Percutaneous left atrial appendage occlusion: impact on left atrial deformation indices

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Abstract

Background: Percutaneous left atrial appendage occlusion (LAAO) is an accepted alternative to thromboprophylaxis in patients with atrial fibrillation (AF) who are: i) intolerant to oral anticoagulation (OAC) (e.g. life-threatening haemorrhage), ii) non-adherent to OAC, or iii) at a high bleeding risk with OAC. Improvement in LA mechanics was shown post-LAAO in the LAFIT-LARIAT study, using the Lariat device. No significant change was seen in LA mechanics after LAAO with the Watchman device in the LAFIT-Watchman study. The impact of LAAO with the Amplatz or Amulet device on LA deformation mechanics has not been investigated.

Purpose: To evaluate the impact of LAAO with the Amplatz or Amulet device on echocardiographic LA deformation indices.

Methods: All patients undergoing percutaneous LAAO from 2013 to 2021 at a single centre were included from an ongoing clinical registry. LA reservoir ($\varepsilon_{reservoir}$), conduit ($\varepsilon_{conduit}$) and contractile strain ($\varepsilon_{contractile}$) and strain rate ($SR_{reservoir}$, $SR_{conduit}$, $SR_{contractile}$) were assessed with two-dimensional speckle tracking echocardiography from an apical four-chamber view. Conduit and contractile strain and strain rates were only recorded for patients without AF at the time of echocardiography. Changes in LA deformation indices over time were compared with a linear mixed model.

Results: 28 LAAO recipients (mean age 73±12 years, 68% male) were analysed. 5 (18%) patients had AF pre- or post-procedure. After a mean follow-up of 1.6±1.4 months, the mean LA $\varepsilon_{reservoir}$ increased from 10.15±6.44% to 10.18±8.72% (p=0.985), the mean LA $\varepsilon_{conduit}$ increased from 5.12±5.48% to 5.31±6.11% (p=0.891) and the mean LA $\varepsilon_{contractile}$ decreased from 5.14±4.32% to 4.95±5.30% (p=0.898). During the same time interval, the mean LA $SR_{reservoir}$ decreased from +0.54±0.23.s^{-1} to +0.48±0.43.s^{-1} (p=0.566), the mean LA $SR_{conduit}$ remained stable: -0.47±0.41.s^{-1} to -0.47±0.32.s^{-1} (p=0.997) and the mean LA $SR_{contractile}$ decreased from -0.66±0.50.s^{-1} to -0.55±0.46.s^{-1} (p=0.660).

Conclusions: No significant improvement in LA mechanical function was seen after LAAO with the Amplatz or Amulet device. Different LAAO devices therefore appear to have divergent effects on LA deformation, the clinical implications of which may warrant further study.

Introduction

Atrial fibrillation (AF) is the most common arrythmia in clinical practice, and it is independently associated with all-cause mortality, heart failure and stroke.1 Percutaneous left atrial appendage occlusion (LAAO) with a dedicated device has emerged as an alternative to oral anticoagulation (OAC) in patients who are intolerant to anticoagulant drugs, non-adherent or have a very high bleeding risk. Improvement in LA mechanics after LAAO was noted in the LAFIT-LARIAT study, using the Lariat device (SentreHEART, Redwood City, CA, USA). Conversely, no significant change was detected in LA deformation after LAAO with the Watchman device (Boston Scientific, St. Paul, MN, USA) in the LAFIT-Watchman

study. The impact of LAAO performed with the Amplatz or Amulet device (Abbot Vascular, St. Paul, MN, USA) on LA deformation mechanics has never been investigated. We therefore analysed changes in echocardiographic LA deformation indices after LAAO with the Amplatz or Amulet device.

Methods

Patients ≥18 years with complete echocardiographic data from the same vendor (in order to allow speckle tracking strain analysis) before and after percutaneous LAAO, were included. Data were extracted from a clinical registry, comprising all patients who underwent percutaneous LAAO between 2013 and 2021 at a single centre (SAEndovascular, Kuils River Netcare Hospital, Cape Town, South Africa). Written, informed consent was obtained pre-procedure for all patients undergoing LAAO. All data that were analysed in the current study were collected for routine clinical purposes and handled anonymously. The study protocol was approved by the Health Research Ethics Committee, Faculty of Medicine and Health Sciences, Stellenbosch University and the Netcare Research Operations Committee.

