ORIGINAL ARTICLE

The Reservoir Function. Functional Evaluation of the Left Atrium by Two-dimensional Strain during Rest and Exercise Stress

La reserva del reservorio. Evaluación funcional por Strain 2D de la aurícula izquierda en reposo y esfuerzo

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ABSTRACT

Background: According to different guidelines, the echocardiographic evaluation of left atrial function based on dimensions, areas, volumes and diastolic function through pulsed-wave Doppler interrogation is fundamental, as left atrial dilatation has been shown to be a predictor of adverse cardiovascular events. The advent of new echocardiographic techniques has allowed the assessment of atrial deformation (strain) with curves that identify the reservoir, conduit and contractile function. However, there is still no consensus to define left atrial strain by speckle tracking in normal patients and its response with exercise.

Objectives: The aim of this study was to establish the left atrial strain reference value at rest and during peak exercise stress echocardiography in healthy patients and to analyze the relationship between deformation and the E/e' ratio to assess changes in atrial stiffness.

Methods: This was a descriptive, prospective, observational study, including patients over 18 years of age, with no cardiovascular risk factors or previous history of comorbidities, who underwent an exercise stress echocardiography test between January and March 2017. A Vivid E 95 ultrasound system (GE Healthcare) was used, with 5MS MHz transducer and image acquisition frame rate between 60 and 70 frames per second at rest, and between 80 and 100 during exercise. Loops were obtained in 4-chamber and 2-chamber views, both at rest and at maximum exercise load, and were analyzed offline with EchoPac 201 software. Strain was measured tracing the borders of the left atrium at 1 mm from the mitral valve annulus, and manually adjusting the width of the region of interest to cover atrial wall thickness. The 6 segments were considered for each view and the average value of the curve corresponding to the reservoir was analyzed, as it was the most representative and reproducible. The average E/e'/left atrial strain × 100 ratio was used to calculate atrial stiffness. For the statistical analysis, categorical variables were expressed as percentages; quantitative variables were expressed as mean±SD and compared using paired t test. Significance was established for $p < 0.05$.

Results: Among the 34 patients meeting the inclusion criteria, 3 were excluded due to poor echocardiographic window at rest and 2 during exercise. Mean age of the remaining 29 patients (85% total feasibility) was 50±10.6 years and 16 were men. Intraobserver variability of reservoir calculated at rest and during exercise was 2.2±1.6% and 2.3±2.5%, respectively, and interobserver variability 6±7% and 4.6±4%.

Conclusions: In normal patients it was possible to assess left atrial reservoir function at rest and during maximum exercise stress with a significant increase of deformation and without changes in atrial stiffness.

Key words: Stress Echocardiography - Left Atrial Function - Left atrial strain.

RESUMEN

Introducción: El estudio ecocardiográfico de la función global auricular izquierda, según guías, se basa en la medición de dimensiones, áreas, volúmenes y la función diastólica mediante la interrogación con Doppler pulsado. Su importancia es trascendental, ya que su dilatación ha demostrado ser un predictor de eventos cardiovasculares adversos.

Con el advenimiento de las nuevas técnicas ecocardiográficas es posible evaluar la mecánica de la deformación de la pared auricular (strain) con curvas que identifican la función de reservorio, conducto y contracción. Sin embargo, aún no hay consenso para definir el valor de strain auricular izquierdo determinado mediante speckle tracking en pacientes normales y su respuesta con el ejercicio.

Objetivos: Establecer el valor de referencia de strain auricular izquierdo en pacientes sanos en reposo y durante el pico de un ecoestrés de esfuerzo. Además, analizar la relación de la deformación con la E/e´ para determinar los cambios de rigidez auricular.

Metodología: Estudio descriptivo, prospectivo, observacional. Se incluyeron los pacientes mayores de 18 años, sanos, sin factores de riesgo cardiovascular, ni antecedentes patológicos a los que se realizó un ecoestrés con ejercicio entre enero y marzo 2017.

