Reviewer’s report

Title: Pilot study using 3D-longitudinal strain computation in a multi-parametric approach for best selecting responders to Cardiac Resynchronization Therapy.

Version: 0 Date: 08 May 2017

Reviewer: Ivan Stankovic

Reviewer's report:

In this study, septal flash and SDIL,peak were the only dyssynchrony parameters associated with volumetric response in the multivariable model which is interesting.

In my opinion, the most important finding of the current study is that 3D strain-derived parameter could differentiate responders from non-responders among 18 patients without septal flash.

Therefore, if these results are confirmed by a validation study, it seems that mechanical dyssynchrony assessment should have 2 steps. As the first step, septal flash should be searched for using a simple visual and/or M-mode approach. If SF is not found, 3D echo should be performed in the next step as an attempt to detect a novel predictor of volumetric response proposed by the authors.

The authors could reshape the discussion section to emphasize these novel findings.

Also, Table 5 should include only parameters that were independent predictors of response, especially septal flash alone which is currently missing (from the results section, with Sn and Sp of 79%, SF was equal to, if not better than, SDIL,peak > 1,037%.s-1). Further, since the accuracy of the SDIL,peak > 1,037%.s-1 and septal flash combined was lower than that of SDIL,peak > 1,037%.s-1 alone, it appears that the latter parameter should mainly be assessed in patients without septal flash to improve detection of potential responders. According to Table 5, 5 (28%) patients without SF, who were initially misclassified as non-responders based on the absence of septal flash, were correctly identified as potential responders based on SDIL,peak > 1,037%.s-1, which is impressive. It would be nice to include video examples of patients without septal flash but with SDIL,peak > 1,037%.s-1 in the revised version of the manuscript.

- Only patients in sinus rhythm with good image quality were included in this study and also in other studies proposing strain-based methods for the quantification of dyssynchrony. In a real world scenario, atrial fibrillation is observed in approx. 25% of patients undergoing CRT implantation. Excluding such large proportion of patients is a serious limitation of any method and deserves to be underlined in the respective section of the manuscript.
- Only volumetric response at 6 months following CRT was assessed. However, it has been shown that almost a half of initial volumetric non-responders (after 1 year of CRT) might become responders after a longer period of time which questions this definition of response (Burns KV et al. JACC Heart Failure 2015). This is acceptable for a pilot study, but further validation studies should include harder end-points, especially given the fact that it has already been shown that the correction of septal flash by CRT is associated with improved long-term survival (PREDICT-CRT, EHJ CI 2016).

- If proposed dyssynchrony parameters are the substrate for volumetric response to CRT, it seems logical that they were corrected by CRT. The correction of dyssynchrony by CRT was not assessed in the present study which is, again, acceptable for the pilot study. However, it would be of interest to report what happened to the septal flash (was it corrected or not) in 3 non-responders who had it at the baseline visit.

- Low-dose dobutamine challenge might be useful to unmask or potentiate dyssynchrony, SF/ApRock (Parsai et al EHJ 2009, Stankovic et al EHJ 2013) in patients with no dyssynchrony at baseline.

Minor

ABSTRACT

"All attempts to improve patient selection for cardiac resynchronization therapy (CRT) using echo-derived indices have failed so far"

- This statement probably refers to the catastrophic results of the PROSPECT trial. There are other multi-center dyssynchrony studies since then and this sentence could be softened a bit.

METHODS

"The morphology was classified as either LBBB or non-LBBB (non-specific intraventricular conduction delay)."

- It should be clarified whether only patients with LBBB and non-specific intraventricular conduction delay were included. What about patients with RBBB?

"…the main aim during the implantation was to obtain the finest QRS at the end of the procedure"
- I guess the authors had "the narrowest" QRS in mind

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