ORIGINAL ARTICLE

Left atrial function - novel ecocardiographic markers for detecting atrial fibrillation in hypertensives

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Abstract: **Objectives –** We thought to evaluate left atrium (LA) as an attempt to find an echocardiographic marker of paroxysmal atrial fibrillation (AF) in hypertensive patients without any significant disease. **Methods –** We prospectively enrolled two groups of hypertensives: forty six patients with hypertension (HTN) without history of arrhythmia (group 1) and twenty three patients with HTN and a recent episode of documented paroxysmal AF (group 2). Left atrial (LA) diameters (anteroposterior, transversal and longitudinal) and LA phasic volumes (maximal, minimal and before atrial contraction) were assessed by 2D echocardiography and left atrial emptying functions (LAEF) (global, active and passive) were calculated; also 3D acquisitions of maximal and minimal volumes of LA were performed. Using the current recommendations of speckle tracking technique, peak longitudinal strain of left atrial walls (PALS) and peak atrial contraction strain (PACS) (mean value from apical four chambers and two chambers view) were analyzed. **Results –** Age (59.5y+-12 vs 67.7ys+-8, p=0.003) and the mean time of HTN diagnosis (42 mo+-6 vs 80 mo+8, p=0.007) were significantly higher in group 2; the other cardiovascular risk factors (smoking, dyslipidemia) were similar as prevalence. We found all 2D and 3D LA volumes significantly greater in group 2 (for all p<0.0001) and global, active and passive LA EF significantly lower in the same group, compared with the other (p<0.0001, p<0.0001 and p<0.02). In comparison with 2D values, 3D volumes and emptying fractions were lower, but with no statistical significance. The peak longitudinal strain values were also significantly lower in AF group versus HTN control (26.1+-7.4 vs 15.7+-5.6, p<0.0001) while peak contraction strain was nonsignificant in the two groups. **Conclusion –** The echocardiographic evaluation of LA function using 2D and 3D volumetric and speckle tracking methods can be successfully used in identifying hypertensive patients at risk of atrial fibrillation.

Keywords: hypertension, atrial fibrillation, atrial remodelling, 3D-echocardiography, strain

Rezumat: **Obiective –** Ne-am propus evaluarea funcţiei atriului stâng, în scopul de a depista noi markeri ecoardiografici de apariţie a fibrilaţiei atriale la pacienţii hipertensivi. **Metode –** În studiul nostru au fost înrolate prospectiv două grupuri de pacienţi hipertensivi: 46 pacienţi cu hipertensiune arterială fără istoric de aritmii (grup1) şi 23 de pacienţi hipertensivi cu un episod recent de fibrilaţie atrială documentată (grup 2). Dimensiunea atriului stâng a fost evaluată ecocardiografic: diametrele anteroposterior, transversal şi longitudinal, precum şi cele trei volume fazice (maxim (vol max), minim (vol min) şi cel dinainte de contracţia atrială (vol pre A)) prin metoda Simpson biplan modificată. Pe baza volumelor au fost calculate fracţiile de golire atrială activă, pasivă şi totală. Achiziţii ecocardiografice 3D ale volumelor maxim şi minim au fost efectuate. De asemenea a fost analizată valoarea strainului sistolic longitudinal atrial şi strainul atrial de contracţie (media obţinută din ferestrele apical patru camere şi două camere) prin metoda speckle tracking, conform standardelor actuale. **Rezultate –** Vârsta (59.5a±12 vs 67.7±8, p=0.003) şi timpul de la debutul hipertensiunii arteriale(42l±6 vs 80l±8, p=0.007) au fost semnificativ mai mari în grupul 2; ceilalţi factori de risc cardiovasculari (fumatul, dislipidemia) au avut o prevalenţă similară în cele două grupuri. Toate volumele atriale evaluate 2D şi 3D au fost semnificativ mai mari în grupul 2 (pentru toate p<0.0001) şi fracţiile de golire globală, activăşi pasivă semnficativ mai mici în acest grup, comparativ cu celălalt (p<0.0001, p<0.0001 and p=0.02.) Valorile peak-strainului longitudinal atrial au fost de asemenea semnficativ mai mici la cei cu fibrilaţie atrială faţă de hipertensivii fără aritmie(26.1%+-7.4 vs 15.7%+-5.6, p<0.0001), iar strainul de contracţie atrială nu a avut semnificaţie statistică între cele două grupuri. **Concluzie –** Evaluarea funcţiei atriului stâng prin ecocardiografia bidimensionala şi tridimensională şi prin metode de tip speckle tracking este utilă în identificarea pacienţilor hipertensivi cu risc de dezvoltare a fibrilaţiei atriale.