Se utilizó un Vivid E 95 (GE Healthcare), con transductor 5MS MHz, con adquisición de las imágenes con un frame rate entre 60 - 70 en reposo y entre 80 - 90 en el esfuerzo. Los loops se obtuvieron en las vistas de 4 cámaras y 2 cámaras, tanto en reposo como a la máxima carga de ejercicio y se analizaron offline (EchoPac Version 201). Para la medición de strain se trazaron los bordes de la AI, a

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1 mm de distancia del anillo de la válvula mitral, ajustando de manera manual el ancho de la zona de interés en relación al espesor de la pared auricular. Se consideraron los 6 segmentos por cada vista y se analizó el valor promedio de la curva correspondiente al reservorio por ser la más representativa y reproducible. Para el valor de rigidez auricular se calculó el promedio E/e´/strain AI x 100. En el análisis estadístico las variables categóricas se expresan como porcentaje y las cuantitativas como media ± DS y se comparan con test de t para muestras pareadas. Se consideró significativa una $p < 0.05$.

Resultados: De 34 pacientes pacientes con criterios de inclusión se excluyeron a 3 por mala ventana ecocardiográfica en reposo y 2 en el esfuerzo. De los 29 pacientes analizados (factibilidad total 85 %) 16 fueron hombres con una media de edad de la población de 50 ± 10.6 años. La variabilidad intraobservador del cálculo del reservorio en reposo y esfuerzo fue del 2.2 %±1.6 y 2.3% ± 2.5 e interobservador de 6% ±7 y 4.6% ± 4 respectivamente.

Conclusiones: En una población normal resultó factible evaluar la función del reservorio de la aurícula izquierda en reposo y durante el esfuerzo máximo con un incremento significativo de la deformación, sin cambios de la rigidez auricular.

Palabras clave: Ecocardiografía de Estrés - Función auricular izquierda - Strain Auricular Izquierdo.

Abbreviations

LA	Left atrium	**bpm**	Beats per minute
SD	Standard deviation	**PASP**	Pulmonary artery systolic pressure
HR	Heart rate	**SPSS**	Statistical Package for the Social Sciences

INTRODUCTION

It is currently recognized that the left atrium (LA) is more than a chamber for the passage of blood flow and that its normal function is essential for the modulation of left ventricular filling. Its function may be divided into three phases: 1) reservoir phase for the venous return during ventricular systole and isovolumic contraction, 2) conduit phase during early diastole and 3) pump phase during atrial contraction, which contributes with 15% to 30% of cardiac output. (1) To achieve these functions, the LA has cylindrical cardiomyocytes, which usually bifurcate at the ends and are connected by intercalated discs, forming syncytia through which the electrical impulse propagates to activate its mechanical action. (2)

The importance of adequate left atrial function has been well established, as its dilatation is a prognostic predictor of different diseases, as transient or permanent cerebrovascular accident, heart failure and atrial fibrillation. (3-5) Therefore, two- and more recently three-dimensional transthoracic echocardiography is essential to assess left atrial function in patients at risk of cardiovascular events.

Today, the study of left atrial function is mainly based on area, volume and diastolic function measurements with pulsed Doppler ultrasound, as established by chamber quantification guidelines. (6) However, the development of new technologies, initially designed to evaluate ventricular function, have provided new tools to analyze atrial myocardial fiber deformation curves in their different phases during the cardiac cycle, allowing a better understanding of atrial function contribution to cardiac mechanics.

Several studies have already defined normal left atrial strain and strain rate values by speckle tracking echocardiography in healthy subjects, (7-9) and although there is as yet no international consensus on these normal values, there are studies showing the usefulness of evaluating atrial mechanical performance as an early predictor of cardiovascular events and of the association between left atrial function at rest and left ventricular filling pressures. (10-14)

Since the beginning of stress echo, new quantitative technologies have been incorporated to decrease the subjectivity of the method and increase diagnostic precision. Several publications have reported the response of left ventricular deformation during exercise and pharmacological stress, but only one recent article published in October 2017 has reported the use of two-dimensional (2D) strain to assess atrial function during exercise stress echo and heart failure with preserved ejection fraction. (19)

The aim of this study was thus to establish the reference value of left atrial strain at rest and during peak exercise stress echo in healthy subjects and analyze the relationship between deformation and the E/e' ratio to determine changes in atrial stiffness.

METHODS

Patients

All patients over 18 years of age, without cardiovascular risk factors or personal history of disease, referred to the echocardiography laboratory of our institution (Investigaciones Médicas, Buenos Aires) to undergo diagnostic exercise stress echocardiography, were prospectively included in the study between January 2 and March 31, 2017. Patients with suboptimal ultrasound window and those with positive stress echo due to ischemia, or with absence of contractile reserve. or left ventricular diastolic dysfunction were excluded from the study.

