European Heart Journal - Cardiovascular Imaging (2022) **23**, 61–70
doi:10.1093/ehjci/jeaa415

Determinants of left atrial reservoir and pump strain and use of atrial strain for evaluation of left ventricular filling pressure

Katsuji Inoue[1,2†], Faraz H. Khan [1†], Espen W. Remme[1], Nobuyuki Ohte[3], Eusebio García-Izquierdo[4], Michael Chetrit[5], Vanessa Moñivas-Palomero[4], Susana Mingo-Santos[4], Øyvind S. Andersen[1], Einar Gude[1], Arne K. Andreassen[1], Tom Kai Ming Wang[6], Shohei Kikuchi[3], Marie Stugaard[7], Jong-Won Ha[8], Allan L. Klein[6], Sherif F. Nagueh[9], and Otto A. Smiseth [1*]

[1]Institute for Surgical Research and Department of Cardiology, Rikshospitalet, Oslo University Hospital, and University of Oslo, N-0027 Oslo, Norway; [2]Department of Cardiology, Pulmonology, Hypertension & Nephrology, Ehime University Graduate School of Medicine, Toon, Japan; [3]Department of Cardiology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; [4]Department of Cardiology, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain; [5]Department of Cardiovascular Medicine, McGill University Health Centre, Montreal, Canada; [6]Section of Cardiovascular Imaging, Department of Cardiovascular Medicine, Heart, Vascular, and Thoracic Institute, Cleveland Clinic, OH, USA.; [7]Department of Cardiology, Ringerike Hospital, Vestre Viken Hospital Trust, Hønefoss, Norway; [8]Cardiology Division, Yonsei University College of Medicine, Seoul, Korea; and [9]Department of Cardiology, Methodist DeBakey Heart and Vascular Center, Houston, Texas, USA

Received 23 October 2020; editorial decision 14 December 2020; accepted 17 December 2020; online publish-ahead-of-print 26 January 2021

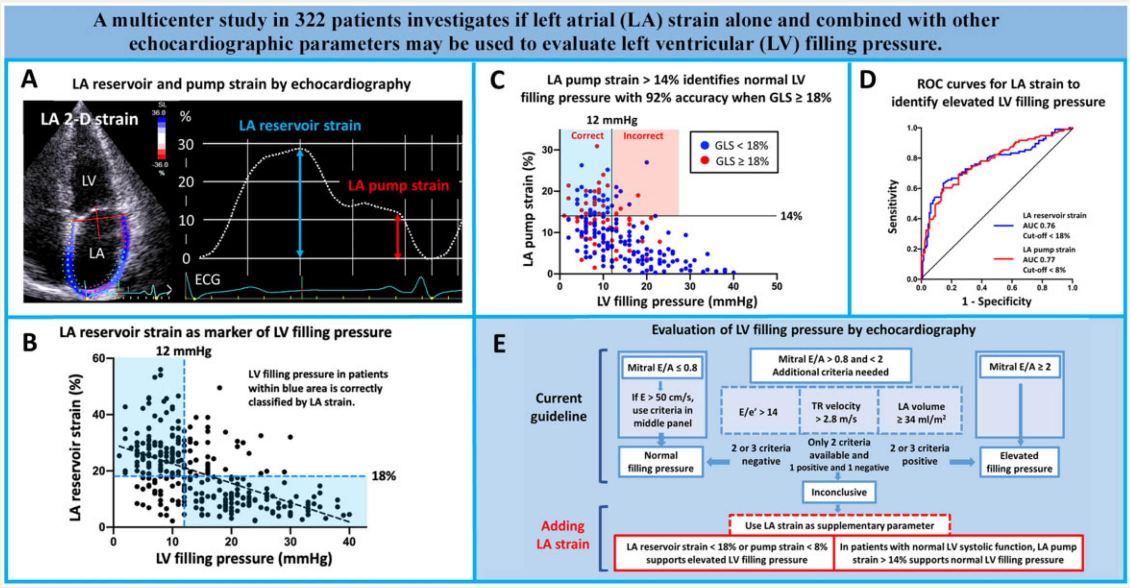
Aims The aim of this study is to investigate determinants of left atrial (LA) reservoir and pump strain and if these parameters may serve as non-invasive markers of left ventricular (LV) filling pressure.

Methods and results In a multicentre study of 322 patients with cardiovascular disease of different aetiologies, LA strain and other echocardiographic parameters were compared with invasively measured LV filling pressure. The strongest determinants of LA reservoir and pump strain were LV global longitudinal strain (GLS) (*r*-values 0.64 and 0.51, respectively) and LV filling pressure (*r*-values -0.52 and -0.57, respectively). Left atrial volume was another independent, but weaker determinant of both LA strains. For both LA strains, association with LV filling pressure was strongest in patients with reduced LV ejection fraction. Left atrial reservoir strain <18% and LA pump strain <8% predicted elevated LV filling pressure better ($P < 0.05$) than LA volume and conventional Doppler parameters. Accuracy to identify elevated LV filling pressure was 75% for LA reservoir strain alone and 72% for pump strain alone. When combined with conventional parameters, accuracy was 82% for both LA strains. In patients with normal LV systolic function by GLS, LA pump strain >14% identified normal LV filling pressure with 92% accuracy.

Conclusion Left atrial reservoir and pump strain are determined predominantly by LV GLS and filling pressure. Accuracy of LA strains to identify elevated LV filling pressure was best in patients with reduced LV systolic function. High values of LA pump strain, however, identified normal LV filling pressure with good accuracy in patients with normal systolic function.

*Corresponding author. Tel: + 47 23 07 00 00; Fax: + 47 23 07 39 17. E-mail: otto.smiseth@ous-hf.no

†These two authors contributed equally to this work and are joint first authors.



