Reviewer’s report

Title: Predicting Clinically Unrecognized Coronary Artery Disease: Use of Two-Dimensional Echocardiography

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Reviewer: Rosa Sicari

Reviewer’s report:

This is an interesting and well written manuscript addressing an important clinical issue such as the usefulness of 2D echo for the risk stratification of patients with suspected CAD. The main limitation of the study is due to the retrospective nature of the analysis, and there are a few issues that authors should address:

1. Patient selection: authors should provide more details on the patient population selection criteria. This is a major flaw in the study since authors do not justify on what basis patients underwent SPECT and coronary angiography.

2. Level of risk: In the analysis authors have included patients with reduced EF (<50%), with previous MI identified by rest wall motion abnormalities. These patients per se have a higher risk of death and this may pollute the statistical analysis by increasing the mortality rate. The real novelty of the study relies on the ability of few, simple echo parameters in the prediction of CAD. Therefore, authors should exclude from the analysis patients with reduced EF and/or history of MI and restrict the analysis to the real prognostic value of MAC, aortic calcification, LVH + conventional risk factors.

SPECT may have a high number of false positive results as outlined in the study limitation but recognise a reduction of coronary flow reserve also in the absence of significant coronary artery disease as in diabetics, hypertensives or hypertrophy as the expression of microvascular disease. Please address.

Provide also separate data on outcome between perfusion abnormalities in the absence of CAD but with MAC, aortic calcification and clinical risk factors from those with significant CAD.

4. On this same line not all coronary arteries are haemodynamically significant and may therefore, not induce perfusion abnormalities. Please address.

5. Please specify the definition of aortic calcification vs. aortic stenosis. Again, also aortic stenosis patients should be excluded from the analysis.

6. The discussion is too long and should be more focused on the clinical impact of calcification recognised by 2D echo when more sophisticated and expensive techniques such as CT are routinely employed to assess the same parameters but at much higher health and environmental costs.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

'I declare that I have no competing interests'