



# Myocardial perfusion imaging and CAC score: Not only a brick in the wall

Emilia Zampella, MD, PhD,<sup>a</sup> Roberta Assante, MD, PhD,<sup>a</sup> and Wanda Acampa, MD, PhD<sup>a</sup>

<sup>a</sup> Department of Advanced Biomedical Sciences, University Federico II, Naples, Italy

Received Sep 18, 2021; accepted Sep 18, 2021  
doi:10.1007/s12350-021-02816-2

---

## See related article, pp. 2448–2456

---

In patients with suspected or known coronary artery disease (CAD) noninvasive assessment of myocardial perfusion is mandatory to rule-out the presence of coronary stenoses and to guide patient's management.<sup>1</sup> Radionuclide myocardial perfusion imaging (MPI) techniques, including single-photon emission computed tomography (SPECT) and positron emission tomography/computed tomography (PET/CT), accounts for the vast majority of tests currently performed for detection of perfusion abnormalities.<sup>2</sup> Despite the presence of myocardial perfusion defect at visual or semiquantitative MPI analysis is strongly related coronary stenoses and it is considered as important determinant of outcome, discrepancy between the anatomic extent of CAD and perfusion abnormalities can be observed.<sup>3</sup> The natural history of CAD is based on atherosclerotic and perfusion changes and the presence of diffuse coronary atherosclerosis could be useful in guiding of management, especially in patients with mildly abnormal MPI studies.<sup>4,5</sup> Coronary artery calcium (CAC) score is well validated index of atherosclerosis and it is considered a powerful tool in risk-stratifying asymptomatic patients at intermediate risk of CAD.<sup>6</sup> Coronary perfusion data may be integrated with anatomic information from CAC measurements to increase diagnostic and prognostic power of radionuclide cardiac imaging.

In the current issue of *Journal of Nuclear Cardiology*<sup>®</sup>, Mouden et al<sup>7</sup> investigated the clinical impact of

CAC score in reporting cardiac SPECT and PET MPI. In particular, the authors investigated how the addition of CAC score could change classification of normal and abnormal MPI scans. Moreover, they evaluated how this combined approach improved the prediction of CAD and outcome, during a short-term follow-up. The analyzed data from 206 patients who underwent cardiac PET/CT imaging and 4,018 subjects who performed SPECT/CT MPI. All SPECT studies were acquired by using a cadmium-zinc-telluride (CZT) camera and attenuation correction was applied. In order to account for differences in clinical risk factors and CAC score values, the authors performed a propensity score analysis between PET and SPECT patients, obtaining a final population of 412 subjects. The effect of adding CAC score to MPI findings have been previously investigated.<sup>4,8–11</sup> If a CAC score of zero is a powerful negative risk marker,<sup>8,9</sup> Ghadri et al<sup>10</sup> demonstrated that high CAC values (> 1,000) are able to identify the presence of CAD also in patients with normal MPI. Shepis et al<sup>4</sup> found that the addition of CAC score improved sensitivity of MPI in detecting CAD in 77 intermediate risk patients with available coronary angiography. The authors identified a CAC score of 709 as optimal cut-off for detecting CAD “missed” by SPECT. Similarly, Sharma et al<sup>11</sup> demonstrated that magnitude of CAC score was related with the frequency of abnormal MPI. Mouden et al<sup>7</sup> evaluated images quality of both PET and SPECT studies by two expert readers. Subsequently, all images were interpreted as normal, abnormal or equivocal according to MPI findings. Despite the introduction of CZT cameras dramatically improved diagnostic accuracy of SPECT MPI,<sup>12,13</sup> images quality resulted to be higher for PET than for SPECT. This point needs to be highlighted, considering that the major contribution of CAC score is expected to be found in patients with non-diagnostic MPI results. According to this hypothesis, the authors found that the percentage of normal SPECT scans was

Reprint requests: Emilia Zampella, MD, PhD, Department of Advanced Biomedical Sciences, University Federico II, Naples, Italy; [emilia.zampella@gmail.com](mailto:emilia.zampella@gmail.com)

J Nucl Cardiol 2022;29:2457–9.

1071-3581/\$34.00

Copyright © 2021 American Society of Nuclear Cardiology.

influenced by the addition of CAC score (82% vs 88%, respectively). The same results were not observed when PET images were considered. In order to evaluate the diagnostic and prognostic impact of CAC score on MPI reporting, the angiographic and follow-up data were collected. The authors considered as end-point the presence of obstructive CAD in a small group of patients with available coronary angiography, and the occurrence of cardiac events during a short term follow-up in the overall population.