Cuvinte cheie: hipertensiune arterială, fibrilaţie atrială, remodelare atrială, ecocardiografie 3D, strain

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BACKGROUND

It is well known that hypertension (HTN) increases the pressure in the left atrium (LA), in time modifying the size of this heart chamber that can lead to appraisal of atrial fibrillation (AF). HTN remains one of the most important factors for development of AF[1,2]. In fact, there is a structural and functional atrial remodeling, with the first changes occurring in the elastic properties of myocardium and reflecting in LA dysfunction, with initial preservation of normal LA size. The left atrial dilatation makes part of the end stage of this process of remodeling. The novel echocardiographic techniques as 3D echocardiography and speckle tracking echocardiography made possible the accurate assessment of LA function by being able to detect even minor changes[3,4]. The study of LA myocardial deformation as two dimensional strain images provides a global but also regional wall function assessment. The clinical importance of this evaluation was established in recent studies that showed its prognostic role in cardiovascular disease[5-8].

MATERIAL AND METHODS

Study population

Forty six hypertensive patients without any other cardiac event were prospectively enrolled as the first group. Other twenty four hypertensive patients with a recent episode of atrial fibrillation, while in sinus rhythm were recruited, forming the second group. Interview, physical examination, electrocardiogram and echocardiography were performed in all patients. Subjects with secondary HTN, thyroid dysfunctions, diabetes mellitus or any other significant heart disease (LV ejection fraction <55%, arrhythmias, pacing, significant valvulopathies, known coronary disease) were excluded. Also, the patients with low quality echocardiographic views were excluded, because left atrial analysis requires optimal visualization of endocardial borders.

Blood pressure was measured at the brachial artery with the Korotkoff method, in the supine position, by performing a mean value of two measurements in conformity with guideline recommendations[9].

Subjects were followed for twelve months.

Echocardiographic study

All patients were investigated by echocardiography, using a Vingmed Vivid 7 and a Vivid E9 unit with the possibility of offline analysis of the recordings. Patients were studied in the left lateral position and the measurements were done according to the current guidelines recommendations[10]. During the evaluation all patients were in sinus rhythm.

