Modern Medicine. 2016, Vol. 23, No. 1 : 5-11

Original Paper

Left Atrial Structural and Functional Remodeling in Hypertensives - An Echocardioghraphic Study

Ioana Petre, Adriana Alexandrescu, Silvia Iancovici, Sebastian Onciul, Oana Florentina Tăutu, Maria Dorobanțu

Department of Cardiology, Clinical Emergency Hospital, Bucharest, Romania

REZUMAT

Remodelarea structurală și funcțională a atriului stâng la hipertensivi - studiu ecocardiografic

Obiective: Acest studiu și-a propus evaluarea remodelării atriului stâng prin metoda ecocardiografică la pacienții hipertensivi optim tratați comparativ cu cei normotensivi.

Metode: În studiul nostru au fost înrolati 35 pacienți cu hipertensiune arterială esențială necomplicată, tratați până la valoarea țintă (<140/90mmHg). Dimensiunea atriului stâng a fost evaluată ecocardiografic: diametrele anteroposterior, transversal și longitudinal, precum și cele trei volume fazice [maxim (vol max), minim (vol min) și cel dinainte de contracția atrială (vol pre A)] prin metoda Simpson biplan modificată. Pe baza volumelor au fost calculate fracțiile de golire atrială activă, pasivă și totală. De asemenea a fost analizată valoarea strainului sistolic longitudinal atrial (media obținută din ferestrele apical patru camere și două camere) prin metoda speckle tracking, conform standardelor actuale. Rezultatele au fost comparate cu cele ale unui grup control ce a cuprins 37 subiecți sănătoși.

Rezultate: Diametrul anteroposterior, precum și toate cele trei volume atriale au fost semnficativ mai mari în grupul hipertensivilor față de control (39.54±4.6 mm vs 35.43±4.5 mm pentru diametrul anteroposterior, 60.51±14.9 ml vs 45.22±13.4 ml pentru vol max, 25.48±10.3 ml vs 14.64±5.3 ml pentru vol min si 42.14±11.4 vs 24.86±8.5 pentru volpre A, pentru toate p<0.0001). Din punct de vedere al funcției fazice atriale, pacienții hipertensivi au avut fracțiile de golire totală si pasivă semnficativ mai mici (49.78±8.4% vs 66.05±7.44, p<0.0001 și respectiv 44.62±8.36% vs 58.79±8.14%, p<0.0001), dar cu valori similare ale fracției de golire activă atrială, comparativ cu normotensivii. Valorile peak-strainului longitudinal atrial au fost de asemenea semnficativ mai mici la hipertensivi față de control (22.7% vs 35.1%, p<0.0001).

Concluzie: Hipertensiunea arterială, chiar forma necomplicată și optim tratată afectează funcția mecanică a atriului stâng. În grupul de hipertensivi al studiului nostru s-au observat dimensiuni crescute ale atriului stâng față de normotensivi, precum și o alterare a funcției atriale globale și pasive, cu menținerea funcției de pompă a atriului stâng. Disfuncția atrială a fost evidențiată și prin alterarea valorii peak-strainului longitudinal atrial.

Cuvinte cheie: hipertensiune arterial, atriu stâng, volume atriale, speckle tracking

ABSTRACT

Objectives: We sought to investigate left atrial (LA) structural and functional abnormalities in a group of optimal treated hypertensives, in comparison to a control group.

Methods: This study included 35 prospectively enrolled subjects with treated, uncomplicated, essential hypertension (HTN). Left atrial diameters (anteroposterior, transversal and longitudinal) and left atrial phasic volumes

Corresponding author: Ioana Petre, MD
Department of Cardiology, Clinical Emergency Hospital, Calea Floreasca, no.8, 014461
Bucharest, Romania e-mail: i_comanescu@yahoo.com

[maximal (LAV max), minimal (LAV min) and before atrial contraction (LAVpreA)] were assessed by echocardiography and LA emptying functions (LAEF) (global, active and passive) were calculated. Using the current recommendations of speckle tracking technique, peak longitudinal strain of LA walls (PALS)(mean value from apical four chambers and two chambers view) were analysed. The results were compared with a group of 37 age-matched healthy controls.