Percutaneous LAAO insertion technique

All LAAO procedures were performed under transoesophageal echocardiography (TOE) guidance. Transseptal puncture was performed via right femoral venous access, and the sheath and dilator advanced into the superior vena cava before being exchanged for a transseptal needle. The interatrial septum was punctured under TOE guidance, whereafter a stiff 0.035” guidewire was advanced into the LAA, facilitated by low-volume radiographic contrast (Imeron, Bracco, Milan, Italy) injections. Systemic anticoagulation was achieved with intravenous heparin administration after successful transseptal puncture. The transseptal sheath was subsequently exchanged for a 14F TorqueVue 45x45 delivery sheath (Abbot Vascular, St. Paul, MN, USA), which was advanced into the LAA. The appendage was delineated with a contrast injection and measured fluoroscopically. Amplatz or Amulet (Abbot Vascular, St. Paul, MN, USA) LAAO devices were deployed via the delivery sheath under fluoroscopic and TOE guidance. After ensuring correct placement of the LAAO with a tug test, fluoroscopic confirmation of mild lobe compression, separation of the lobe and disc, a concave shape of the disc and deployment of the lobe at a right angle to the LAA axis was performed. Finally, major peri-device leaks were excluded with TOE before the device was released and the delivery cable and sheath retracted from the LA.

Echocardiographic data acquisition and analysis

Transthoracic echocardiography was performed with commercially available echocardiography equipment (Vivid E95, General Electric Vingmed Ultrasound, Milwaukee, USA) in the left lateral decubitus position. Two-dimensional (2D) echocardiographic data were acquired with an M5S transducer, and depth and gain settings optimized as required. All echocardiographic data were ECG-triggered, including at least three consecutive RR intervals and were archived digitally to allow for off-line analysis (EchoPac 202, General Electric Vingmed Ultrasound, Milwaukee, USA). LA volumes were calculated by means of the

Simpson's biplane method of discs from apical two- and 4-chamber views. Various phasic, volume-derived LA functional indices were calculated from 2D echocardiographic data. The LA ejection fraction (LAEF) was defined as: (LA maximum volume – LA minimum volume)/LA maximum volume, expressed as a percentage. The LA expansion index (LAEI) was calculated as follows: (LA maximum volume – LA minimum volume)/LA minimum volume, and expressed as a percentage. Similarly, the LA passive emptying fraction (LAPEF) was calculated with the following formula: (LA maximum volume – LA pre-atrial contraction volume)/LA maximum volume and expressed as a percentage. Lastly, the LA active emptying fraction (LAAEF) was calculated as: (LA pre-atrial contraction volume – LA minimum volume)/LA pre-atrial contraction volume, and expressed as a percentage.[2] LA speckle tracking strain analysis was performed in an apical 4-chamber view, with ECG gating using the R-wave of the QRS complex as the reference point. Pulmonary vein ostia and the LAA were excluded from the tracings, and the region of interest was reduced manually to encompass the LA wall. LA reservoir strain ($\varepsilon_{reservoir}$), conduit strain ($\varepsilon_{conduit}$) and contractile strain ($\varepsilon_{contractile}$) were measured from a strain versus time plot (**Figure 1**), while LA strain rates ($SR_{reservoir}$, $SR_{conduit}$, $SR_{contractile}$) were derived from the same data points (**Figure 2**). $\varepsilon_{conduit}$ and $\varepsilon_{contractile}$ and strain rates were only recorded for patients in sinus rhythm at the time of echocardiography, since LA contractile function is lost during AF.[3]

Statistical analysis

Normality was assessed by visual comparison of data histograms to a normal probability curve, as well as Q-Q plots and detrended normal Q-Q plots. Continuous data are presented as means and standard deviations (when normally distributed) and as medians and interquartile ranges (IQR) when not normally distributed. Categorical data are expressed as frequencies and percentages. The inter-observer and intra-observer variability LA phasic parameters as well as LA strain and strain rate measurement were assessed by calculating the intra-class correlation coefficient (ICC) on 5 randomly selected patients. Student's t-tests were used for comparison of continuous variables and χ^2 or Fischer's exact tests, as appropriate, for the comparison of categorical variables. Changes in deformation indices over time were evaluated with a linear mixed model. All tests were two-sided and a p-value of <0.05 was considered statistically significant. All analyses were performed with SPSS for Windows version 25.0 (SPSS, Armonk, NY, USA).