Stress echo

An exercise stress echo was performed with supine cycle ergometry. Exercise consisted in 3-minute stages, increasing 25 Watts per stage, to achieve at least 85% of the maximum cardiac heart rate (HR) estimated for patient age (modified Astrand protocol). A complete echocardiographic evaluation of cardiac chamber diameters, areas and volumes and systolic and diastolic function was performed before starting the exercise. A Vivid E 95 (GE Health Care, Milwaukee, USA) ultrasound system, equipped with M5S MHz multi-frequency transducer was used for the studies.

Our conventional institutional protocol of ventricular image acquisition was performed, together with targeted left atrial images in 4- and 2-chamber views at rest and prior to the maximum load achieved by the patient. Baseline images were captured at a frame rate of 60 to 70 per second and during exercise stress between 80 and 90 per second. The values of septal e', lateral e' and the E wave of mitral inflow with the average of the two e's ratio (E/ e'average) were calculated by tissue Doppler echocardiography. The E/e'/ LA strain × 100 index was used to assess atrial stiffness and the stiffness/LA volume index was determined. Complete Doppler echocardiography was achieved at rest and during exercise stress, including pulmonary pressure measurements whenever tricuspid valve reflow velocity could be recorded. Simultaneously, a 12-lead electrocardiogram was performed in each patient and blood pressure was measured in each exercise stage.

Two-dimensional left atrial longitudinal strain

The analysis of left atrial deformation was performed offline in an EchoPac workstation (GE Healthcare) tracing atrial borders 1 mm below the mitral valve plane, and manually adjusting the region of interest width to the atrial wall thickness of all the segments analyzed.

The onset of the QRS complex was used as reference point for the analysis of left atrial strain. Six segments per view were considered and the strain (%) curves were analyzed in the atrial reservoir phase at rest and at the maximum load attained during exercise. In addition, indexed biplane atrial volumes and E/e' data were explored to obtain atrial stiffness indexes.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation or median and interquartile range, and categorical variables are presented as percentages. Differences between groups for continuous variables with normal distribution were analyzed with Student's t test for related data. A p value <0.05 was considered as statistically significant. SPSS 18 (SPSS Inc. 5 Chicago, IL) software package was used for statistical analyses.

Ethical considerations

The study was evaluated and approved by the institutional Ethics Committee. All patients signed an informed consent before entering the study.

RESULTS

Stress echo

The patients did not present complications during the exercise stress test.

Population characteristics

A total of 550 exercise stress echocardiograms were performed in our laboratory between January 2 and March 31, 2017. Among the 34 patients meeting the inclusion criteria, 3 were excluded due to bad echocardiographic window at rest and 2 during exercise. Mean age of the remaining 29 patients was 50±10.6 years, and 16 were men. Mean HR at rest was 67± 16 beats per minute (bpm) and at maximum exercise load 115±28 bpm.

Atrial volume, tissue Doppler, strain and stiffness

Table 1 shows the values of tissue Doppler septal e', lateral e', E wave velocity and E/e' average ratio at rest and exercise stress in 29 patients with normal stress echo. As shown in Table 1, pulmonary artery systolic pressure (PASP) could also be obtained in 27 patients at rest during exercise. Atrial volume indexed by body surface area was calculated from 4-and