The prognostic implications of the addition of CAC score to MPI have been previously investigated in several populations.<sup>5,14–19</sup> It should be noted that in most of these previous reports CAC score measurements have been obtained by using the CT component during cardiac PET acquisition. Thus, hybrid imaging modalities allow the possibility to evaluate myocardial perfusion and CAC quantification as a part of the same examination, with a significant reduction in radiation exposure and procedural costs.<sup>5,14–19</sup> Moreover, the larger amount of data has been obtained by PET/CT imaging, that is considered the gold standard for absolute quantification of myocardial blood flow (MBF) and myocardial flow reserve (MFR).

Mouden et al<sup>7</sup> obtained results partially discordant from these previous reports. The authors found that the addition of CAC score increased the percentage of normal SPECT scan. Differently, the probability obstructive CAD, as well as the occurrence of late events, resulted to be comparable among normal PET and SPECT MPI. Moreover, the increased percentage of scans interpreted as normal when adding CAC score to the SPECT images did not influence the rate of obstructive CAD or cardiac events. This means that the addition of CAC score seems to have not a significant impact on prognosis when normal scans were considered. Differently, in patients with abnormal scans, the rate of events was higher for PET as compared to SPECT, suggesting that cardiac PET has a higher prognostic value. However, no differences in outcome were observed when the addition of CAC score was considered. These data are partially discordant with previous reports in which the incremental value of CAC score over perfusion findings has been tested.<sup>17–19</sup> In particular, Brodov et al<sup>17</sup> found that both regional perfusion and CAC score improved the diagnostic accuracy of cardiac PET imaging in detecting obstructive CAD. In two more recent reports,<sup>18,19</sup> regional CAC score and semiquantitative perfusion variables have been combined with MFR data in order to investigate the diagnostic and prognostic impact of this combined approach. The authors found that, despite a preserved MFR was useful in excluding the presence of CAD, the addition of CAC score had an incremental diagnostic

value in particular in vessels with impaired MFR and without severe ischemia. Moreover, coronary lesions with higher CAC score values and impaired coronary vascular function showed the worst prognosis.

The results obtained by Mouden et al<sup>7</sup> can be explained considering that they provide results from real clinical data in a heterogeneous population. Nowadays, it should be considered that real clinical practice, with the availability of advanced technologies as PET/CT and SPECT cameras with CZT, would mean possibility to provide semiquantitative or quantitative data. These technologies demonstrated to provide a very small number of low-quality images and the reproducibility of quantitative data are guarantee of high accuracy for diagnostic and prognostic purposes.<sup>12</sup> In previous reports<sup>17–19</sup> the authors performed a per-vessel analysis in which semiquantitative and quantitative regional data have been considered. From these data it emerged that addition of MFR<sup>18,19</sup> seems to be more strongly related to the total atherosclerotic burden than semiquantitative perfusion alone. This association may have contributed to provide a more powerful measure of CAD risk than each variable considered alone.

Mouden et al<sup>7</sup> helped to outline the real clinical impact of CAC scoring on MPI evaluation, leading to consider that CAC score is not a sterile measure of atherosclerosis, but it may represent a unique opportunity to combine anatomical and functional imaging in one examination. Moreover, we must focus that beyond semiquantitative perfusion data, several functional and quantitative variables can be obtained by MPI.<sup>20,21</sup> A full integration in reporting, risk prediction, and decision-making will provide novel insights into lesion behavior, with the potential to improve management of patients with CAD.

## Disclosure

*Authors declare that they have no conflict of interest.*

## References

1. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J* 2020;41:407-77.
2. Petretta M, Acampa W, Daniele S, Zampella E, Assante R, Nappi C. Long-term survival benefit of coronary revascularization in patients undergoing stress myocardial perfusion imaging. *Circ J* 2016;80:485-93.
3. Doukky R, Hayes K, Frogge N, Balakrishnan G, Dontaraju VS, Rangel MO, et al. Impact of appropriate use on the prognostic value of single-photon emission computed tomography myocardial perfusion imaging. *Circulation* 2013;128:1634-43.