Results: LA anteroposterior diameter as well as all three phasic LA volumes were significantly greater in HTN group (39.54±4.6 mm vs 35.43±4.5 mm for anteroposterior diameter, 60.51±14.9 ml vs 45.22±13.4 ml for LAV max, 25.48±10.3 ml vs 14.64±5.3 ml for LAVmin and 42.14±11.4 vs 24.86±8.5 for LAVpreA , for all p<0.0001), while the transversal and longitudinal diameters were similar. We found significantly lower total and passive EF in hypertensives than in control group (total LAEF 49.78±8.4% vs 66.05±7.44, p<0.001and passive LAEF 44.62±8.36% vs 58.79± 8.14%, p<0.001), but the active LAEF was preserved. The peak systolic strain values were also significantly lower in HTN group versus control (22.7% versus 35.1%, p<0.0001)

Conclusion: Hypertension, even correctly treated, affects the mechanical function of left atrium. In our hypertensive group we observed the dilation of left atrium and an altered passive and total atrial function, with preservation of atrial pump function compared to control group. LA dysfunction was also demonstrated through low peak strain values.

Key words: hypertension, left atrium, phasic volumes, speckle tracking

BACKGROUND

Arterial hypertension (HTN) is a common cardiovascular pathology that usually complicates with cardiac dysfunction. HTN alters atrial dynamics significantly, leading to left atrial (LA) morphological and functional abnormalities.

Echocardiography proved to be an adequate method of evaluation of LA remodeling, by its means of assessing with accuracy LA size, volumes and its multiple functions. LA size has been consistently shown to be a powerful cardiovascular morbidity and mortality predictor (1-5) and most recently functional assessment of LA has been shown to be at least o marker of cardiovascular outcomes (3,6). Current available data suggest that the combined evaluation of LA size and function will augment prognostication, being important in clinical setting. (7)

MATERIALS AND METHODS

Study population

In the first study group were included 35 consecutive patientswith well-controlled essential hypertension (blood pressure at initial evaluation <=140/90 mmHg). Two blood pressure measurement were performed 5 minutes apart and the mean value was noted. All patients were under pharmacological treatment. Diabetes mellitus and secondary causes of hypertension were excluded, as well as any other significant cardiac pathology: LV ejection fraction <50%, arrhythmias, pacing, cardiomyopathies, significant valvulopathies (moderate or severe), any history or evidence of ischemic heart disease. Because the left atrium function evaluation needs a high quality acquisition, with a good view of endocardial borders only the patients with optimal echocardiographic views were included.

The second group (control subjects) comprised 37 normotensives, with normal clinical exam and echocardiography, with no significant medical history or treatment.

Left atrium size and phasic volumes

Two dimensional echocardiography was performed, using a VIVID7 (General Electric) machine, with respect of the recommendations of available guidelines. Three LA diameters were measured, using bidimensional method: anteroposterior diameter (from parasternal long axis view), transversal and longitudinal diameter (from apical 4 chamber view).

LA volumes were measured from the apical four and two chamber view. For measuring LA volumes we used the Simpson biplane method because it has the advantage of being more objective (by reliance on the computerized summation of discs for the total volume and not requiring input of a specific length for volume calculation). (8)

LA volumes were measured at 3 points:

- maximal LA volume (LAV max) - the volume that occurs at the end of ventricular systole, just before mitral valve opening (the end of the T wave of the eCG); (**Fig.1** and **Fig. 2**)
- minimal LA volume (LAV min) that occurs at mitral valve closure (in telediastole); (**Fig. 3** and **Fig. 4**)
- the volume before active atrial contraction (LAV preA) - timed to the onset of the P wave. (**Fig. 5** and **Fig. 6**)

The left atrium acts as a reservoir when the valve is closed, as a conduit when the mitral valve is open, until the start of atrial contraction when it acts as a pump. From these volumes total, passive and active emptying fraction (LAEF) were calculated (**Table 1**), which give important information about atrial functions.

All atrial volumes were indexed to body surface area.