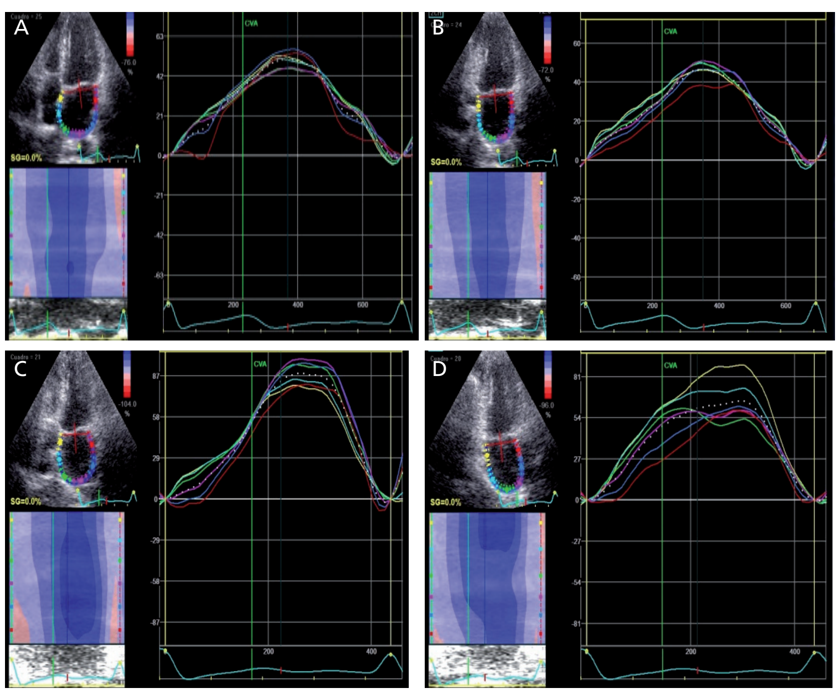

Fig. 1. Rest and exercise stress left atrial strain by speckle tracking in the reservoir phase. The analysis of left atrial (LA) strain curves in the reservoir phase was performed in 12 segments, 6 in 4-chamber view (4C) and 6 in 2-chamber view (2C), both at rest and during exercise stress. The point of greatest deformation of the dotted white curve in each image marks mean strain in the reservoir. (**A**) 4C left atrial strain at rest. (**B**) 2C left atrial strain at rest. (**C**) 4C left atrial strain during exercise stress. (**D**) 2C left atrial strain during exercise stress. Mean LA strain at rest was 44.9±7.8% and during exercise stress 58.9±9.4% (p <0.0001), with a difference of 14 points.

2-chamber views, with mean value of 26.6±6.8 ml/m2 at rest and 22.1±5.8 ml/m2 at maximum load (p=0.009). Mean left atrial longitudinal strain by 4- and 2-chamber speckle tracking echocardiography, calculated from the average of the 12 segments analyzed, was 44.9±7.8 % at rest and 58.9±9.4 % at maximum load (p <0.0001) (Figura 2).

Atrial stiffness and the stiffness/volume ratio at rest were 17.6±6 and 0.82±0.4, respectively and at maximum load 15.8±4.2 and 0.75±0.3, respectively, without significant statistical differences (Figure3).

Feasibility and intra and interobserver variability

The feasibility of measuring atrial strain at maximum load was 85%.

Intraobserver variability of reservoir calculation at rest and exercise stress was 2.2±1.6% and 2.3±2.5%, respectively, and interobserver variability was 6±7% and 4.6±4%, respectively.

DISCUSSION

New echocardiographic tools allow the quantification of cardiac mechanics with values comparable to other more complex and less available cardiovascular imaging techniques.

Table 1. Results

	HR	E cm/s	Septal e' cm/s	Lateral e' cm/s	E/.e' average	PASP mmHg	Indexed LA volume ml/m2	Mean LA strain %	Stiffness	Stiffness/Volume
Baseline	67 ± 1.06	75.04 ± 15.69	9.45 ± 3.4	11.2 ± 3.8	7.7 ± 2.2	26.7 ± 8.75	26.6 ± 6.8	44.9 ± 7.8	17.8 ± 6	0.82 ± 0.4
Peak	115 ± 28	102 ± 17.99	11 ± 2.0	12 ± 2.1	9.1 ± 1.8	44.18 ± 11.84	22.1 ± 5.8	58.9 ± 9.4	15.8 ± 4.2	0.75 ± 0.3
p	<0.0001	<0.0001	0.01	NS	0.003	<0.0001	0.009	<0.0001	NS	NS

Baseline and peak maximum exercise values of the variables assessed. Left atrial (LA) strain is the mean of the 12 segments analyzed. Stiffness: (E/e´ / LA strain ×100) HR: Heart rate. PASP: Pulmonary artery systolic pressure

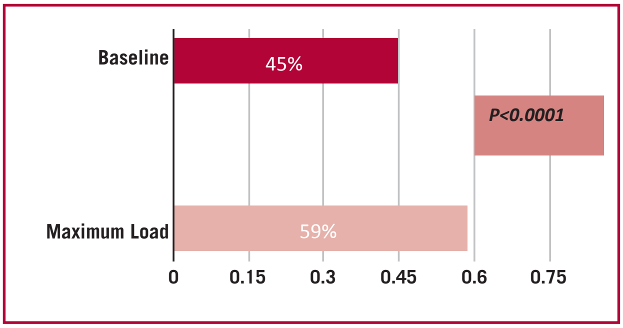

Fig. 2. Mean left atrial strain by speckle tracking in the reservoir phase, comparing baseline and exercise stress at maximum load.