Results

Baseline patient characteristics and procedural aspects

A total of 28 LAAO recipients (mean age 73±12 years, 68% male) were analysed. 5 (18%) patients had AF either pre- or post-procedure. The majority of patients were in permanent AF (n=24, 86%). Recurrent haemorrhage and a contraindication to OAC were the most common indications for LAAO, and a major haemorrhagic episode and erratic international normalized ratio the most frequent contraindications to OAC. The mean device size was 22±2 mm and the procedural success rate was 100%. One (4%) patient experienced a serious procedural complication, i.e. device embolization. Baseline characteristics are

summarized in **Table 1**. The ICC for inter-observer variability of LA $\varepsilon_{reservoir}$, LA $\varepsilon_{contractile}$, LA $SR_{reservoir}$, LA $SR_{conduit}$ and LA $SR_{contractile}$ were 0.98 (95% confidence interval (CI): 0.88-0.99, p<0.001), 0.89 (95% CI: 0.28-0.99, p=0.009), 0.96 (95% CI: 0.68-0.99, p<0.001), 0.91 (95% CI: 0.38-0.99, p<0.006) and 0.98 (95% CI: 0.79-0.99, p<0.001). The ICC for intra-observer variability of LA $\varepsilon_{reservoir}$, LA $\varepsilon_{contractile}$, LA $SR_{reservoir}$, LA $SR_{conduit}$ and LA $SR_{contractile}$ were 0.99 (95% CI: 0.99-1.00, p<0.001), 0.99 (95% CI: 0.99-1.00, p<0.001), 0.93 (95% CI: 0.47-0.99, p=0.004), 0.97 (95% CI: 0.74-0.99, p<0.001) and 0.97 (95% CI: 0.71-0.99, p<0.001).

LA size and phasic-derived function before and after LAAO

After a mean follow-up of 1.6±1.4 months, the LA maximum volume increased from 70±27 ml to 77±29 ml (p=0.083), the LA minimum volume increased from 48±21 ml to 50±22 ml (p=0.671) and the LA pre-atrial contraction volume increased from 59±21 ml to 63±23 ml (p=0.215). During the same time interval, the LAEF increased from 31±24% to 36±20% (p=0.481), the LAEI increased from 62±57% to 81±99% (p=0.473), the LAPEF increased from 12±41% to 14±39% (p=0.777) and the LAAEF increased from 8±44% to 16±33% (p=0.333).

Impact of LAAO on LA deformation

After a mean follow-up of 1.6±1.4 months, the mean LA $\varepsilon_{reservoir}$ increased from 10.15±6.44% to 10.18±8.72% (p=0.985), the mean LA $\varepsilon_{conduit}$ increased from 5.12±5.48% to 5.31±6.11% (p=0.891) and the mean LA $\varepsilon_{contractile}$ decreased from 5.14±4.32% to 4.95±5.30% (p=0.898) (**Figure 3**). During the same time interval, the mean LA $SR_{reservoir}$ decreased from $+0.54\pm0.23.s^{-1}$ to $+0.48\pm0.43.s^{-1}$ (p=0.566), the mean LA $SR_{conduit}$ remained stable: $-0.47\pm0.41.s^{-1}$ to $-0.47\pm0.32.s^{-1}$ (p=0.997) and the mean LA $SR_{contractile}$ decreased from $-0.66\pm0.50.s^{-1}$ to $-0.55\pm0.46.s^{-1}$ (p=0.660) (**Figure 4**).

Discussion

The principal findings of the current study are: i) LA size increased after percutaneous LAAO, ii) LA mechanical function, assessed by 2D phasic-derived volume indices (LAEF, LAEI, LAPEF and LAAEF) remained stable post-LAAO and iii) there was no significant change in LA deformation indices after LAAO with an Amplatz or Amulet device.

LAAO and stroke prevention

AF predisposes to systemic thromboembolism, especially ischaemic stroke. This risk can be mitigated with OAC: either traditional vitamin K antagonists or novel oral anticoagulants, the latter of which are preferred, except for moderate-to-severe mitral stenosis and mechanical valve prostheses. Patients with AF who are intolerant or non-adherent to OAC, or who have an unacceptably high bleeding risk, may be considered for LAAO. The LAA is an area of the LA with low blood flow, making it prone to stasis and

thrombus formation. Only approximately 10% of emboli in non-valvular AF originate outside of the LAA, and exclusion or occlusion of the LAA is a viable alternative to OAC.[4-7] Data on the safety and efficacy of LAAO have accrued from large trials, e.g. WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation (PROTECT AF), Evaluation of the WATCHMAN LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy (PREVAIL) and the Interventional Left Atrial Appendage Closure vs. Novel Anticoagulation Agents in High-risk Patients With Atrial Fibrillation (PRAGUE-17) study.[8-10]

