Received: 29 August 2022 | Accepted: 16 December 2022

DOI: 10.1111/cpf.12806

ORIGINAL ARTICLE

Clinical Physiology and Functional Imaging

Left atrial contraction strain during a Valsalva manoeuvre: A study in healthy humans

Peter Gottfridsson[1] | Lucy Law[2] | Roman A'roch[1] | Tomi Myrberg[3] | Magnus Hultin[1] | Per Lindqvist[2] | Michael Haney[1]

[1]Department of Surgical and Perioperative Sciences, Anesthesiology and Intensive Care Medicine Unit, Umeå University, Umea, Sweden

[2]Department of Surgical and Perioperative Sciences, Clinical Physiology Section, Umeå University, Umea, Sweden

[3]Department of Surgical and Perioperative Sciences, Anesthesiology and Intensive Care Medicine Unit, Umeå University (Sunderby sjukhus), Umea, Sweden

Correspondence

Peter Gottfridsson, Department of Surgical and Perioperative Sciences, Anesthesiology and Intensive Care Medicine Unit, Umeå University, 901 85 Umeå, Sweden.
Email: Peter.Gottfridsson@umu.se

Funding information

Västerbotten Läns Landsting

Abstract

Background: Cardiac mechanics are influenced by loading conditions as well as sympathetic tone. Left atrial (LA) contractile function assessed by two-dimensional (2D) strain has been described in the setting of controlled preload alterations; however, studies show conflicting findings about change or direction of change. We hypothesized that the controlled preload reduction and the sympathetic nervous system activation that occurs during a standardized Valsalva manoeuvre would bring about a change in LA contraction strain.

Methods: Healthy young adults of both sexes were recruited. Transthoracic echocardiographic ultrasound images were collected before and during a Valsalva manoeuvre. Standard imaging windows for LA strain assessment were used and the images were copied and stored for later offline analysis. These were assessed for adequate atrial wall visualization in 2D strain assessment. Paired comparisons were carried out using Student's *T* test.

Result: Thirty-eight participants were included and there were 22 complete studies with paired pre- and during Valsalva manoeuvre. LA contraction strain at baseline was $10.5 \pm 2.8\%$ (standard deviation) and during the Valsalva manoeuvre $10.6 \pm 4.6\%$, $p = 0.86$.

Conclusion: The Valsalva manoeuvre, a combination of preload reduction and sympathetic nervous system activation, seems not to be associated with a change in LA contraction strain in healthy young individuals. LA contraction strain should be interpreted in the context of both atrial loading conditions and prevailing autonomic nervous system activity.

KEYWORDS

contractile function, echocardiography, left atrium, preload, speckle tracking, sympathetic nervous system

1 | INTRODUCTION

Cardiac mechanics are influenced by loading conditions as well as sympathetic tone (Meyer et al., 2010; Smiseth et al., 2021). How cardiac mechanics are affected by different loadings conditions is not yet completely understood, neither in healthy nor in critically ill individuals. When assessing critically ill patients with altered hemodynamics, cardiac echocardiography may be useful to guide therapy (Cecconi et al., 2014).

Left atrial (LA) contractile function assessed by two-dimensional (2D) strain (left atrial contraction strain, LASct), has been described in the setting of controlled preload alterations; however, studies show conflicting findings concerning LASct changes (Dermlim et al., 2019; Genovese et al., 2018; Gottfridsson et al., 2022; Mah et al., 2020; Obokata et al., 2013). LA strain may be a measurement that could provide insight into LA and even left ventricular function, with the advantage of allowing serial assessments in individuals to guide diagnosis or treatment. When atrial afterload is elevated, for example, in advanced ventricular dysfunction, LASct has been found to be reduced (Cameli et al., 2016; Inoue et al., 2021). However, how changes in autonomic nervous system input to the heart affect LASct has not yet been well described. One study with controlled preload reductions and general anaesthesia (reduced autonomic nerve system output) describes possible LASct reduction (Howard-Quijano et al., 2015).

