

## Coronary artery calcium screening: sufficient evidence for accurate risk assessment?

Ernst E. van der Wall · Joanne D. Schuijf ·  
J. Wouter Jukema · Jeroen J. Bax

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Accurate risk assessment in coronary artery disease is very much needed in decreasing cardiovascular events through more appropriate targeting of preventive measures. Needless to say that high risk patients (those with >20% 10-year risk of future cardiovascular event) need more aggressive preventive therapy anyway. However, a majority of cardiovascular events occur in individuals at intermediate risk, i.e., a 10–20% 10-year risk. Consequently, cardiac risk assessment is mostly warranted in asymptomatic patients, particularly in those at intermediate risk. It has been suggested that traditional risk assessment may be refined with the selective use of newer imaging methods, such as coronary artery calcium scoring and noninvasive angiography with computed tomography (CT) techniques [1–6]. These technologies, which allow quantification of atherosclerotic burden, can predict risk of cardiac events and might provide an approach to more widespread coronary atherosclerosis screening [7].

Coronary calcification is a marker of atherosclerosis that can be quantified with the use of cardiac CT and it is proportional to the extent and severity of atherosclerotic disease. Because of the noninvasive

nature of CT and the large societal burden of coronary atherosclerosis, there is great interest in developing CT-based techniques for detection of coronary artery calcium, a known marker of underlying atherosclerosis. However, important questions remain including the role of calcium in the process of acute plaque rupture [8], the utility of this technique both the asymptomatic and symptomatic population [9], and the statistical distribution of calcium scores and hard cardiac events in the general population [10].

Sofar, the published studies demonstrate a high sensitivity of coronary artery calcium for the presence of coronary artery disease but a lower specificity for obstructive CAD depending on the magnitude of the coronary artery calcium. Several large clinical trials found true incremental predictive value of coronary artery calcium over the Framingham risk score when used in asymptomatic patients [10]. Based on multiple observational studies, patients with increased plaque burden (increased coronary artery calcium) are approximately 10 times more likely to suffer a cardiac event over the next 3–5 years [11]. Coronary calcium scores have outperformed conventional risk factors, highly sensitive C-reactive protein (CRP), apolipoproteins [12], and carotid intima-media thickness as a predictor of cardiovascular events [13]. The relevant prognostic information may be used to initiate or intensify appropriate treatment strategies to slow the progression of atherosclerotic vascular disease. Current data

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E. E. van der Wall (✉) · J. D. Schuijf ·  
J. W. Jukema · J. J. Bax  
Department of Cardiology, Leiden University Medical  
Center, P.O. Box 9600, Leiden, The Netherlands  
e-mail: e.e.van\_der\_wall@lumc.nl

suggests intermediate risk patients may benefit most from further risk stratification with cardiac CT, as coronary artery calcium testing is effective at identifying increased risk and in motivating effective behavioral changes. It has been shown that for both general and special populations a zero score excludes most clinically relevant coronary artery disease. Budoff et al. [10] showed a 10-year survival (after adjustment for risk factors, including age) of 99.4% for a calcium score of 0 which worsened to 87.8% for a score of >1,000. However, it should be realized that absence of coronary calcium does not completely eliminate the possibility of flow-limiting coronary artery disease. Importantly, a stepwise increase occurs in the risk of adverse events with increasing calcium scores in patients with and without ischemia on PET myocardial perfusion imaging [14]. On the other side of the spectrum, high calcium scores do not confer an increased risk for cardiac events among patients with normal scintigraphic myocardial perfusion studies [15]. Although, patients with increased calcium scores may be considered for intensive medical therapy to prevent future coronary artery disease events, a normal perfusion study in such patients suggests no need for more aggressive interventions. Nevertheless, there is nowadays sufficient evidence that coronary artery calcium may be considered as useful predictor of coronary artery disease in certain population of patients such as patients with diabetes, hypertension, and in elderly patients [16–24].