Quantification of LA function with echocardiography

Phasic changes in echocardiographic LA volumes during the cardiac cycle are used to derive LAEF, LAEI, LAPEF and LAAEF, which are parameters of global LA function, LA reservoir function, LA conduit function and LA contractile function, respectively.[2] LA deformation indices can be obtained from apical 2D echocardiographic images by using speckle tracking strain analysis. LA $\varepsilon_{reservoir}$ reflects chamber compliance, $\varepsilon_{conduit}$ LA elastance and $\varepsilon_{contractile}$ LA systolic function.[11] LA deformation analysis has a number of advantages over conventional, phasic-change derived parameters for the evaluation of LA function: 1) it reflects only active myocardial deformation, and not passive motion due to tethering, 2) it is less load-dependent and 3) it has been shown to be more sensitive in detecting LA functional abnormalities in a variety of cardiac disease states.[12]

LA function: the impact of percutaneous LAAO

LA exclusion by means of epicardial suture ligation with the Lariat device has been demonstrated to decrease the burden of AF, as well as arterial blood pressure.[13, 14] Since the LAA is a neurohormonally active structure, the antihypertensive effect of the Lariat device may reflect its impact on atrial natriuretic peptide release (of which approximately 30% is stored in the LAA). The reduction in AF burden has been postulated to reflect exclusion (and eventual ischaemic necrosis and atrophy) of the LAA as a source of AF initiation (trigger and/or substrate).[13, 14] A decrease in AF burden may translate into improved LA mechanical function, and conversely, LAA exclusion could lead to better LA function, thereby decreasing AF burden (e.g. by decreasing the number of AF drivers).[13] An analysis of LA function from 66 patients in the LAFIT-LARIAT registry (who underwent epicardial LAA exclusion with the Lariat device), demonstrated a decrease in median LA volume index (35.4 (IQR 29.4-37.2)ml/m^2 to 29.2 (IQR 28.2-35.9)ml/m^2, p=0.023) as well as an improvement in median LA $SR_{reservoir}$ (+0.72 (IQR 0.63-0.83).s^{-1} to +0.81 (IQR 0.73-0.98).s^{-1}, p=0.043) and median LA $SR_{conduit}$ (-0.74 (IQR 0.67-0.99).s^{-1} to -0.89 (IQR 0.82-1.07).s^{-1}, p=0.025).[15] These data suggest that improved LA mechanical function follows on LAA exclusion with the Lariat device. Use of the Lariat device is a more invasive procedure than insertion of other percutaneous LAAO devices, e.g. Watchman, and safety concerns have been raised: pericardial effusion requiring drainage has been documented in up to 20% of Lariat recipients.[16] In a study (LAFIT Watchman) of 25 patients who underwent LAAO with the Watchman device, improvements in median phasic LA volume-derived functional indices were seen from baseline to

post-LAAO: LAEF (36 (IQR 27-45)% increased to 42 (IQR 34-49)%, p=0.005), LAEI (58.1 (IQR 37.8-85.2)% increased to 75.3 (IQR 52.3-98.0)%, p=0.03), LAPEF (21.0 (IQR 13.8-34.7)% increased to 28.6 (IQR 21.9-35.9)%, p=0.03) and LAAEF (12.6 (IQR 8.8-25.5)% increased to 13.3 (IQR 9.7-29.9)%, p=0.04).[17] These changes suggest an improvement in LA global function, LA reservoir function, LA conduit function and LA contractile function after percutaneous LAAO. Surprisingly, taking into account the fact that LA deformation parameters are more sensitive to changes in LA function than phasic-derived indices, no significant changes were recorded in median LA $\varepsilon_{reservoir}$ (14.5 (IQR 10.3-19.9)% to 12.6 (IQR 9.8-18.3)%, p=0.798), LA $\varepsilon_{conduit}$ (4.8 (IQR 2.3-9.0)% to 3.6 (IQR 2.6-8.6)%, p=0.882), LA $\varepsilon_{contractile}$ (8.9 (IQR 6.8-13.3)% to 9.0 (IQR 6.4-11.3)%, p=0.657), LA $SR_{reservoir}$ (+0.52 (IQR 0.35-0.86).s^{-1} to +0.58 (IQR 0.28-0.40).s^{-1}, p=0.851), LA $SR_{conduit}$ (-0.56 (IQR 0.43-0.93).s^{-1} to -0.58 (IQR 0.46-0.87).s^{-1}, p=0.518), or LA $SR_{contractile}$ (-0.30 (IQR 0.08-0.44).s^{-1} to
-0.43 (IQR 0.12-0.79).s^{-1}, p=0.427).[17] The latter results are in agreement with those from our study, using a different percutaneous LAAO device (Amplatz/Amulet), i.e. no significant change in LA deformation parameters.

