Annals of Nuclear Cardiology Vol. 8 No. 1 113–116

REVIEW ARTICLE

Relationship Among Coronary Artery Calcium Score, Myocardial Perfusion SPECT and Risk Stratification of Coronary Artery Disease

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Received: June 30, 2022/Revised manuscript received: August 3, 2022/Accepted: August 3, 2022

Abstract

Since Agatston et al. first reported quantification of the coronary artery calcification score (CACS) in 1990, discussion of its clinical significance and use in diagnostic management has continued. Recent papers have reported the relationship between CACS and myocardial perfusion single photon emission computed tomography (SPECT: MPS) and its combined diagnostic value. When interpreting CACS results, it should be noted that the frequency of significant ischemia detected by MPS, likelihood of coronary artery disease (CAD), and event rate gradually increased from mild to moderate CACS (1-400). At present, high CACS is considered to be moderately consistent with abnormal MPS, and abnormal CACS in normal MPS may contribute to CAD risk stratification. However, it should be noted that CACS=0 does not completely exclude CAD, which is particularly important when using CACS as a gatekeeper for MPS. Both stand-alone computed tomography (CT) scanner and hybrid SPECT-CT scanner are available for combined risk stratification of CACS and MPS in addition to improvement of image quality with attenuation correction.

Keywords: Coronary artery calcium score, Coronary artery disease, Hybrid SPECT-CT, Myocardial perfusion single photon emission computed tomography, Risk stratification

Ann Nucl Cardiol 2022; 8 (1): 113–116

Since Agatston et al. first reported quantification of the coronary artery calcification score (CACS) in 1990, discussion of its clinical significance and use in diagnostic management has continued (1–4). CACS can be easily measured by electrocardiogram (ECG) -gated computed tomography (CT) without contrast, and in addition to being useful alone for event risk stratification in coronary artery disease (CAD), it is also known to have additional prognostic ability for other noninvasive physiologic tests, including treadmill exercise ECG test (5). In addition, previous reports have shown that CACS is an independent predictor of dementia (6). Recent papers have reported the relationship between CACS and myocardial perfusion single photon emission computed tomography (SPECT: MPS) and its combined diagnostic value. This review article summarizes the findings to date, focusing on the relationship between CACS and MPS, and also describes the clinical implications of using CACS in combination with MPS for risk stratification of CAD.

Clinical significance of CACS for asymptomatic patients

In 2017, an expert consensus statement on the society of cardiovascular CT (SCCT) suggested that CACS is useful in accurately predicting CAD risk, even in asymptomatic patients, and helps guide treatment decisions (7). In addition, Dudum et al. reported that CACS is a reliable predictor of all-cause death, cardiovascular death, and CAD for asymptomatic populations in the United States with a family history of CAD (8).

doi: 10.17996/anc.22-00166

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Relationship between CACS and MPS results

In order to understand the relationship between CACS value and MPS result, it is important to organize significant cut-off values for CACS. In several previous reports, a CACS cut-off value of 400 was used for the validation of the assessment of significant ischemia or CAD events (9–11). In addition, the 2013 European Society of Cardiology (ESC) guidelines on the management of stable CAD and the Japanese Circulation Society (JCS) 2018 guidelines on the diagnosis of chronic coronary heart disease describes a CACS cut-off value 400 as a criterion for the recommendation of myocardial perfusion imaging in asymptomatic patients (12, 13). Although a CACS cutoff value of 400 has been used symbolically in several previous studies, the Society of Cardiovascular CT and Society of Thoracic Radiology guidelines in 2016 classified CACS ≥300 as moderate to severely increased risk (14). When interpreting CACS results, it should be noted that the frequency of significant ischemia detected by MPS, likelihood of CAD, and event rate gradually increased from mild to moderate CACS (1-400) (5, 15–19). In addition, previous study from Hecht et al reported that detection rate of abnormal MPS in the patients with CACS ≥400 was approximately 35% (17). Furthermore, Blumenthal et al previously reported that there was only modest agreement between abnormal exercise stress MPS results and high CACS (20). According to their report, an abnormal exercise stress MPS result occurred in >50% of subjects with a CACS >100, but also in 12% with CACS =0, 9% of with CACS 1 to 10, and 20% with CACS 11 to 100 (20). Interestingly, even when patients with normal MPS have a very high CACS, such as CACS >1000, the association with severe coronary artery disease has been reported to be only moderate (21). Another significant cut-off value is CACS=0. It should also be noted that although CACS =0 has been reported to be associated with a low incidence of significant ischemia in MPS and a risk of CAD events, they cannot be completely ruled out (15, 20, 22).

