated, the addition of routine reporting of LVM estimates in clinical MPI reports would be reasonable and may be useful in clinical care.

Disclosures

A. Tavoosi, Y. Kadoya and T.D. Ruddy declare that they have no conflict of interest.

References

1. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implication of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med* 1990;322:1561-6.
2. Haider AW, Larson MG, Benjamin EJ, Levy D. Increased left ventricular mass and hypertrophy are associated with increased risk for sudden death. *JACC* 1998;32:1454-9.
3. Turakhia MP, Schiller NB, Whooley MA. Prognostic significance of increased left ventricular mass index to mortality and sudden death in patients with stable coronary heart disease (from the Heart and Soul Study). *Am J Cardiol* 2008;102:1131-5.
4. Charoenpanichkit C, Morgan TM, Hamilton CA, Wallace EL, Robinson K, Ntim WO. Left ventricular hypertrophy influences cardiac prognosis in patients undergoing dobutamine cardiac stress testing. *Circ Cardiovasc Imaging* 2010;3:392-7.
5. Gerds E, Rossebø AB, Pedersen TR, Cioffi G, Lønnebakken MT, Cramariuc D, et al. Relation of left ventricular mass to prognosis in initially asymptomatic mild to moderate aortic stenosis. *Circ Cardiovasc Imaging* 2015;8:e003644.
6. Abdi-Ali A, Miller RJH, Southern D, Zhang M, Mikami Y, Knudtson M, et al. LV mass independently predicts mortality and need for future revascularization in patients undergoing diagnostic coronary angiography. *JACC Cardiovasc Imaging* 2018;11:423-33.
7. Wolfe CL, Corbett JR, Lewis SE, Buja LM, Willerson JT. Determination of left ventricular mass by single-photon emission computed tomography with thallium-201. *Am J Cardiol* 1984;53:1365-8.
8. Faber TL, Cooke CD, Folks RD, Vansant JP, Nichols KJ, DePuey EG, et al. Left ventricular function and perfusion from gated SPECT perfusion images: An integrated method. *J Nucl Med* 1999;40:650-9.
9. Akinboboye O, Germano G, Idris O, Nichols K, Gopal A, Berman D. Left ventricular mass measured by myocardial perfusion gated SPECT. Relation to three-dimensional echocardiography. *Clin Nucl Med* 2003;5:392-7.
10. Maruyama K, Hasegawa S, Nakatani D, Paul A, Kusuoka H, Nishimura T, et al. Left ventricular mass index measured by quantitative gated myocardial SPECT with ^{99m}Tc-tetrofosmin: A comparison with echocardiography. *Ann Nucl Med* 2003;17:31-9.
11. Schepis T, Gaemperli O, Koepfli P, Valenta I, Strobel K, Brunner A, et al. Comparison of 64-slice CT with gated SPECT for evaluation of left ventricular function. *J Nucl Med* 2006;47:1288-94.
12. Okwuosa TM, Hampole CV, Ali J, Williams KA. Left ventricular mass from gated SPECT myocardial perfusion imaging:

- Comparison with cardiac computed tomography. *J Nucl Cardiol* 2009;16:775-83.
13. Slomka PJ, Miller RJH, Hu L-H, Germano G, Berman DS. Solid-state detector SPECT myocardial perfusion imaging. *J Nucl Med* 2019;60:1194-204.
 14. Gimelli A, Liga R, Magro S, Novo S, Pedrinelli R, Petronio AS, et al. Evaluation of left ventricular mass on cadmium–zinc–telluride imaging: Validation against cardiac magnetic resonance. *J Nucl Cardiol* 2019;26:899-905.
 15. Danad I, Raijmakers PG, Driessen RS, Leipsic J, Raju R, Naoum C, et al. Comparison of coronary CT angiography, SPECT, PET, and hybrid imaging for diagnosis of ischemic heart disease determined by fractional flow reserve. *JAMA Cardiol* 2017;2:1100-7.
 16. Harms HJ, Knaapen P, de Haan S, Halbmeijer R, Lammertsma AA, Lubberink M. Automatic generation of absolute myocardial blood flow images using [¹⁵O]H₂O and a clinical PET/CT scanner. *Eur J Nucl Med Mol Imaging* 2011;38:930-9.
 17. Harms HJ, de Haan S, Knaapen P, Allaaart CP, Lammertsma AA, Lubberink M. Parametric images of myocardial viability using a single ¹⁵O–H₂O PET/CT scan. *J Nucl Med* 2011;52:745-9.
 18. Harms HJ, Hansson NHS, Tolbod LP, Kim WY, Jakobsen S, Bouchelouche K, et al. Automatic extraction of myocardial mass and volume using parametric images from dynamic nongated PET. *J Nucl Med* 2016;57:1382-7.
 19. Malahfji M, Ahmed AI, Han Y, Jung AK, Alnabelsi T, Nabi F, et al. Left ventricular mass on positron emission tomography: Validation against cardiovascular magnetic resonance. *J Nucl Cardiol* 2021. <https://doi.org/10.1007/s12350-021-02537-6>.
 20. Byrne C, Kjaer A, Forman JL, Hasbak P. Reproducibility of LVEF, LV volumes, and LV mass between Rubidium-82 PET/CT scans in young healthy volunteers using two commercially available software packages. *J Nucl Cardiol* 2020;27:1237-45.
 21. Rozanski A, Gransar H, Hayes SW, Min J, Friedman JD, Thomson LEJ, et al. Temporal trends in the frequency of inducible myocardial ischemia during cardiac stress testing 1991 to 2009. *J Am Coll Cardiol* 2013;61:1054-65.
 22. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007;356:1503-16.
 23. Maron DJ, Hochman JS, Reynolds HR, Bangalore S, O'Brien SM, Boden WE, et al. Initial invasive or conservative strategy for stable coronary disease. *N Engl J Med* 2020;382:1395-407.
 24. Tilkemeier PL, Bourque J, Doukky R, Sanghani R, Weinberg RL. ASNC imaging guidelines for nuclear cardiology procedures. Standardized reporting of nuclear cardiology procedures. *J Nucl Cardiol* 2017;24:2064-128.

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