Our study focuses on the combination of both controlled preload reduction and sympathetic nervous system activation, and their effects of them on LASct. In acute critical illness, it is common that the neuroendocrine stress response, in combination with intravascular fluid shifts, leads to a reduced venous return to the heart and increased sympathetic tone (Merx & Weber, 2007). Our aim was to determine if there was a predictable change in LASct in response to an experimentally controlled reduction in preload with a simultaneous increase in sympathetic nervous system activity achieved via the Valsalva manoeuvre in healthy volunteers. We hypothesized that the controlled preload reduction and the sympathetic nervous system activation that occurs during a standardized Valsalva manoeuvre would bring about a change in LASct.

2 | METHODS

The project received ethical approval from the Regional Board of Ethics in Umeå, Research with Humans (Dnr 2017-327-31M). Trial design and analysis details were registered at www.clinicaltrails.gov (NCT03436030).

For this study, healthy and consenting young adults of both sexes were recruited for assessment through an advertisement to medical students at Umeå University. Inclusion criteria were age over 18 and self-reported general health, and exclusion criteria were pathology detected on the screening baseline echocardiographic assessment done before data collection. Transthoracic echocardiographic ultrasound images were collected by one expert operator (Lucy Law) using a Vivid 9 ultrasound machine with an M5S cardiac ultrasound probe (GE Healthcare). Patients were supine, or if required for image quality, slightly left decubitus for all imaging. Standard imaging windows were used with a particular focus on the apical four-chamber view and optimization of the LA. At least three heart cycles were recorded and stored for later offline analysis as DICOM files. The measurements were made using commercial software (Echo Pac 203 rev 66.4 GE Healthcare).

The Valsalva manoeuvre was carried out using a resistance tube connected to a manometer which the participants exhaled against. The goal of 40 cm H_2O generated airway pressure was the threshold considered for successful and adequate manoeuvre performance. The physiologic response to the Valsalva manoeuvre can be divided into four phases, as illustrated in Figure 2, where Phase 1 consists of an initial preload increase of the left ventricle (LV) lasting a few heart strokes after starting the manoeuvre. Phase 2 consists of a preload decrease and sympathetic nervous system activation. Phase 3 is the immediate response after stopping the manoeuvre and Phase 4 is the slow recovery (Ghazal, 2017).

A full echocardiographic study was recorded at rest. Then targeted imaging was performed as a baseline at rest, and again during the Valsalva manoeuvre Phase 2. The manoeuvre was repeated as required until all the images were acquired. The volunteers had at least 1 min of recovery between each attempt and an average of two attempts were required. The following images were recorded: LV, LA, Doppler measurements over the mitral valve, aortic valve and tissue Doppler over the lateral LV base. Noninvasive blood pressure measurement was recorded for each measurement sequence using automatic software (Finapres Medical Systems).

Longitudinal strain analysis of the LV and LA were measured as per published guidelines (Badano et al., 2018; Voigt et al., 2020, 2015). Specific heart cycles were chosen to optimize image quality. The myocardial walls were traced manually by a "point and click" method in the analysis software. The chamber wall region of interest width for analysis was manually adjusted to approximately 3 mm. The tracing was managed in five segments. Care was taken to make sure that the traced regions of interest followed the observed myocardial wall during the heart cycle. If one segment did not trace well, the whole series was rejected.

2.1 | Analysis

Grouped results for the different variables were assessed using descriptive statistics and tested for normal distribution with the Shapiro–Wilks test. Paired comparisons were carried out using Student's *T* test (IBM SPSS Statistics for Windows, Version 27.0). Summary results are presented as means with standard deviation.

A power calculation to support sample size estimation was done using a power of 0.8; α, 0.05; baseline LASct estimate, 12.0 and intervention LASct estimate change, 2.5, with a standard deviation of 4 in both groups (based on pilot observations). This supported an estimated sample size of 23, and inclusion was planned for

40 participants given the risk of dropouts and image quality-analysis challenges.

