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Reproducibility of global left atrial strain and strain rate between novice and expert using multi-vendor analysis software

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Abstract

Left atrial (LA) strain is an emerging technique with potential applications including arrhythmia prediction in atrial fibrillation and early identification of atrial dysfunction. The aim of this study was to evaluate reproducibility of LA strain and strain rate (SR) using multi-vendor analysis software between novice and expert. For LA strain to be a reliable tool, the technique must be reproducible by observers with variable experience. Use of multi-vendor analysis software allows serial strain assessment when echocardiographic images are acquired using different vendors. Fifty subjects underwent 2D-Speckle tracking echocardiographic (STE) derived LA strain and SR analysis measured from apical four and two-chamber views. Three strain parameters of LA function were assessed: reservoir (S-LAs, SR-LAs), contractile (S-LAa, SR-LAa) and conduit (S-LAs–S-LAa, SR-LAe). Strain analyses were performed by 2 independent, blinded novice and expert observers using multi-vendor analysis software. Intraobserver and interobserver analyses were performed using intra class correlation coefficients (ICC) and Bland–Altman analysis. LA strain and SR measured by novice observer demonstrated excellent intraobserver reproducibility (ICC for all strain and SR values > 0.88). There was good interobserver agreement of LA strain values between novice and expert (S-LAs:ICC 0.81, S-LAe:ICC 0.82, S-LAa:ICC 0.74). SR values also demonstrated good interobserver agreement (SR-LAs:ICC 0.83, SR-LAe:ICC 0.79, SR-LAa:ICC 0.86). Of all parameters, SR-LAa had the best interobserver and intraobserver agreement (ICC 0.86, 0.96). Global LA strain and SR values were highly reproducible by novice strain reader using multi-vendor analysis software. Interobserver reproducibility between novice and experts were good and acceptable within limits of agreement.

Keywords Left atrial strain · Atrial function · Atrial deformation · Left atrium · Strain · Reproducibility

Introduction

The left atrium (LA) plays an important role in overall cardiac performance, including contribution to left ventricular (LV) stroke volume with atrial contraction. Loss of LA function has been shown to be an important determinant of morbidity and mortality in normal populations and in various pathologic conditions [1]. To date, methods for assessing LA function have been limited. The most universally utilised

surrogate for LA remodelling and dysfunction has been the LA volume indexed to body surface area (LAVI). There is increasing evidence that LAVI is an insensitive marker for detecting early LA dysfunction, hence the demand for other methods to assess LA function. LA strain is an emerging tool for assessment of LA function in pathologies such as atrial fibrillation and in detection of sub-clinical cardiac involvement in a variety of disease states [2–4].

LA strain research has rapidly evolved in the last few years and, with an expanding number of possible applications, will likely progress to the clinical arena. Importantly, two recent publications by Pathan et al. and Sugimoto et al. have documented normal ranges for LA function in healthy subjects [5, 6].

There are several aspects of this study that are important to assist in uptake of LA strain into practice. For LA strain to be practical and applied outside the research arena, the technique must be easy to learn and reproducible over

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time, by observers with variable experience. Reproducibility studies and documentation of the learning curve for LV global longitudinal strain (GLS) analysis have been vital for uptake into clinical practice [7, 8]. Inter-vendor consistency is another technical aspect that limits routine clinical practice of LV GLS. These challenges in widespread standardisation and implementation of LA strain led to formation of an EACVI/ASE/Industry combined Joint Task Force. This group of experts have published a consensus document in an effort to standardise LA strain among vendors [9]. Adoption of multi-vendor acquisition software may help overcome this issue.

The aim of this study was to evaluate the reproducibility of LA strain and strain rate (SR) between expert and novice strain observers using multi-vendor acquisition software.