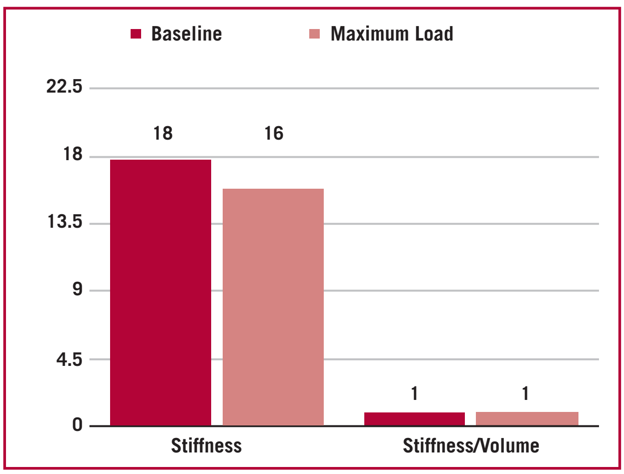

Fig. 3. Comparative values of stiffness (E/e´/LA strain × 100) and the Stiffness/Volume index at rest and during exercise stress.

Two-dimensional strain, calculated from the analysis of longitudinal deformation, is the most widely used variable to assess left ventricular function. This deformation is the change in length corrected by the original length or the percent change from the initial dimension.

Non-Doppler 2D strain is a novel technique analyzing the movement of natural acoustic markers (speckles) distributed in the myocardium, which allow assessing the magnitude and sense of local wall motion to estimate tissue motion velocity and deformation, independently of the insonation angle.

Classical parameters of diastolic ventricular function are not always premature, and show variations depending on loading conditions and HR, yielding controversial results. Neither are dimension and volume calculations useful to assess atrial function when patient evaluation with subclinical disease is attempted, as they are frequently non-pathological. In most cases these measurements are only altered when the patient presents morphological changes of the LA. Therefore, different investigators, as Dr. Jae Oh et al. (20) have started to use left atrial longitudinal strain by speckle tracking to calculate atrial stiffness indices. These indices have been analyzed and reproduced with great feasibility by other authors, as Dr. Héctor Deschle et al., who published his experience in asymptomatic, young, hypertensive patients, and also studied the new stiffness/LA volume ratio index. (21)

Previous descriptions have been reported on left atrial behavior in resting normal conditions, (22) but we thought it was important to assess its conduct during exercise stress echocardiography in healthy subjects.

Exercise stress echocardiography has shown to be useful not only for the diagnosis of ischemic heart disease, but also in many other diseases, with the advantage of providing more information of the patient's hemodynamic condition than pharmacological studies. (23)

The aim of the present study was to establish the reference value of left atrial strain in healthy subjects at rest and at peak exercise stress. In addition, strain was compared with other important parameters, as the relationship of deformation with E/e' to establish changes in atrial stiffness.

Numerous studies have evaluated diastolic function by means of the relationship between the E wave of mitral valve inflow and the average tissue velocity at the level of the septal and lateral mitral valve annulus, both at rest and during exercise. (24, 25) It has also been shown that patients with decreased strain have lower exercise capacity, equivalent to an increase in E/e'. (26)

In the present work we observed a significant increase in the E/e' ratio during exercise stress from 7.7±2.2 to 9.1±1.8 ($p=0.003$), but within values considered normal. It is known that an E/e' increase above 13 or 14 is a parameter of diastolic dysfunction, with prognosis similar to an ischemic response, and with high rate of complications during evolution. (27, 28)

The values of global left atrial strain correlate well with Doppler echocardiography indices, representing atrial and ventricular diastolic function. Therefore, it was expected that in healthy individuals assessed at rest and exercise stress, the increase of left atrial function evaluated by 2D strain was manifested as normal E/e' ratio and atrial stiffness, and with adequate increase in pulmonary artery pressure during stress (see Table 1).