3 | RESULTS

Thirty-eight participants were included, 18 females and 20 males. The mean age was 25.3 ± 3.6 years and the mean body mass index was 23.8 ± 1.9 kg/m^2. All participants stated that they were healthy and there was no pathology detected with the full echocardiographic exam. All participants completed the interventions without difficulty. Ultrasound files were lost for two participants when transferring from the ultrasound machine to the hard drive, resulting in ultrasound material for 36 individual participants being included for further assessment. These were assessed for adequate atrial wall visualization in 2D strain assessment. It was not possible to get an acoustic window adequate for LA strain analysis in 14 participants during the Valsalva manoeuvre, despite rigorous effort. There were 22 complete studies with the paired pre- and during Valsalva LA strain measurements (Figure 1).

Timing for the typical echocardiographic targeted imaging sequence is demonstrated in Figure 2. A representative example of LA strain measurement in a single heart cycle is shown in Figure 3.

The main result was that the Valsalva manoeuvre was not associated with a change in LASct, even though LA loading, measured as a decrease in LA area, was reduced (Table 1). Stroke volume was reduced during the Valsalva measurement as demonstrated by left ventricular outflow tract velocity–time integral values.

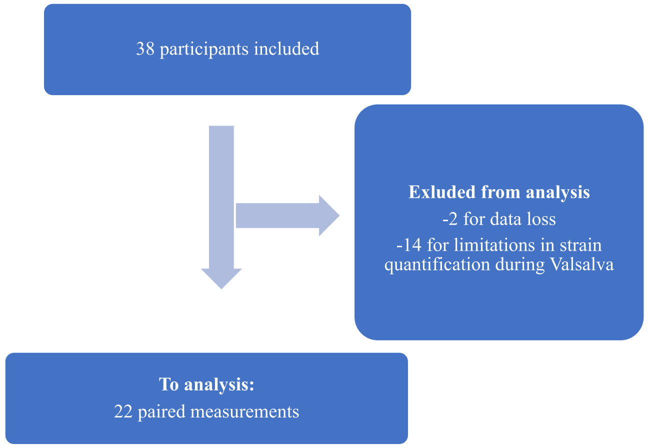

FIGURE 1 A flowchart showing participant inclusion and assessment process.

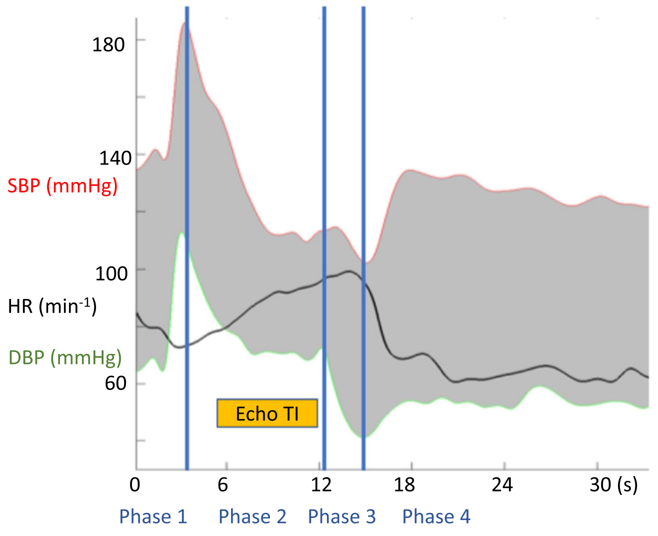

FIGURE 2 An example of Finapres measurements recorded during the Valsalva manoeuvre for one participant. A targeted echocardiographic imaging recording were done during Phase 2 of the Valsalva sequence. DBP, diastolic blood pressure; Echo TI, echocardiographic targeted imaging; HR, heart rate; min, minutes; mmHg, millimetre of mercury; SBP, systolic blood pressure.

4 | DISCUSSION

We successfully conducted structural and functional ultrasound-based assessments during Phase 2 of the Valsalva manoeuvre, as demonstrated by the early transmitral flow (E) and LA area changes when compared to baseline. The main finding was that LASct demonstrated no systematic change between baseline compared to that measured during phase 2 of a Valsalva manoeuvre. The Valsalva manoeuvre is understood to, and used for, bringing about simultaneous preload reduction and sympathetic nervous system activation with input to cardiac contractile function (Ghazal, 2017).

