Reviewer’s report

Title: The value of left ventricular strain–volume loops in predicting response to cardiac resynchronization therapy

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Reviewer: Gianni Pedrizzetti

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This manuscript analyses a group of original mechanical parameters that can be improved predictors of CRT response. The parameters were constructed by the correlation between LV volume and principal strain (PS) at all instants of the cardiac cycle, both in global and segmental combinations, evaluated by speckle tracking of 3D echocardiography of the LV. The study is performed on 40 patients and 20 subjects are included as controls.

Overall, the analysis is interesting and the new parameter given by the correlation between MidLateral PS and Global volume loop (called R²-S/D coupling of MidSeptal PS-Global volume loop) provides better predictive power to CRT outcome. On the other side, also the simple MidLateral PS peak (1st item in table 3 and in table 4) presents a comparable ability to differentiate responder from non-responders at baseline. The new parameter (R²-S/D coupling of MidSeptal PS-Global volume) also performs slightly better than the simple MidLateral PS peak that is number two in performance in univariate logistic regression and not much worse in multivariate. Even the simple GLS value appears to significantly differentiate responder from non-responders at baseline (table 2 and 5).

Main Concerns:

1) The introduction of the new approach seems to work well only in the specific combination MidLateral PS-Global volume loop and this appears a consequence of the underlying differences in MidLateral contraction in these subjects. Therefore, the results do not provide a conclusive evidence of superiority of this approach to more simple measures. Authors should also test different measures of MidLateral strain (different direction, and synchrony/timing parameters) to confirm the superiority of using the "loop" approach with respect to the many possible strain-based measures.

2) The good results obtained by GLS appears in contradiction with existing results where GLS is definitely not a predictor of response to CRT. This suggests that the dataset may not fully represent the general behavior observable in this type of patients. Authors should better verify the basic results with respect to literature.

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