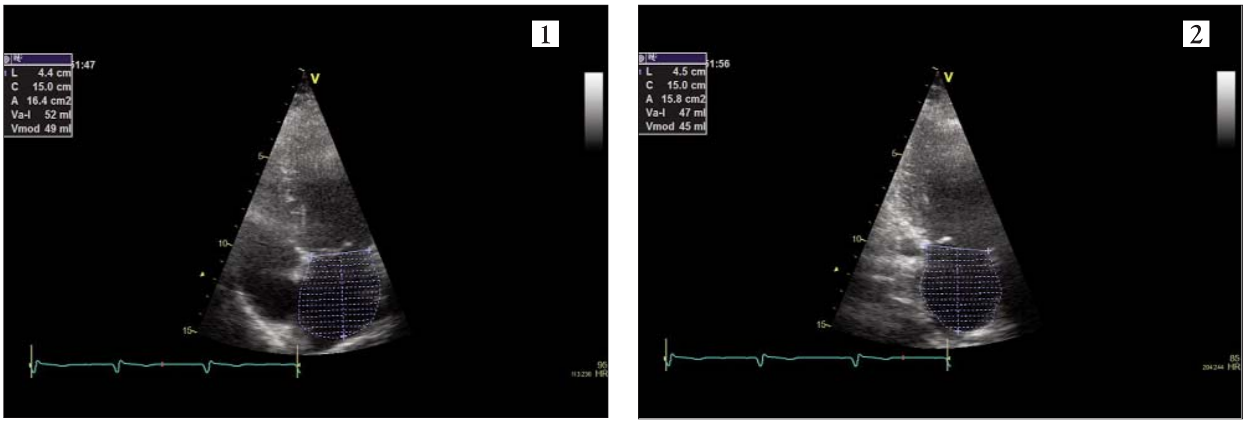

Figure 1 and 2. Measuring LA maximal volume (LAV max) at the end of ventricular systole in apical 4c and apical 2c views

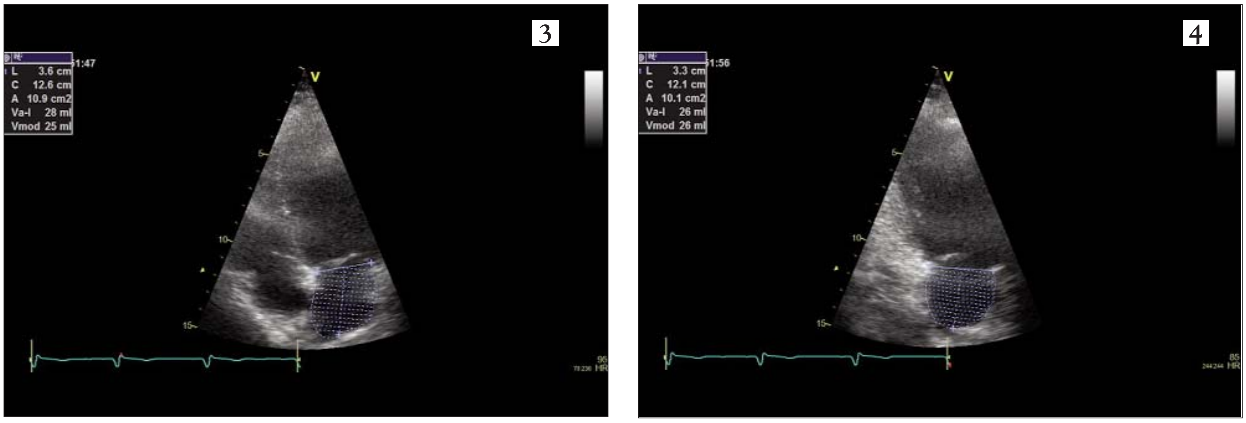

Figure 3 and 4. Measuring LA minimum volume (LAV min) at the end of the dyastole, in apical 4c and 2c views