In 2007, a clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain has been published [25]. This document consists of a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA). In this consensus document, the role of coronary calcium quantification is evaluated in identifying risk in asymptomatic patients, symptomatic patients, and selected subgroups such as women, ethnic groups, elderly patients, and patients with diabetes. Sequential to this document, a Task force on training in advanced cardiovascular imaging has recently been published with emphasis on training in cardiac CT [26].

In the current issue of this journal, new recommendations provided by the European Society of

Cardiac Radiology (ESCR) and North American Society for Cardiovascular Imaging (NASCI) are published [27]. In this extensive and interesting document the existing guidelines and the most relevant literature (142 references!) on coronary calcium screening for cardiac risk assessment are reviewed for both general and special populations. The coronary calcium score remains a strong predictor of incident coronary heart disease and provides predictive information beyond that provided by standard risk factors. For both general and special populations a zero score excludes most clinically relevant coronary artery disease. Regarding impact on therapy, it is clearly stated that there is currently still little evidence to alter prescription based on knowledge of the calcium score. Along those lines, the evidence is inconclusive as to the most accurate method to define progression of coronary artery calcium, putting into question the value of serial testing. Finally, the document addresses the importance of standardization of coronary artery calcium measurements by multi-detector CT.

To summarize, the new recommendations provide a wealth of useful information on the value of coronary artery calcium screening in patients suspected for and known with coronary artery disease. Therefore, this document deserves to be adopted by the European cardiology community.

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## References

1. Slart RH, Bax JJ, van Veldhuisen DJ, van der Wall EE, Dierckx RA, Jager PL (2006) Imaging techniques in nuclear cardiology for the assessment of myocardial viability. *Int J Cardiovasc Imaging* 22:63–80
2. van Werkhoven JM, Schuijff JD, Jukema JW et al (2008) Anatomic correlates of a normal perfusion scan using 64-slice computed tomographic coronary angiography. *Am J Cardiol* 101:404–405
3. Pundziute G, Schuijff JD, Jukema JW et al (2007) Prognostic value of multislice computed tomography coronary angiography in patients with known or suspected coronary artery disease. *J Am Coll Cardiol* 49:62–70
4. Schuijff JD, Pundziute G, Jukema JW et al (2006) Diagnostic accuracy of 64-slice multislice computed