Graphical abstract Determinants and clinical application of LA reservoir and pump strain: Panel A: Apical 4-chamber image with colour coded region of interest for LA strain and the LA strain trace. Panel B: Relationship between LA reservoir strain and LV filling pressure in the total population. Panel C: Left atrial pump strain > 14% identifies normal LV filling pressure. Panel D: ROC curves for classification of LV filling pressure as normal or elevated. For comparison, curves are from the 235 patients where pump strain could be assessed. Panel E: Illustrates how LA strain may be incorporated in the decision algorithm for evaluation of LV filling pressure from the 2016 ASE/EACVI guideline (2).

Keywords heart failure • left ventricular filling pressure • diastolic dysfunction • catheterization • left atrial strain

Introduction

Demonstration of elevated left ventricular (LV) filling pressure is important for the heart failure (HF) diagnosis. In a joint recommendation from the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI), it was proposed to use a combination of several echocardiographic parameters to evaluate LV filling pressure.[1] The validity of this approach was recently confirmed in two multicentre studies with invasive pressure as gold standard.[2,3] However, a limitation of this multi-marker approach for estimation of LV filling pressure is that a number of patients remain uncategorized due to lack of one or more of the required echocardiographic parameters. Left atrial (LA) reservoir and pump strain measured by speckle tracking echocardiography are proposed as supplementary markers of LV filling pressure.

For application in clinical diagnostics, it is important to understand which factors other than LV filling pressure determine the magnitude of the LA strain components. Therefore, the present multicentre study investigates determinants of LA reservoir and pump strain by studying patients with a wide range of cardiac disorders. Furthermore, the study investigates how LA strain may be used in combination with other echocardiographic parameters in the evaluation of LV filling pressure. The study is done with echocardiographic equipment from different vendors, and invasive pressure is used as gold standard for LV filling pressure.

Methods

Patient population

The multicentre study was conducted at Oslo University Hospital, Rikshospitalet (Oslo, Norway), Methodist DeBakey Heart and Vascular centre (Houston, TX, USA), Yonsei University College of Medicine (Seoul, South-Korea), Cleveland Clinic (Cleveland, OH, USA), Hospital Universitario Puerta de Hierro, Majadahonda (Madrid, Spain), and Nagoya City University, Graduate School of Medical Sciences (Nagoya, Japan).

A total of 322 patients (154 prospectively and 168 retrospectively from recent studies from the participating centres) referred for diagnostic right- or left-sided heart catheterization were included. Patients where adequate echocardiographic images could not be obtained and patients with complex congenital heart disease, cardiac transplants, end-stage liver disease, mitral stenosis, or prosthetic mitral valve were excluded. Echocardiography was performed either during ($n = 90$) or within 1 day ($n = 232$) of catheterization.

The proposed protocol including standardization of how to measure strain, and other echocardiographic and haemodynamic parameters was agreed on by all the participating centres. The parameters were sent to

Table 1 Clinical, haemodynamic, and echocardiographic characteristics

Variables	Number of patients	Median (interquartile range) or number (percentage)
Clinical		
Age (years)	322	62 (53–70)
Female gender, *n* (%)	322	132 (41)
Body surface area (m^2)	322	1.9 (1.7–2.0)
Hypertension, *n* (%)	322	140 (44)
Chronic kidney disease, *n* (%)	314	64 (20)
Coronary artery disease	322	78 (24%)
Atrial fibrillation[a]	322	43 (13%)
Haemodynamic		
Heart rate (beats/min)	321	71 (60–81)
Systolic blood pressure (mmHg)	314	122 (106–140)
Diastolic blood pressure (mmHg)	306	71 (63–81)
Cardiac index (L/min)	174	2.8 (2.2–3.5)
PCWP (mmHg)	276	12 (8–21)
LV pre-A (mmHg)	66	10 (7–13)
LV end-diastolic pressure (mmHg)	73	15 (12–20)
Mean pulmonary artery pressure (mmHg)	210	28 (19–39)
Systolic pulmonary artery pressure (mmHg)	256	44 (33–63)
Diastolic pulmonary artery pressure (mmHg)	250	17 (11–25)
Mean right atrial pressure (mmHg)	246	7 (3–11)
Echocardiography		
LV end-diastolic volume (mL)	319	99 (76–135)
LV end-systolic volume (mL)	319	42 (28–81)
LV ejection fraction (%)	322	55 (40–64)
E velocity (cm/s)	317	76 (59–92)
A velocity (cm/s)	268	68 (51–88)
E/A	268	1.0 (0.8–1.6)
Average *E/e′*	297	11 (8–16)
Peak TR velocity (m/s)	273	2.7 (2.4–3.2)
LA volume (mL/m^2)	321	35 (27–44)
LV GLS (%)	321	15.6 (11.5–18.9)
LA reservoir strain (%)	309	21.7 (13.5–28.8)
LA pump strain (%)	235	9.4 (5.3–13.6)

GLS, global longitudinal strain; LA, left atrial; LV, left ventricular; PCWP, pulmonary capillary wedge pressure; TR, tricuspid regurgitation.
[a]Two of the patients with atrial fibrillation also had history of atrial flutter.

the core laboratory (Oslo University Hospital), where all statistical analyses were performed.

The study was approved by the Regional Ethics Committees and Institutional Review Boards.

Echocardiographic imaging

Echocardiography equipment was from GE Healthcare (Echopac), Philips (QLAB), and Siemens (VVI, Tomtec). Echocardiographic recordings were analysed without knowledge of invasive haemodynamic data.

Mitral peak early (*E*) and atrial induced (*A*) flow velocities, septal and lateral mitral annular velocities and their average (*e′*), peak tricuspid regurgitation (TR) velocity, and LA volume indexed to body surface area (LAVI) were measured. The ratios *E/A* and *E/e′* were calculated.

Left atrial reservoir and pump strains and LV global longitudinal strain (GLS) were measured by speckle tracking echocardiography using frame rates from 40 to 80/s. Left atrial strain was calculated from apical 4-chamber view as recommended in the ASE/EACVI consensus report[4] and GLS from LV apical 4-chamber, 2-chamber, and long-axis views. Left atrial reservoir strain was calculated from LV-end diastole, and pump strain after onset of the p-wave in the electrocardiogram at the sharp downslope of the strain trace. Shortening strains are reported as absolute numbers. Measurements were averaged over three cardiac cycles when the patient had sinus rhythm and five cycles when there was atrial fibrillation.