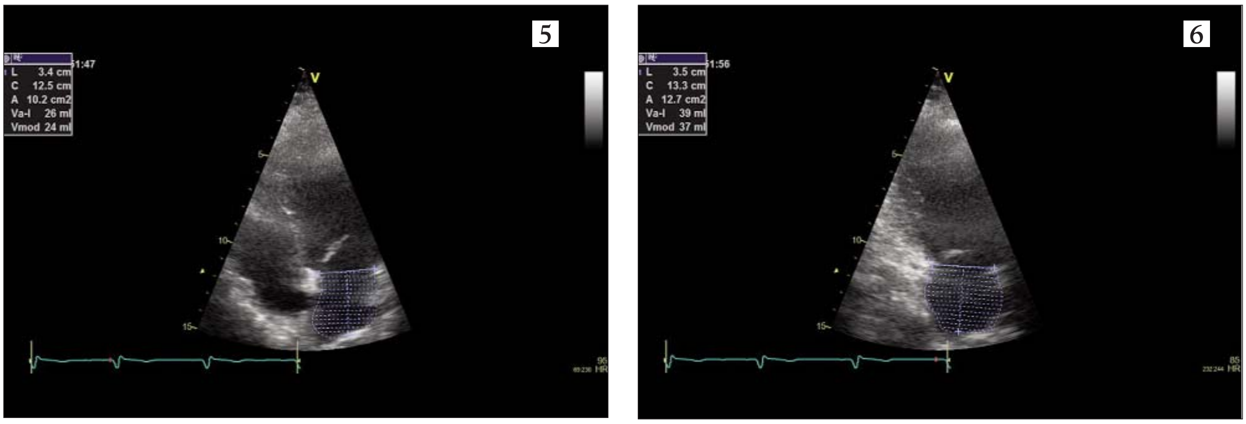

Figure 5 and 6. Measuring the LA volume just before atrial contraction (LAV preA) in apical 4c and 2c views

Table 1. Volumetric assessment of LA phasic function

FUNCTION	PARAMETER	FORMULA
Reservoir Function	Total emptying fraction	(LAV max-LAv min)/LAV max x100%
Conduit Function	Passive Emptying Fraction	(LAV max-LAV preA)/LAV max x100%
Pump Function	Active Emptying Fraction	(LAV preA-LAv min)/LAvpreAx100%

Two dimensional speckle tracking technique

Speckle tracking is a novel echocardiographic method that analyses myocardial motion within a user-defined region of interest, without angle dependency. (6,9)

We assessed longitudinal atrial strain, using offline analysis (data from Echopac, GE Medical Systems), after apical 4c and 2c images were recorded. The acquisitions were of good quality, with frame rates of about 50-70 frames/s, using a narrow sector, optimizing visualization of LA cavity and avoiding foreshortening of the LA. The LA endocardial border was manually traced at endsystole in both apical views; the software generated an automatically epicardial surface tracing, delineating a region of interest of 6 segments in each apical view. The examiner selected a default thickness for the LA myocardium (2-3 mm) and the system performed the wall motion tracking analysis throughout the entire cardiac cycle. Longitudinal strain curves were generated for each atrial segment.

The LA strain pattern is characterized by a predominant positive wave that peaks at the end of ventricular systole (PALS), followed by two distinct descending phases in early diastole and late systole. The mean measurements of the six segments was automated generated as a separate white curve (**Fig. 7** and **Fig. 8**). The mean value of all 12 segments of PALS was used in the statistical analysis.

Statistical analysis

The quantitative continue variables were expressed as mean value ± standard deviation and the categorical variables as percentage. The categorical variables were compared using chisqured test or Fisher test as appropriate. All the p values were 2-tailed, with statistical significance defined by a p value $<=0.05$.

RESULTS

Baseline characteristics

The general characteristics are summarized in **Table 2**.

The frequency of female individuals was similar in both groups (68.1% comparative to 70%, respective 25 subjects for both groups), but HTN group comprised an

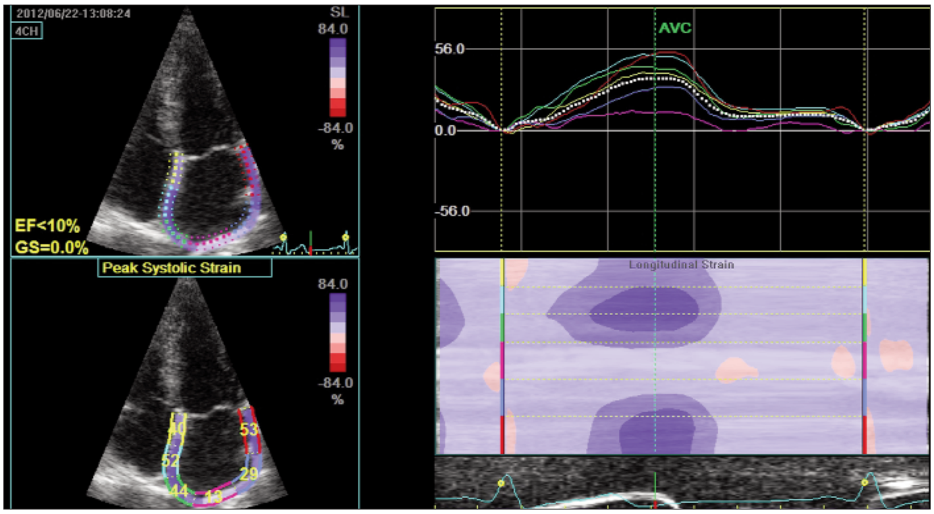

Figure 7. Peak systolic atrial strain in apical 4c view (curves and values for 6 atrial segments and the mean white curve)

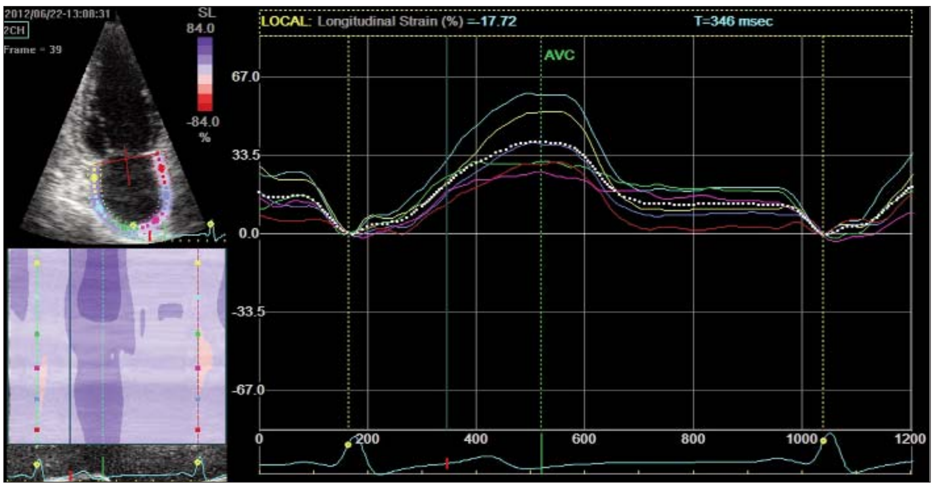

Figure 8. Peak systolic atrial strain in apical 2 view(curves for 6 atrial segments and the mean white curve)

Table 2. General characteristics

	Control N=37	HTN N=35	P
Age (years)	41.4±13.4	54.5±13.4	
Gender			
Female	25(67.6%)	25(71.4%)	NS
Male	12(32.4%)	10(29.6%)	
BSA, m²	1.82±0.2	1.85±0.2	NS
BP systolic	111±8.5	129±17.6	<0.001
diastolic	63±2.3	74±8.1	<0.001
Time from HTN dgn (months)	-	33	

Data are presented as mean ± standard deviation for numerical data and percentage for categorical data; N: total number from the group; NS: statistically nonsignificant (p>0.05); BSA=body surface area; BP=blood pressure; dgn=diagnosis

older population (mean value of 54 ± 13 years in the HTN group and 41 ± 13 years in control group). All the echocardiographic parameters were age and sex-matched.

In our HTN group the mean time of arterial HTN diagnosis was 33 months and the mean blood pressure (under treatment) was 129/74 mmHg.

LA volumes and diameters

LA anteroposterior diameter, as well as all the volumes (Vol max, Vol min and VolpreA) and indexed values were significantly greater in hypertensives, compared to controls (p<0.0001), while the transversal and longitudinal diameters were similar (**Table 3**).

LA active EF was similar between the two groups, while we found significantly lower LA passive and total EF in hypertensives, than in control group (p<0.0001) (**Table 4**).

Peak longitudinal atrial strain

The positive peak atrial strain values (the mean value for 12 atrial segments) were also significantly lower in the HTN group versus control, ranging from 22.36% to 44% in control group (with a mean value of 35.2±5.6 % and the most frequent value of 34.5%) and from 8.8% to 43% in HTN group with the mean value of 22.7±13.9 and most often the value of 26%.(**Table 5**)

DISCUSSIONS

In the recent years many studies focused on the analysis of the left atrium among hypertensives or patients with atrial arrhythmias, trying to find elements of clinical relevance and new markers of prognosis. LA size proved to be an independent predictor of atrial fibrillation (8,10,11), stroke (12), heart failure (4, 13, 14), prognosis in cardiomyopathies (15, 16) and total as well as cardiovascular mortality (3, 5, 17, 18).

LA linear size measurement - the anteroposterior diameter - has been validated in many old studies. This was confirmed also in our study - the anteroposterior diameter being the single increased diameter in HTN group, with a statistical significance comparative to control. However, the current guidelines recommend assessment of LA maximal volume using optimal 4-chamber view and using this value indexed by BSA (LAVI). In our HTN group (patients with optimal treated HTN) comparing LAVI with the reference range from literature we find that 45%(15 subjects) had LA dilatation, the rest of the subjects having a normal LA size. LA dilatation was defined as recommended by the last chamber quantification guideline (19), as LAVI>=34 ml/m²; between them 73.3% (11

Table 3. LA size (phasic volumes and diameters)

	Control N=37	HTN N=35	P
LAV preA(ml)	24.86±8.5	42.14±11.4	<0.0001
LAV preA(ml/m²)	13.62±4.2	22.7±5.86	<0.0001
LAV max(ml)	45.22±13.4	60.51±14.9	<0.0001
LAV max(ml/m²)	24.66±6.08	32.6±7.4	<0.0001
LAV min(ml)	14.64±5.3	25.48±10.3	<0.0001
LAV min(ml/m²)	8.03±2.67	13.79±5.3	<0.0001
LA ant-post diam	35.43±4.5	39.54±4.6	<0.0001
LA longitudinal diam	40.13±3.9	41.09±3.58	NS
LA transversal diam	46±4.8	49.5±6.15	NS

Data are presented as mean ± standard deviation for numerical data and percentage for categorical data; N: total number from the group; NS: statistically nonsignificant (p>0.05); LA = left atrium; LAV = left atrial volume; max = maximal; min = minimal; preA = before atrial contraction; ant-post = anteroposterior; diam = diameter

Table 4. LA phasic emptying fractions

	Control N=37	HTN N=35	P
LA active EF biplane	40.75±7.5	40.106±11	NS
LA passive EF biplane	58.79±8.14	44.62±8.36	<0.0001
LA total EF biplane	66.05±7.44	49.78±8.4	<0.0001

Data are presented as mean ± standard deviation for numerical data and percentage for categorical data; N: total number from the group; NS: statistically nonsignificant (p>0.05); LA=left atrium; EF=emptying fraction

Table 5. Peak systolic atrial strain (average of 12 atrial segments)

	Control N=37	HTN N=35	P
PALS (%)	35.2±5.6	22.7±13.9	<0.0001

Data are presented as mean ± standard deviation for numerical data and percentage for categorical data; N: total number from the group; NS: statistically nonsignificant (p>0.05); PALS = peak atrial longitudinal strain subjects) had only mild dilatation (34-41 ml/m^2). The explanation for the preserved LAVI in more of the half of the HTN patients and the mild dilatation in the other half could be the short time of the HTN diagnosis (a mean of 33 months) and the optimal treated HTN.

A comprehensive measuring of LA volume using 4-chamber and 2-chamber views (without foreshoretening) at different points of cardiac cycle brings more reliable information about the left atrium structure. As expected, in our study all left atrial biplane volumes (maximal, minimal and preA volumes as well as indexed values) were found to be higher in hypertensive group compared to our normotensive group.

Many echocardiographic parameters can be analysed for an accurate prediction of left atrium function. The study of left atrium myocardium mechanics identified three atrial functions: reservoir function, conduit function and contractile function. LA function assessment based on echocardiographic volumetric formula has been used in several studies. Even if there are no validated normal values for emptying fractions, because there were no large multicentric studies, our control EF values were closed to the one reported in the literature. (7,8)

Most of the studies among hypertensives demonstrated a decrease in conduit and passive volumes, with an increase in active emptying fraction. (20,2 1). This augmented contractile atrial function is one of the mechanisms compensating for decreased early filling in patients with reduced left ventricular compliance and is considered to becaused by the increase of LA volume (Frank-Starling's law). However, the results in literature about the changes of the phasic LA functions among HTN are inconclusive. For patients with mild hypertension no change was noted in passive emptying or conduit volumes with an increase in active emptying volume, with an overall LA increase compared with normal (22). On the other hand, extreme dilatation and pathological abnormalities of LA muscle may account for the decreased LA booster function in hypertensive patients with paroxysmal atrial fibrillation (23). In our study we found a decrease in reservoir and passive volumes among hypertensives, but with the preservation of active emptying fraction (without an compensatory response of the contractile atrial function). In a recent study, all LA emptying fractions were decreased in hypertensives (24).

