Left Atrial Appendage strain and strain rate using Cardiovascular Magnetic Resonance feature tracking: a preliminary study on feasibility and reproducibility.

Abbreviations

LAA left atrial appendage

SR strain rate

ICC interclass correlation coefficient

CMR cardiac magnetic resonance

FT feature tracking

2D-CMR-FT 2-dimensional cardiac magnetic resonance feature tracking

LV left ventricle

SSFP steady-state free precession

Keywords: Left atrial appendage; CMR; Myocardial strain; feature-tracking.

Introduction

Over the past decade, left atrial appendage (LAA) function has been widely recognized as an important marker to predict the onset of adverse cardiovascular events [1]. Its active contraction prevents thrombus formation. When it is lacking, such as in atrial fibrillation[2], the thromboembolic risk is markedly increased. The mechanical properties of the LAA may regulate hemodynamic function through modulation of left atrial pressure in conditions of volume overload and increased left atrial pressure [2]. In addition to its mechanical properties, the LAA has a role in volume homeostasis through the secretion of atrial natriuretic factor [2].

As a consequence, clinicians should certainly focus their attention on LAA anatomy and function[1].

So far, different researches have evaluated LAA deformation by means of transthoracic echocardiography Doppler and Tissue-Doppler [2,1,] with some intrinsic limitations, such as the angle dependency that limit LAA assessment due to its oblique anatomy[3].

Nevertheless, since then there has been continuous research on new methods to assess LAA function [3,4]. Recently, strain and strain rate (SR) analysis have been proposed as a tool to assess LAA phasic function, but so far only a few studies evaluated LAA strain feasibility and reproducibility with speckle tracking echocardiography [3–5]. Conversely, no studies have assessed yet the potential role of Cardiac Magnetic Resonance (CMR), which has shown to be the reference standard in assessing ventricular and atria volumes [6,7,8]. In this setting, CMR already proved to be the mainstay in assessing ventricular and atrial functions. The purpose of our preliminary study was to evaluate the feasibility and reproducibility of CMR with Feature Tracking (FT) in evaluating LAA phasic function.

Material and Method

Study population

In this retrospective single-center study, we searched in our database all patients with a "chicken wing" morphology of LAA who underwent CMR between March 3rd, 2020, and February 7th,2021. Twenty healthy subjects and 40 patients with a clinical indication for CMR were retrospectively enrolled. The patient group included 20 consecutive patients from each of the following categories according to current diagnostic guidelines: acute myocarditis[9] and acute myocardial infarction[10]. Exclusion criteria included: subjects < 18 years old; contraindication to CMR (implantable devices, severe claustrophobia), or a history of renal disease with a current eGFR < 30 mL/min/1.73 m2. The control group comprised healthy subjects who had CMR to exclude scar-related ventricular tachycardia without known cardiovascular risk factors and had negative studies, were used as negative controls. Informed consent was waived because of the retrospective nature of the study. Flowchart of the patient enrolled was reported in **figure 1.**

CMR acquisition

CMR scans were performed using a digital 1.5 T scanner system (Philips Achieva dStream, *Philips Healthcare, Best, The Netherlands*). An 8 channels anterior cardiac coil arrays were used. Cine-CMR examinations were electrocardiogram triggered and performed during breath-holding.

Thirty phases were derived for each cardiac cycle. CMR protocol included functional sequences, such as cine bright blood steady-state free precession (SSFP) on the short axis and long axes (2 chambers, 3 chambers, and 4 chambers).

For feasibility assessment, the imaging quality of SSFP sequences was quality assessed[11]. Image quality was graded as not analysable (0), fair (1), good (2), and excellent (3).

CMR image post-processing

We used the commercially available software Circle CVI42 (*CVI42, Circle Cardiovascular Imaging Inc., Calgary, Canada*) for 2D-CMR-FT data analysis. 2D-CMR-FT analyses of left atrial appendage deformation were conducted offline. As shown in **Figure 2**, the ideal acquisition plan for a comprehensive assessment of chicken-wing LAAs corresponds to the acquisition plan of the two-chamber left ventricle (LV) view. The two-chamber LV view is prescribed from the four-chamber view (passing through the center of the mitral valve and the LV apex) and short-axis images (parallel to the ventricular septum)[12]. LAA endocardial borders were manually traced on long-axis view of the cine images when the LAA was at its largest area. In particular, the two-chamber views were used to derive LA longitudinal strain. We decided to include in our research only one morphological variant of LAA, represented by the most common subtype named "chicken wing".[13]

Figure 3 showed an example of LAA segmentation in healthy subject.