We consider that the analysis of left atrial myocardial deformation during exercise stress could provide in the future valuable and early information for the diagnosis of numerous diseases. But, as it could probably have a very different performance in patients with ischemic response, it was first necessary to know the behavior in normal subjects.

Our results showed that left atrial reservoir reserve by 2D strain was feasible and reproducible.

It was seen that mean left atrial reservoir deformation was 44.9±7.8% at rest, similar to the value of 46.17±10.05% reported by Deschle et al. (21) and slightly more elevated than the one (39.6±7.8%) referred by Mondillo et al. (29)

Concordant values have been reported by other authors calculating reservoir strain from fewer segments because they exclude the atrial roof, as in the study of J. P. Sun et al. which reported an average strain of 46.8±7.7% (7). Moreover, other authors also discarded the interatrial septum, (21) while in our study we incorporated the 6 segments per chamber analyzed, following the recommendations of S. Mondillo's Italian group. (29)

An average increase of 15 percent points between rest and peak exercise, from 44.9±7.8% to 58.9±9.4%, revealed that healthy individuals have an important left atrial reservoir reserve.

A very recent work published by investigators of the University of Milan, also registered an increase ranging from 31±5.6% to 39±8% in 4-chamber views during exercise stress in normal controls, showing the relevance of determining left atrial strain during exercise as a novel parameter of left atrial dysfunction limiting exercise capacity. (19)

In the present study we also evaluated left atrial stiffness as the increase in pressure required to elicit a certain rise in volume, and the value of 17.8±6 was similar to the one (19.9±4) reported by Deschle et al., the small difference probably related with patient age (50±10.6 years vs. 43.72±5.02 years).

It is known that a decrease of ventricular contractile reserve evaluated by strain, assessed with either pharmacological or exercise stress echo plays an important prognostic role in different scenarios, as heart failure with preserved ejection fraction and normal values at rest, (30) coronary artery disease and heart valve disease patients. (31-33)

In our laboratory, we are now focused in determining what happens with left atrial remodeling, expressed by changes in strain during exercise in elite athletes and in patients with hypertension, heart valve disease, ischemia and heart failure with preserved ejection fraction. This is the new challenge.

Limitations

A limitation of this study is the small number of patients, because as it is a highly specialized diagnostic center, the number of normal individuals that could be analyzed in the study period was not very high.

The left ventricular algorithm available in the workstations was used to calculate left atrial strain, as there is no specific software dedicated to the atrium.

Strain by speckle tracking was assessed only in the reservoir phase of the LA since, among the three phases of left atrial function it is the longest one, with good feasibility and reproducibility.

The onset of the QRS complex was used as reference point for left atrial strain analysis, whereas other authors postulate the p wave to start tracing the strain curves. (11) We computed the average of the 6 atrial walls although different works discarded the atrial roof due to the discontinuity produced by the entry of the pulmonary veins and in others, the interatrial septum was not considered as it shared the structure with the right atrial chamber; (7, 21) however, our results were not different from these works.

The images to calculate left atrial deformation were acquired during exercise in supine position prior to peak stress, so the HR was not always the maximum achieved by the patient.

Technically, the analysis of 2D longitudinal deformation depends on the ultrasound window, so elevated HR usually generates artifacts and lower quality images for post-processing.

CONCLUSIONS

The assessment of the left atrial reservoir function at rest and during exercise stress was feasible and reproducible in healthy subjects, with a significant increase of strain but without changes in atrial stiffness with exercise.

Conflicts of interests

None declared.

(See authors' conflicts of interest forms on the web/Supplementary material).

