

Peer Review File

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Reviewer A

In this study the authors describe a retrospective study to explore the prognostic value of the left atrial strain rate in patients with severe DCM by cardiac magnetic resonance feature tracking (CMR-FT). A total of 58 patients were enrolled in this study, with a median follow-up length of 43 months (13-72 months). They discovered that LASRs had a good predictive value for cardiac events in individuals with severe DCM when the two models were adjusted for clinical risk factors and imaging measures. The manuscript may be useful for adding to the published knowledge database in similar areas. It does, however, have some limitations. There were a few misunderstandings and/or queries that the author needed to clarify:

- 1) Methods / study population: Is it LVEF > 35 percent in CMR or (e) LVEF < 35 percent in CMR when it comes to the exclusion criteria for patients? Please check.
- 2) Results/ CMR imaging: LA maximum volume index/ LA diastatic volume index/ LA minimum volume index were significant ($p < 0.05$) in univariable cox regression (Table 2). Why didn't the LA diastatic volume index include in multivariable cox regression? Please clarify.
- 3) Besides LA strain indices, please add LV strain in the analysis.
- 4) Results/ Analysis of correlation: Are there any correlation between LA strain rate and LV strain (like LV GLS, LV GCS)?
- 5) Is there some study of LA strain rate in DCM by speckle tracking using ultrasound? If so, what are the strengths of this study?

Response: Thank you for your recognition of our revised manuscript. We really appreciate all that you have done to improve our manuscript.

1. Methods / study population: Is it LVEF > 35 percent in CMR or (e) LVEF < 35 percent in CMR when it comes to the exclusion criteria for patients? Please check. Response: Thank you very much for the suggestion. The patients with LVEF < 35% were included and patients with LVEF \geq 35% were excluded in the present study. This typo has been corrected in the revised manuscript. (see Page 4, line 111)

2. Results/ CMR imaging: LA maximum volume index/ LA diastatic volume index/ LA minimum volume index were significant ($p < 0.05$) in univariable cox regression (Table 2). Why didn't the LA diastatic volume index include in multivariable cox regression? Please clarify. Response: Thank you very much for the reminder. In our study, the LA maximum volume index/ LA diastatic volume index/ LA minimum volume index were all significant ($p < 0.05$) in univariate analysis. The variance inflation factor (vif) was assessed to avoid collinearity. A parameter with a variance inflation factor greater than 4 was excluded from the multivariate analysis(1). (see Page 5, line 162-163). The vif of LA maximum volume index/ LA diastatic volume index/ LA minimum volume index were 18.31/2.39/18.47, respectively. Meanwhile, previous articles reported that LA maximum volume index was an important prognostic factor for dilated cardiomyopathy(2) (3). So the LA maximum volume index and LA diastatic volume index were included in multivariate analysis.(see Page 6, line 189-195 and table 3 Note) Reference : .1. Akinwande MO, Dikko HG, Samson A. Variance Inflation Factor: As a Condition for the Inclusion of Suppressor Variable(s) in Regression Analysis. Open Journal of Statistics 2015;Vol.05No.07:14. 2. Gulati A, Ismail TF, Jabbour A, et al. Clinical utility and prognostic value of left atrial volume assessment by cardiovascular magnetic resonance in non-ischaemic dilated cardiomyopathy. Eur J Heart Fail 2013;15:660-70.

3. Left Atrial Size Is the Major Predictor of Cardiac Death and Overall Clinical Outcome in Patients with Dilated Cardiomyopathy : A Long-Term Follow-Up Study. 1997. 3. Besides LA strain indices,

please add LV strain in the analysis. Response: Thanks for your suggestion, we have added the analyze of LVGLS, LVGCS and LVGRS under your suggestion in the revised manuscript (see method section, results section, table1, table2) .