After manual segmentation, the software automatically tracked the myocardial borders throughout the whole cardiac cycle. The quality of the tracking and contouring was visually validated and manually corrected by a radiologist with 3 years of experience in cardiac imaging to cover the full thickness of the LAA wall. Global longitudinal strain was assessed by measuring the most negative peak during the LAA contractile period, as previously reported by Jankajova et al. in their transoesophageal study.[4]

The corresponding strain rate (SR) parameters were derived. All measurements were repeated twice, and the averaged value was used for calculation. For intra-observer analysis, the same observer, with 3 years of experience in cardiovascular imaging, performed strain analysis, repeating all measurements twice 1 month apart in random order to avoid recall bias.

For inter-observer analysis, two additional blinded observers with 5 and 1 years of experience in cardiovascular imaging respectively performed the same LAA strain analysis in a randomly set of 15 patients.

Statistical analysis

Continuous variables were presented as mean ± standard deviation (SD). Kolmogorov-Smirnov tests were used to check continuous variables for normal distribution.

Intra-observer and inter-observer variability were assessed by intraclass correlation coefficients (ICCs) and Bland-Altman analysis. ICC estimates and their 95% confident intervals (CI) were reported. Reliability was graded as poor if ICC <0.50, moderate if it was 0.50–0.75, good if 0.75–0.90, and excellent if >0.90. A p-value <0.05 was considered statistically significant. All statistical analysis was performed using IBM SPSS Statistics version 22 (SPSS Inc., Chicago, IL, USA)

Results

Patient included

We included 20 healthy subjects (13 males, mean age 39.7 ± SD 14,2 years.), 20 patients with AM (13 males, mean age 44,5 ± SD 20,4 years), and 20 acute myocardial infarctions (9 males, mean age 57,6 ± SD 6 years). 10 patients had to be excluded due to insufficient image quality of LAA, especially for inadequate scan plane. 10 patients were excluded owing to a morphological subtype of LAA different from the “chicken wing” variant.

Feasibility of LAA 2D-CMR-FT

2D-CMR-FT of LAA strain could be assessed and analysed successfully in all enrolled subjects and patients. **Figure 4** showed an example of the LAA strain in two subjects.

Imaging quality was graded good to excellent in 80% of patients and moderate to good in 20% of patients. Tracking quality was sufficient in all cases, based on visual checking and manual corrections. The average time taken to perform LAA strain analysis was 233 ± 132 seconds.

2D-CMR-FT *of LAA*

Table 1 shows global longitudinal LAA strain and its related SR average value per group. Both intra-observer and inter-observer ICC values were good to excellent (ICC = 0,91, and ICC =0,89, ICC =0,79, and respectively) for strain. Intra-observer reproducibility for global longitudinal LAA strain parameters per group of pertinence is also reported in **Table 2**. In all the groups under analysis, the reproducibility was good, and no significant differences were seen with respect to the group of pertinence. With respect to LAA SR values, both intra-observer and inter-observer reliability was moderate (ICC = 0,72, ICC = 0,53, and ICC = 0,56, respectively). Intra-observer reproducibility for global longitudinal LAA strain rate parameters per group of pertinence is also reported in **Table 2**.

Bland-Altmann plots showed no systematic errors and minimal differences for LAA strain and SR measurement as shown in **Figure 5.**

Discussion

To our knowledge, this is the first study aimed at evaluating LAA deformation measurement using 2D-CMR-FT and consequently, at assessing feasibility and reproducibility of CMR-derived LAA strain parameters. Overall, moderate to good intra-observer reproducibility of 2D-CMR-FT measurements of global LAA strain and SR was found. Reproducibility was better for strain rather than strain rate measurements and no difference in reproducibility were observed among different subgroups of patients and healthy subjects.

Transoesophageal echocardiography represents the reference standard in the evaluation of LAA contractile function, with some limitations such as its invasive nature, requiring oesophageal intubation[14]. Recently, CMR has emerged as a useful cardiac imaging technique for the non-invasive assessment of cardiac function and volumes, with the added value of tissue characterization in comparison with transoesophageal echocardiography. [14,7,8]

Myocardial strain by CMR is a growing field of interest that is experiencing a steady development, due to technological innovations the most. It allows deformation evaluation without requiring additional image acquisition [15,16].

2D-CMR-FT was applied in different cardiovascular diseases (CVD) resonance to assist health workers in diagnosis, treatment, and decision-making. Myocardial strain is able to detect subtle and early changes in ventricular and atrial cardiac muscle with high sensitivity in the subclinical phase of many CVD [17–19].