Cardiac catheterization

In 276 (86%) patients, LV filling pressure was measured during right heart catheterization as end-expiratory pulmonary capillary wedge pressure (PCWP). In 46 patients, filling pressure was measured during left heart catheterization as LV pre-atrial contraction (pre-A) pressure and in 6 patients where pre-A pressure was not possible to assess, as LV end-

Table 2 Determinants of LA reservoir and LA pump strain in the total population: multivariate analysis

	LA reservoir strain			LA pump strain		
	Unstandardized, coefficients (95% CI)	Standardized, coefficients (β)	*P* value	Unstandardized, coefficients (95% CI)	Standardized, coefficients (β)	*P* value
Overall						
LV filling pressure	-0.28 (-0.41 to -0.15)	-0.21	<0.001	-0.29 (-0.38 to -0.20)	-0.38	<0.001
LV GLS	0.99 (0.79 to 1.19)	0.48	<0.001	0.32 (0.19 to 0.45)	0.28	<0.001
LA volume index	-0.11 (-0.16 to -0.06)	-0.18	<0.001	-0.05 (-0.09 to -0.01)	-0.15	0.009
LV EF <50%						
LV filling pressure	-0.31 (-0.42 to -0.20)	-0.42	<0.001	-0.32 (-0.41 to -0.22)	-0.58	<0.001
LV GLS	0.51 (0.27 to 0.75)	0.32	<0.001	0.19 (-0.02 to 0.40)	0.17	0.072
LA volume index	-0.06 (-0.11 to -0.01)	-0.17	0.017	-0.05 (-0.09 to -0.00)	-0.18	0.035
LV EF ≥50%						
LV filling pressure	-0.22 (-0.46 to 0.02)	-0.12	0.077	-0.27 (-0.43 to -0.11)	-0.27	0.001
LV GLS	1.05 (0.71 to 1.39)	0.40	<0.001	0.38 (0.15 to 0.60)	0.25	0.001
LA volume index	-0.15 (-0.24 to -0.06)	-0.23	0.001	-0.07 (-0.13 to 0.01)	-0.15	0.053

GLS, global longitudinal strain; LA, left atrial; LV, left ventricular.

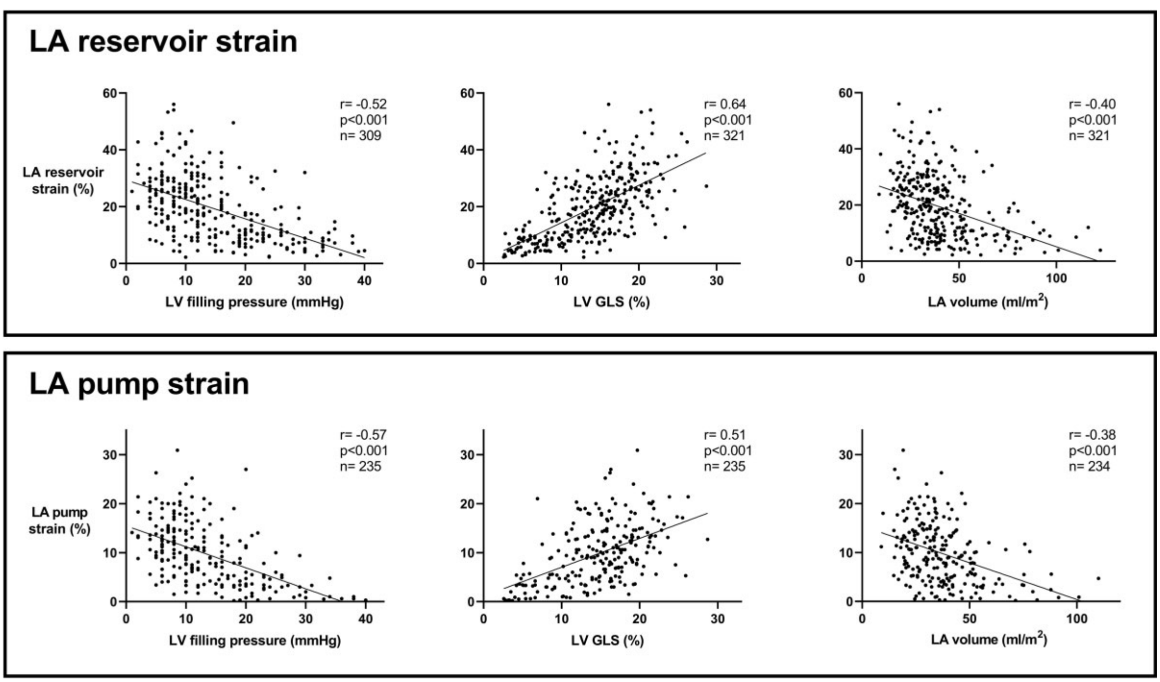


Figure 1 Determinants of LA strain. Relation between LA reservoir strain and its determinants (upper panels) and LA pump strain and its determinants (lower panels). GLS, global longitudinal strain; LA, left atrial; LV, left ventricular.

diastolic pressure.[5] PCWP or LV pre-A pressure >12 mmHg or LV end-diastolic pressure >16 mmHg were considered elevated.[6]

Analyses

First, we investigated the cardiac mechanical determinants of LA strain, and in this analysis, it was considered important to include a wide range of different cardiac disorders. Therefore, in this analysis, we included the 'total study population'. In a second analysis, we investigated whether LA reservoir and pump strain could improve evaluation of LV filling pressure when used in combination with other echocardiographic indices according to the general recommendation in the 2016 ASE/EACVI guideline.[1] For this analysis, to be in keeping with the 2016 ASE/EACVI guideline, patients with one or more of the following 'specific cardiovascular diseases' were excluded: atrial fibrillation, non-cardiac pulmonary hypertension, severe mitral regurgitation, mitral annular calcification (MAC), restrictive or hypertrophic cardiomyopathies, left bundle branch block (LBBB), or paced rhythms. In this population of 196 patients, LA strain as marker of LV filling pressure was tested in combination with mitral *E/A*, *E/e′*, TR velocity, and LA volume as recommended in the 2016 ASE/EACVI guideline.[1]

Statistical analysis

Univariate linear regression analyses were performed, followed by a multivariable linear regression analysis to assess which parameters were independent determinants of LA reservoir and pump strains. Fischer's *r* to *z* transformation was used to investigate the significance of difference between correlation coefficients. Area under the receiver operating characteristic (ROC) curve (AUC) was calculated to evaluate the ability of LA strain to estimate LV filling pressure. All analyses were performed with IBM SPSS software (Version 25.0, IBM Corp., Armonk, NY, USA) and Graphpad Prism (Version 8.2.0).