4. Schepis T, Gaemperli O, Koepfli P, Namdar M, Valenta I, Scheffel H, et al. Added value of coronary artery calcium score as an adjunct to gated SPECT for the evaluation of coronary artery disease in an intermediate-risk population. *J Nucl Med* 2007;48:1424-30.
5. Assante R, Acampa W, Zampella E, Arumugam P, Nappi C, Gaudieri V, et al. Prognostic value of atherosclerotic burden and coronary vascular function in patients with suspected coronary artery disease. *Eur J Nucl Med Mol Imaging* 2017;44:2290-8.
6. Polonsky TS, McClelland RL, Jorgensen NW, Bild DE, Burke GL, Guerci AD, et al. Coronary artery calcium score and risk classification for coronary heart disease prediction. *JAMA* 2010;303:1610-6.
7. Mouden M, Jager PL, van Dalen JA, van Dijk JD. Added value of coronary artery calcium score in the reporting of SPECT versus PET myocardial perfusion imaging. *J Nucl Cardiol* 2021. <https://doi.org/10.1007/s12350-021-02789-2>.
8. Mittal TK, Pottle A, Nicol E, Barbir M, Ariff B, Mirsadraee S, et al. Prevalence of obstructive coronary artery disease and prognosis in patients with stable symptoms and a zero-coronary calcium score. *Eur Heart J Cardiovasc Imaging* 2017;18:922-9.
9. Nappi C, Nicolai E, Daniele S, Acampa W, Gaudieri V, Assante R, et al. Long-term prognostic value of coronary artery calcium scanning, coronary computed tomographic angiography and stress myocardial perfusion imaging in patients with suspected coronary artery disease. *J Nucl Cardiol* 2018;25:833-41.
10. Ghadri JR, Pazhenkottil AP, Nkoulou RN, Goetti R, Buechel RR, Husmann L, et al. Very high coronary calcium score unmasks obstructive coronary artery disease in patients with normal SPECT MPI. *Heart* 2011;97:998-1003.
11. Sharma V, Mughal L, Dimitropoulos G, Sheikh A, Griffin M, Moss A, et al. The additive prognostic value of coronary calcium score (CCS) to single photon emission computed tomography myocardial perfusion imaging (SPECT-MPI)-real world data from a single center. *J Nucl Cardiol* 2019. <https://doi.org/10.1007/s12350-019-01965-9>.
12. Cantoni V, Green R, Acampa W, Zampella E, Assante R, Nappi C, et al. Diagnostic performance of myocardial perfusion imaging with conventional and CZT single-photon emission computed tomography in detecting coronary artery disease: A meta-analysis. *J Nucl Cardiol* 2019;14:1-8.
13. Mannarino T, Assante R, Ricciardi C, Zampella E, Nappi C, Gaudieri V, et al. Head-to-head comparison of diagnostic accuracy of stress-only myocardial perfusion imaging with conventional and cadmium-zinc telluride single-photon emission computed tomography in women with suspected coronary artery disease. *J Nucl Cardiol* 2021;28:888-97.
14. Gaudieri V, Acampa W, Rozza F, Nappi C, Zampella E, Assante R, et al. Coronary vascular function in patients with resistant hypertension and normal myocardial perfusion: A propensity score analysis. *Eur Heart J Cardiovasc Imaging* 2019;20:949-58.
15. Assante R, Acampa W, Zampella E, Arumugam P, Nappi C, Gaudieri V, et al. Coronary atherosclerotic burden vs. coronary vascular function in diabetic and nondiabetic patients with normal myocardial perfusion: A propensity score analysis. *Eur J Nucl Med Mol Imaging* 2017;44:1129-35.
16. Dekker M, Waissi F, Bank IEM, Lessmann N, Išgum I, Velthuis BK, et al. Automated calcium scores collected during myocardial perfusion imaging improve identification of obstructive coronary artery disease. *Int J Cardiol Heart Vasc* 2019;26:100434.
17. Brodov Y, Gransar H, Dey D, Shalev A, Germano G, Friedman JD, et al. Combined quantitative assessment of myocardial perfusion and coronary artery calcium score by hybrid 82Rb PET/CT improves detection of coronary artery disease. *J Nucl Med* 2015;56:1345-50.
18. Zampella E, Acampa W, Assante R, Nappi C, Gaudieri V, Mainolfi CG, et al. Combined evaluation of regional coronary artery calcium and myocardial perfusion by 82Rb PET/CT in the identification of obstructive coronary artery disease. *Eur J Nucl Med Mol Imaging* 2018;45:521-9.
19. Zampella E, Acampa W, Assante R, Gaudieri V, Nappi C, Mannarino T, et al. Combined evaluation of regional coronary artery calcium and myocardial perfusion by 82Rb PET/CT in predicting lesion-related outcome. *Eur J Nucl Med Mol Imaging* 2020;47:1698-704.
20. Otaki Y, Betancur J, Sharir T, Hu LH, Gransar H, Liang JX, et al. 5-Year prognostic value of quantitative versus visual MPI in subtle perfusion defects: Results from REFINE SPECT. *JACC Cardiovasc Imaging* 2020;13:774-85.
21. Nappi C, Gaudieri V, Acampa W, Assante R, Zampella E, Mainolfi CG, et al. Comparison of left ventricular shape by gated SPECT imaging in diabetic and nondiabetic patients with normal myocardial perfusion: A propensity score analysis. *J Nucl Cardiol* 2018;25:394-403.

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