Author’s response to reviews

Title: 2-Dimensional Speckle Tracking Echocardiography Predicts Severe Coronary Artery Disease in Women with Normal Left Ventricular Function: A case-control study.

Authors:

Ryan Hubbard (Hubbard.Ryan@mayo.edu)
Maria Arciniegas Calle (Calle.maria@mayo.edu)
Sergio Barros Gomes (Gomez.sergio@mayo.edu)
Joyce Kukuzke (Kukuzke.joyce@mayo.edu)
Patricia Pellikka (Pellika.patricia@mayo.edu)
Rajiv Gulati (Gulati.rajiv@mayo.edu)
Hector Villarraga (villarraga.hector@mayo.edu)

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Author’s response to reviews:

Dear Sirs:

Thank you very much for your reviews and comments; this has definitively improved our manuscript significantly. Please find the response to your comments below. The changes will be found as tracked changes in the manuscript.

Reviewer #1: Authors define severe CAD as >50% blockage in one or more coronary arteries. Angiographic definition of a significant CAD is >70% stenosis in any epicardial coronary artery and >50% stenosis in the left main artery. I wouldn't use the word "severe CAD" as it gives the audience a wrong message.. I would rather use the word "CAD" for any patients with >50% stenosis..

Thank you very much for your feedback. This classification was based on current practice guidelines which place patients with higher than 50% stenosis at high risk for adverse cardiac events. Please refer to the references below.
References:


Also, authors mention that age was significant predictor for CAD and they adjusted for age during multivariate analysis, but they must mention the odds ratio for the same.

Thank you for your feedback. The odds ratio for age and CAD was 1.25 (CI 1.14-1.49). We have added it to the manuscript.

Reviewer #2: This is an interesting paper. The manuscript is well structured and written, the methods are thoroughly described and the statistical methods seem appropriate.

The work, however, contains some important limitations that affect the strength of the data presented.

1. Sample size is too small; furthermore the study group and the control group are too different. The control group should consist of elements that present the same characteristics
of the study group, except for the variable applied to the latter. In this work the control group is completely different from the study group, so it cannot be considered as a control group.

Thank you very much for your feedback. The sample size in our study was one of the limitations. It was driven by the difficulty in finding controls that had a normal coronary angiogram. We felt it was necessary to have objective evidence of no coronary artery disease in the controls. Unfortunately, in order to have the healthiest controls possible we could not match for age or any other risk factor. Our findings should be corroborated with further studies; however, we believe that the strong association found between GLS and dyssynchrony with CAD in women can become an important variable to measure in the workup of women patients with suspected CAD. In addition, we believe that the fact that dyssynchrony was still significant after adjusting for age, in a multivariate model, is an important finding.

2. The authors stated that the differences in strain and strain rate parameters remained significant after adjustment for heart rate, blood pressure, LVEF, and body mass index in a multivariate model, but the presence of left ventricular hypertrophy (LVH) is not specified despite the high presence of hypertension in the study group. This is a fundamental factor because LVH is associated with impaired myocardial strain and may be responsible for itself for lower values of myocardial deformation parameters described in the study, independently of the presence of CAD.

Thank you for your feedback. This is an excellent point. We acquired data for the left ventricular mass index in order to classify patients with a value of > 95 g/ m2 as having left ventricular hypertrophy. According to his classification, six patients in the CAD group had left ventricular hypertrophy. However, the mean LVMi was 92 g/m2 (SD 31 g/m2) in the CAD group and 74 g/m2 (SD 15 g/m2). When we added LVMi to the multivariate model, dyssynchrony remained significant with a p value < 0.01 (0.0061).

Reviewer #3: This is a really interesting paper about Speckle-tracking echocardiography. I have some minor concerns:

- First of all, when did you perform exercise stress echocardiography? Because in "Methods" you wrote about a Bruce protocol treadmill exercise stress test (stress ECG test?), not about stress echocardiography.

Thank you very much for your feedback. We performed a complete exercise stress echocardiography in all patients. This has been clarified in the manuscript.
- You defined "severe CAD" an occlusion of more than 50% in one or more vessel, while usually it could be consider severe a stenosis greater than 70%. How many patients of "CAD group" did receive percutaneous coronary angioplasty?

Thank you for your feedback. This classification was based on current practice guidelines which place patients with higher than 50% stenosis at high risk for adverse cardiac events. Please refer to the references below.

References:


- Your main findings were significant reduction in longitudinal S, CS and dyssynchrony in CAD group. It is difficult to find a homogeneous control group, but GLS may be lower in the "CAD group" also because of age (patients are significantly older than control group). In
particular, after adjusting for age, only mechanical dyssynchrony (1 SD of the GLS TTP) remained significant. And what about GLS value? Please clarify this aspect.

Thank you very much for your feedback. In order to have the healthiest controls possible, with a normal angiogram, we could not match for age or any other risk factor. Our findings should be corroborated with further studies; however, we believe that the strong association found between GLS and dyssynchrony with CAD in women can become an important variable to measure in the workup of women patients with suspected CAD. In addition, we believe that the fact that dyssynchrony was still significant after adjusting for age is an important finding. GLS did not remain significant after adjusting for age only dyssynchrony maintained its significance with a p value of 0.0061.

- Standard echocardiographic data: I don’t understand "EF 60 mmHg vs. 63 mmHg". Did you refer to ejection fraction? Please correct measurement unit.

Thank you. The units have been corrected.

- It is a retrospective collection of data, starting from angiography results; perhaps it could be consider another limitation of the study.

Thank you, we will add this to the limitations.

Sincerely,

Hector R. Villarraga, MD