

**REPLY: Can Deep Learning Improve 2D Echocardiographic RV Assessment?****First Important Steps**

We thank Drs Kampaktsis and Giannakidis for their observations and comments on our recently published study,<sup>1</sup> in which we trained and validated a deep learning (DL) model for predicting right ventricular ejection fraction (RVEF) from 2D apical 4-chamber (A4C) view echocardiographic videos. We were well aware that we chose a very ambitious objective (ie, to infer a 3D analysis-derived parameter from a 2D image sequence depicting only a slice of the right ventricle [RV]), which should also be taken into consideration when interpreting our results.

We agree that comparing the  $R^2$  of our model with that of fractional area change (FAC) would be of interest. However, the referenced  $R^2$  of 0.760 for FAC should be interpreted with caution because it belongs to a linear regression model that was fitted to the data of 40 patients with pulmonary hypertension to assess the association between FAC and cardiac magnetic resonance imaging-derived RVEF.<sup>2</sup> When we applied this model to our external validation set, we got an  $R^2$  of 0.154 at the examination level. Nevertheless, it would not be appropriate to compare either of these  $R^2$  values with those reported in our study, given the considerations mentioned earlier.

It is worth speculating about multiple aspects of the benchmarking against simple visual assessment. First, we think that it was the right call to keep the evaluating cardiologist blinded to the rest of the echocardiographic study, all quantitative indices, and the clinical characteristics of the patients, because the DL model had no access to these either. Second, it should also be emphasized that the cardiologist had more than 10 years of experience in 3D echocardiography-based RV assessment. Thus, having a similar accuracy and higher sensitivity (at the expense of lower specificity) than such an expert is a great result and implies that our model can aid less experienced physicians in detecting RV dysfunction, even without the need for any quantitative indices of RV function, which are often challenging to measure in point-of-care settings and bear several other shortcomings.<sup>3</sup> Third, benchmarking against visual assessment is quite meaningful given that according to a recent worldwide survey, more than 40% of responders still assessed RV size and function qualitatively while performing echocardiography.<sup>4</sup> Finally, our model was benchmarked against visual assessment in detecting RV dysfunction only, but not in predicting RVEF on a continuous scale (ie, the primary task of the DL model).

Although there is little doubt that using multiple 2D views would improve performance, we intentionally opted for a simpler approach. Our hypothesis was that there is more RV-related information within a single A4C video than we would think at first. As indicated by the saliency maps, our DL model captured latent information from other cardiac structures, which resulted in good performance. One of the many advantages of a single-view-based approach is that it is well suited for point-of-care examinations performed with limited echocardiographic windows, under time pressure, and often by physicians with less experience in echocardiography. Importantly, the predicted RVEF values inherited the prognostic power of the ground truth, suggesting that we found an optimal balance between complexity and performance, and justifying the clinical usefulness of our model.

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