Materials and methods

Study population

We retrospectively selected 70 patients who underwent coronary angiography and two-dimensional (2D) transthoracic echocardiography for a variety of clinical indications which included acute coronary syndromes, heart failure, and valvular heart disease. 50 patients were included for LA strain analysis. 20 patients were excluded due to arrhythmia (n=6) or suboptimal atrial image quality (n=12). Atrial fibrillation was excluded to enable assessment of sinus rhythm-specific LA strain parameters in all patients.

Study design

This is a retrospective study in which LA strain was analysed in 50 patients who underwent transthoracic echocardiography image acquisitions carried out by different sonographers, using different vendors' echocardiographic machines. Echocardiograms were obtained as a part of routine clinical practice. There were two observers (one expert and one novice) who undertook offline strain analysis using multi-vendor analysis software (TomTec Imaging Systems, Germany) on the same 50 patients. The novice and expert strain assessors were blinded to patient clinical details and the results of the other observer at time of strain analysis. Another blinded repeat analysis at least 1 week later was performed by the novice using the same images from the same cardiac cycle. Intra and interobserver agreement was evaluated between the novice and expert observers.

The expert observer has experience equivalent to Level III training in echocardiography with > 3 years of extensive clinical and research experience in strain analysis. The novice observer was a cardiology fellow in training with competency in echocardiography acquisition but no prior experience in performing strain analysis. The novice received one, 30-min education session on LA strain measurement prior to commencing which included a hands-on, supervised offline strain analysis on three consecutive patients. The study was approved by the ethics committee of the local institution.

Echocardiography/LA strain

Echocardiograms were performed using several commercially available high end ultrasound systems. Images were acquired in Digital Imaging and Communications in Medicine (DICOM) format with an average frame rate of 53 frames per second. LA deformation assessment was carried out using the latest 2D-STE multi-vendor analysis software, TomTec, which utilises algorithms designed for LA analysis (2D Cardiac Performance Analysis, TomTec-Arena version 4.6, TomTec Imaging systems, Unterschleissheim, Germany). Images were excluded from analysis if any part of the LA wall was out of the field of view.

2D-STE derived LA strain, and SR were measured by manually tracing the LA endocardial borders in the apical four (A4C) and two-chamber (A2C) views using a point-and-click technique a software determined end systolic frame (illustrated in Fig. 1). The software automatically generated tracking of the LA endocardium with an additional epicardial line creating the region of interest. The pulmonary veins and LA appendage were excluded from the analysis. For each LA strain analysis in the A4C or A2C view, the Tomtec software divides the LA myocardium into three segments: the left wall, right wall and the roof. Four LA longitudinal deformation curves are subsequently generated—one for each of the three LA segments and an average GLS curve. GLS curves (not regional strain) were analysed. Strain calculations were initiated from the onset of the QRS (R–R gating). When using QRS gating, the strain values are all positive and timing is described according to ventricular systole/diastole. Average strain and SR measurements were collected for the three major LA functions: reservoir, conduit and contractile [3, 4]. In this study they were denoted as follows:

- *LA Reservoir function* (S-LAs and SR-LAs): represents LA expansion as the mitral valve is closed and the LA fills via the pulmonary veins. During systolic filling, the LA wall is "stretched" lengthening in the longitudinal direction and this gives a positive strain value. Estimated using the peak positive strain value corresponding to the period between the R wave and T wave on the ECG. Reservoir SR is the peak positive value in systole.
- *LA Conduit function* (S-LAe = [S-LAs–S-LAa] and SR-LAe): represents the transfer of blood from the LA to the LV during early diastole due to a small pressure gradient.