Clinical implications

LA function has been linked to systemic embolism and mortality risk in patients with AF.[18] An improvement in LA function after percutaneous LAAO would therefore be desirable and may have beneficial long-term effects. Patients selected for percutaneous LAAO often have persistent or permanent AF, such as in our cohort, where 86% of patients had permanent AF. In the LAFIT Watchman study, 56% of patients had persistent AF.[17] Since longstanding AF often leads to electrical and structural remodelling of the LA, it is likely that many LAAO recipients have fibrosed, remodelled atria that have little capacity for functional improvement post-procedure.[19] In the LAFIT-LARIAT registry, however, improved LA function was seen after exclusion of the LAA. Despite the fact that the Lariat device cannot be directly compared to the Watchman or Amplatz/Amulet device, the possibility exists that patients with greater baseline LA functional reserve were included in the LAFIT-LARIAT study, compared to the LAFIT Watchman or ours. Larger studies, including cardiac magnetic resonance imaging with late gadolinium enhancement of the LA to demonstrate the fibrotic LA substrate (which is correlated with the ability of the LA to improve its function e.g. post-ablation) will be required to elucidate the impact of LA functional reserve on LA function after LAAO.[20]

Study limitations

This was a single-centre, retrospective analysis. The limited sample size precluded multivariable analysis to ascertain the impact of factors other than LAAO on the size and mechanical function of the LA, e.g. age, LV diastolic function, mitral valve disease, pulmonary vein isolation and pharmacotherapy. A longer follow-up time might have revealed more significant changes in LA functional parameters, although it was similar to that in the LAFIT Watchman study, where patients underwent follow-up echocardiography within 30 days of the procedure.[17] Despite the limited sample size, it still represents the largest study to

date on LA deformation changes in percutaneous LAAO devices. Systematic three-dimensional echocardiographic data were not acquired, and phasic LA volume-derived parameters were calculated from 2D data.

Conclusions

No significant improvement in LA mechanical function was seen after LAAO with the Amplatz or Amulet device. Different LAAO devices therefore appear to have divergent effects on LA deformation, the clinical implications of which may warrant further study.

Declarations

Disclosures

MJH received financial support from Medtronic and is a Hamilton Naki scholar. The remaining authors have nothing to disclose.

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Tables

Table 1: Baseline patient characteristics

Characteristic	
Age (years)	73±12 years
Male, n%	19 (68%)
Heart failure, n%	16 (57%)
Diabetes mellitus, n%	9 (32%)
Dyslipidaemia, n%	24 (86%)
Prior stroke or TIA, n%	6 (21%)
Statin, n%	23 (82%)
Beta-blocker, n%	22 (79%)
Aspirin, n%	21 (75%)
Clopidogrel, n%	11 (39%)
AF type	
- Paroxysmal - Persistent - Permanent	4 (14%) 0 (0%) 24 (86%)
CHA_2DS_2-VASc	3.5±1.5
Warfarin, n%	20 (71%)
NOAC, n%	9 (3%)
Indication for LAAO	
- Recurrent haemorrhage, n% - Prior severe haemorrhage, n% - Combined dual antiplatelet therapy, n% - Poor adherence to OAC, n% - High risk of falls or previous falls, n% - Contraindication to OAC, n%	7 (25%) 2 (7%) 3 (11%) 5 (18%) 4 (14%) 7 (25%)
Contraindication to OAC	
- Major haemorrhagic episode, n% - Erratic INR or logistical, n% - Cerebrovascular haemorrhage, n% - Drug interactions, n% - Haematological, n% - GIT haemorrhage, n%	9 (32%) 9 (32%) 2 (7%)

	4 (14%)
	2 (7%)
	1 (4%)

All values are expressed as mean±standard deviation, or median and interquartile range. AF, atrial fibrillation; GIT, gastrointestinal; INR, international normalized ratio; LAAO, left atrial appendage occlusion; NOAC, novel oral anticoagulant; OAC, oral anticoagulation; TIA, transient ischaemic attack

