Author’s response to reviews

Title: Global Longitudinal Strain is a more reproducible Measure of Left Ventricular Function than Ejection Fraction regardless of Echocardiographic Training

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Version: 1 Date: 07 Aug 2019

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Comments and responses to the reviewer’s comments

Reviewer #1: Global longitudinal strain is a more reproducible measure of LV function than EF regardless of echocardiographic training

This is not a highly original study but a well-done one. The results have been somehow published previously by the EACVI/ASE taskforce for strain. Nevertheless, the present results are well-displayed, convincing.

It would be nice to add other simple measurement done in echo to compare the robustness of GLS as compare to LVEF but also, as compare to LV end diastolic dimeter, LA volume, or E/A ratio.

Thank you for constructive suggestions which we believe will improve the manuscript. As suggested, we added two more echocardiographical parameters. LV end diastolic diameter (EDD) and E/e´ are implemented in the article under the sections of method and results. We choose to add E/e´ instead of E/A ratio since it can be measured in patients with atrial fibrillation. It is of interest to see how simple parameters are influenced by levels of expertise. GLS and LVEF describe systolic function and EDD and E/e´ are hemodynamic markers that partially describe diastolic function and filling pressures. The supplementary data added is
limited to the scenario when trainee analyze both trainee and expert images. Our results indicate this scenario to be the major source of variability. The main focus in this study was to investigate how levels of expertise influenced the evaluation of left ventricular systolic function with regional LV dysfunction due to ischemic heart disease.

The following is added in the manuscript: in the section “Method”: “Left ventricular end diastolic diameter was measured perpendicular to the left ventricle in parasternal long axis image measuring the distance from the septal endocardium to the endocardium of posterior wall in the end diastole at the level of the tips of the mitral valve. E wave express early diastolic mitral inflow velocity measured by pulsed doppler. e´ represent early diastolic septal mitral annular velocity. (Page 8, lines 5-10)

The results of statistical analysis of the added parameters was added in section “Results”: “When trainee comparing left ventricular end diastolic diameter in expert and trainee images ICC was 0.91 (0.85-0.95) with a systematic bias of -0.43 mm. ICC of E/e´ was 0.92 (0.85-0.95) with a systematic bias of 0.25 (Figure 6).” (page 10, lines 10-12)

Why did the authors focus on 47 patients and not 50, are there patients that were OK for the analysis according to expert and not to trainees?

This study was a sub study during a 5-year follow-up of an original echocardiographic study of acute coronary syndrome and strain. 126 patients participated in the original study. 21 patients declined further participation or were lost. 104 patients accepted participation in a follow up study, but only 47 were available for echocardiographic examination of both sonographers.

No patients were excluded by expert or trainee due to acoustic difficulties. Feasibility and image quality are reported in section of “Results” and in table 3 in the manuscript. Following is added in the manuscript:

Analyzing trainee images, trainee analyzed 17.3 (±1.2) segments versus expert 17.1 (±1.5), p=0.45. In expert images the trainee analyzed 17.4 (±1.0) versus expert 17.6 (±1.1), p=0.38. (page 9, lines 9-11)

Reviewer #2: This study demonstrates a superior reproducibility of GLS in comparison with LV EF in a population of 47 patients with CAD.
Concerns:

1. The authors should also present their own data on feasibility of both GLS and EF in the population assessed. It should be important also to report the rate of inadequacy of regional longitudinal strain measurements.

As noted in the manuscript section “Results, Echocardiographic data” (page 9, lines 5-6) there were no patients or images rejected for LVEF or GLS measurements. Image quality in LVEF measurements is reported in the manuscript in table 3 and was evaluated by the expert sonographer.

Several papers have reported high variability in segmental longitudinal strain [1, 2] even among expert readers. GLS is a sensitive marker of systolic function and ischemia and the main focus in our paper. Segmental longitudinal strain was, however, not specifically focused in our study because of recent data reporting low reproducibility on regional function by strain (Mirea and Voigt, JACCi). We do agree, however, that more detailed data on segmental longitudinal strain measurement feasibility should be reported. The following is added in the section “Results”:

Analyzing trainee images, trainee analyzed 17.3 (±1.2) segments versus expert 17.1 (±1.5), p=0.45. In expert images the trainee analyzed 17.4 (±1.0) versus expert 17.6 (±1.1), p=0.38. (page 9, lines 9-11)

2. A recent study (Negishi T et al, JACC CV Imaging 2017) showed that the precision in GLS measurements is improved after training, regardless the experience, in a multi-center study. This study shall be quoted in the reference list.

This study from major contributors in strain research is quoted/included in the reference list according to your good advice. (page 5, line 22 page 13, line 19 and page 15, line 36)

3. The lack of automatic LV EF measurements by 2D echo is a limitation which should be acknowledged in the "Limitations" section.

This is an important remark and the following has been added to the manuscript under section “Limitations”:

At present there are limited software available that allows automated LVEF measurement that could reduce inter observer reproducibility. (page 14, lines 6-8)
In Table 1, heart rate of the study population should also be reported. Moreover, the range of continuous variables could be welcome in this table. Heart rate is a factor that can influence strain measurements. We agree that this parameter should be reported. The parameter is added in Table 1 as well as range for all continuous data.
