Reviewer's report

**Title:** Diagnostic and Predictive Value of Speckle Tracking Echocardiography in Cardiac Sarcoidosis

**Version:** 0  **Date:** 01 Oct 2019

**Reviewer:** Sahar Abdelmoneim

**Reviewer's report:**

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Manuscript Number: BCAR-D-19-00759

Title "Diagnostic and Predictive Value of Speckle Tracking Echocardiography in Cardiac Sarcoidosis"

This is a single center retrospective study (time frame 2005-2016) evaluating 2-dimensional speckle tracking Echocardiography (2D-STE) and conventional echocardiographic parameters (LV and RV) in consecutive patients with definite or probable (defined as ≥50% likelihood) cardiac sarcoidosis (CS). CS was diagnosed per the Heart Rhythm Society consensus statement in 83 patients (25 with definite CS on Endomyocardial biopsy, and 58 Probable CS). A comparative age and sex matched cohort (n=97) without comorbidities or CS and normal echocardiographic findings were evaluated as control group. The authors further evaluated the prognostic value of 2D-STE parameters for cardiac events during a median follow-up of 26 months.

The authors concluded that abnormal left ventricular global longitudinal strain (LV GLS), inferoseptal and inferior wall strain and right ventricle global longitudinal strain (RV GLS) are good predictors of CS even if LV EF or RV systolic parameters are within normal limits. A cutoff of GLS (more positive than −14%) correlated with outcomes of heart failure and hospital admission.

The topic of the study is of great interest. The prevalence of CS reported and acknowledged by the authors in this current study is relatively high (68%) but closely correlates with the prevalence of CS reported in autopsy studies (70-85%).

Prior studies involved patients with sarcoidosis without cardiac involvement and tested the role of 2D-STE as a pre-clinical detection tool of myocardial impairment prior to LV dysfunction. In this study, the authors thoroughly assessed all 2D-STE strain and strain rate parameters for the
LV and RV in all comers of cardiac sarcoidosis patients (irrespective of the degree of cardiac involvements), which adds to the strength and uniqueness of the study.

Some minor comments for your consideration:

Introduction:

* Well written. Recommend adding a line on the study hypothesis.

Methods and statistics:

* Recommend adding a flow chart to describe the selection of the study cohort and illustrate the different study subgroups

* Blood pressure levels could influence LV longitudinal and circumferential strain values. Please clarify if matching by the degree of systolic blood pressure was attempted.

* Recommend adding: "consecutive" control patients were identified from the echo lab during the same time frame as the CS cases.

* For completeness of data please list the initial referral reason for Echocardiography in both the CS and control cohorts.

* In the section of "LV Deformation Parameters Assessed With 2D-STE": clarify the software module utilized for strain analysis (i.e. did the author utilize the auto strain feature or the CPA "cardiac Performance analysis" package) within Tom Tec Imaging System?

* Also please clarify if the RV 2-D STE analysis were done from endocardial border tracing only? Or endocardial as well as epicardial borders.

* Recommend adding a "Followup section" in the methods to list the outcomes of interest, definitions of the outcomes, and methods utilized to ascertain the outcome data (through medical chart or phone calls, etc.).

* Please clarify the statistical section of univariate analysis utilized and list if multivariate analysis were used.

Results:

* Accurate speckle tracking is dependent on the image quality. Please briefly comment on the feasibility of strain analysis in both CS and control groups.
Recommend adding a case example illustrating MRI or FDG uptake on FDG-PET and echo image with strain analysis to show correlative strain measurements with other.

Recommend reporting on the Lab inter-observer or intra-observer variability (inter class correlation coefficient) for 2D-STE parameters.

It is interesting to know if there is evidence of RV involvement or pattern of hyper-enhancement on other imaging in the group of patients having the cardiac MRI or PFDG PET available, and how did this correlate with RV involvement on.

It would be of interest, also to briefly comment on the Receiver operating characteristic curves or AUC for LV and RV GLS in the 23 patients with early stage of CS.

Also, was there any isolated RV involvement?

The authors reported a median follow period of 26 months and commented on outcomes of heart failure and hospital admission for cardiac complication. Please clarify this section further and classify the outcome per groups of CS. Also clarify if cardiac death as an outcome was documented?

Recommends expanding the result section pertaining the univariate logistic regression analysis. How did the RV GLS perform? and did the author adjust for other risk factors in those 83 patients.

Figures and Table; appropriate and clear. Recommend listing the total sample size utilized in Figure 1 for the Bull's eye illustration.

Discussion:

The authors acknowledged study limitations well.

Sarcoid myocardial infiltration was reported to begin in medial myocardial fibers affecting mainly longitudinal and radial LV deformations. Please comment on this considering the results displayed showing no significance for circumferential parameters.

Recommend, if possible, briefly discuss if the clinical applications of utilizing LV and RV GLS in CS can be expanded to differentiate between early active cardiac inflammation from fibrotic scar.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Acceptable

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