REFERENCES

1. Mehrzad R1, Rajab M2, Spodick DH. The three integrated phases of left atrial macrophysiology and their interactions. Int J Mol Sci 2014;15:15146-60. http://doi.org/f6k8n2
2. Goette A, Kalman JM, Aguinaga L, Akar J, Cabrera JA, Chen SA, et al. EHRA/HRS/APHRS/SOLAECE expert consensus on atrial cardiomyopathies: definition, characterization, and clinical implication. Europace 2016;18:1455-90. http://doi.org/chns
3. Tsang TS, Abhayaratna WP, Barnes ME, Miyasaka Y, Gersh BJ, Bailey KR, et al. Prediction of cardiovascular outcomes with left atrial size: Is volume superior to area or diameter? J Am Coll Cardiol 2006;47:1018–23. http://doi.org/dwd3qk
4. Laukkanen JA, Kurl S, Eranen J, Huttunen M, Salonen JT. Left atrium size and the risk of cardiovascular death in middle-aged men. Arch Intern Med 2005;165:1788–93. http://doi.org/dq7ch3
5. Benjamin EJ, D'Agostino RB, Belanger AJ, Wolf PA, Levy D. Left atrial size and the risk of stroke and death. The Framingham Heart Study. Circulation 1995;92:835–41. http://doi.org/q3p
6. Lang R, Badano L, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1-39. http://doi.org/bhj5
7. Sun JP, Yang Y, Guo R, Wang D, Lee AP, Wang XY, et al. Left atrial regional phasic strain, strain rate and velocity by speckle-tracking echocardiography: normal values and effects of aging in a large group of normal subjects. Int J Cardiol 2013;168:3473-9. http://doi.org/f5ghbz
8. Vianna-Pinton R, Moreno CA, Baxter CM, Lee KS, Tsang TS, Appleton CP. Two-dimensional speckle-tracking echocardiography of the left atrium: feasibility and regional contraction and relaxation differences in normal subjects. J Am Soc Echocardiogr 2009;22:299-305. http://doi.org/fpt9w6
9. Saraiva RM, Demirkol S, Buakhamsri A, Greenberg N, Popović ZB, Thomas JD, et al. Left atrial strain measured by two-dimensional speckle tracking represents a new tool to evaluate left atrial function. J Am Soc Echocardiogr 2010;23:172-80. http://doi.org/c59w4n
10. Inaba Y, Yuda S, Kobayashi N, Hashimoto A, Uno K, Nakata T, et al. Strain Rate Imaging for Noinvasive Funtional Quatification of the left atrium: comparative studies in control and patients with atrial fibrillation. J Am Soc Echocardiogr 2005;18:729–36. http://doi.org/bcns9z
11. Kim DG, Lee KJ, Lee S, Jeong SY, Lee YS, Choi YJ, et al. Feasibility of two-dimensional global longitudinal strain and strain rate imaging for the assessment of left atrial function: a study in subjects with a low probability of cardiovascular disease and normal exercise capacity. Echocardiography 2009;26:1179-87. http://doi.org/c59w4n
12. Kurt M, Wang J, Torre-Amione G, Nagueh SF. Left atrial function in diastolic heart failure. Circ Cardiovasc Imaging 2009;2:10-5. http://doi.org/dd5q4m
13. Cameli M, Ciccone M, Maiello M, Modesti P, Muiesan M, Scicchitano P, et al. Speckle tracking analysis: a new tool for left atrial function analysis in systemic hypertension: an overview. J Cardiovasc Med 2016;17:339-43. http://doi.org/f8f5px
14. Otani K, Takeuchi M, Kaku K, Haruki N, Yoshitani H, Tamura M, et al. Impact of diastolic dysfunction grade on left atrial mechanics assessed by two-dimensional speckle tracking echocardiography. J Am Soc Echocardiogr 2010;23:961-7. http://doi.org/b7f4qc
15. Caniggia C, Amor M, Lowenstein Haber D, Alasia D, Galello M, Darú V, et al. Factibilidad y aportes del análisis de la deformación longitudinal 2D global y regional durante el eco estrés con ejercicio. Rev Argent Cardiol 2014;82:126-32.
16. Uusitalo V, Luotolahti M, Pietilä M, Wendelin-Saarenhovi M, Hartiala J, Saraste M, et al. Two-Dimensional Speckle-Tracking during Dobutamine Stress Echocardiography in the Detection of Myocardial Ischemia in Patients with Suspected Coronary Artery Disease. J Am Soc Echocardiogr 2016;29:470-9. http://doi.org/f8kzkf
17. Govind SC, Gopal AS, Netyö A, Nowak J, Brodin LA, Patrianakos A, et al. Quantification of low-dose dobutamine stress using speckle tracking echocardiography in coronary artery disease. Eur J Echocardiogr 2009;10:607-12. http://doi.org/cv28sh