Results

Table 1 summarizes clinical, echocardiographic, and haemodynamic data. Median LV EF was 55% and there was elevated LV filling pressure in 58% of the patients. Several patients (8%) had LV filling pressure ≥30 mmHg, consistent with severe or end-stage HF.

The 'total study population' consisted of 322 patients and included 126 with one or more of the following 'specific cardiovascular diseases'; atrial fibrillation ($n = 43$), LBBB or right ventricular or biventricular paced rhythm ($n = 23$), non-cardiac pulmonary hypertension ($n = 36$), restrictive or hypertrophic cardiomyopathy ($n = 23$), and mitral regurgitation or MAC of at least moderate grade ($n = 27$).

Left atrial reservoir strain could be measured in almost all patients ($n = 309$), with only a few excluded due to inability to obtain optimal images. LA pump strain could be measured in 235 patients as it could not be assessed in the 43 with atrial fibrillation and judged as technically suboptimal in another 31 patients.

In the group where echocardiography was not performed simultaneously with catheterization, but within 1 day ($n = 232$), there was no significant difference in heart rate, systolic, or diastolic pressure at the two time points.

Determinants of LA reservoir and pump strain

There was a strong correlation between LA reservoir and pump strains ($r = 0.81$, $P < 0.001$), indicating tight coupling between the two strain components. Multivariable regression analysis of the total study population showed that LV GLS, LV filling pressure, and LAVI were all statistically independent determinants of both LA strain components (*Table 2*). As illustrated in *Figure 1*, LV GLS was the strongest ($P < 0.05$) determinant of LA reservoir strain, whereas for pump strain, LV filling pressure and GLS were the two strongest, with no significant difference between them. Left atrial volume had relatively weak correlations with LA reservoir and pump strains.

Correlation with LV filling pressure

For both LA reservoir and pump strain, progressively lower strains were associated with increasingly higher LV filling pressure (*Figure 1*). When excluding patients with atrial fibrillation, the correlation between LA reservoir strain and LV filling pressure did not change significantly (from r=-0.52 to -0.54, P=ns) (Supplementary data online, *Figure S1*). This limited influence on the r-value reflects the small portion of atrial fibrillation patients in the study population. In patients with atrial fibrillation, however, Left atrial reservoir strain was <20% regardless of level of filling pressure in all but one patient.

The associations between reservoir and pump strain and LV filling pressure were strongest in patients with reduced LV EF and GLS (*Table 3*). Thus, in patients with normal EF, the correlation was weaker, and with GLS ≥18%, there was no significant correlation

Table 3 Correlation values of echocardiographic parameters to LV filling pressure

Echocardiographic parameter	Correlation in total population (*r*-value)	Correlation in EF ≥ 50% (*r*-value)	Correlation in EF <50% (*r*-value)
Total population ($n = 322$)			
LA pump strain	-0.57	-0.32	-0.71
LA reservoir strain	-0.52	-0.33	-0.61
Average *E/e′*	0.40	0.40	0.25
LA volume index	0.36	0.35	0.24
LV GLS	-0.50	-0.28	-0.42
TR velocity	0.24	0.19	0.33
Without patients with specific cardiovascular diseases ($n = 196$)			
LA pump strain	-0.52	-0.33	-0.72
LA reservoir strain	-0.48	-0.26	-0.69
Average *E/e′*	0.42	0.40	0.28
LA volume index	0.32	0.30	0.21
LV GLS	-0.49	-0.24	-0.50
TR velocity	0.46	0.31	0.54

All *r*-values are statistically significant ($P < 0.01$).
GLS, global longitudinal strain; LA, left atrial; LV, left ventricular; TR, tricuspid regurgitation.

Table 4 Cut-off value for and accuracy of echocardiographic parameters in classifying LV filling pressure as normal or elevated

Echocardiographic parameter	Cut-off value	Accuracy in total population (%)	Accuracy in EF ≥50% (%)	Accuracy in EF <50% (%)
Total population ($n = 322$)				
LA pump strain	<8%	72	66	85
LA reservoir strain	<18%	75	72	81
Average *E*/*e*′	>14	68	68	68
LA volume index	>34 mL/m^2	69	69	68
LV GLS	<16%	63	56	73
TR velocity	>2.8 m/s	62	64	60
Without specific populations ($n = 196$)				
LA pump strain	<8%	72	65	85
LA reservoir strain	<18%	74	70	83
Average *E*/*e*′	>14	69	70	67
LA volume index	>34 mL/m^2	68	70	64
LV GLS	<16%	61	55	74
TR velocity	>2.8 m/s	70	73	65

GLS, global longitudinal strain; LA, left atrial; LV, left ventricular; TR, tricuspid regurgitation.