4. Results/ Analysis of correlation: Are there any correlation between LA strain rate and LV strain (like LV GLS, LV GCS). Response: Thanks for your reminder, we have now added this correlation between LA strain rate and LV strain in the revised manuscript. (see table 4, page 6, line 206-211). LA SRs and LA SRe were both weak correlation with LVGLS, LVGCS; LA SRa was weak correlation with LVGCS. Parameter LA SRs LA SRe LA SRa r Value p-Value r Value p-Value r Value p-Value
LVGLS -0.33 0.012 0.32 0.013 0.22 0.102 LVGCS -0.38 0.003 0.30 0.025 0.28 0.036 LVGRS 0.28 0.077 -0.21 0.194 -0.26 0.100

5. Is there some study of LA strain rate in DCM by speckle tracking using ultrasound? If so, what are the strengths of this study? Response: Thanks for your suggestion. (a) Left atrial speckle tracking is applied to DCM, mainly in the difference of left atrial strain between idiopathic DCM and ischemic DCM(4), and the significance of left atrial strain in identifying whether DCM is complicated with atrial fibrillation(5).But there is rare study on the prognosis value of LA strain rate in DCM as far as we know. (b)The main strength of this study is that 1) DCM is often accompanied by an enlarged left atrium that cannot be detected by ultrasonography, heavy interference of gas exchange in the lungs, and a low signal-to-noise ratio. 2) CMR-FT could provide prognostic information regardless of LA size(6) and be superior to 2-dimensional echocardiography and exhibited outstanding inter-study reliability in normal, dilated, and hypertrophic hearts(7).(see Page 4, Line97-99,Page 7, Line252-259) Reference: 4.idiopathic dilated cardiomyopathy patients: A two-dimensional speckle tracking imaging study. J Clin Ultrasound 2016;44:437-45.

5. Kurzawski J, Janion-Sadowska A, Gackowski A, et al. Left atrial longitudinal strain in dilated cardiomyopathy patients: is there a discrimination threshold for atrial fibrillation? Int J Cardiovasc Imaging 2019;35:319-25. 6. Grothues F, Smith GC, Moon JC, et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol 2002;90:29-34. 7. Grothues F, Smith GC, Moon JC, et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol 2002;90:29-34.

Reviewer B:

1. Abstract: It should be made clear that it is all about idiopathic DMC. all abbreviations need to be defined when used first. yet, there is not enough evidence to suggest that LA strain can be used to guide therapy, etc.

Response: (a)Thank you very much for the suggestion. The patients included in our study were idiopathic DCM patients (LVEF<35%) . We include the term "idiopathic" in our definitions of DCM in the article. (see Page 4, line 111) (b)We apologized for this misunderstanding by our mistake in expression. As you said there is not enough evidence to suggest that LA strain can be used to guide therapy, etc. LA reservoir strain rate and active strain rate were powerful prognostic markers. The LASRs by MRI-FT provided independent prognostic value in patients with severe idiopathic DCM. (see Page8 , line 268-269)

2. Background: an introduction into the LA physiology would be good for the general reader. M&M: inclusion idiopathic DMC, exclusion ER <35% (typo?). Exclusion Afib? Results: Table X (typo?). The paragraph about LA volume is confusing.

Response: Thank you very much for the suggestion. (a) We added the LA physiology in introduction as "DCM is often associated with left atrial enlargement and impairment of left atrium reservoir function, conduit function, and pump function (8) (5). Previous articles reported that left atrial volume index was a prognostic factor for dilated cardiomyopathy(3). But the left atrial function cannot be fully explained by the degree of left atrial dilation in dilated cardiomyopathy(9). Strain and strain rate reflect various aspects of myocardial deformation and both measure different aspects of overall heart function, which can be used to assess risk, fatality rate, and prognosis of heart attack (10-12)." (see Page 3, line 83-85;- Page 4, line86-91) (b) The patients with LVEF< 35 were included in our study. This typo has been corrected in the revised manuscript. (see Page 4, line 111) (c) Bland-

