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Optimizing coronary artery calcium scanning to meet the challenges of population screening

Coronary artery calcium (CAC) scoring by CT currently provides a valuable tool for risk-based therapeutic management for patients "on the fence", specifically, selected adult patients without symptoms of atherosclerotic cardiovascular disease but for whom, after quantitative risk assessment using risk-factor based tools such as Pooled Cohort Equations, the shared physician-patient decision to initiate preventive treatment remains uncertain. Indeed, both ACC/AHA cardiovascular risk guidelines[1] and Joint ESC cardiovascular disease prevention guidelines,[2] documents endorsed by a total of 19 professional societies, suggest that CAC scoring "may be considered" to inform treatment decision making in this context. CAC scoring may be especially helpful in selected patients with family history of premature coronary disease, patients who, based on guidelines, are advised to be on statin therapy but who prefer to avoid it, and patients deemed "statin intolerant" who could however potentially be re-challenged.[3] A large evidence base exceeding 2500 peer-reviewed papers[4] informs CAC-scoring practice. This literature demonstrates strong prognostic capability of CAC testing[4] as well as salutary effects on medication and lifestyle change initiation,[5] long-term statin adherence and weight loss,[6] and risk factor control[7] from a patient's visualization of his or her CAC.

A much larger potential future role for CAC scoring has been proposed which would involve broad-based population screening of asymptomatic but clinically intermediate-risk patients. This approach would require rigorous testing and validation in the form of a randomized controlled trial. While a US trial has not yet been funded, the 39,000 patient Risk Or Benefit IN Screening for CArdiovascular Diseases (ROBINSCA) trial is currently underway in the Netherlands,[8] aimed at determining whether CAC screening in asymptomatic women and men followed by preventive treatment will reduce coronary heart disease mortality and morbidity on 5-year follow-up.

Nevertheless, CAC scanning remains controversial, insurance coverage is poor, and its use in US clinical practice low.[4] Recommendations issued by the US Preventive Services Task Force (USPSTF) in July 2018 on risk assessment for cardiovascular disease with nontraditional risk factors concluded that "the current evidence is insufficient to assess the balance of benefits and harms of using the … CAC score in risk assessment for cardiovascular disease …"[9] Based on the CAC literature, USPSTF's conclusions have been vigorously objected to by professional societies.[10]

USPSTF, in these recommendations, stated that "the main potential harm of adding nontraditional risk factors to CVD risk assessment is radiation exposure from CAC score testing."[9] Concern for radiation from CT scanning for CAC scoring was raised as well in the ACC/AHA[1] and ESC[2] guidelines. Radiation exposure from CAC scoring is as of yet not well characterized across clinical populations. While early data found radiation effective doses ranging over more than an order of magnitude,[11] the highest doses observed (> 10 mSv) were from older multidetector-row scanner technology that is highly unlikely to be in use in 2018, and typical doses today are far lower. Nevertheless, claims[4] of routine low doses of ≤1 mSv are also unlikely to be an accurate description of contemporary practice. Wherever observed, there is considerable variability in clinical practices related to patient radiation exposure from all modalities,[12] and it is unlikely that CAC scanning is any exception. Indeed, a survey among ROBINSCA sites found "quite a few differences" between sites in current clinical CAC scanning protocols for same-generation CT systems from the same vendor.[8] The spectrum of doses in contemporary CAC scanning will be addressed in a worldwide cross-sectional study, planned for 2019 as part of the International Atomic Energy Agency Noninvasive Cardiology Protocols Study 2 (INCAPS 2).

What techniques have been studied to reduce radiation from CAC scoring, and what are their effects on dose, calcium scores, and risk reclassification? This is the focus of an important systematic review by Vonder et al., part of the team conducting ROBINSCA, in Volume 12, issue 5 of *JCCT*.[13] The authors identified 28 English-language studies published over the past 15 years comparing "full-dose" to "reduced-dose" protocols which reported quantification of radiation dose reduction, CAC scores, and/or cardiovascular risk stratification. These included both phantom studies and patient studies ranging from 15 to 200 patients. Five dose-reduction techniques were identified: x-ray tube-voltage reduction alone, with iterative reconstruction (IR), and with tin-filtration spectral shaping (4, 2, and 4 studies, respectively), and tube-current reduction with and without IR (4 and 13 studies). The authors appropriately chose the scanner-reported volume CT dose index ($CTDI_{vol}$) as the measure of dose; to approximately translate $CTDI_{vol}$ to effective dose using contemporary methodology,[14] one can divide by 3 and change units from mGy to mSv. Average $CTDI_{vol}$ for full-dose protocols in the 11 patient studies published in the past 5 years ranged from 2.2 to 13.9 mGy, and for reduced-dose protocols from 0.6 to 5.7 mGy.[13]

Tube-voltage reduction studies were characterized by a diversity of approaches to the problem of greater calcium attenuation at lower voltage that results in seemingly higher CAC scores. Some studies retained standard threshold values, other studies increased the lowest threshold (the standard is 130 HU), and others increased all 4 thresholds for Agatston scoring, using a variety of threshold values; no approach reflects comprehensive modeling of the underlying physics or between-scanner differences. This resulted in variable findings of significantly increased, decreased, or similar CAC scores between standard and low-voltage scans. The lowest doses were observed in recent studies using a tin filter to remove low-energy photons that contribute little to the final image, however 3 of 4 such studies noted a significant change in Agatston score. Nevertheless, the two patient studies had low reclassification rates (3% and 4%).