Speckle tracking (ST) technique was initially used for the strain evaluation of left ventricle. From 2009 it has been validated as a feasible technique for the assessment of longitudinal myocardial LA deformation. Reference ranges of strain indices were reported by Cameli (25) and were similar with the values from our control group (PALS 42.2±6.1% in Cameli study and 35.2±5.6 %in our study). The advantage brought by speckle tracking is the analysis of every element of atrial function, with a higher frame rate - so a better temporal evaluation at a particular moment from the cardiac cycle. More importantly, the ST strain imaging technique allows detection of LA functional impairment at very early stage, even in the absence of LA enlargement and before clinical appraisal of symptoms. The speckle tracking parameter investigated in our study was the mean value from the 12 atrial segments of the peak longitudinal atrial strain (the positive value from the ventricular systole).

In previous studies patients with HTN showed significantly lower values of strain and strain rate during reservoir function compared with controls, even when the LA dimensions were not increased (26), irrespective of left ventricular hypertrophy (27). Consistently with the results from the literature, we found that PALS was reduced among the hypertensives comparing with controls (22.7% versus 35.2%, $p<0.0001$), with a high statistical significance, demonstrating an altered reservoir function of LA among HTN.

Limitations

The small number of patients in both groups and the heterogenity of the hypertensives (all classes of hypertension, that were treated with different drug combinations) represent some limitations of this study. Also, we excluded the diabetes mellitus, but we did not analyse the presence of other classical risk factors among the subjects.

Between the two groups there was a statistically significant difference of the age of the population. Even we tried to compensate this finding by age-matching all the parameters, the increased age of hypertensives comparing to controls might have influenced the results.

We could have had a better evaluation of LA function by analyzing also the other strain parameters and this will be our purpose for the next HTN study.

CONCLUSION

Hypertension, even well treated, is associated with impaired LA size and function. Using multiple echocardiographic techniques, we found that hypertensive patients have structural and functional LA abnormalities. LA enlargement (increased LA biplane volumes at different cardiac cycles) was closely related to LA dysfunctions. Decreased peak atrial longitudinal systolic strain and total emptying atrial fraction demonstrate an altered LA reservoir function. Also our study has shown a reduced passive EF with preservation of active EF (atrial pump) among hypertensives - results that are not well defined in literature.

Our observation onthe close association between LA size and functional impairment is similar with the results of numerous previous studies involving measuring techniques.

Our findings suggest that a more thorough echocardiographic evaluation of LA may be necessary and useful along with the choice of antihypertensive drugs and target blood value in hypertension.

Acknowledgement

This paper is partly supported by the Sectorial Operational Programme Human Resources Development (SOPHRD), financed by the European Social Fund and the Romanian Government under the contract number POSDRU 141531"/ "MENȚIUNE: Această lucrare este parțial sprijinită de către Programul Operațional Sectorial Dezvoltarea Resurselor Umane (POSDRU) finanțat din Fondul Social European și de către Guvernul Romaniei prin contractul nr. POSDRU 141531".