Figures

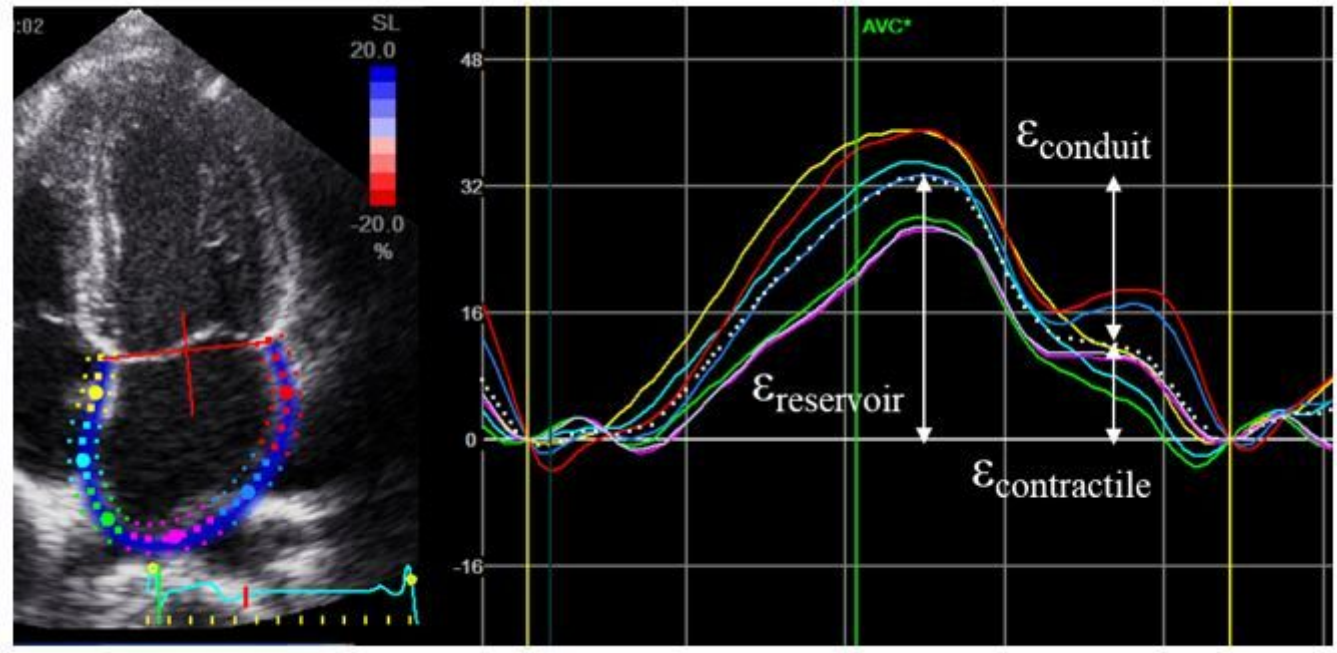

Figure 1

Left atrial speckle tracking strain analysis. Speckle tracking strain analysis was performed in an apical four-chamber view, and gating performed according to the RR-intervals on the ECG. Left atrial reservoir strain ($\varepsilon_{reservoir}$), conduit strain ($\varepsilon_{conduit}$) and contractile strain ($\varepsilon_{contractile}$) were measured. AVC, aortic valve closure