Fig. 1 Apical four and two-chamber view of the LA are used to manually trace the LA endocardial borders in end systole using a point-and-click technique
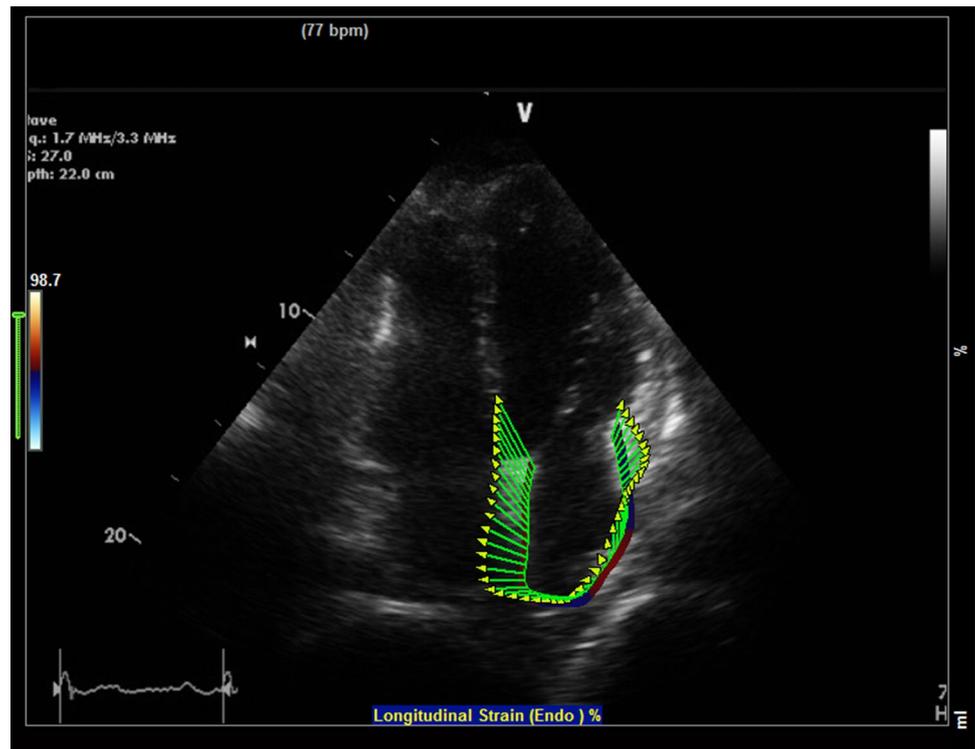
Is the difference between the reservoir and contractile strain values. The corresponding SR value is negative (as it occurs during passive LA emptying where there is a reduction in LA size and La myocardial shortening in the longitudinal direction) and is assessed in early diastole.

- *LA Contractile function* (S-LAa and SR-LAa): active LA contraction augments LV stroke volume at end LV diastole, with the strain and SR curve values corresponding to the ECG P-wave. The corresponding SR value is also negative as the LA is contracting and the LA myocardium further shortens in the longitudinal direction.

Figure 2 illustrates the LA strain and SR curves and measurement of the three atrial functions with comparison to traditional Doppler parameters. Figure 3a, b illustrate typical LA strain and SR curves and the determination of the LA function values.

Statistical analysis

Continuous data were presented as mean values $\pm$ SD. Data were analysed using standard statistical software (SPSS Version 13; SPSS, Inc, Chicago, IL). For all strain measurements the interobserver and intraobserver variability was assessed using intraclass correlation coefficients (ICCs) and Bland–Altman analysis. Absolute mean strain measurements were compared between novice and expert using

paired t-test. A p value of < 0.05 was considered statistically significant.

Results

### Demographics, clinical and echocardiographic parameters

The final study population consisted of 50 transthoracic echocardiograms from a heterogenous group of subjects. There were high rates of cardiovascular risk factors in this patient group as is highlighted in Table 1. Significant valvular disease was present in 6% (n = 3) of the patients. LV systolic dysfunction was seen in 30% of patients (50% dilated cardiomyopathy; 44% ischemic cardiomyopathy, 6% other).

Echocardiographic images were acquired using commercially available high end ultrasound systems (GE Vivid E95: n = 38, Phillips iE33: n = 10 and Siemens SC2000 Systems: n = 2).

Inter observer and intra observer variability

LA strain measured by the novice strain reader demonstrated excellent intraobserver reproducibility. The ICC for all strain and SR values was > 0.88. The SR-LAa showed the highest intraobserver variability (ICC = 0.96 [95% CI 0.92–0.98]).