Clinically useful setting for combination of CACS and MPS

Understanding the variability in the frequency of abnormalities relative to each other's results of MPS and CACS, we should be aware that there are reports that the combination of CACS and MPS is useful in several conditions. There were several reports suggesting the additive value of CACS to normal or mild to moderate abnormal MPS for detection of cardiac event risk. Chang et al reported that severe CACS >400 added incremental prognostic information in subjects with normal MPS with a 3.55-fold relative increase for any cardiac event in comparison to the subjects with minimal CACS (≤10) (23). In addition, Barros et al reported CACS ≥400 was significant predictor of major adverse cardiac event in patients with mild to moderate abnormality in MPS (24). Furthermore, previous reports by Suzuki et al and Sharma et al suggested that combination of CACS and MPS results significantly stratify the risk of coronary revascularization, mortality and myocardial infarction in patients with normal MPS using moderate range of CACS cut-off value (200-300) (22, 25). Figure 1 shows an example of a male patient in his 80s with atypical chest pain and normal MPS. The patient's CACS was 901. Coronary angiography revealed significant stenosis in right coronary artery (Figure 2). CACS obtained from attenuation scan in perfusion scan is highly predictive of risk, including in patients for whom there is no evidence of ischemia.

CACS as a gatekeeper to MPS

In addition to a combination of CACS and MPS to determine risk stratification, the use of CACS as a gatekeeper for MPS has also been reported. Previous studies reported that CACS=0 was associated with a low prevalence of obstructive CAD (<5%) and a low risk of death or nonfatal myocardial infarction (<1% annual risk) (26, 27). According to the 2019 ESC guidelines, CACS measurement for the purpose of reclassifying CAD risk in the management of chronic coronary syndrome is a test that can be considered (2). Harmark et al previously reported that the combination of CACS (cut-off value <10) and N-terminal pro-B type natriuretic peptide (NT-pro BNP: cut-off value <26) could tentatively avoid 8% of MPS scan (28).

Modality selection for combination of CACS and MPS

The SPECT-CT hybrid machine not only improves the image quality of MPS with attenuation correction, but also enables risk assessment using a combination of CACS and MPS by one-stop shop (25). In addition, previous study by Schepis et al reported that attenuation maps from stand-alone CT scanner for CACS allows accurate attenuation correction of MPS images (29). Therefore, both types of imaging modalities are considered to be useful for risk stratification combining CACS and MPS and for improving the image quality of MPS using attenuation correction.

Conclusion

In this article, the relationship between CACS and MPS has been summarized, in addition to the clinical implication of the combination of CACS and MPS for risk stratification of CAD. Previous reports to date suggest that abnormalities in CACS and MPS are in moderate agreement, and CACS may stratify CAD risk in normal MPS.

Acknowledgments

None.

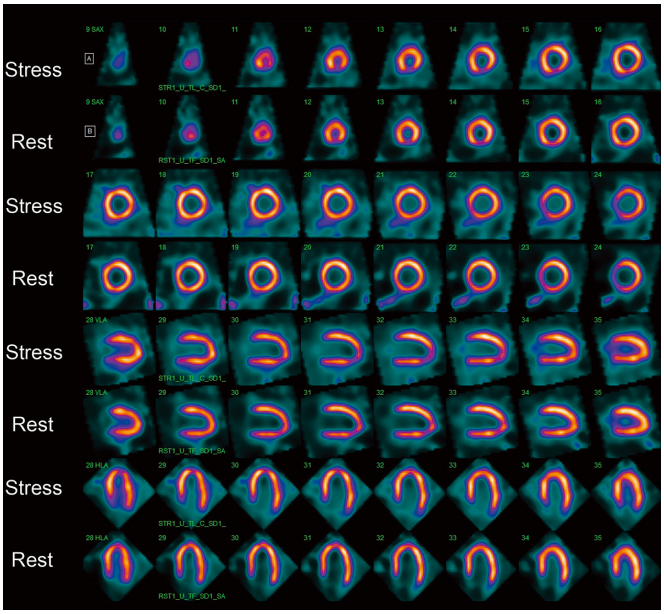

Figure 1 An example of a male patient in his 80s with atypical chest pain and normal MPS. The patient's CACS was 901.

