Reviewer's report

Title: The Importance of Achieving a Target Heart Rate to Determine the Normal Limit Value of Coronary Flow Reserve in the Territory of the Left Anterior Descending Coronary Artery During Dobutamine Stress Echocardiography

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Reviewer: Rosa Sicari

Reviewer's report:

This is an interesting study addressing a methodologic more than a pathophysiologic one when assessing CFR during dobutamine stress echocardiography. Authors demonstrate that the feasibility is very high or at least comparable with vasodilator stress testing more feasible than inotropic stressing. However there are several issues that authors should address:

In order to assess a pathophysiologic pattern of normality authors should have studied healthy volunteers. It is not clear which patients have been selected for the study. Please clarify what was the indication to stress echocardiography, and if you selected only subjects with normal function at rest and negative dobutamine stress echo.

To assess the feasibility of such a method the patient sample studied is too small. This feasibility is built inside ideal conditions that may hard to reproduce on consecutive patients.

Authors mention to medical therapy only in the discussion section of the manuscript but they should inform us on how many were an medical therapy, which therapy and if it was withheld before testing.

Authors excluded 1 patient because he did not show a normal CFR: please explain why.

In dobutamine as well as in exercise stress echocardiography the lack of achieving target heart rate may identify patients with worse prognosis as demonstrated by several groups, provided that medical therapy may influence it. Please comment.

The need to achieve target heart rate or at least a delta of 50 bpm is reasonable but authors should explain the pathophysiologic basis.

The correlation between HR and CFR is strong but we do not know how it works in positive tests or in patients with impairment of microcirculation. Please address.

In line with the previous comment the way results are presented is confusing. Please state that CFR was assessed at each stage and that the correlation were created on the overall sampling (as it appears from figures).

Due to authors' experience with vasodilator stress testing what is the potential advantage of using dobutamine stress echo when it appears that it is less
feasible and more demanding. Please comment.
The conclusion in the abstract are not clear and should be rephrased.
The title is too long
The references are incomplete and should be extensively revised. Please note
that Pellikka et al. Published on the use of CFR during dobutamine stress echo.
You may be interested in replacing ref.# 20 with a more recent one by F. Rigo:
tricks and pitfalls of CFR. Cardiovascularultrasound 2008

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests’