

# Left Atrial Longitudinal Strain: Early Alterations in Young Patients with Mild Hypertension

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## ABSTRACT

### Objectives

The aim of this study was to evaluate early changes in left atrial longitudinal strain based on speckle tracking and the atrial stiffness index in patients with mild hypertension.

### Methods

One hundred and one patients, between 30 to 50 years of age, were prospectively enrolled in the study: 32 healthy sedentary patients (Group 1), 35 healthy recreational athletes (Group 2) and 34 controlled hypertensive patients (Group 3). Sixty eight patients were men (67.3%). Conventional echocardiographic assessments were performed, color tissue Doppler and lateral and septal pulsed tissue Doppler were recorded and atrial volume was calculated. Left ventricular strain and strain rate and left atrial peak strain during the reservoir period were obtained by speckle tracking. The atrial stiffness index was calculated based on the (E/e)/ peak atrial strain ratio. Data was analyzed using ANOVA followed by the Bonferroni test. A p value <0.01 was considered statistically significant.

### Results

The E/A ratio and the tissue e wave velocity were higher and the E/e ratio was lower in the athlete group. Left ventricular mass index did not show statistical differences among groups. Left atrial volume was higher in athletes without attaining significant difference. In hypertensive patients, atrial strain was lower ( $36.94 \pm 7.71$  vs.  $46.17 \pm 10.05$  in Group 1 and  $46.80 \pm 8.44$  in Group 2; 95% CI 3.96-14.47;  $p < 0.0001$ ) and the stiffness index was higher ( $30.49 \pm 11.93$  vs.  $19.94 \pm 8.12$  in Group 1 and  $18.99 \pm 5.88$  in Group 2; 95% CI 5.05-16.05;  $p < 0.0001$ ).

### Conclusions

Left atrial longitudinal strain during the reservoir period and the atrial stiffness index are altered in patients with mild controlled hypertension before the detection of other echocardiographic changes.

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## Key words

> Echocardiography – Hypertension – Atrial appendage

## Abbreviations

EF	Ejection fraction	LV	Left ventricle
HF	Heart failure	TD	Tissue Doppler
LA	Left atrium		

## INTRODUCTION

The left atrium (LA) plays an important role in maintaining cardiac output, acting as a blood reservoir during left ventricular systolic contraction and as a contractile chamber increasing left ventricular filling

towards end diastole.

Changes occurring in response to clinical situations with different hemodynamic conditions are assessed by echocardiography with conventional methods such as area and volume calculations. (1)

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Left atrial size has shown to be a predictor of cardiovascular events and death (2) and related to the extent of diastolic dysfunction. (3, 4) However, between 25 and 30% of patients with diastolic dysfunction have normal atrial size. (5)

The study of atrial function has allowed a better understanding of diastolic dysfunction and heart failure (HF) with preserved ejection fraction (EF). A recent study showed that left atrial dysfunction was a predictor of hospitalization for HF in a group of patients with coronary artery disease and preserved EF. (6)

New echocardiographic techniques allow quantification of atrial myocardial strain and velocity at different periods of the atrial cycle. The study of its application in different clinical scenarios has promoted the interest of many researchers in recent years, mostly because some parameters derived from these new technologies have proved to be early markers of disease and have prognostic value. The usefulness of atrial strain during the reservoir period and the stiffness index to identify patients with diastolic dysfunction with and without HF has been previously demonstrated. (7)

The LA modulates left ventricular filling through three components: a phase of reservoir or expansion during ventricular systole, a conduit phase during passive ventricular filling, and an active contractile component (when there is atrial contraction). (Figure 1)

During exercise, the atrial reservoir function and active contraction increase. Enhanced reservoir function plays an important role in left ventricular filling by helping to maintain a proper atrioventricular pressure gradient during diastole and an adequate

stroke volume.

Decreased left atrial compliance may be important as a mechanism of hemodynamic changes. (8, 9)

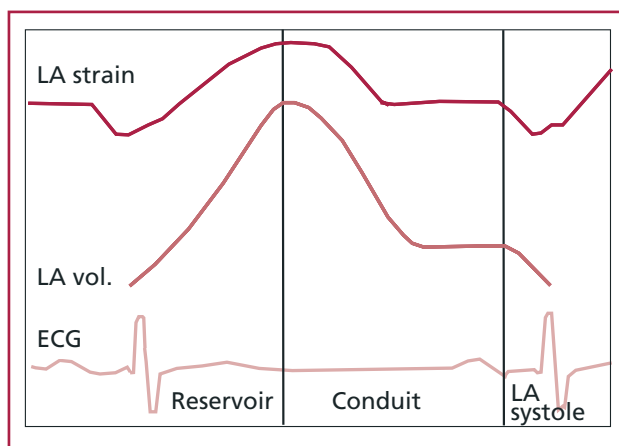
The purpose of this study was to evaluate early changes of atrial strain and stiffness in a group of controlled hypertensive patients with no significant changes in other echocardiographic parameters and without HF. They were compared with a control group of healthy subjects and a group of recreational athletes of similar age and gender. The inclusion of the latter group allowed the comparison of patients with increased left atrial volume and to assess its influence on strain and atrial stiffness.

**METHODS**

A prospective register was performed from January 2011 to August 2012 from an echocardiographic database of 150 patients between 30 to 50 years of age. Forty nine patients were excluded due to technical errors in image acquisition, low frame rate (FR) or inadequate ultrasound window. Among the remaining 101 patients, 32 were healthy, sedentary subjects (Group 1), 35 healthy recreational athletes (Group 2) and 34 controlled hypertensive patients (Group 3). Group 2 was defined as follows: subjects performing isotonic aerobic physical activity more than one hour daily, more than three times a week at least during the last year. The majority of patients were male. (67.3%) The different group characteristics are detailed in Table 1. All patients underwent an echocardiographic study using a GE Vivid E9 ultrasound system according to standard technique. Usual echocardiographic measurements were performed and the color tissue Doppler (TD) was recorded with a FR over 40 frames per second. Pulsed lateral and septal TD was calculated off-line from the acquired color TD loops. Left atrial volume was measured in 4 and 2 chamber views using the modified Simpson rule. The E/A ratio of left ventricular filling flow and the E/e ratio (ratio between maximum velocity of the mitral flow E wave and maximum velocity of the pulsed TD e wave, used to estimate ventricular filling pressure or mean left atrial pressure) were calculated. Mean lateral and septal mitral annulus tissue e wave was used to make calculations. Ventricular longitudinal systolic strain and strain rate were obtained by speckle tracking in the three conventional apical views. Mean maximum lateral, inferior and posterior atrial strain were similarly calculated during the reservoir period (Fig. 2)

These measurements were performed on cine loops acquired with a frame rate over 50 frames per second using the software provided by the equipment, adapting the width of the area of interest to atrial wall thickness. All off-line analyses were performed by the same operator on at least two stored beats. The stiffness index was calculated according to the (E/e)/mean atrial longitudinal strain formula during the reservoir period. The atrial stiffness index was previously postulated and validated by Kurt et al. (7) using catheterization.

Left atrial volumes and left ventricular mass were indexed to body surface area calculated with the Mosteller formula. Finally, the ratio between the stiffness index and

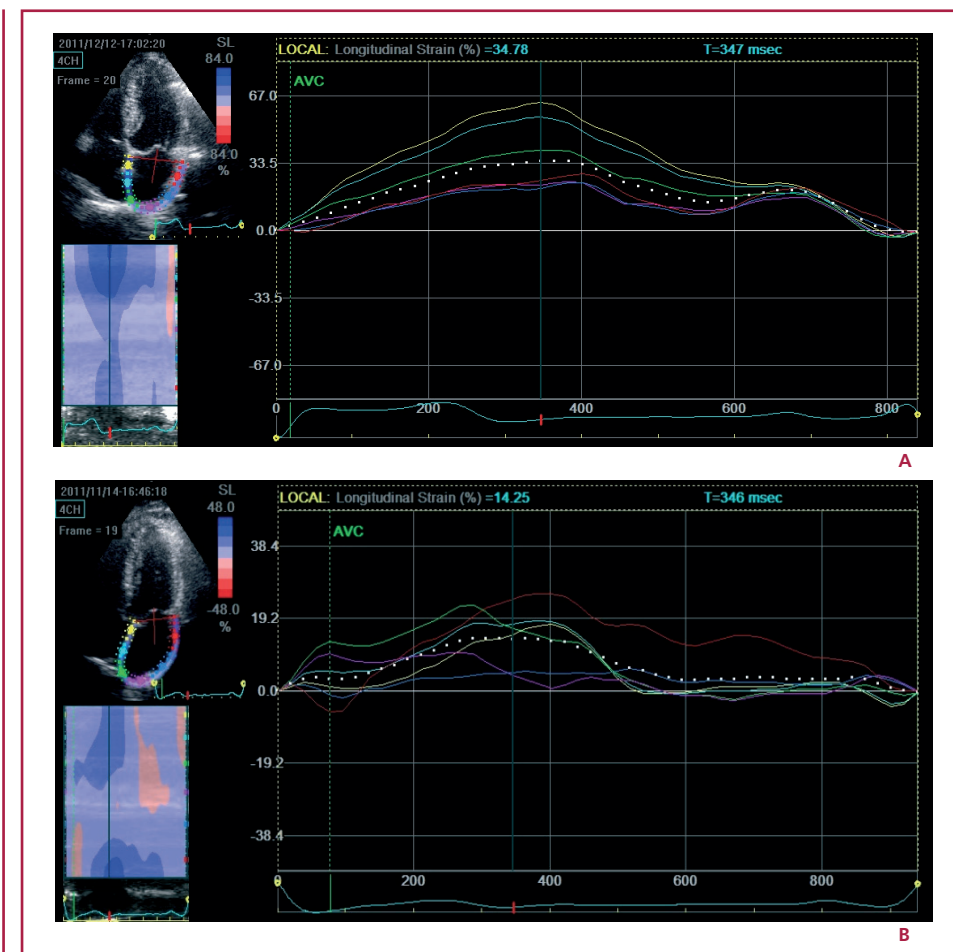


**Fig. 1.** Atrial volume increases progressively until ventricular end-systole (reservoir phase), followed by two successive emptying phases (conduit phase and atrial systole). LA: Left atrial. ECG: Electrocardiogram

	Healthy	Athletes	Hypertensive
Age, years	43.72 ± 5.02	41.51 ± 6.25	44.24 ± 5.56
Male gender, % (n)	62.5 (20)	74.3 (26)	64.7 (22)

**Table 1.** Age and gender distribution in the different groups

**Fig. 2. A:** Atrial strain by speckle tracking in a normal subject. **B:** Atrial strain by speckle tracking in a hypertensive patient.



left atrial indexed volume was obtained to differentiate sedentary from athlete normal subjects. ANOVA followed by the Bonferroni test was used to compare means between groups. A p value < 0.01 was considered statistically significant.

**RESULTS**

Depending on the amount of physical activity, athletes had greater ventricular mass and atrial volume than the other two groups, though the differences were not statistically significant probably due to the reduced number of patients. There were no differences in these parameters between hypertensive and normal sedentary subjects. Left ventricular longitudinal strain rate was not significantly different among groups. The E/A ratio and the velocity isolated from the mean tissue e wave were significantly higher and the E/e ratio was significantly lower in the athlete group compared with hypertensive patients. Global left ventricular longitudinal strain was significantly higher in normal than in hypertensive patients, but there were no significant differences compared to athletes.

Atrial strain was lower and atrial stiffness was higher in the hypertensive group. Both parameters were better than the rest of analyzed variables to single out hypertensive patients from the other two groups (Table 2 and Figure 3). On the other hand, the ratio between the stiffness index and the indexed left

atrial volume significantly separated the athlete group from the hypertensive group (Table 2 and Figure 4). Ten percent of patients were analyzed in two different occasions using the same stored loops, with no significant differences in the results.

The analysis of atrial strain was simple and reproducible when an adequate ultrasound window was available with a correct FR (> 50 cycles per second). The software used in the study did not allow the analysis of the equipment and the need to perform it in a work station is difficult and time-consuming.

**DISCUSSION**

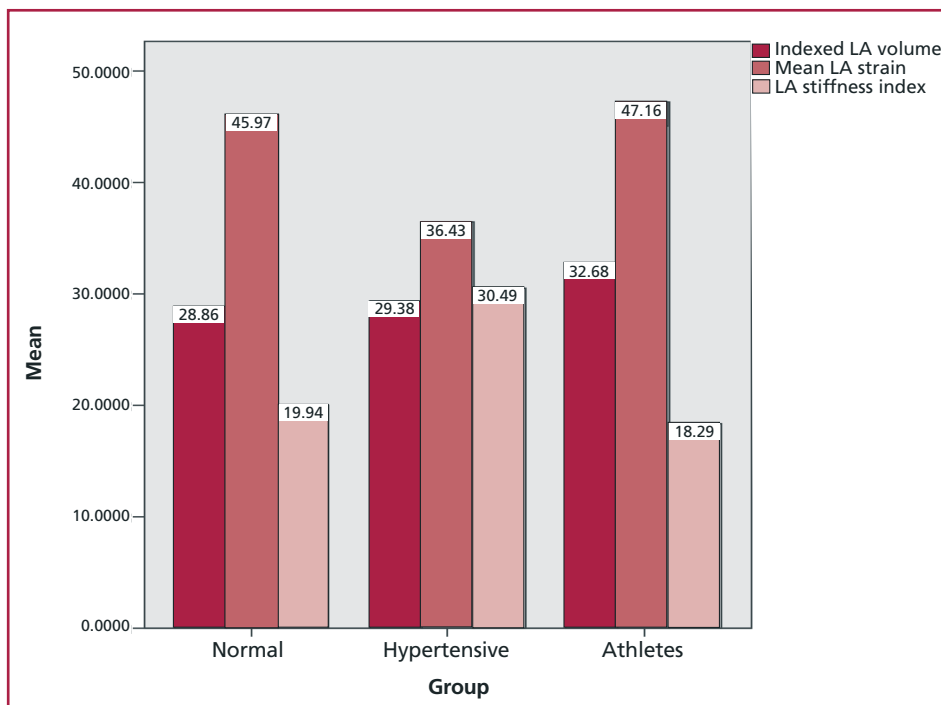
There has been a growing interest in the study of diastolic dysfunction given that a significant number of patients presenting this condition develop signs and symptoms of pump failure. For this reason the number of patients with HF and preserved EF admitted to the hospital has increased in recent years surpassing, in some cases, the admission of patients with HF and reduced EF. (10).

Several series have shown that hypertension is present in a large percentage of patients who reach this condition. (11-14) Therefore, assessment of diastolic function and early diagnosis of the degree of dysfunction in these patients is of particular interest, since it favors the beginning of appropriate treatment

	Healthy (Group 1)	Athletes (Group 2)	Hypertensive (Group 3)	p
LV mass index (gr/m <sup>2</sup> )	83.88±17.53	94.71±25.25	90.51±24.04	ns
E/A ratio	1.36±0.40	1.60±0.49	1.24±0.40	<b>0.005</b> (2 vs.3)
Pulsed TD e (cm/seg)	9.95±1.96	10.48±1.88	8.59±2.00	<b>0.001</b> (2 vs. 3)
E/e	8.62±2.06	8.30±1.72	10.48±2.98	<b>0.001</b> (2 vs. 3)
LA vol./m <sup>2</sup> (ml/ m <sup>2</sup> )	28.91±4.71	32.78±7.75	29.21±7.45	ns
LV strain (%)	-21.01±1.96	-20.06±2.80	-18.95±2.10	<b>0.003</b> (1 vs 3)
LV strain rate (x/1)	1.34±0.36	1.39±0.40	1.14±0.34	<b>0.02</b> (2 vs3)
LA strain (%)	46.17±10.05	46.80±8.44	36.94±7.71	<b>&lt;0.000</b> (3 vs.1 y 2)
E/e/LA strain x100	19.94±8.12	18.99±5.88	30.49±11.93	<b>&lt;0.000</b> (3 vs.1 y 2)
Stiffness/LA vol. ratio	0.70±0.26	0.59±0.22	1.09±0.47	<b>&lt;0.000</b> (3 vs.1 y 2)

**Table 2.** Comparison of mean echocardiographic variables

LA: Left atrial. LV: Left ventricular. TD: Tissue Doppler. V: vol.



**Fig. 3.** Indexed atrial volume, atrial strain and stiffness index values. Notice the difference of this index in hypertensive patients and the similarity in healthy sedentary and athlete subjects. The negative sign was eliminated from atrial strain for comparison purposes.

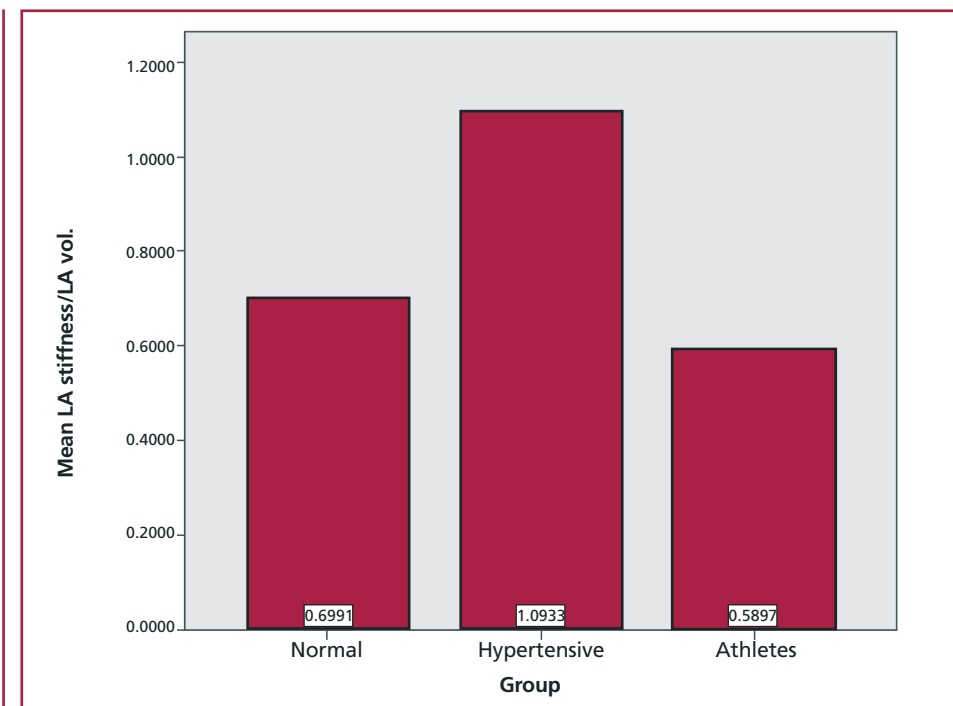
in the early stages of the disease.

It is known that patients with diastolic dysfunction have increased left ventricular mass and left atrial volume compared with control subjects, but not versus athlete subjects who present with left ventricular hypertrophy without diastolic failure. (7)

The classical evaluation parameters of dias-

tolic dysfunction appear late and show variations depending on loading conditions and other situations such as heart rate, so at times, they may not be conclusive. (15) This occurs not only with the E/A ratio of mitral inflow but also with tissue Doppler wave velocities. It should be noted that approximately one third of patients with HF and preserved EF have no

**Fig. 4.** Stiffness index/LA volume ratio. Notice the marked different between hypertensive patients and athlete subjects. LA: left atrium. vol: volume



alteration of the classical parameters of diastolic function or atrial dilation. (16) Although the E/e ratio (indicator of left ventricular end-diastolic pressure) is a highly reproducible parameter, easy to obtain and very helpful in patients with preserved EF, it has a wide band of indefinite gray values, requiring other measurements. (17, 18)

We know the great impact on the LA caused by diastolic left ventricular dysfunction, generating its dilation and increased pressure.

New tools incorporated into the equipments, as myocardial strain based on speckle tracking, have brought new insights in particular situations. It has been reported that these atrial strain measurements would allow predicting the probability of maintaining sinus rhythm after successful cardioversion. (19)

Of particular interest is the left atrial peak strain during the reservoir period, i.e. at the end of ventricular systole, end of atrial diastole.

Some studies have shown that atrial strain using speckle tracking detects alterations of atrial function in hypertensive patients before traditional parameters, even in patients without atrial dilation. (20, 21) However, this strain is not altered in elite athletes. (22)

The Nagueh group has taken a further step by proposing a very simple atrial stiffness index validated with direct catheterization measurements. Stiffness is defined as the increase in pressure required to provoke a specific increase in volume, in this case of the LA, and is expressed in mmHg/ml. In the study, the ratio between pulmonary capillary wedge pressure and atrial strain during the reservoir period was used, which seems a reasonable analogy. (23) Finally, the

pulmonary capillary wedge pressure was substituted by the E/e ratio and the results were similar.

This index was used to study patients with diastolic dysfunction without HF, patients with HF and preserved EF, and patients with HF and reduced EF, comparing them with a control group. The values of left atrial stiffness differentiated these groups better than isolated atrial strain. (24) Since in the study of patients with suspected diastolic dysfunction the E/e ratio must be reported, this stiffness index is very easy to obtain and in our series allowed us to identify diastolic dysfunction at a very early stage of hypertension, when the isolated E/e ratio was very slightly altered and of course ventricular hypertrophy or atrial dilation were not yet present. The fact that we have studied young subjects makes the group very homogeneous with no other associated diseases, even those that might be unknown to patients.

It is remarkable that recreational athletes had a greater mass index than the other groups (hypertensive patients were adequately treated) and also increased indexed left atrial volume, though this difference did not reach statistical significance. Hypertensive patients with less mass and less atrial volume had a significant increase in atrial stiffness perhaps due to increased fibrotic mass of the atrial myocardium, as observed in the ventricle of patients with HF and preserved EF. (25) This suggests that hypertension is a more aggressive disease than widely acknowledged in daily practice.

We believe that the contribution of our work is precisely to describe that increased atrial stiffness allows identifying diastolic function alterations better than classical diastolic dysfunction parameters in

hypertensive patients.

In conclusion, this index could be very useful, it is easy to perform and perhaps in the future will facilitate the identification of patients with a higher propensity to develop HF, for which additional studies, so far not available, will be required.

We also postulate the ratio between the stiffness index and the indexed left atrial volume. This ratio clearly distinguished athlete patients from hypertensive patients. With future validated studies, it could be useful in differentiating pathological from physiological hypertrophy.

## CONCLUSIONS

Atrial longitudinal strain during the reservoir period by speckle tracking and the atrial stiffness index are easily quantifiable, and are altered in controlled mild hypertensive patients before other echocardiographic abnormalities are detected.

The differences appear to reflect a change in atrial function by the disease process itself and independently of other adaptive changes.

## RESUMEN

### Análisis de la deformación auricular longitudinal: alteraciones precoces en hipertensos jóvenes controlados

#### Introducción

Evaluar alteraciones precoces del strain auricular longitudinal en base al speckle tracking y el índice de rigidez auricular en hipertensos leves.

#### Material y métodos

Ingresaron prospectivamente 101 pacientes de entre 30 y 50 años: 32 sujetos sanos sedentarios (Grupo 1), 35 sanos deportistas (Grupo 2) y 34 hipertensos controlados (Grupo 3). Sexo masculino: 68 (67,3%). Se efectuaron mediciones ecocardiográficas convencionales, se registraron el Doppler tisular color y el Doppler tisular pulsado lateral y septal y se calculó el volumen auricular. Se obtuvieron el strain y el strain rate ventricular sistólico y el strain auricular máximo durante el período de reservorio por speckle tracking. Se calculó el índice de rigidez auricular en base a la relación (E/e)/strain auricular máximo. Se utilizó el análisis de ANOVA seguido de la prueba de Bonferroni, considerándose significativa una  $p < 0,01$ .

#### Resultados

La relación E/A y la velocidad de la onda e tisular fueron mayores y la relación E/e fue menor en el grupo de deportistas. El índice de masa del ventrículo izquierdo no mostró diferencias significativas. El volumen de la aurícula izquierda fue mayor en deportistas sin alcanzar significación estadística. El strain auricular fue menor en hipertensos ( $36,94 \pm 7,71$  vs.  $46,17 \pm 10,05$  en el Grupo 1 y  $46,80 \pm 8,44$  en el Grupo 2; IC 95% 3,96-14,47;  $p < 0,0001$ ) y el índice de rigidez auricular fue significativamente más alto en este grupo ( $30,49 \pm 11,93$  vs.  $19,94 \pm 8,12$  en el Grupo 1 y  $18,99 \pm 5,88$  en Grupo 2; IC 95% 5,05-16,05;  $p < 0,0001$ ).

#### Conclusiones

La deformación auricular longitudinal durante el período de

reservorio y el índice de rigidez auricular se hallan alterados en hipertensos leves controlados antes de que se detecten otras alteraciones ecocardiográficas.

**Palabras clave** > Ecocardiografía - Hipertensión - Apéndice atrial

#### Conflicts of interest

None declared.

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