In our preliminary study, intra-observer reproducibility was higher for strain measurement than strain rate parameters. This result is in accordance with other reports, which were focused on studying ventricular and atria function [20,21,22,23]. Interestingly, we observed no difference in reproducibility between healthy subjects and patient groups under analysis. This point may be crucial for the reproducibility of LAA strain in the assessment and follow-up of patients that suffering from different cardiovascular diseases.

The assessment of LAA strain and SR parameters might be improved: (1) using dedicated SSFP sequences focused on LAA; (2) even better, taking care of the plane of 2-chambers acquisition, looking for including all LAA in the same slice. This method does not require further CMR image acquisition and does not increase the examination time.

Our study has some weaknesses. The major limitation is the relatively small and heterogeneous sample size and the retrospective selection of the patients' cohort. Again, we assessed the reproducibility of the used imaging technique without analysing the diagnostic and prognostic role of LAA between the groups under analysis. Although 2D-CMR-FT models have been validated for global strain in the left ventricle, to the best of our knowledge there is no software available for the analysis of LAA strain. Consequently, we used the ventricular endocardial borders segmentation tool. Finally, we used a single cardiac MRI software to analyse LAA strain without the possibility to assess inter-vendors feasibility and reproducibility.

Conclusion

2D-CMR-FT allows to quickly assessment LAA strain and SR parameters from moderate to good intra-observer reproducibility It is equally feasible in healthy subjects and in those suffering from different CVD, namely heart attack and acute myocarditis. Further studies to evaluate and develop the application of 2D-CMR-FT in assessing LAA strain parameters are mandatory to improve and validate this method in clinical routine.

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Figure Legends

Figure 1: Flowchart of the patients enrolled in our preliminary study.

Figure 2: A demonstration of enrolled and excluded patients from the study in relation to LAA images quality.

Figure 3: Example of Left atrial appendage strain (LAA). We selected only patients with "chicken wing" morphological type of LAA (figure 2a). LAA endocardial borders were manually traced on 2-chamber view. After manual segmentation, the software automatically tracked the myocardial borders throughout the entire cardiac cycle. The quality of the tracking and contouring was visually validated and manually corrected (figure 2b)

Figure 4: Example of left atrial appendage (LAA) strain (figure 3a) and strain rate parameters (Figure 3b) in two subjects. Global longitudinal strain as well as its strain rate measurements was assessed by measuring the most negative peak during the LAA contractile period (arrow in figure 3a and 3b).

Figure 5: Bland-Altman plots for intra- (fig 5a) and inter-observer (fig 5b) reproducibility of LAA strain and strain rate

Tables

Table 1: Comparison of healthy subjects and patients groups regarding demographics characteristics and left atrial appendage strain parameters.

	Global	Control	Acute Myocarditis	Myocardial infarction
Age	47,26 ± 13,53	39.7 ± 14,2	44,5 ± 20,4	57,6 ± 6
Males	40/60, 66 %	13/20, 65%	12/20, 60%	9/20, 45%
LAA Strain	-7,33 ± 4,8	-7,81 ± 5,35	-8,2 ± 5,5	-4,5 ± 1,6
LAA SR	-1,62 ± 0,76	-1,9 ± 0,84	-1,39 ± 0,42	-1,07 ± 0,43

LAA left atrial appendage, SR strain rate.

Mean +/- DS

Table 2: ICCs for Intra- and inter-observer reproducibility of LAA strain and SR parameters

	Intra-observer	Inter-observer 1	Inter-observer 2
LAA strain	0,79 (0,60 – 0,89)	0,89 (0,69 – 0,96)	0,91 (0,77 – 0,97)
LAA strain rate	0,53 (0,26 – 0,72)	0,72 (0,16 - 0,96)	0,56 (0,90 – 0,82)

	Intra-observer			Inter-observer			Inter-observer		
	Control subjects	Acute myocarditis	Myocardial infarction	Control subjects	Acute myocarditis	Myocardial infarction	Control subjects	Acute myocarditis	Myocardial infarction
LAA strain	0,70 (0,22 – 0,88)	0,82 (0,18 - 0,92)	0,79 (0,18 – 0,95)	0,83 (0,22 – 0,96)	0,95 (0,60 – 0,99)	0,72 (0,2 – 0,96)	0,91 (0,38 – 0,99)	0,96 (0,52 – 0,99)	0,59 (0,2- 0,82)
LAA strain rate	0,61 (0,10 – 0,74)	0,54 (-0,29 - 0,88)	0,68 (-0,27 – 0,92)	0,67 (0,11 – 0,81)	0,49 (-0,22 – 0,85)	0,63 (0,3 – 0,81)	0,51 (- 0,21 – 0,82)	0,52 (-0,11 – 0,94)	0,49 (0,10 - 0,68)

ICC intraclass coefficent, LAA left atrial appendage; SR Booster strain rate