Reviewer's report

Title: SPECT myocardial perfusion imaging as an adjunct to coronary calcium score for the detection of hemodynamically significant coronary artery stenosis

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Reviewer: Maksymilian Opolski

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Major Compulsory Revisions
Coronary artery disease (CAD) accounts for the majority of deaths from cardiovascular diseases. Thus, early detection of CAD is crucial for both risk modification and tailored medical therapies. The enthusiastic adoption of coronary computed tomography angiography (CCTA) enables a noninvasive diagnosis of CAD in a symptomatic patient population with intermediate pretest probability of CAD. In contrast, the application of noncontrast coronary calcium scoring (CS) has been validated for risk stratification in asymptomatic patients. Thus, current guidelines on cardiac CT recommend two distinct algorithms for CAD diagnosis depending on clinical manifestation of angina pectoris (asymptomatic or symptomatic patients) that should be regarded as non-interchangeable.

In the manuscript of von Ziegler et al, the impact of adding myocardial perfusion imaging (MPI) with single photon emission computed tomography (SPECT) to coronary CS for the assessment of significant CAD as detected by invasive coronary angiography (ICA) was determined. The analysis was based on a consecutive cohort of 351 symptomatic patients with clinical indication for ICA who based on the study protocol underwent both SPECT MPI and coronary CS.

In conclusion, the authors state that while coronary CS is an excellent tool to rule out CAD, it has still low positive predictive value (with many false-positive results) for assessment of angiographically significant coronary lesions. In contrast, the addition of SPECT MPI in a subgroup of patients with CS>0 led to a significant reduction of false-positive findings, i.e. the number of patients needing ICA compared to a CS strategy alone. This is an interesting and valuable observation. The main advantages of the study should be listed as follows: an accurate study protocol, large cohort of patients, precise statistical analysis, sound data presentation, and high quality of written English.

However, there is a major limitation that may affect the practical application of the presented results and needs authors clarification before a decision on publication can be reached. It results from the methodological pitfall in which the authors precipitately assumed that the diagnostic performance of coronary CS for the detection of significant CAD in symptomatic patients needs further improvement. However, according to current guidelines coronary CS has not a single clinical application in a symptomatic patient population. Thus, the idea of improving any imaging modality with no robust data for clinical implementation in the studied population...
seems logically unsound. On the other hand, the assumption of enhancing the diagnostic performance of SPECT MPI (which has already been validated in a symptomatic patient population) with CS is methodologically explicable and correct, and should be at least commented by von Ziegler et al.

Minor Essential Revisions

1. Significant CAD was defined as at least 75% of luminal obstruction in quantitative coronary analysis. This is opposite to the definition of significant CAD applied by the majority of the studies and needs clarification. Suppose the authors had used the cut-off value of 50% for luminal stenosis, the number of false-positive findings for CS should have been significantly lower resulting in initially higher specificity/positive predictive value of CS that, as I reckon, could have been hardly improved by SPECT MPI. This is an important methodological bias with a potential for misinterpretation of the presented results and should be commented by the authors.

2. The idea of performing coronary revascularization solely on the basis of luminal coronary artery stenosis in case of equivocal stress tests (as in the presented study) seems rather controversial in the “myocardial ischemic era”.

3. At the end the presented diagnostic performance of CS plus SPECT MPI turns out to be comparable to SPECT MPI strategy alone for the detection of significant CAD with no significant superiority in the number of false-positive findings in the CS plus SPECT MPI group. However, the authors do not report this observation by only comparing the CS plus SPECT MPI strategy vs CS alone. Thus, one could cite a famous quote - “we found both similarities and differences, but at the end there is no much difference between them”.

4. The limitation section is too laconic and needs substantial extension.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.