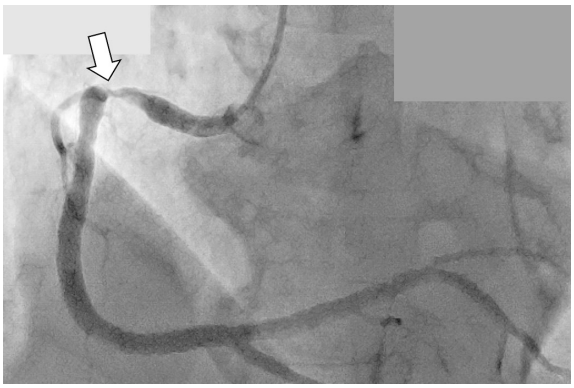

Figure 2 Coronary angiography revealed significant stenosis in right coronary artery (white arrow).

Sources of funding

None.

Conflicts of interest

None.

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References

1. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990; 15: 827–32.
2. 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.
3. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019; 139: e1082–143.
4. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA Guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019; 140: e596–646.
5. Chang SM, Nabi F, Xu J, Pratt CM, Mahmarian AC, Frias ME, et al. Value of CACS compared with ETT and myocardial perfusion imaging for predicting long-term cardiac outcome in asymptomatic and symptomatic patients at low risk for coronary disease: clinical implications in a multimodality imaging world. JACC Cardiovasc Imaging 2015; 8: 134–44.
6. Kuller LH, Lopez OL, Mackey RH, Rosano C, Edmundowicz D, Becker JT, et al. Subclinical cardiovascular disease and death, dementia, and coronary heart disease in patients 80+ years. J Am Coll Cardiol 2016; 67: 1013–22.
7. Hecht H, Blaha MJ, Berman DS, Nasir K, Budoff M, Leipsic J, et al. Clinical indications for coronary artery calcium scoring in asymptomatic patients: expert consensus statement from the Society of Cardiovascular Computed Tomography. J Cardiovasc Comput Tomogr 2017; 11: 157–68.
8. Dudum R, Dzaye O, Mirbolouk M, et al. Coronary artery calcium scoring in low risk patients with family history of