Altman plot analysis as well as Intraclass correlation coefficient for strain rate measurements are shown in Table E1 (online). (see Page6, line 214-215); After additional adjustment for significant cardiac function factors, including mitral valve regurgitation, LA maximum volume index, LA diastatic volume index, the LASRs [HR 0.13, 95% CI (0.02,0.82), p=0.030]; the LASRa [HR 2.40, 95% CI (0.65, 8.83), p=0.189] (Table 3).(see,Page6 ,Line189-195, Page 3 Line 63-64) Reference: 8. Abdelghani Abdelzaher M, Atteia WM. Left atrial geometry and pump function in ischemic cardiomyopathy. *Int J Cardiol Heart Vasc* 2014;5:45-50. 9. Triposkiadis F, Pitsavos C, Boudoulas H, et al. Left atrial myopathy in idiopathic dilated cardiomyopathy. *Am Heart J* 1994;128:308-15. 10. Hoit BD. Left atrial size and function: role in prognosis. *J Am Coll Cardiol* 2014;63:493-505. 11. Ramkumar S, Yang H, Wang Y, et al. Association of the Active and Passive Components of Left Atrial Deformation with Left Ventricular Function. *J Am Soc Echocardiogr* 2017;30:659-66. 12. Chirinos JA, Sardana M, Ansari B, et al. Left Atrial Phasic Function by Cardiac Magnetic Resonance Feature Tracking Is a Strong Predictor of Incident Cardiovascular Events. *Circ Cardiovasc Imaging* 2018;11:e007512. 3.

3. Discussion: non ischemic and idiopathic is not the same.

Response: Thanks for your suggestion reminder, we apologized for our misunderstanding. Under your suggestion, We have modified and deleted the sentence “and might be damaged more in nonischemic dilated cardiomyopathy patients” in the manuscript. (Page 7, Line 248)

4. Conclusion: There is not enough evidence to suggest that LA strain may serve clinical parameter. Results are only applicable to patients with severe idiopathic DMC. How much time does it take for the additional sequences and assessment of the parameters? What is the correlation with probnp (mentioned in M&M)?

Response: Thanks for your suggestion reminder (a). There is not enough evidence to suggest that LA strain may serve clinical parameter. The conclusion was identified as “LA reservoir strain rate and active strain rate were powerful prognostic markers. The LASRs by MRI-FT provided independent prognostic value in patients with severe idiopathic DCM.” (Page 8, Line 268-269) (b).As we described in the M&M““The severe idiopathic DCM was diagnosed based on the World Health Organization/International Society and Federation of Cardiology criteria (13). The exclusion criteria were as follows: (i) patients with congenital heart disease (CHD); (ii) patients with valvular disease; (iii) patients having significant coronary artery disease (defined as showing at least 50% luminal stenosis), previous coronary revascularization, or myocardial infarction; (iiii) patients with an estimated glomerular filtration rate less than 30 mL/min/1.73 m² or implanted devices; (iiiiii) LVEF \geq 35% in CMR.”. Our research was indeed conducted on severe idiopathic DCM. (see Page 4,Line 104-112) (c)As we described in the M&M of the paper“A stack of short-axis single-shot balanced-standard steady-state free-precession sequence images was collected from apex to base with the two-,three-and four-chamber views.”that the left atrial sequence is included in the routine sequence without additional time. (Page 4, Line 114-118) It’s may take 5 mints to assessment of LA strain parameters. This was added in the in the revised manuscript(Page 5, Line137-138). (d)LA SRs was mild decreased with NT-proBNP value (r=-0.3, p=0.03). LA SRe and LA SRa were not significant correlated with NT-proBNP value .we have now added this correlation between LA strain rate and NT-proBNP value in the revised manuscript. (Page 6, Line 206, table 4) Parameter LA SRs LA SRe LA SRa r Value p-Value r Value p-Value r Value p-Value NT-proBNP value -0.30 0.030 0.24 0.093 0.20 0.149 13. Richardson P, McKenna W, Bristow M, et al. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies. *Circulation* 1996;93:841-2. 5.Table 1: Caption incomplete

Response: Thanks for your suggestion, we have modified the captions as your suggestion in table 1.