Fig. 2 LA strain and SR curves
and measurement of the three
atrial functions with comparison
to traditional Doppler param-
eters view on the mitral inflow
and pulmonary venous pulse
wave Doppler traces
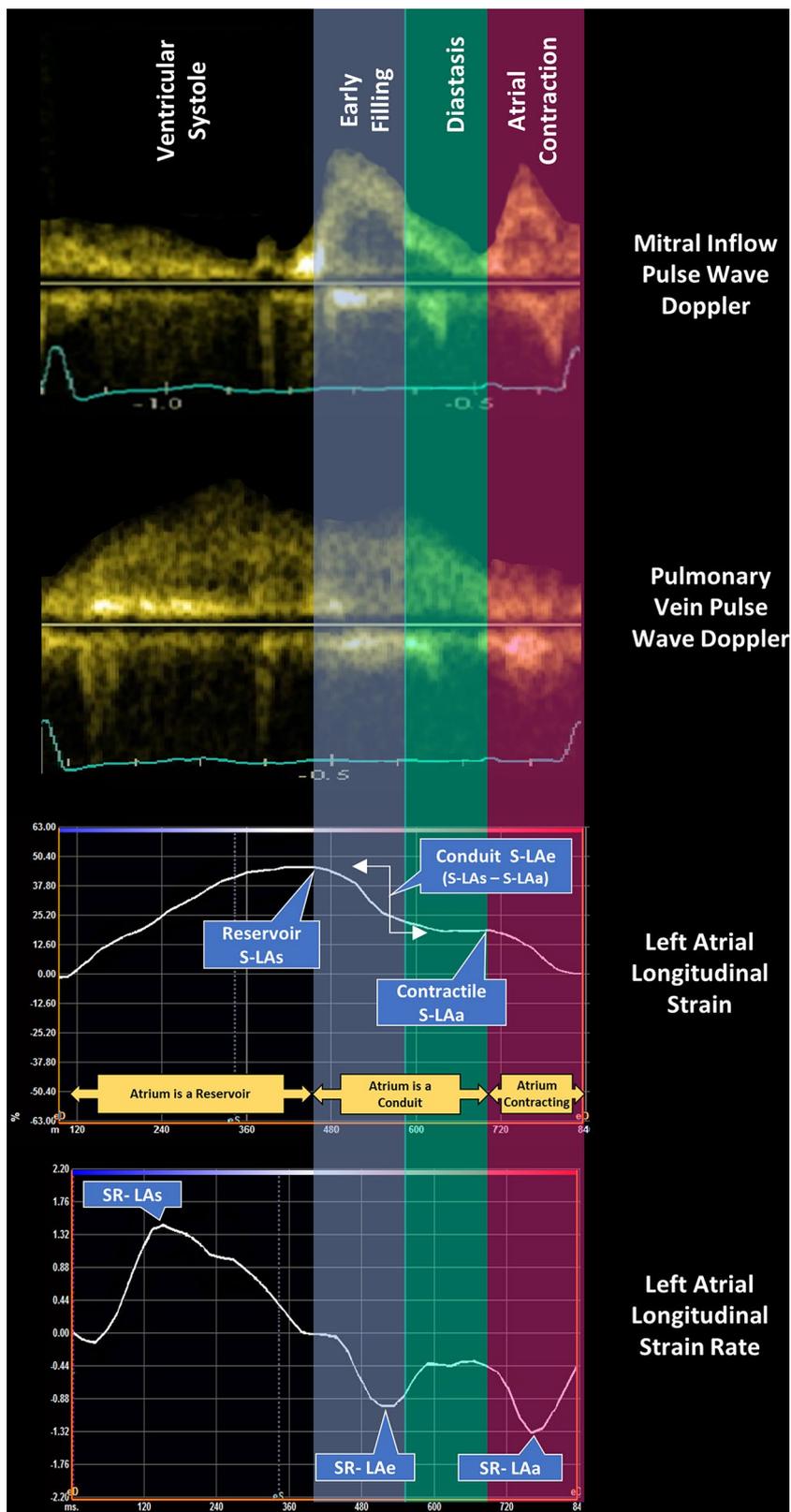
Intraobserver agreement was better than interobserver agree-
ment for all strain and SR values. (Tables 2, 3).

