Reviewer’s report

Title: Clinical implication of disturbed left atrial phasic functions in the heterogeneous population associated with hypertension or atrial fibrillation

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Reviewer: Alex PW Lee

Reviewers report:

Zhu et al studied LA phasic strains and strain rates using STE in 4 cohorts - HT without AF, HT with AF, lone AF, and healthy subjects. They found that (1) the passive conduit and reservoir LA strains are impaired, with preserved pump functions, in HT subjects without AF; (2) LA pump function and synchrony were impaired in HT subjects with AF; (3) LA strains were impaired despite normal LA volume in lone AF patients; (4) ROC curve analysis of various phasic LA strain parameters show they could be used to discriminate HT subjects with vs without AF, or lone AF vs healthy patients.

This is an interesting paper, and of clinical relevance. It provides important data on the alteration in the LA phasic function in relation to occurrence of AF in HT patients and lone AF. The diagnostic cut-off values proposed by this paper is of potential diagnostic relevance in patients with suspected atrial arrhythmia in the setting of hypertension.

However, I have the following comments that would need the authors to address:

- page 4 line 73. please define new-onset AF in this study

- page 6 line 129-152: this is the main part of the results, with a lot of parameters and data that sometimes may appear confusing and difficult to follow. I would suggest the authors to more concisely summaries the major findings in the text, in a more logical sense that readers can more easily follow, while referring to the tables for detail data.

- please clarify whether patients are prospectively or retrospectively recruited.
- page 5 line 101-108: the authors calculate global strain and SR by averaging 12 segments from the 4 and 2 chamber views, but calculate the dyssynchrony by SD of the time to peak strain/SR of 15 segments of the 4, 3, and 2 chamber views - what is the rationale behind the different views and LA wall segments used in strain/SR vs dyssynchrony?

- Strain/SR ratio indices: why chose these ratio indices? while 3 ratios were analyzed for strain (pump/res, pump/cond, cond/res), only one ratio (SRpump/cond) was calculated? authors should add a paragraph explaining the physiological implication of these ratios they used.

- page 7-8, line 178-180: "Our findings suggest that (1) in early stage of hypertension, conduit function is first and most severely impaired, followed by reservoir function, while booster pump function is still preserved and contribution proportion of pump phase shows a compensatory increase.". This statement is not supported by data as this is not a longitudinal study.

- page 8, line 192-193: "In our study, the depression in PALSres, PALScond and PALScond shown in hypertensive patients suggested that LA conduit function was first and most severely impaired, followed by reservoir function." Again, a natural history of LA phasic function impairment with conduit strain impairment taking place first before reservoir strain is implied by the authors but not supported by data. Although the chronicity of HT is longer in the HT+AF group than the isolated HT group in this study (by merely 3 years and +/-4.5y SD), the comparison is still only cross-sectional between the two cohorts rather than longitudinal within the same cohort. One cannot conclude or imply that the isolated HT group will "progress" later to HT+AF group.

- LA reservoir strain is passive and primarily a reflection of the LV longitudinal systolic strain -- systolic LV longitudinal deformation pulls down the mitral annulus and thus stretch the LA. The impairment of LA reservoir strain and SR are likely reflecting impaired LV longitudinal strain in hypertensive subjects. The relations of LV GLS and LA passive strains as described by recent studies (Tang et al J Am Soc Echocardiogr 2019;32:503-513) and (Ersboll M et al. Circ Cardiovasc Imaging 2013;6:26-33) should be discussed.

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