- tomography in the noninvasive evaluation of significant coronary artery disease. *Am J Cardiol* 98:145–148
5. Schuijf JD, Wijns W, Jukema JW et al (2006) Relationship between noninvasive coronary angiography with multislice computed tomography and myocardial perfusion imaging. *J Am Coll Cardiol* 48:2508–2514
  6. Jongbloed MR, Lamb HJ, Bax JJ et al (2005) Noninvasive visualization of the cardiac venous system using multislice computed tomography. *J Am Coll Cardiol* 45:749–753
  7. Groen JM, Greuter MJ, Vliegenthart R et al (2008) Calcium scoring using 64-slice MDCT, dual source CT and EBT: a comparative phantom study. *Int J Cardiovasc Imaging* 24:547–556
  8. de Nooijer R, Verkleij CJ, von der Thüsen JH et al (2006) Lesional overexpression of matrix metalloproteinase-9 promotes intraplaque hemorrhage in advanced lesions but not at earlier stages of atherogenesis. *Arterioscler Thromb Vasc Biol* 26:340–346
  9. Henneman MM, Schuijf JD, Pundziute G et al (2008) Noninvasive evaluation with multislice computed tomography in suspected acute coronary syndrome: plaque morphology on multislice computed tomography versus coronary calcium score. *J Am Coll Cardiol* 52:216–222
  10. Budoff MJ, Shaw LJ, Liu ST et al (2007) Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. *J Am Coll Cardiol* 49:1860–1870
  11. Akram K, Voros S (2008) Absolute coronary artery calcium scores are superior to MESA percentile rank in predicting obstructive coronary artery disease. *Int J Cardiovasc Imaging*. doi:10.1007/s10554-008-9305-5
  12. van Lennep JE, Westerveld HT, van Lennep HW, Zwinderman AH, Erkelens DW, van der Wall EE (2000) Apolipoprotein concentrations during treatment and recurrent coronary artery disease events. *Arterioscler Thromb Vasc Biol* 20:2408–2413
  13. Folsom AR, Kronmal RA, Detrano RC et al (2008) Coronary artery calcification compared with carotid intima-media thickness in the prediction of cardiovascular disease incidence: the Multi-Ethnic Study of Atherosclerosis (MESA). *Arch Intern Med* 168:1333–1339
  14. Schenker MP, Dorbala S, Hong EC et al (2008) Interrelation of coronary calcification, myocardial ischemia, and outcomes in patients with intermediate likelihood of coronary artery disease: a combined positron emission tomography/computed tomography study. *Circulation* 117:1693–1700
  15. Rozanski A, Gransar H, Wong ND et al (2007) Clinical outcomes after both coronary calcium scanning and exercise myocardial perfusion scintigraphy. *J Am Coll Cardiol* 49:1352–1361
  16. Djaber R, Beishuizen ED, Pereira AM et al (2008) Non-invasive cardiac imaging techniques and vascular tools for the assessment of cardiovascular disease in type 2 diabetes mellitus. *Diabetologia*. doi:10.1007/s00125-008-1062-4
  17. Scholte AJ, Schuijf JD, Kharagjitsingh AV et al (2008) Prevalence of coronary artery disease and plaque morphology assessed by multi-slice computed tomography coronary angiography and calcium scoring in asymptomatic patients with type 2 diabetes. *Heart* 94:290–295
  18. Bax JJ, Young LH, Frye RL et al (2007) Screening for coronary artery disease in patients with diabetes. *Diabetes Care* 30:2729–2736
  19. Scholte AJ, Bax JJ, Wackers FJ (2006) Screening of asymptomatic patients with type 2 diabetes mellitus for silent coronary artery disease: combined use of stress myocardial perfusion imaging and coronary calcium scoring. *J Nucl Cardiol* 13:11–18
  20. Husmann L, Scheffel H, Valenta I et al (2008) Impact of hypertension on the diagnostic accuracy of coronary angiography with computed tomography. *Int J Cardiovasc Imaging*. doi:10.1007/s10554-008-9307-3
  21. Raggi P, Gongora MC, Gopal A, Callister TQ, Budoff M, Shaw LJ (2008) Coronary artery calcium to predict all-cause mortality in elderly men and women. *J Am Coll Cardiol* 52:17–23
  22. Brown ER, Kronmal RA, Bluemke DA et al (2008) Coronary calcium coverage score: determination, correlates, and predictive accuracy in the Multi-Ethnic Study of Atherosclerosis. *Radiology* 247:669–675
  23. Detrano R, Guerci AD, Carr JJ et al (2008) Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med* 358:1336–1345
  24. Sirineni GK, Raggi P, Shaw LJ, Stillman AE (2008) Calculation of coronary age using calcium scores in multiple ethnicities. *Int J Cardiovasc Imaging* 24:107–111
  25. Greenland P, Bonow RO, Brundage BH et al (2007) ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography). Society of Atherosclerosis Imaging and Prevention; Society of Cardiovascular Computed Tomography. *Circulation* 115:402–426
  26. Budoff MJ, Achenbach S, Berman DS et al (2008) Task force 13: training in advanced cardiovascular imaging (computed tomography) endorsed by the American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, and Society of Cardiovascular Computed Tomography. *J Am Coll Cardiol* 51:409–414
  27. Oudkerk M, Stillman AE, Halliburton SS et al (2008) Coronary artery calcium screening: current status and recommendations from the European Society of Cardiac Radiology and North American Society for Cardiovascular Imaging. *Int J Cardiovasc Imaging* 24:645–671