Strain values showed good interobserver agreement:
S-LAa had the lowest agreement (ICC 0.74 [95% CI

Fig. 3 a Typical LA strain curve with determination of the three LA functions: reservoir, conduit and contractile strain. **b** Typical LA SR curve with illustration of the reservoir (peak systolic, SR-LAs), conduit (early diastolic, SR-LAe) and contractile (late diastolic, SR-LAa) SR measurements
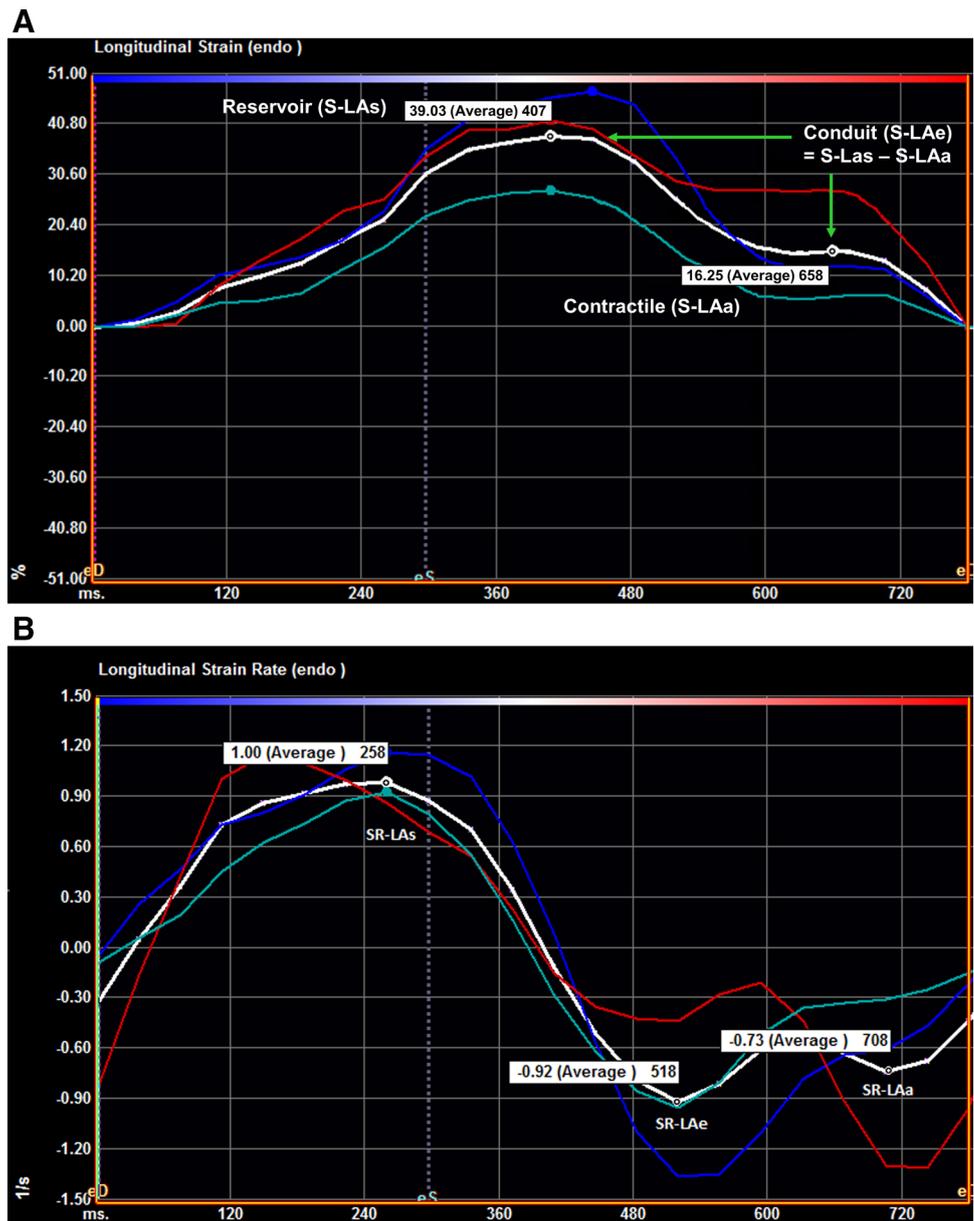