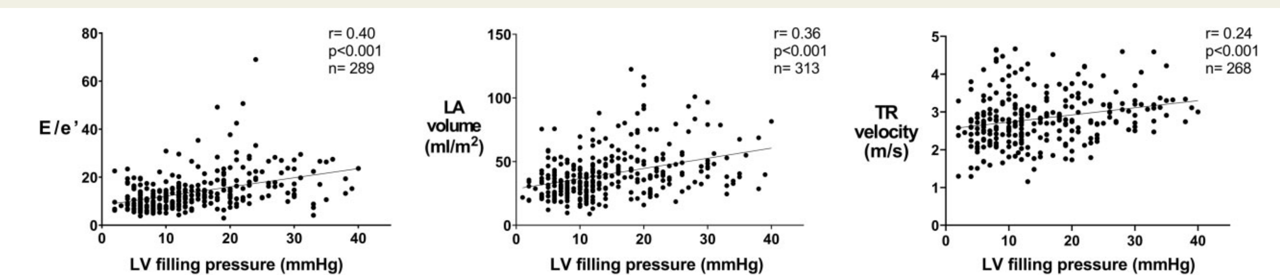


Figure 2 Relations between conventional echocardiographic markers and LV filling pressure. LA, left atrial; LV, left ventricular; TR, tricuspid regurgitation.

between LA strains and filling pressure. When considering patients with GLS ≥16%, there was a weak correlation between LA pump strain and LV filling pressure ($r = 0.30$, $P < 0.01$) but no significant correlation between reservoir strain and filling pressure.

In the 'total study population', LA reservoir and pump strain had stronger correlation with LV filling pressure than LA volume and TR velocity ($P < 0.05$), but not significantly stronger than the correlation between *E*/*e*′ and LV filling pressure ($P = 0.06$) and between LV GLS and filling pressure (*Figures 1 and 2* and *Table 3*). In patients with EF ≥ 50%, the correlations between LA strains and LV filling pressure were not stronger than for the other echocardiographic parameters (*Table 3*).

Since *E*/*e*′ is not recommended as marker of LV filling pressure in patients with significant mitral regurgitation or MAC, LBBB or ventricular pacing,[1] we also analysed the data when these groups were excluded, and the correlation between *E*/*e*′ and LV filling pressure in the 'total study population' improved ($r = 0.50$, $P < 0.001$).

Strain cut-off values for assessing LV filling pressure

According to ROC analysis, optimal cut-off to differentiate between normal and elevated LV filling pressure was 18% for LA reservoir strain when defining PCWP >12 mmHg as elevated, and 16% when using PCWP ≥15 mmHg, or LVEDP ≥16 mmHg as alternative definition.[7]

When using cut-off <18%, the accuracy of LA reservoir strain to differentiate between normal and elevated (>12 mmHg) filling pressure was 75% when applied in the 'total study population', 81% in patients with EF < 50%, but only 72% in patients with EF ≥ 50% (*Table 4*).

The best cut-off value for 'pump strain' to differentiate between normal and elevated LV filling pressure was 8%. Results with respect to differentiation between normal and elevated LV filling pressure was 72% for pump strain in the 'total study population', and AUC was similar for pump strain and reservoir strain. Similar to reservoir

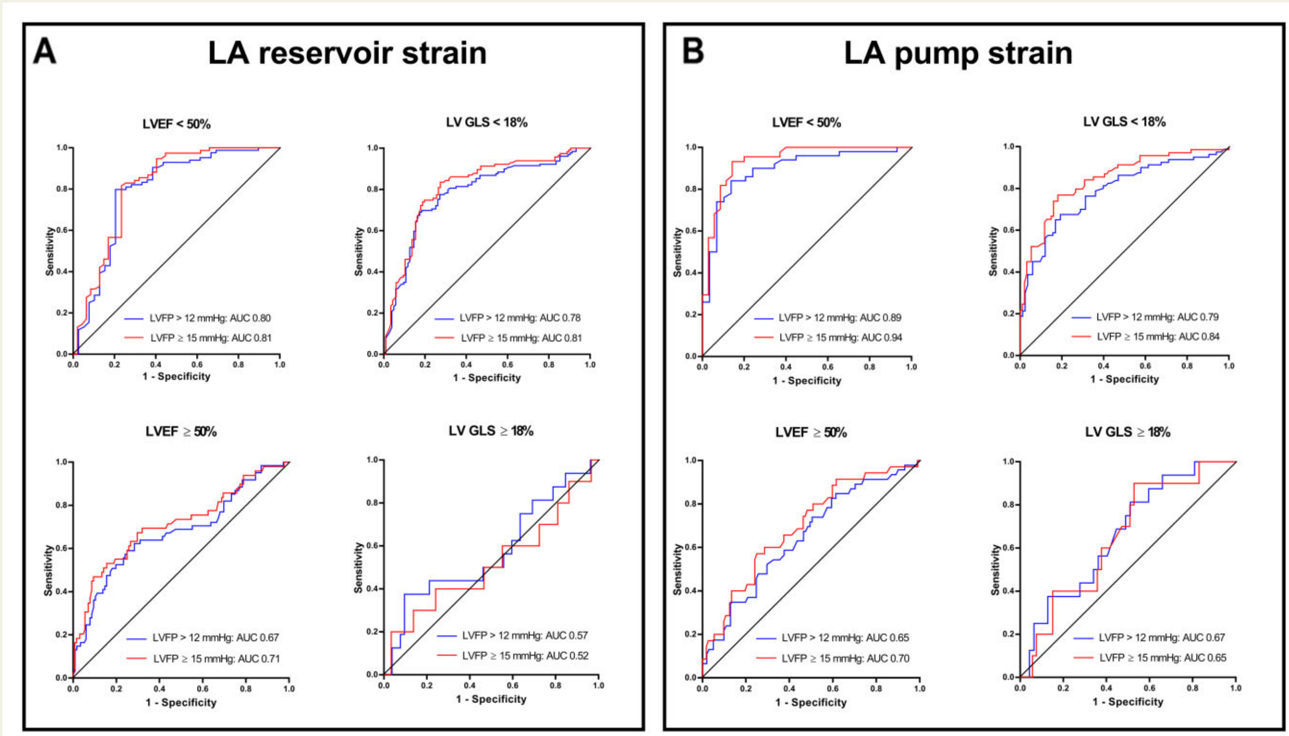


Figure 3 Classification of LV filling pressure by LA reservoir and pump strain. ROC curves showing ability of LA reservoir strain ($n = 309$) (*A*) and LA pump strain ($n = 235$) (*B*) to classify LV filling pressure as normal or elevated. Each panel includes two ROC curves according to different definitions of LV filling pressure as normal or elevated, using cut-offs of >12 and ≥15 mmHg. Systolic function is classified using LV EF (left) and LV GLS (right). Classification was best in patients with reduced systolic function as reflected in larger AUC in ROC curves. There was no significant difference in classifying LV filling pressure between the two cut-off values. AUC, area under the curve; GLS, global longitudinal strain; LA, left atrial; LV, left ventricular; ROC, receiver operating characteristic.

