Author’s response to reviews

Title: Associations of 2D speckle tracking echocardiography-based right heart deformation parameters and invasively assessed hemodynamic measurements in patients with pulmonary hypertension

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Version: 1 Date: 13 Apr 2020

Author’s response to reviews:

Dear Dr. Sicari,

We are submitting a revised version of our manuscript entitled “Associations of 2D speckle tracking echocardiography-based right heart deformation parameters and invasively assessed hemodynamic measurements in patients with pulmonary hypertension” (MS: CARU-D-20-00026). We were pleased by the evaluations and highly appreciate the constructive comments and suggestions made by the reviewers.

As detailed below, in the revised manuscript we have addressed all points raised by the reviewers (additionally, a track change version of the revised manuscript has been attached to this letter). According to the suggestion of reviewer No. 1, the manuscript was also revised by two fluent English speakers for language improvements. We look forward to receiving your response to our submission.

Sincerely,

Lena Theres, MD
Anna Brand, MD
Fabian Knebel, MD
Bernd Hewing, MD
Reviewer 1:

"This is an interesting original descriptive work related to noninvasive assessment of atrial and ventricular deformation in patients with invasively determined post-capillary PH. You have demonstrated at least moderate association between atrial/ventricular strains and PCWP/mPAP at the same time indicating that correlation results could be underestimated. What could be a potential source of underestimation? This issue needs to be explained and discussed. In theory, RA/RV myocardial strain should reflect the mechanical adaptation of right chambers to chronic pulmonary pressure overload. There are several adaptive mechanisms that are launched in this chronic process of post-capillary PH: geometry and shape change, myocardial wall hypertrophy, myocardial contractility. All these variables have an impact on myocardial strain measurements. Thus, I would not expect very strong relationship with pulmonary pressure components. Strain will probably never become a marker of elevated pulmonary pressure."

--We thank the reviewer for drawing our attention to this important point. We agree with the reviewer that there are several determinants of RA and RV strain besides RV afterload, such as RV and RA geometric assumptions, and that pulmonary pressure overload represents only one of the possible parameters impacting on right heart strain, independent of sample volume. We now discuss the reason for our moderate association findings in the discussion section (page 13, lines 324-328): “The reported moderate associations of RAS and RVS with invasive pulmonary pressures may be explainable by the fact that RAS and RVS are, next to an increase of RV afterload, significantly associated with geometric and structural properties of the RA and the RV (such as hypertrophy and remodeling processes) with impact on compliance and wall tension, as well as on systolic RV and LV performance.”

"It would be worth adding also data on RV stroke volume / RVOT TVI, RV diastolic function to see the relationship with RA/RV strain and PCWP/mPAP."

--We agree with the reviewer that associations of other RV parameters, such as RVOT VTI / stroke volume or diastolic RV function parameters, with RA and RV strain and invasive pressure measurements are worth to investigate. We therefore added data on RVOT VTI, as well as on RV e’ and RV a’ evaluated by TDI, to Table 2, and assessed correlation coefficients of these parameters with RA and RV strain, and with pulmonary pressures (revised results section, page 10, lines 264 – 266: “RVOT VTI and RV-a’ showed weak to moderate correlation with RAS and RVS (RVOT VTI: r=0.244, p=0.042; r=-0.306, p=0.015 for RAS and RVS; RV-a’: r=0.405, p=0.001; and r=-0.256, p=0.055 for RAS and RVS; respectively)” and Table 4).

Reviewer 2:

"The authors analyze the possibility of using 2D-STE in association with invasive parameters in the evaluation of patients with pulmonary hypertension. They found a good correlation between 2D-STE and hemodynamic parameters in patients with pulmonary hypertension, not in patients without. It should be noted that the group with HP has double difference from that without, regard to atrial fibrillation and CAD and MI and CABG. A multiparametric evaluation would probably have been helpful in assessing the weight of these differences between the two groups."
We are thankful for the suggestions of the reviewer and added a multiparametric analysis including the parameters RAS or RVS, respectively, in addition to atrial fibrillation, CAD, myocardial infarction, and history of CABG as supplementary material (Table S1 and S2). We found that none of the parameters had a significant impact on the diagnosis of pulmonary hypertension in this analysis. We further mention this issue in the revised results section: “Some of the clinical characteristics with possible impact on PH diagnosis were different between groups; however, none of these parameters showed significant associations with the diagnosis of PH in a multivariate logistic regression model (see Supplement, Tables S1 and S2)” (page 10 and 11; lines 266 – 269).