coronary heart disease: validation of the SCCT guideline approach in the coronary artery calcium consortium. J Cardiovasc Comput Tomogr 2019; 13: 21–5.
9. Erbel R, Möhlenkamp S, Moebus S, Schmermund A, Lehmann N, Stang A, et al. Coronary risk stratification, discrimination, and reclassification improvement based on quantification of subclinical coronary atherosclerosis: the Heinz Nixdorf Recall study. J Am Coll Cardiol 2010; 56: 1397–406.
10. Min JK, Labounty TM, Gomez MJ, Achenbach S, Al-Mallah M, Budoff MJ, et al. Incremental prognostic value of coronary computed tomographic angiography over coronary artery calcium score for risk prediction of major adverse cardiac events in asymptomatic diabetic individuals. Atherosclerosis 2014; 232: 298–304.
11. Bavishi C, Argulian E, Chatterjee S, Rozanski A. CACS and the frequency of stress-induced myocardial ischemia during MPI: a meta-analysis. JACC Cardiovasc Imaging 2016; 9: 580–9.
12. Yamagishi M, Tamaki N, Akasaka T, Ikeda T, Ueshima K, Uemura S, et al. JCS 2018 Guideline on diagnosis of chronic coronary heart disease. Circ J 2021; 85: 402–572.
13. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J 2013; 34: 2949–3003.
14. Hecht HS, Cronin P, Blaha MJ, Budoff MJ, Kazerooni E, Narula J, et al. 2016 SCCT/STR guidelines for coronary artery calcium scoring of noncontrast noncardiac chest CT scans: a report of the Society of Cardiovascular Computed Tomography and Society of Thoracic Radiology. J Cardiovasc Comput Tomogr 2017; 11: 74–84.
15. Berman DS, Wong ND, Gransar H, Miranda-Peats R, Dahlbeck J, Hayes SW, et al. Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. J Am Coll Cardiol 2004; 44: 923–30.
16. Winther S, Schmidt SE, Mayrhofer T, Bøtker HE, Hoffmann U, Douglas PS, et al. Incorporating coronary calcification into pre-test assessment of the likelihood of coronary artery disease. J Am Coll Cardiol 2020; 76: 2421–32.
17. Hecht HS. Coronary artery calcium scanning: past, present, and future. JACC Cardiovasc Imaging 2015; 8: 579–96.
18. Matsuo S, Nakajima K, Okuda K, Kinuya S. The relationship between stress-induced myocardial ischemia and coronary artery atherosclerosis measured by hybrid SPECT/CT camera. Ann Nucl Med 2011; 25: 650–6.
19. Mitchell JD, Paisley R, Moon P, Novak E, Villines TC. Coronary artery calcium and long-term risk of death, myocardial infarction, and stroke: the walter reed cohort study. JACC Cardiovasc Imaging 2018; 11: 1799–806.
20. Blumenthal RS, Becker DM, Yanek LR, Moy TF, Michos ED, Fishman EK, et al. Comparison of coronary calcium and stress myocardial perfusion imaging in apparently healthy siblings of individuals with premature coronary artery disease. Am J Cardiol 2006; 97: 328–33.
21. Yuoness SA, Goha AM, Romsa JG, Akincioglu C, Warrington JC, Datta S, et al. Very high coronary artery calcium score with normal myocardial perfusion SPECT imaging is associated with a moderate incidence of severe coronary artery disease. Eur J Nucl Med Mol Imaging 2015; 42: 1542–50.
22. Suzuki Y, Matsumoto N, Nagumo S, Matsuo R, Kuronuma K, Ashida T, et al. Incremental predictive value of coronary calcium score in risk stratification of coronary revascularization in patients with normal or mild ischemia using nuclear myocardial perfusion single photon emission computed tomography. Circ J 2021; 85: 877–82.
23. Chang SM, Nabi F, Xu J, Peterson LE, Achari A, Pratt CM, et al. The coronary artery calcium score and stress myocardial perfusion imaging provide independent and complementary prediction of cardiac risk. J Am Coll Cardiol 2009; 54: 1872–82.
24. Barros MVL, Nunes M do C, Braga G, Rabelo DR, Magalhães K, Scaramello F, et al. Role of coronary artery calcium score for risk stratification in patients with non significant perfusion defects by myocardial perfusion single photon emission computed tomography. Cardiol J 2015; 22: 330–5.
25. 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 2021; 28: 2086–96.
26. Budoff MJ, Mayrhofer T, Ferencik M, Bittner D, Lee KL, Lu MT, et al. Prognostic value of coronary artery calcium in the PROMISE study (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). Circulation 2017; 136: 1993–2005.
27. Villines TC, Hulten EA, Shaw LJ, Goyal M, Dunning A, Achenbach S, et al. Prevalence and severity of coronary artery disease and adverse events among symptomatic patients with coronary artery calcification scores of zero undergoing coronary computed tomography angiography: results from the CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter) registry. J Am Coll Cardiol 2011; 58: 2533–40.
28. Haarmark C, Andersen KF, Madsen C, Zerahn B. Coronary artery calcium score and N-terminal pro-B-type natriuretic peptide as potential gatekeepers for myocardial perfusion imaging. Clin Physiol Funct Imaging 2017; 37: 710–6.
29. Schepis T, Gaemperli O, Koepfli P, Rüegg C, Burger C, Leschka S, et al. Use of coronary calcium score scans from stand-alone multislice computed tomography for attenuation correction of myocardial perfusion SPECT. Eur J Nucl Med Mol Imaging 2007; 34: 11–9.