REFERENCES

1. B. Ristow, S. Ali, M. a Whooley et al, "Usefulness of left atrial volume index to predict heart failure hospitalization and mortality in ambulatory patients with coronary heart disease and comparison to left ventricular ejection fraction (from the Heart and Soul Study)", Am. J. Cardiol., 2008, 102(1):70–6
2. B. Paul, "Left Atrial Volume - A New Index in Echocardiography", JAPI, 2009, 57: 463–465
3. S. Gupta, S. A. Matulevicius, C. R. Ayers et al, "Left atrial structure and function and clinical outcomes in the general population", Eur. Hear. J. , 2013, 34(4): 278–285
4. Y. Takemoto, M. E. Barnes, J. B. Seward et al, "Usefulness of Left Atrial Volume in Predicting First Congestive Heart Failure in Patients ≥ 65 Years of Age With Well-Preserved Left Ventricular Systolic Function", Am. J. Cardiol., 2014, 96(6):832–836
5 A. Rossi, P. L. Temporelli, M. Quintana et al, "Independent relationship of left atrial size and mortality in patients with heart failure: an individual patient meta-analysis of longitudinal data (MeRGE Heart Failure)", Eur. J. Heart Fail., 2009, 11(10):929–36
6. B. D. Hoit, "Left atrial size and function: role in prognosis", J. Am. Coll. Cardiol., 2014, 63(6):493–505
7. G.G. Blume, C.J. Mcleod, M.E.Barnes et al, "Left atrial function: physiology, assessment, and clinical implications", Eur. Hear.J., 2011, 12:421-430
8. E.S.Tucay, "Left Atrial Volume and Left Atrial Function as Predictor of Postoperative Atrial Fibrillation", 2012, http://www.phc.gov.ph/journal/publication
9. M. Cameli, M. Lisi, F. M. Righini et al, "Novel echocardiographic techniques to assess left atrial size, anatomy and function", Cardiovasc. Ultrasound, 2012, 10(1): 4
10. Y-S Lee, D W Hyun, B C Jung et al, "Left atrial volume index as a predictor for occurrence of atrial fibrillation after ablation of typical atrial flutter", Journal of Cardiology, 2010, 56(3):348-353
11. AJ Sanfilippo, VM Abascal, M Sheehan, "Atrial enlargment as a consequence of atrial fibrillation. A prospective echocardiographic study", Circulation, 1990, 82:792-797
12. G Piotrowski, M Banach, E. Gerdts et al "Left atrial size in hypertension and stroke", J Hypertens, 2011, 29(10):1988-93
13. B. Ristow, S. Ali, M. A. Whooley et al, "Usefulness of Left Atrial Volume Index to Predict Heart Failure Hospitalization and Mortality in Ambulatory Patients With Coronary Heart Disease and Comparison to Left Ventricular Ejection Fraction (from the Heart and Soul Study)," Am. J. Cardiol., 2014, 102(1):70–76
14. H. Tamura, T. Watanabe, S. Nishiyama et al, "Increased Left Atrial Volume Index Predicts a Poor Prognosis in Patients With Heart Failure", J. Card. Fail., 2014, 17(3):210–216
15. AM Losi, S Betocchi, G Barbati et al, "Prognostic significance of left atrial volume dilatation in patients with hypertrophic cardiomyopathy", J Am Soc Echocardiogr, 2009, 22(1):76-81
16. F. Ferreira, A.Galrinho, R.Soares et al, "Prognostic valueof left atrial volume in patients with dilated cardiomyopathy", Rev Port Cardiol, 2013; 32:865-72
17. DA Patel, CJ LAvie, RV Milani et al, "Clinical Implications of left atrial enlargement: a review", Ochsner J, 2009, 9(4):191-196
18. DA Patel, CJ LAvie, RV Milani et al, "Left atrial volume index preditive of mortality independent of left ventricular geometry in a large clinical cohort with preserved ejection fraction", Mayo Clin Proc, 2011, 86(8):730-737
19. R.M. Lang, L.P. Badano, V. Mor-Avi 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 Echocard, 2015, 28(1)
20. MK Erol, M Yilmaz, M Acikel et al, "Left atrial mechanical function in patients with essential hypertension", Acta Cardiol, 2002, 57(5): 323-7
21. G. Cioffi, GF Mureddu, C Stefenelli et al, "Relationship between left ventricular geometry and let atrial size in patients with systemic hypertension", J Hypertens, 2004, 22:1589-1596
22. S. Eshoo, S.L.Ross, L.Thomas, "Impact of Mild Hypertension on Left Atrial Size and Function", Circ Cardiovasc Imaging, 2009, 2:93-99
23. Q.Cui, H.Wang, W.Zhang et al, "Enhanced Left Atrial Reservoir, Increased Conduit, and Weakened Booster Pump Function in Hypertensive Patients with Paroxysmal Atrial Fibrillation", Hypertension Research, 2008, 31: 395-400
24. T-Y Xu, J Sun, A P-W Lee et al, "Left atrial Function as Assessed by Speckle-Tracking Echocardiography in Hypertension", Medicine, 2015, 94(6):526
25. M. Cameli, M. Caputo, S. Mondillo et al,"Feasibility and reference values of left atrial longitudinal strain imaging by two-dimensional speckle tracking", Cardiovasc. Ultrasound, 2009, 7:6
26. M Sahebjam, A Mazareei, M Lotfi-Tokaldany et al, "Comparison of Left Atrial Function between Hypetensive Patients with Normal Atrial Size and Normotensive Subjects Using Strain Rate Imaging", Arch Cardiovasc Imaging, 2014, 2(1):ee16081
27. N Kokubu, S Yuda, K Tsuchihashi et al, "Noninvasive assessement of Left atrial function by strain rate imaging in patients with hypertension: a possible beneficial effect of renin-angiotensin system inhibition on left atrial function", Hypertens Res, 2007; 30(1):13-21