Table 1 Clinical and resting echocardiographic characteristics

Variable	Value
Age (years)	59 ± 12
Body surface area (m²)	2.0 ± 0.3
Heart rate (beats per minute)	70 ± 11
Valvular disease	6 (12%)
Coronary artery disease	28 (56%)
Type 2 diabetes	16 (32%)
Hypertension	30 (60%)
Ejection fraction (%)	54 ± 12 (range 22–75)
LA volume indexed to BSA (LAVI; ml/m²)	35 ± 10 (range 16–69)
Enlarged LA volume (LAVI > 34)	26 (52%)

Data are expressed as mean $\pm$ SD or as a number (percentage)

0.31–0.88]) whilst S-LAs and S-LAe had better agreement (ICC = 0.81 [95% CI 0.20–0.94] and ICC = 0.82 [95% CI 0.68–0.90] respectively). SR values also showed good interobserver agreement (ICC ranging from 0.79 to 0.86). SR-LAa had the highest interobserver agreement whilst SR-LAe had the lowest agreement. SR values were generally more reproducible than strain values between the novice and expert readers. Notably, the strain values for all parameters measured by the novice observer were statistically significantly lower than those by the expert but the absolute difference is minimal. (Table 3).

Table 2 Novice intraobserver variability for LA strain and strain rate (SR) values

Variable	Novice 1	Novice 2	p value	R value	LOA	ICC
S-LAs (%)	32 ± 10.7	31.2 ± 9.4	0.98	0.92	-8.37 to 8.34	0.91 (0.85–0.95)
S-LAe (%)	16.6 ± 6.8	16.4 ± 7.1	0.62	0.88	-6.69 to 6.23	0.88 (0.79–0.93)
S-LAa (%)	15.5 ± 7.1	15.7 ± 6.6	0.62	0.90	-5.77 to 6.20	0.90 (0.84–0.94)
SR-LAs (S^{-1})	1.13 ± 0.35	1.11 ± 0.32	0.27	0.88	-0.35 to 0.3	0.88 (0.79–0.93)
SR-LAe (S^{-1})	-0.88 ± 0.31	-0.88 ± 0.32	0.95	0.88	-0.30 to 0.30	0.88 (0.80–0.93)
SR-LAa (S^{-1})	-1.21 ± 0.58	-1.22 ± 0.58	0.48	0.96	-0.36 to 0.32	0.96 (0.92–0.98)

LOA limits of agreement, *ICC* interclass correlation coefficient, *S-LAs* peak systolic or 'reservoir strain', *S-LAe* conduit strain, *S-LAa* contractile strain, *SR-LAs* peak systolic SR, *SR-LAe* early diastolic SR, *SR-LAa* late diastolic SR

Table 3 Interobserver variability for LA strain and strain rate (SR) values between expert and novice