Concerning secondary results, there was no difference in grouped heart rate values, as an indication that the echocardiographic targeted imaging was in the middle of Phase 2 (Ghazal, 2017). Interestingly, the Valsalva manoeuvre, as conducted with this study protocol, seems to be associated with a significant reduction of the early diastolic maximal lateral mitral annular tissue velocities. However, no reduction was measured in the systolic tissue doppler velocities.

There may be several possible explanations for why the Valsalva manoeuvre did not bring about a clear change in LASct. This might be due to a net zero change, as the combined decrease in load and increase and sympathetic tone caused by the performance of the manoeuvre cancel each other out. This would mean that interpreting change in LASct needs to be made in the context of both load and sympathetic tone.

In healthy subjects, the atrial systolic contribution to ventricular filling is relatively small. In conditions where ventricular compliance is reduced and filling pressures are higher, for example, with ventricular diastolic dysfunction, there can be a clinically important ventricular filling contribution from atrial systole. For this reason, LA strain and strain rate measures are sometimes presented together with left ventricular global strain values (Lindqvist & Henein, 2021; Mălăescu et al., 2022). Our study question was focused on LA strain independently in the setting of healthy heart chambers and LASct was not assessed where LV dysfunction was present.

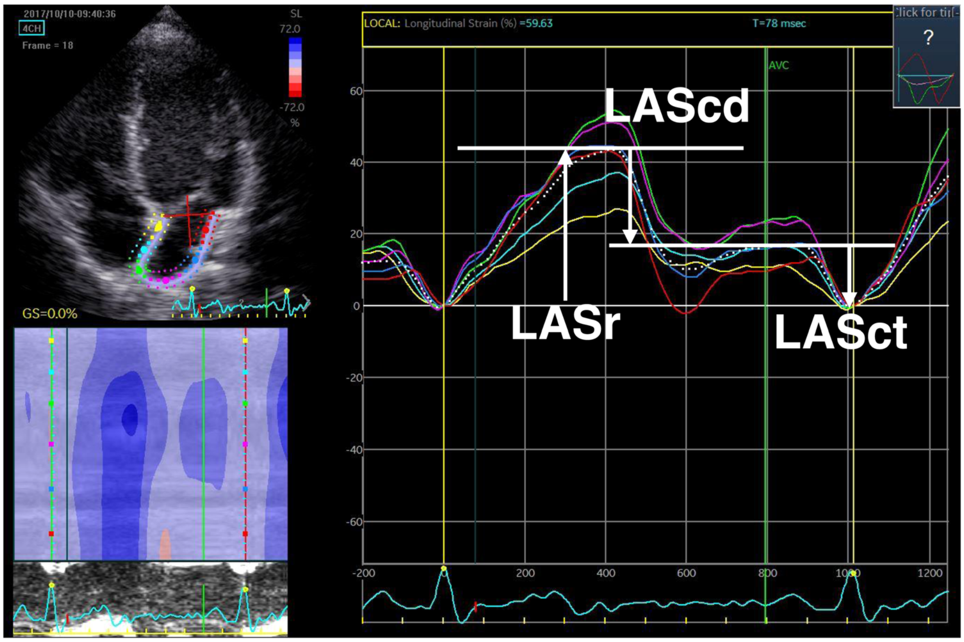

FIGURE 3 Strain imaging over a single heart cycle. This example shows the left atrial contraction strain measurement based on summary values from segmental interrogation. LAScd, left atrial conduction strain; LASct, left atrial contraction strain; LASr, left atrial reservoir strain.