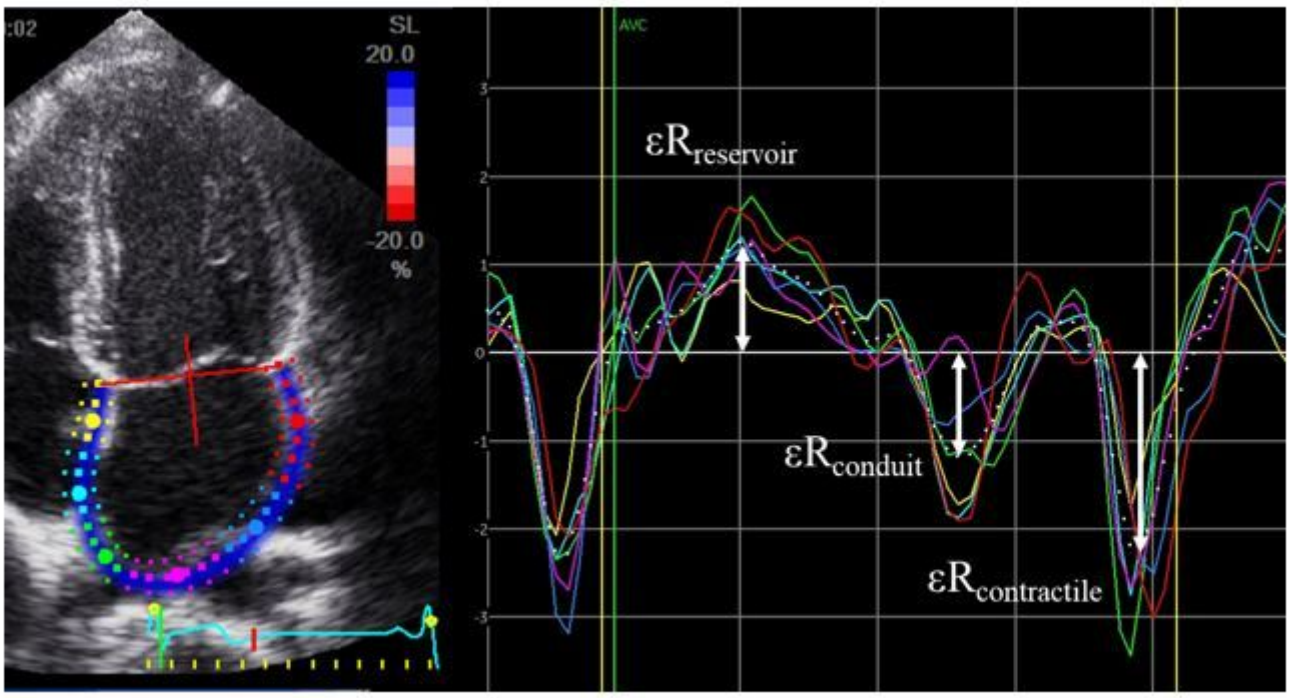

Figure 2

Left atrial (LA) speckle tracking strain rate analysis. Speckle tracking strain rate analysis was performed in an apical four-chamber view, and gating performed according to the RR-intervals on the ECG. LA reservoir strain rate ($\varepsilon R_{reservoir}$), LA conduit strain rate ($\varepsilon R_{conduit}$) and LA contractile strain rate ($\varepsilon R_{contractile}$) were measured. AVC, aortic valve closure