Variable	Novice	Expert	p value	R value	LOA	ICC
S-LAs (%)	32.1 ± 10.7	37.3 ± 11.4	< 0.0001	0.91	-4.25 to 14.76	0.81 (0.20–0.94)
S-LAe (%)	16.6 ± 6.8	18.3 ± 8.2	0.0089	0.85	-6.84 to 10.18	0.82 (0.68–0.90)
S-LAa (%)	15.5 ± 7.1	19.1 ± 7.7	< 0.0001	0.82	-5.10 to 12.26	0.74 (0.31–0.88)
SR-LAs (S^{-1})	1.13 ± 0.35	1.28 ± 0.35	< 0.0001	0.91	-0.14 to 0.44	0.83 (0.29–0.94)
SR-LAe (S^{-1})	-0.88 ± 0.31	-0.97 ± 0.35	0.0022	0.83	-0.48 to 0.30	0.79 (0.62–0.89)
SR-LAa (S^{-1})	-1.21 ± 0.58	-1.39 ± 0.56	< 0.0001	0.90	-0.68 to 0.31	0.86 (0.57–0.94)

LOA limits of agreement, *ICC* interclass correlation coefficient, *S-LAs* peak systolic or 'reservoir strain', *S-LAe* conduit strain, *S-LAa* contractile strain, *SR-LAs* peak systolic SR, *SR-LAe* early diastolic SR, *SR-LAa* late diastolic SR

Discussion

LA strain is an evolving echocardiographic technique for assessment of LA function that has been studied in a variety of clinical settings [10]. In this retrospective study we sought to investigate the reproducibility of LA strain between an expert and novice LA strain reader. The results demonstrated that LA strain and SR measurements were highly reproducible by a novice strain reader after a short training session. The ability to measure LA function is important as the LA contributes to maintenance of cardiac output, and abnormalities in LA function play an important role many cardiac pathological conditions. Quantification of LA functions is challenging. LAVI has been widely utilised as a surrogate for LA function though there is increasing evidence that LAVI is not a sensitive marker for detecting early LA dysfunction [2, 11]. There are many studies investigating the clinical relevance and application of LA strain and SR over and above LAVI, hence the importance of demonstrating that LA strain measurements are reproducible [12–18].

Despite the plethora of recent literature confirming the potential benefit of LA strain imaging, the technique must be demonstrated to be reproducible and easy to learn in order for the technology to progress from a research tool to routine clinical practice. In a busy echocardiography laboratory where a multitude of measurements are taken as a part of any one study, additional measures must be of high yield, and be accurately measurable by observers of varying skill levels at serial time points. For example, a junior sonographer and a senior strain reader should achieve similar values. There has been work in this area suggesting good to excellent reproducibility. Kadappu et al. assessed reproducibility using EchoPAC LV strain software (GE Vingmed Ultrasound AS, Horten, Norway) in 76 patients with CKD. They found inter observer variabililty to be excellent for LA reservoir strain (ICC > 0.95) and LA SR values (ICC > 0.88) [15]. Notably, strain was more reproducible than strain rate. Sareban et al. and Oxborough et al. assessed STE derived atrial strain in 20 patients and also found very good intraobserver variability (ICCs > 0.9) [18, 19]. Sareban et al. also found moderate inter observer variability (ICCs 0.8–0.9) [18].

LA size and function can be assessed using other imaging modalities, particularly cardiac MRI (CMR). LA strain assessment by CMR has been validated in several studies with reported excellent reproducibility [20, 21] A multiethnic study of atherosclerosis (MESA) sub study reported ICC > 0.9 for reproducibility for this CMR technique [21]. This is an area for further study, however CMR has the limitations of lower availability, higher cost and requirement for gadolinium contrast.

The findings of our current study confirm that LA strain is reproducible and easy to learn for a novice observer even in a diverse heterogeneous patient population with a multitude of pathologies. There was a small absolute difference in all strain parameters, with underestimation by the novice reader compared to the expert. This is most likely related to technique and may be improved by additional supervised training for the novice. LV strain has been through a similar development and validation process, including documentation of the learning curve required to achieve strain analysis competency by Chan et al. [8]. Determination of a left atrial strain learning curve would useful for further validation of left atrial strain as a reproducible technique.