TABLE 1 Ultrasound results

N = 22	Pre Valsalva	During Valsalva	*p* Value
LASct (%)	10.5 (2.8)	10.6 (4.6)	0.86
LASr (%)	44.9 (6.5)	35.4 (7.7)	<0.001
LA area (cm^{-2})	17.9 (3.5)	11.5 (2.9)	<0.001
LV GLS (%)	−19.5 (2.1)	−17.5 (2.9)	<0.001
LVOT VTI (cm)	23.0 (5.9)	16.7 (4.1)	<0.001
E (m/s)	0.78 (0.04)	0.57 (0.07)	<0.001
A (m/s)	0.39 (0.08)	0.41 (0.07)	0.79
e (m/s)	0.15 (0.01)	0.10 (0.02)	<0.001
a (m/s)	0.054 (0.01)	0.047 (0.01)	0.14
S (m/s)	0.096 (0.01)	0.101 (0.02)	0.59
HR (min^{-1})	63.5 (9.9)	65.2 (5.8)	0.35
LV EDV (ml)	107.3 (31.6)	82.3 (19.7)	<0.001

Note: Results are presented as mean values with standard deviation. Abbreviations: A, late trans mitral maximum flow velocity; a, late diastolic maximal lateral mitral annular tissue velocity with atrial contraction; E, early trans mitral maximum flow velocity; e, early diastolic maximal lateral mitral annular tissue velocity; HR, heart rate; LA area, left atrial end-systolic area; LASct, left atrial contraction strain; LV EDV, left ventricular end-diastolic volume; LV GLS, left ventricular global longitudinal strain; LVOT VTI, left ventricular outflow tract velocity–time integral; S, maximal systolic lateral mitral annular tissue.

When implementing the Valsalva manoeuvre as a controlled intervention, care needs to be taken to sample the specific phase of interest in the study context, since it is widely recognized that there are multiple phases within the manoeuvre that correspond with different loading conditions, as well as autonomic nervous system activity. The goal was to generate a condition where sympathetic nerve system input to the heart was transiently increased, where at the same time there was a preload restriction. This is a clinical situation that is not uncommon in cases of critical illness and positive pressure ventilatory support. In this data collection and analysis, much attention was given to this experimental condition for data collection. The major limitation was image quality during Phase 2 since good resolution of atrial wall movement is needed for strain analysis. This is why the two-chamber view was not used in the analysis, though two-chamber views were acquired and assessed.

A strength of the study design was that paired measurements for participants could be acquired, increasing the power of the analysis to identify changes in ultrasound variables using paired comparison. One limitation of this study design was a relatively small sample size, however even considering this, it is unlikely that the study would have missed a large effect on LASct due to the Valsalva manoeuvre. In addition, no reproducibility analysis is presented for the LASct measurement which could have added confidence to the numerical result. Since this cohort included only healthy young individuals, no generalization can be made regarding cohorts with increased age or cardiovascular disease. The present findings reflect normal healthy conditions and provide reference values for the effects of the Valsalva manoeuvre on LA strain in a healthy young population.

We conclude that with the Valsalva manoeuvre, where a combination of preload reduction and sympathetic nervous system activation occurs, there does not seem to be a notable change in LA contraction strain in healthy young individuals. We further conclude that LA contraction strain measurements should be interpreted in the context of both load and sympathetic nervous tone conditions.

ACKNOWLEDGEMENTS

In the department, in which the authors are affiliated, Alexander A'roch helped with data gathering during the experiment, Göran Johansson helped with database management and statistical assistance and Marcus Karlsson helped with Finapres data management.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

All data are available on reasonable request from the corresponding author.

ORCID

Peter Gottfridsson http://orcid.org/0000-0002-4606-9308
Tomi Myrberg http://orcid.org/0000-0002-8802-2321

REFERENCES

Badano, L.P., Kolias, T.J., Muraru, D., Abraham, T.P., Aurigemma, G. & Edvardsen, T. et al. (2018) 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. *European Heart Journal. Cardiovascular Imaging*, 19, 591–600.

Cameli, M., Sparla, S., Losito, M., Righini, F.M., Menci, D., Lisi, M. et al. (2016) Correlation of left atrial strain and Doppler measurements with invasive measurement of left ventricular end-diastolic pressure in patients stratified for different values of ejection fraction. *Echocardiography*, 33, 398–405.

Cecconi, M., De Backer, D., Antonelli, M., Beale, R., Bakker, J., Hofer, C. et al. (2014) Consensus on circulatory shock and hemodynamic monitoring. Task force of the european society of intensive care medicine. *Intensive Care Medicine*, 40, 1795–1815.