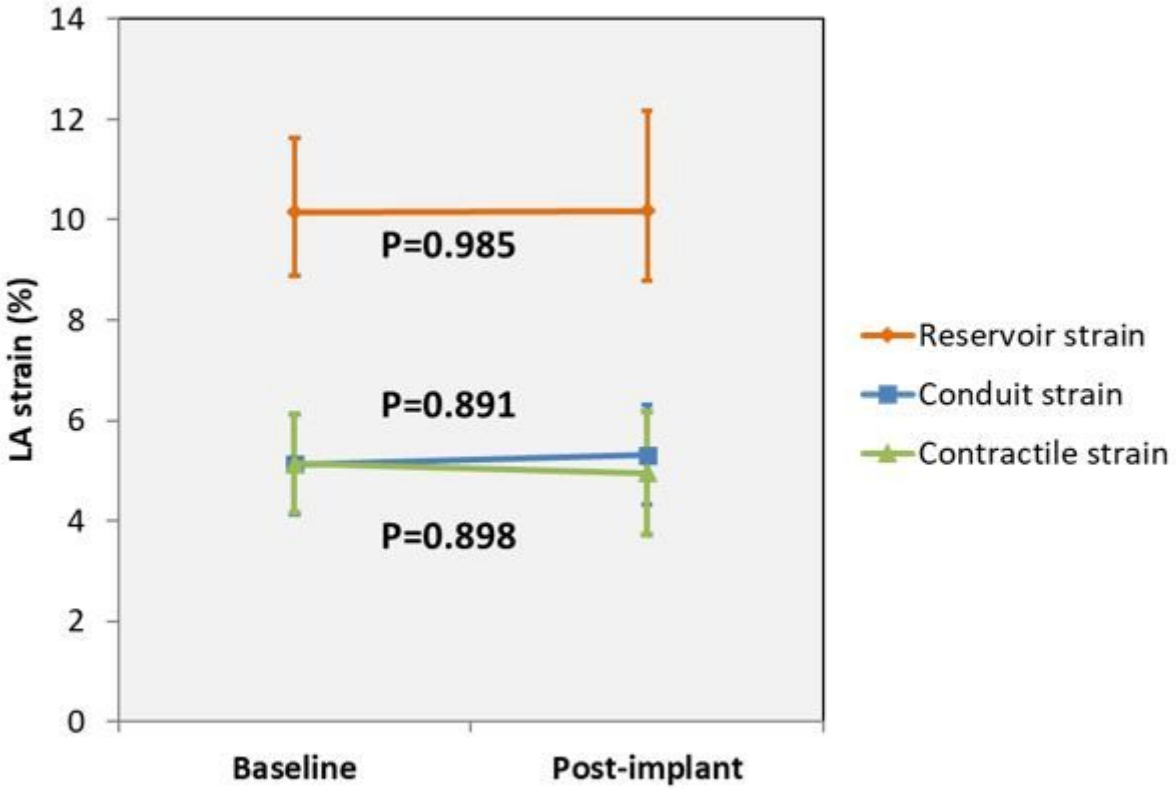

Figure 3

Changes in left atrial (LA) strain. The change in LA reservoir strain ($\varepsilon_{reservoir}$), LA conduit strain ($\varepsilon_{conduit}$) and LA contractile strain ($\varepsilon_{contractile}$) were measured from baseline to post-left atrial occluder implantation. Vertical bars represent standard error of the mean.

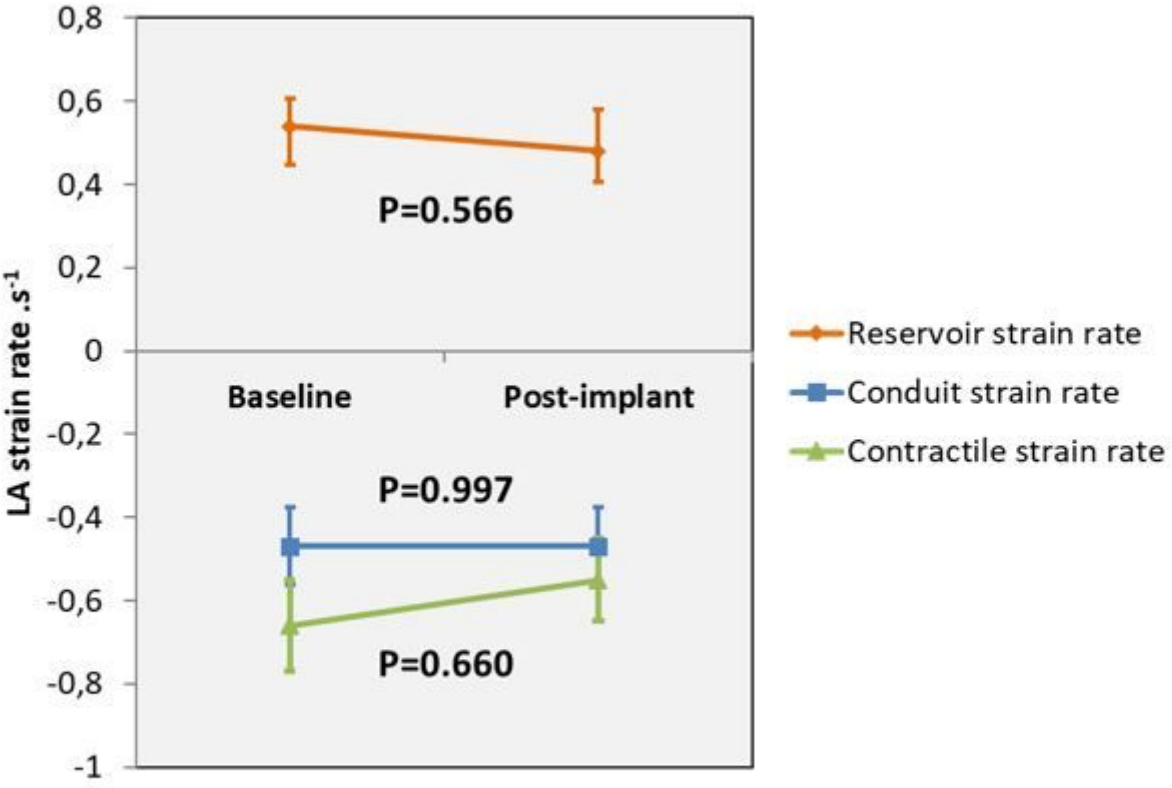

Figure 4

Changes in left atrial (LA) strain rate. The change in LA reservoir strain rate ($\varepsilon_{reservoir}$), LA conduit strain rate ($\varepsilon_{conduit}$) and LA contractile strain rate ($\varepsilon_{contractile}$) were measured from baseline to post-left atrial occluder implantation. Vertical bars represent standard error of the mean.