Reviewer's report

Title: High-resolution grey scale or angio mode power modulation? Head to head comparisons of two modalities of real-time perfusion adenosine stress echocardiography with simultaneous SPECT

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Reviewer: lucia venneri

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In this manuscript the Authors compared, in patients with known or suspected coronary artery disease, two power modulation techniques, angiomode (AM) and high resolution gray scale (HR) during adenosine stress echocardiography (ASE), for the evaluation of myocardial ischemia, considering as gold standard 99mTc-tetrofosmin SPECT.

They suggest that RTP-ASE with its highly availability and with its safety profile (despite of the recent warning) , is an excellent alternative in clinical arena when SPECT is not feasible.

There are several issues that Authors should comment.

In myocardial contrast stress echocardiography the combination of perfusion assessment (showing higher sensitivity) with wall motion evaluation (showing higher specificity) is very appealing for the diagnosis of coronary artery disease. Despite of this important point, the available literature shows that this technique, even in the large-volume stress echocardiography laboratory, is not considered as the natural extension of the classic stress echocardiographic examination. There are no convincing data showing that the ability of contrast echocardiography to supplement wall motion information by providing information on perfusion can add additive diagnostic value to stress echocardiography. In fact, recent EAE Guidelines regarding stress echocardiography do no recommend the use of echo contrast agents to stress echocardiography except for endocardial border enhancement, whenever there are suboptimal resting or peak stress images.

- This is another paper in which RTP stress echo accuracy is not validated versus coronary angiography but vs. myocardial perfusion scintigraphy. Therefore, it is a good concordance study between the two techniques. However, both techniques suffer from the same limitation: they are unable to distinguish between micro and macrovascular coronary disease. It is well known that SPECT is able to detect perfusion abnormalities, which are not necessarily caused by epicardial coronary artery disease. The perfusion defects could be related to microvascular disease and do not cause obvious wall motion abnormalities. Considering this point, the Authors should better state the diagnostic endpoints of stress echocardiographic testing. In other words, do they consider positive for
myocardial ischemia a stress test when stress-inducible perfusion deficit is found, even in absence of any new onset of wall-motion abnormality?

- It would be interesting make an head to head comparisons of the RTP stress echo with magnetic resonance stress testing, which is becoming widely accepted in clinical practice. Both techniques are able to evaluate at the same time perfusion and regional mechanical function

- When authors in table define the percentage of patients with heart failure: how was diagnosis made: symptoms and signs of heart failure or left ventricular dysfunction? Please, be more clear.

- Author report: “Normal findings at stress were not followed by a rest study”. Considering that 60% of patients show wall motion abnormality and perfusion defect at rest, normal findings at stress could be a sign of myocardial viability.

- There is still a number of methodological problems that currently hamper clinical application of RTP stress echo (for instance, off-line analysis, contrast agent costs, availability of dedicated software). Please comment.

- The Authors specify medications at time of testing in the table, but they should discuss the limitations of the stress test imaging, which is highly influenced by anti.anginal therapy.

**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