Dermlim, A., Osuga, T., Nakamura, K., Morita, T., Nisa, K., Sasaoka, K. et al. (2019) Effect of acute volume loading on left atrial strain values derived from two-dimensional speckle tracking echocardiography in dogs. *Journal of Veterinary Medical Science*, 81, 949–957.

Genovese, D., Singh, A., Volpato, V., Kruse, E., Weinert, L., Yamat, M. et al. (2018) Load dependency of left atrial strain in normal subjects. *Journal of the American Society of Echocardiography*, 31, 1221–1228.

Ghazal, S.N. (2017) Valsalva maneuver in echocardiography. *Journal of Echocardiography*, 15, 1–5.

Gottfridsson, P., A'roch, R., Lindqvist, P., Law, L., Myrberg, T., Hultin, M. et al. (2022) Left atrial contraction strain and controlled preload alterations, a study in healthy individuals. *Cardiovascular Ultrasound*, 20, 8.

Howard-Quijano, K., Anderson-Dam, J., McCabe, M., Hall, M., Mazor, E. & Mahajan, A. (2015) Speckle-tracking strain imaging identifies alterations in left atrial mechanics with general anesthesia and positive-pressure ventilation. *Journal of Cardiothoracic and Vascular Anesthesia*, 29, 845–851.

Inoue, K., Khan, F.H., Remme, E.W., Ohte, N., García-Izquierdo, E. & Chetrit, M. et al. (2021) Determinants of left atrial reservoir and pump strain and use of atrial strain for evaluation of left ventricular filling pressure. *European Heart Journal. Cardiovascular Imaging*, 23, 61–70.

Lindqvist, P. & Henein, M. (2021) Left atrial strain rate during atrial contraction predicts raised pulmonary capillary wedge pressure: evidence for left atrio-ventricular interaction. *The International Journal of Cardiovascular Imaging*, 37, 1529–1538.

Mah, K., Bruce, A., Zahari, N., Venner, M.A., Chow, K., Thompson, R.B. et al. (2020) Tilt-table echocardiography unmasks early diastolic dysfunction in patients with hemoglobinopathies. *Journal of Pediatric Hematology/Oncology*, 42, 391–397.

Mălăescu, G., Mirea, O., Capotă, R., Petrescu, A.M., Duchenne, J. & Voigt, J.U. (2022) Left atrial strain determinants during the cardiac phases. *JACC: Cardiovascular Imaging*, 15, 381–391.

Merx, M.W. & Weber, C. (2007) Sepsis and the heart. *Circulation*, 116, 793–802.

Meyer, C., Rana, O.R., Saygili, E., Gemein, C., Becker, M., Nolte, K.W. et al. (2010) Augmentation of left ventricular contractility by cardiac sympathetic neural stimulation. *Circulation*, 121, 1286–1294.

Obokata, M., Negishi, K., Kurosawa, K., Arima, H., Tateno, R., Ui, G. et al. (2013) Incremental diagnostic value of la strain with leg lifts in heart failure with preserved ejection fraction. *JACC: Cardiovascular Imaging*, 6, 749–758.

Smiseth, O.A., Baron, T., Marino, P.N., Marwick, T.H. & Flachskampf, F.A. (2021) Imaging of the left atrium: pathophysiology insights and clinical utility. *European Heart Journal. Cardiovascular Imaging*, 23, 2–13.

Voigt, J.U., Mălăescu, G., Haugaa, K. & Badano, L. (2020) How to do LA strain. *European Heart Journal. Cardiovascular Imaging*, 21, 715–717.

Voigt, J.U., Pedrizzetti, G., Lysyansky, P., Marwick, T.H., Houle, H., Baumann, R. et al. (2015) Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/industry task force to standardize deformation imaging. *European Heart Journal. Cardiovascular Imaging*, 16, 1–11.

How to cite this article: Gottfridsson, P., Law, L., A'roch, R., Myrberg, T., Hultin, M., Lindqvist, P. et al. (2023) Left atrial contraction strain during a Valsalva manoeuvre: a study in healthy humans. *Clinical Physiology and Functional Imaging*, 43, 165–169. https://doi.org/10.1111/cpf.12806