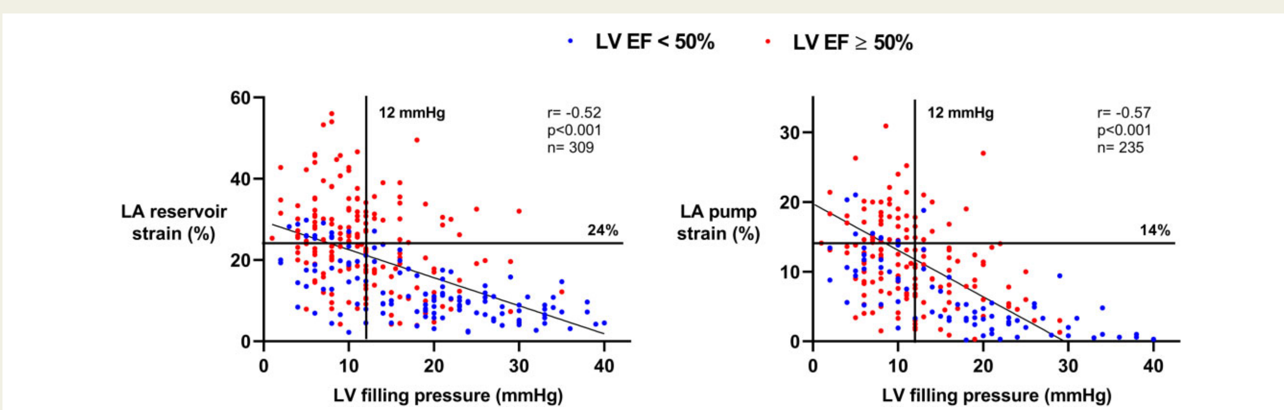


Figure 4 Diagnostic value of a high LA reservoir and pump strain. When LA reservoir strain exceeds 24% or pump strain exceeds 14%, few patients have elevated LV filling pressure. LA, left atrial; LV, left ventricular.

strain, pump strain as marker of elevated LV filling pressure was best in patients with reduced systolic function (*Figure 3*).

In patients with normal systolic function, LA reservoir and pump strain had limited ability to identify elevated LV filling pressure (*Figure 3*). Importantly, when considering patients with normal LV filling pressure, high normal values for LA pump strain >14% identified normal LV filling pressure (≤12 mmHg) with 87% accuracy for the total study population, and 92% accuracy in patients with GLS ≥ 18%.

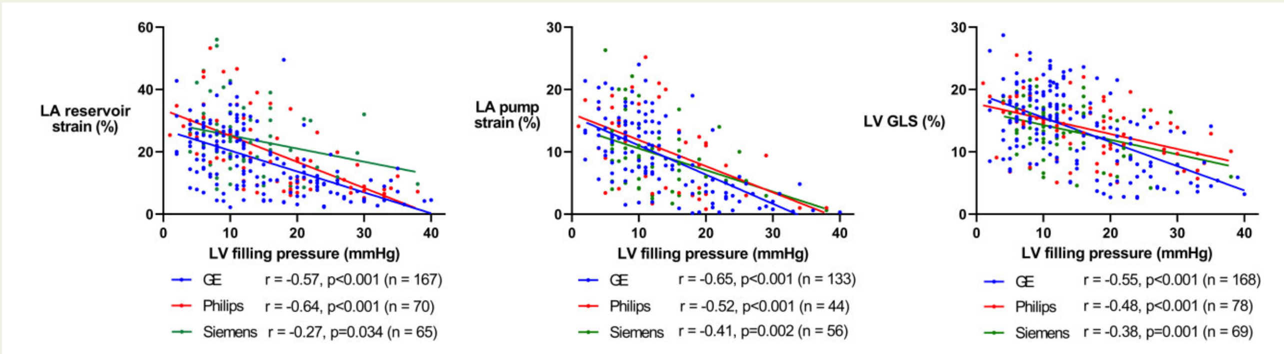


Figure 5 Correlations between LA strains and LV GLS to LV filling pressure among different vendors. GLS, global longitudinal strain; LA, left atrial; LV, left ventricular.

High normal values of LA reservoir strain > 24% were also associated with normal LV filling pressure, but there was more overlap with elevated filling pressure (*Figure 4*). Figure 3 also compares results for >12 and ≥15 mmHg as definition of elevated LV filling pressure.

When comparing recordings done with echocardiographic equipment from different vendors, the relationships between strain parameters and LV filling pressure were essentially similar (*Figure 5*).

Combining LA strain with other parameters of LV filling pressure

In the 196 patients without 'specific cardiovascular diseases', LA strain as marker of LV filling pressure was tested in combination with the other echocardiographic parameters in the 2016 ASE/EACVI guideline.[1] When applying the recommendations in the guideline, accuracy to differentiate between normal and elevated LV filling pressure was 83%. There was, however, no further improvement in accuracy by adding LA strain, but feasibility improved. Thus, in 10% of patients, evaluation of LV filling pressure according to current guideline[1] was inconclusive due to missing echocardiographic parameters, most often TR velocity. When the missing parameter was replaced by LA reservoir strain or pump strain, 99% of patients could be classified, indicating high feasibility, and accuracy was 82%. To test whether LA reservoir strain could replace any missing parameter, we replaced LA volume, TR velocity, or *E/e′* with LA reservoir strain one by one, and found similar accuracy of 82%. The *Graphical Abstract*, Panel E, suggests how LA strains may be incorporated into clinical assessment of LV filling pressure.