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Studies of tube-current reduction without IR found modest dose reduction but similar Agatston scores between standard- and reduced-current scans, however risk reclassification was not reported for any of these studies. Tube-current reduction with IR was characterized by higher dose reduction but underestimation of Agatston scores in 8 of 13 studies; risk reclassification where reported ranged from 3% to 21%. As in tube-voltage reduction, better analytical methods, here ideally tailored to the specific IR method, are needed to adjust Agatston scoring for the changes to reconstructed images related to IR.

Where does this emerging literature on CAC dose-reduction approaches, so nicely compiled and organized by Vonder et al., leave us? Tube voltage reduction approaches have promise, with potential effective doses as low as 0.2 mSv, but they require further development before being ready for clinical practice. Tube current optimization should be performed for all studies. While habitus- and topogram-based automatic selection of tube current for CAC is built into most new scanners, the tolerated noise level is often by default set unnecessarily low, resulting in doses that are unnecessarily high. Preferably in conjunction with a qualified medical physicist, all laboratories should review their default scan protocols and parameters, and in particular how tube current is selected, to achieve adequate image quality for CAC scoring at optimized radiation dose. Given the variable impact on CAC scoring of the different IR algorithms used in different scanners, ideally each laboratory should calibrate its own CAC scores processed with both filtered backpropagation and IR in a series of patients, and use this information to decide whether IR with a reduced tube current would result in sufficiently reliable CAC scores for clinical use.

While radiation concerns may well be overplayed for CAC scanning which is commonly performed at low doses, in particular to optimize the benefit-risk balance and potential appeal of CAC scoring as a population screening test, reduced-dose scanning approaches must be further developed and validated. Illustrating this, Galper et al.,[15] in a microsimulation and risk projection modeling study comparing strategies for primary prevention of coronary heart disease including CAC-based approaches, found that statin and aspirin therapy based on widescale CAC scoring as suggested by Society for Heart Attack Prevention and Eradication (SHAPE) guidelines would prevent 3 million myocardial infarctions and result in 8 million quality-adjusted life years gained over 30 years, in comparison to US *status quo* use of statin and aspirins for primary prevention. This would far outweigh the estimated 11,000 radiation-attributable cancers estimated from CAC scoring, assuming an average effective dose of 2.3 mSv. Nevertheless, other preventive approaches were yet more effective, and notwithstanding this highly favorable benefit-risk calculus, even a modest reduction in average dose could translate to thousands fewer radiation-attributable cancers from screening. CAC scoring has real potential as a screening test for coronary artery disease, albeit one still requiring support from randomized trials and better definition of the targeted population. It is a desideratum for the cardiac CT community to further develop and validate dose-reduction methods to strengthen CAC scanning as a candidate for this role.

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References

1. Goff Jr DC, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;129(Suppl. 2):S49–S73.
2. Piepoli MF, Hoes AW, Agewall S, et al. European Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J.* 2016;37:2315–2381 2016.
3. Blankstein R, Gupta A, Rana JS, et al. The implication of coronary artery calcium testing for cardiovascular disease prevention and diabetes. *Endocrin Metab.* 2017;32:47–57.
4. Hecht HS. Coronary artery calcium scanning: past, present, and future. *JACC Cardiovasc Imag.* 2015;8:579–596.
5. Orakzai RH, Nasir K, Orakzai SH, et al. Effect of patient visualization of coronary calcium by electron beam computed tomography on changes in beneficial lifestyle behaviors. *Am J Cardiol.* 2008;101:999–1002.
6. Kalia NK, Cespedes L, Youssef G, et al. Motivational effects of coronary artery calcium scores on statin adherence and weight loss. *Coron Artery Dis.* 2015;26:225–230.
7. Rozanski A, Gransar H, Shaw LJ, et al. Impact of coronary artery calcium scanning on coronary risk factors and downstream testing: a prospective randomized trial. *J Am Coll Cardiol.* 2011;57:1622–1632.
8. Vonder M, van der Aalst CM, Vliegenthart R, et al. Coronary artery calcium imaging in the ROBINSCA trial: rationale, design, and technical background. *Acad Radiol.* 2018;25:118–128.
9. U.S. Preventive Services Task Force. Risk assessment for cardiovascular disease with nontraditional risk factors: US Preventive Services Task Force recommendation statement. *JAMA.* 2018;320:272–280.
10. https://cdn.ymaws.com/scct.org/resource/resmgr/Advo_Forms/USPSTF_CAC_comments_final_Fe.pdf. Accessed 26 June 2018.
11. Kim KP, Einstein AJ, Berrington de Gonzalez A. Coronary artery calcification screening: estimated radiation dose and cancer risk. *Arch Intern Med.* 2009;169:1188–1194.
12. Carpeggiani C, Picano E, Brambilla M, et al. Variability of radiation doses of cardiac diagnositic imaging tests: the RADIO-EVINCI study (RADIationdOse subproject of the EVINCI study). *BMC Cardiovasc Disord.* 2017;17:63.
13. Vonder M, van der Werf NR, Leiner T, et al. The impact of dose reduction on the quantification of coronary artery calcifications and risk categorization: a systematic review. *J Cardiovasc Comput Tomogr.* 2018;12:352–363.
14. Trattner S, Halliburton S, Thompson CM, et al. Cardiac-specific conversion factors to estimate radiation effective dose from dose-length product in computed tomography. *JACC Cardiovasc Imag.* 2018;11:64–74.
15. Galper BZ, Wang YC, Einstein AJ. Strategies for primary prevention of coronary heart disease based on risk stratification by the ACC/AHA lipid guidelines, ATP III guidelines, coronary calcium scoring, and C-Reactive Protein, and a global treat-all strategy: a comparative-effectiveness modeling study. *PloS One.* 2015;10:e0138092.

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