The ICC range was noted to be wider for the reservoir and contractile strain values when examining the inter-observer variability (Table 3). The ICC values for these LA functions were particularly lower on the apical-4-chamber compared with the apical-2-chamber measurements. As the echocardiographic images used were taken as a part of routine clinical practice, this variability may be due to inadequate optimisation of LA image acquisition i.e. use of dedicated, non-foreshortened LA views and optimal image temporal resolution. The apical-4-chamber LA strain analysis requires exclusion of the LA appendage and pulmonary veins, which will be more difficult with suboptimal image quality.

Many studies have demonstrated differences in LV strain values when directly comparing acquisition from different vendors, particularly when evaluating segmental LV strain [22–24]. Shiino et al. have shown that although inter-vendor agreement in GLS and regional strain measurements have improved, a significantly wide variation in measurements still exists and this remains relevant for serial measurements on the individual patient [25]. For this reason it has been advised that serial strain measurements should be followed up using the same vendor and even same version of software, but this is not always feasible in a large multi-vendor echocardiography laboratory [7, 26, 27]. Vendor-independent analysis software may be of use to circumnavigate the problem of inter-vendor inconsistencies with strain measurements. Pathan et al. assessed LA strain reproducibility for 20 cases using multi-vendor analysis software (Tomtec) and found good to excellent inter observer reproducibility with this software [17]. The recent EACVI/ASE 2018 task force document aiming to standardise LA strain parameters, measurement and software packages is an important step forward in the field of LA strain research [9]. This document not only outlines suggested standard nomenclature and acquisition of LA strain parameters, but also highlights that differences between vendor software for strain assessment remain a very important barrier to widespread use and applicability of LA strain [7]. Our study utilised a multi-vendor analysis software (TomTec) for strain analysis which provided an easy to use platform and allowed rapid LA strain assessment by a novice user even when echocardiographic images were acquired from different vendors. Use of multi-vendor analysis software to assess LA strain may potentially help overcome issues with inter-vendor incompatibility that has been observed with LV strain assessment.

Study limitations

The study was not designed to assess the accuracy of LA strain measurements as there was no comparison to gold standard. This study was focused on determining the reproducibility of LA strain measurements between an experienced and a novice observer. Adequate image quality is important for STE because the LA is in the far field and is a thin walled structure, thus prospective image acquisition with a focus on LA optimisation would benefit further LA strain study [12].

The results are only applicable to multi-vendor strain analysis software (TomTec). As strain analysis was not repeated using vendor specific software, the results cannot be generalized to other vendor specific software for LA strain analysis. With regards to multi-vendor image acquisition, it would be more ideal if we had a balanced number of subjects with each of the three different vendors used for image acquisition and this could allow comparison also between vendors. The echo images for 38 of 50 subjects were acquired by a single vendor.

All cases included in this study were in sinus rhythm and further studies are needed to assess use of LA strain in patients who are not in sinus rhythm. Adequate image quality is important for STE because the LA is in the far field and is a thin walled structure, thus prospective image acquisition with a focus on LA optimisation would benefit further LA strain study [12].

It is important to keep in mind that the published studies regarding LA strain are widely heterogeneous in terms of software, terminology, and methodology used to calculate strain [5]. Different LA strain parameters were used for measurements of LA function and there is a strong need to standardize terminology and measurements to facilitate uniform comparison between studies prior to adoption of widespread clinical application.

Conclusion

Demonstration of the reproducibility of novel techniques, such as LA strain, is of major importance prior to introduction into clinical practice. This study demonstrated that global LA strain and SR values acquired using multiple echocardiographic vendors in a heterogeneous cohort of patients were highly reproducible by a novice strain reader using multi-vendor analysis software. This study suggests

that LA strain assessment is relatively easy to learn, a factor that is important in a busy echocardiography laboratory. Documentation of the LA strain learning curve would be useful to further aid the adoption of LA strain into clinical practice as the technique can be applied to multiple cardiac pathologies.

Compliance with ethical standards

Conflict of interest The authors declared that they have no conflict of interest.

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