18. Cusmà Piccione M, Zito C, Khandheria B, Madaffari A, Oteri A, et al. Cardiovascular maladaptation to exercise in young hypertensive patients. Int J Cardiol 2017;232:280-8. http://doi.org/gbhfsk
19. Sugimoto T, Bandera F, Generati G, Alfonzetti E, Bussadori C, Guazzi M. Left Atrial Function Dyamics During Exercise in Heart Failure. JACC Cardiovasc Imaging 2017;10:1253-64. http://doi.org/chnq
20. Oh JK, Park SJ, Nagueh SF. Established and novel clinical applications of diastolic function assessment by echocardiography. Circ Cardiovasc Imaging 2011;4:444-55. http://doi.org/fkhtp2
21. Deschle H, Gantesti J, Culaciati G, Casso No, Alfie L, Gingins M, et al. Análisis de la deformalción auricular longitudinal: alteraciones precoces en hipertensos jóvenes controlados. Rev Argent Cardiol 2014;82:126-32.
22. Cameli M, Caputo M, Mondillo S, Ballo P, Palmerini E, Lisi M, et al. Feasibility and reference values of left atrial longitudinal strain imaging by twodimensional speckle tracking. Cardiovasc Ultrasound 2009;7:6. http://doi.org/b5c9vc.
23. Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, et al. The clinical use of stress echocardiography in non-ischaemic heart disease: recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. Eur Heart J Cardiovasc Imaging 2016;17:1191-229. http://doi.org/chnn
24. Burgess MI, Jenkins C, Sharman JE, Marwick TH. Diastolic stress echocardiography: hemodynamic validation and clinical significance of estimation of ventricular filling pressure with exercise. J Am Coll Cardiol 2006;47:1891-900. http://doi.org/fgbf7g
25. Leung M, Phan V, Whatmough M, Heritier S, Wong VW, Leung DY. Left ventricular diastolic reserve in patients with type 2 diabetes mellitus. Open Heart 2015;2:e000214. http://doi.org/chnm
26. Kusunose K, Motoki H, Popovic ZB, Thomas JD, Klein AL, Marwick TH. Independent association of left atrial function with exercise capacity in patients with preserved ejection fraction. Heart 2012;98:1311-7. http://doi.org/f36348
27. Holland DJ, Prasad SB, Marwick TH. Prognostic implications of left ventricular filling pressure with exercise. Circ Cardiovasc Imaging 2010;3:149-56. http://doi.org/c35zrh
28. Ha JW, Oh JK, Pellikka PA, Ommen SR, Stussy VL, Bailey KR, et al. Diastolic stress echocardiography: a novel noninvasive diagnostic test for diastolic dysfunction using supine bicycle exercise. Doppler echocardiography. J Am Soc Echocardiogr 2005;18:63-8. http://doi.org/ctvg64
29. Mondillo S, Cameli M, Caputo ML, Lisi M, Palmerini E, Padeletti M, et al. Early detection of left atrial strain abnormalities by speckle-tracking in hypertensive and diabetic patients with normal left atrial size. J Am Soc Echocardiogr 2011;24:898-908. http://doi.org/czr2w2
30. Tan YT, Wenzelburger F, Lee E, Heatlie G, Leyva F, Patel K, et al. The pathophysiology of heart failure with normal ejection fraction:exercise echocardiography reveals complex abnormalities of both systolic and diastolic ventricular function involving torsion,

untwist, and longitudinal motion. J Am Coll Cardiol 2009;54:36-46. http://doi.org/bttghk
31. Szymczyk E, Lipiec P, Michalski B, Szymczyk K, Shim A, Woźniakowski B, et al. 2D speckle tracking echocardiography for the assessment of regional contractile reserve after myocardial infarction. J Cardiovasc Med (Hagerstown). 2016;17:374-81. http://doi.org/f8f43c
32. Lafitte S, Perlant M, Reant P, Serri K, Douard H, DeMaria A, et al. Impact of impaired myocardial deformations on exercise tolerance and prognosis in patients with asymptomatic aortic stenosis. Eur J Echocardiogr 2009;10:414-9. http://doi.org/cr83pv
33. Lancellotti P, Cosyns B, Zacharakis D, Attena E, Van Camp G, Gach O, et al. Importance of left ventricular longitudinal function and functional reserve in patients with degenerative mitral regurgitation: assessment by two-dimensional speckle tracking .J Am Soc Echocardiogr 2008;21:1331. http://doi.org/c88w77