When comparing LA reservoir strain with the ratio *E*/LA reservoir strain, there was no significant difference between the two indices as markers of elevated LV filling pressure.

Reproducibility of LA reservoir and pump strain

Two observers analysed 25 randomly selected patients in the core lab. The interobserver ICCs for LA reservoir and pump strain was 0.89 and 0.82, respectively. The corresponding intraobserver ICCs were 0.93 and 0.92, respectively.

Discussion

As demonstrated in the present study, LA reservoir and pump strains are determined by both LV systolic and diastolic function. In patients with reduced LV EF, LA reservoir and pump strain had better correlation with LV filling pressure than the established echocardiographic parameters, and demonstrated good accuracy to differentiate between normal and elevated LV filling pressure. In contrast, for patients with EF ≥ 50%, LA reservoir and pump strain had limited ability to identify elevated LV filling pressure. High values of LA pump strain >14%, however, identified normal LV filling pressure with good accuracy in patients with normal and in those with reduced LV systolic function.

When assessing LV diastolic function according to the 2016 ASE/EACVI recommendations,[1] and using LA reservoir strain instead of TR velocity, which is frequently missing or inadequately visualized, there was improvement in the feasibility of echocardiographic assessment of LV filling pressure, suggesting a clinical role for LA strain. With the exception of better performance of LA pump strain to identify normal filling pressure, atrial pump strain provided essentially similar information as reservoir strain.

Determinants of LA reservoir and pump strain

The results showed that LV filling pressure, LV GLS and LA volume were independent determinants of LA reservoir and pump strains. For LA reservoir strain, LV GLS was the strongest determinant. This is expected since ventricle and atrium are anatomically connected, and with the LV apex essentially stationary during the cardiac cycle, longitudinal shortening of the LV implies stretching of the LA.

The correlation between LA reservoir strain and LV filling pressure may in part be explained by the association between LV filling pressure and LV systolic function as patients with high LV filling pressure also tend to have reduced GLS. This cannot be the entire explanation, however, since LV filling pressure was an independent determinant of LA reservoir strain. A likely contributing mechanism is increased atrial stiffness caused by remodelling of the atrial wall induced by increased wall stress due to elevated LA pressure. Furthermore, elevated LA pressure puts stretch on the atrial wall and thus increases operative LA stiffness. For a given stretching force as result of LV longitudinal contraction, a stiff atrium is expected to show less lengthening.

The mechanism behind LA volume as a third independent determinant of LA reservoir strain may be geometry. Since strain is a percentage change from baseline, with larger LA volume, the same absolute change in LA size implies lower strain.

Finally, as suggested by previous studies, active LA relaxation contributes to atrial filling in the early reservoir phase.[8] The fall in LA pressure following atrial systole increases the pulmonary venous to LA pressure gradient, which increases LA filling. Therefore, LA systolic function is a determinant of LA reservoir strain. The observed strong correlation between pump strain and reservoir strain is consistent with this notion. This implies that atrial systolic function should be considered the fourth mechanical determinant of LA reservoir strain.

In the present study LV filling pressure showed slightly stronger correlation with LA pump strain than with LA reservoir strain, but the difference was not statistically significant. When applying LA pump strain clinically, it is important to consider if atrial myopathy or atrial stunning following atrial arrhythmia rather than high filling pressure can explain low values of LA pump strain.[9]

Use of LA strain parameters to evaluate LV filling pressure

A number of echocardiographic parameters, including LA volume, mitral flow velocities, *E/e′* and peak TR velocity, may be used for evaluation of LV filling pressure. As shown in this study, LA reservoir and pump strain add to this list, and LA strain values <18% and <8%, respectively, are consistent with elevated LV filling pressure. The association with LV filling pressure, however, was not sufficiently strong to recommend LA reservoir strain as stand-alone index of LV filling pressure in a general population. There were too many patients with low values for LA reservoir strain (<18%) who had normal filling pressure. In patients with EF < 50%, however, both LA reservoir and pump strain had good accuracy to identify elevated LV filling pressure.

In patients with normal LV systolic function there were only weak associations between LA reservoir or pump strains and LV filling pressure. The exception was high normal values for LA pump strain, which identified normal LV filling pressure with good accuracy in patients with normal EF, suggesting a role for LA strain in patients with normal LV function.

Even the combination of echocardiographic indices has limitations, and therefore clinical data and other relevant information must always be incorporated when these markers are used to make clinical decisions. One of the clinical applications of LA reservoir strain may be to serve as a substitute for missing TR velocity or any other missing parameter when using the algorithm for estimation of LV filling pressure recommended in the 2016 ASE/EACVI guideline.[1] When LA strain was used to replace a missing parameter, the accuracy to identify elevated LV filling pressure did not improve, indicating that LA strain was equivalent, but no better than the parameter that was replaced.

Evaluation of pulmonary venous velocities was not part of the design of the present study, but recordings were available in 123 patients. When comparing correlation with LV filling for pulmonary venous systolic/diastolic flow velocity ratio and LA reservoir strain for these patients there was no significant difference (*r*-values 0.63 and 0.68, respectively). Similar to LA strain, the pulmonary venous velocity ratio works well with reduced EF, but is of limited value in patients with EF ≥ 50%.[1] Higher feasibility for LA strain could make it more useful than pulmonary venous velocity ratio in clinical routine.

Comparison with previous studies

A number of smaller studies have shown somewhat inconsistent results regarding the association between LV filling pressure and LA reservoir strain.[10–13] This could reflect in part the small size of these studies and differences with regard to degree of systolic dysfunction. As shown in the present study, the association between LA reservoir strain and LV filling pressure depends on degree of LV systolic dysfunction. There is so far published only one study of >100 patients with invasive validation of the LA strain as marker of LV filling pressure.[14] In that study, which did a comprehensive evaluation of the role of LA strain in HF with preserved LV EF, they also compared LA strain with LV filling pressure. In their study, however, the median time between echocardiography and measurement of LV filling pressure was 6 days which is a significant limitation.

Limitations

Previous studies have shown feasibility of LA reservoir strain ∼92–95%,[15,16] which means that measurement of LA strain should be realistic in the majority of echocardiographic examinations. Feasibility was apparently slightly better (96%) in the present study, probably reflecting the exclusion of patients with technically inadequate echocardiograms.

Different software was used to determine LA strain at the participating centres. There were essentially similar relationships between atrial strains and LV filling pressure when comparing recordings by equipment and software from different vendors. Smaller differences, however, cannot be excluded since the study was not primarily designed to do direct comparison of equipment.

The present study included patients referred for cardiac catheterization for different reasons, not only referrals for HF. The results could have been slightly different if the study had been limited to patients suspected of HF which was done in a previous study.[2] Inclusion of clinical information, in particular whether there is known myocardial disease and HF symptoms, most likely will give even better accuracy when using LA strain in combination with other echocardiographic parameters for the assessment of LV filling pressure.

The subgroups with LBBB, non-cardiac pulmonary hypertension, restrictive or hypertrophic cardiomyopathy, and mitral regurgitation were too small to make definite conclusions about the utility of LA strain for the evaluation of LV filling pressure in these disorders. In the subgroup with atrial fibrillation, which was somewhat larger, the LA reservoir strain values were <20% regardless of LV filling pressure (Supplementary data online, *Figure S1*). This indicates that LA strain cannot be used to assess LV filling pressure in patients with atrial fibrillation. Patients with cardiac hyperdynamic states such as severe valvular regurgitations or septic shock were not included. Evaluation of LV filling pressure in such patients may not be feasible with the approach suggested in this article.

Conclusions

In patients with reduced LV systolic function, LA reservoir and pump strain predicted LV filling pressure better than conventional echocardiographic markers. High normal values of LA pump strain identified normal filling pressure with high accuracy. When used in combination with the conventional markers, LA strain increases the feasibility of using echo Doppler parameters to estimate LV filling pressure as it provides an additional variable to consider when one of the others is missing.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

Funding

F.H.K. and Ø.S.A. were supported by grants from the South-Eastern Norway Regional Health Authority (Project Numbers 2018018 and 2014068, respectively).

Conflict of interest: none declared.

References

1. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2016;**17**:1321–60.
2. Andersen OS, Smiseth OA, Dokainish H, Abudiab MM, Schutt RC, Kumar A *et al.* Estimating left ventricular filling pressure by echocardiography. *J Am Coll Cardiol* 2017;**69**:1937–48.
3. Lancellotti P, Galderisi M, Edvardsen T, Donal E, Goliasch G, Cardim N *et al.* Echo-Doppler estimation of left ventricular filling pressure: results of the multicentre EACVI Euro-Filling study. *Eur Heart J Cardiovasc Imaging* 2017;**18**:961–8.
4. Badano LP, Kolias TJ, Muraru D, Abraham TP, Aurigemma G, Edvardsen T, Industry representatives *et al.* Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *Eur Heart J Cardiovasc Imaging* 2018;**19**: 591–600.
5. Rahimtoola SH, Loeb HS, Ehsani A, Sinno MZ, Chuquimia R, Lal R *et al.* Relationship of pulmonary artery to left ventricular diastolic pressures in acute myocardial infarction. *Circulation* 1972;**46**:283–90.
6. Paulus WJ, Tschöpe C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers RE *et al.* How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. *Eur Heart J* 2007;**28**:2539–50.
7. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS *et al.* 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2016;**37**:2129–200.
8. Smiseth OA, Thompson CR, Ling H, Robinson M, Miyagishima RT. A potential method to calculate transmural left ventricular filling pressure during positive end-expiratory pressure ventilation: an intraoperative study in humans. *J Am Coll Cardiol* 1996;**27**:155–60.
9. Shen MJ, Arora R, Jalife J. Atrial myopathy. *JACC Basic Transl Sci* 2019;**4**:640–54.
10. Lundberg A, Johnson J, Hage C, Bäck M, Merkely B, Venkateshvaran A *et al.* Left atrial strain improves estimation of filling pressures in heart failure: a simultaneous echocardiographic and invasive haemodynamic study. *Clin Res Cardiol* 2019; **108**:703–15.
11. Singh A, Medvedofsky D, Mediratta A, Balaney B, Kruse E, Ciszek B *et al.* Peak left atrial strain as a single measure for the non-invasive assessment of left ventricular filling pressures. *Int J Cardiovasc Imaging* 2019;**35**:23–32.
12. Telles F, Nanayakkara S, Evans S, Patel HC, Mariani JA, Vizi D *et al.* Impaired left atrial strain predicts abnormal exercise haemodynamics in heart failure with preserved ejection fraction. *Eur J Heart Fail* 2019;**21**:495–505.
13. Cameli M, Lisi M, Mondillo S, Padeletti M, Ballo P, Tsioulpas C *et al.* Left atrial longitudinal strain by speckle tracking echocardiography correlates well with left ventricular filling pressures in patients with heart failure. *Cardiovasc Ultrasound* 2010;**8**:14.
14. Reddy YNV, Obokata M, Egbe A, Egbe A, Yang JH, Pislaru S *et al.* Left atrial strain and compliance in the diagnostic evaluation of heart failure with preserved ejection fraction. *Eur J Heart Fail* 2019;**21**:891–900.
15. Morris DA, Belyavskiy E, Aravind-Kumar R, Kropf M, Frydas A, Braunauer K *et al.* Potential usefulness and clinical relevance of adding left atrial strain to left atrial volume index in the detection of left ventricular diastolic dysfunction. *JACC Cardiovasc Imaging* 2018;**11**:1405–15.
16. Singh A, Addetia K, Maffessanti F, Mor-Avi V, Lang RM. LA strain for categorization of LV diastolic dysfunction. *JACC Cardiovasc Imaging* 2017;**10**: 735–43.