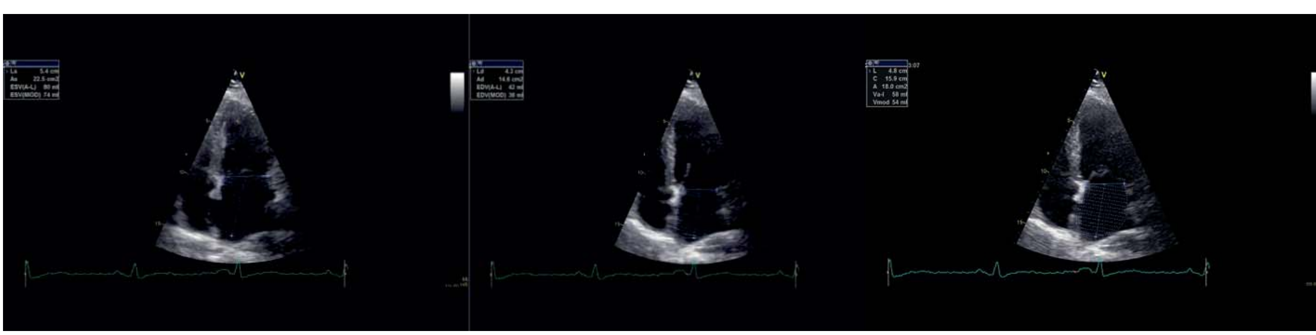

Figure 1. Phasic atrial volumes in 4c apical views: a) LAVmax, b) LAV min, c) LAV preA.

Figure 2. Phasic atrial volumes in 2c apical views: a) LAVmax, b) LAV min, c) LAV preA.

2D left atrial phasic volumes and emptying fractions

LA volumes were evaluated in the apical four and two chamber views, using the Simpson biplane method.

During a cardiac cycle, three volumes were measured:

- maximal LA volume (LAVmax) - the volume that occurs at the end of ventricular systole, just before mitral valve opening (the end of the T wave of the ECG) (Figure 1a and Figure 2a).
- minimal LA volume (LAVmin) that occurs at mitral valve closure(in enddiastole) (Figure 1b and Figure 2b).
- the volume before active atrial contraction (LAV preA) - timed to the onset of the P wave (Figure 3a and Figure 3b).

All the volumes were divided to the body surface area, obtaining LAVmax, LAV min and LAVpreA indices. The LA phasic functions were appreciated: the reservoir, the conduit and the booster pump function by calculation total, passive and active emptying fraction (Table 1).

3D left atrial assessment

3D echocardiography brings the advantage of measuring cardiac cavities with accuracy, without making assumptions, by reconstructing volumes from endocardial contours of the entire chamber. The examinations were performed using a 3D matrix array transducer with a temporal resolution of 8-22 frames/s. A wide angled full volume acquisition mode was used, in apnea, with six cardiac cycles recording. Offline data was analyzed-the pyramidal volume was displayed in three different cross-sections (two orthogonal apical and one short axis) that could be modified by manual shifting of vertical and horizontal lines. Five points were manually placed for left atrium: two points to identify mitral annulus in each apical views and one point to identify the centrum of the posterior wall in either view, than the software automatically identified the endocardial surface. Manual adjustments were made in order to exclude atrial appendage and pulmonary veins from the cavity volumes. The frame with the biggest and smallest atrial dimension were selected and analyzed in this way and atrial maximum (3DLAVmax) and minimum (3DLAVmin) volumes were obtained and atrial EF were derived from the two volumes.

Table 1. Volumetric LA function

LA function	LA emptying fraction	Calculation
Reservoir Function	Total EF	(LAV max-LAVmin)/ LAVmax
Conduit function	Passive EF	(LAVmax-LAVpreA)/ LAVmax
Booster Pump function	Active EF	(LAVpreA-LAVmin)/ LAVpreA

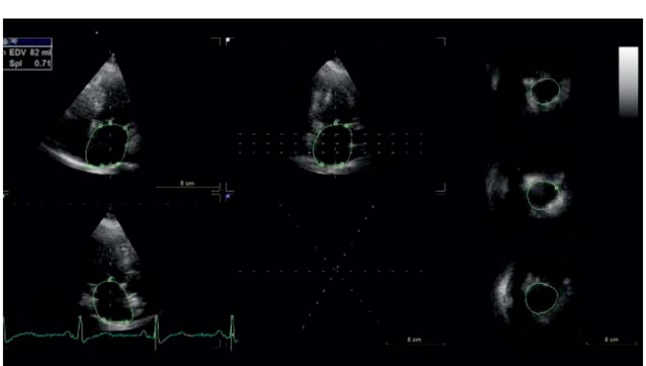

Figure 3. 3D echocardiographic evaluation of left atrium-endocardial border in the 2D cross-sections.

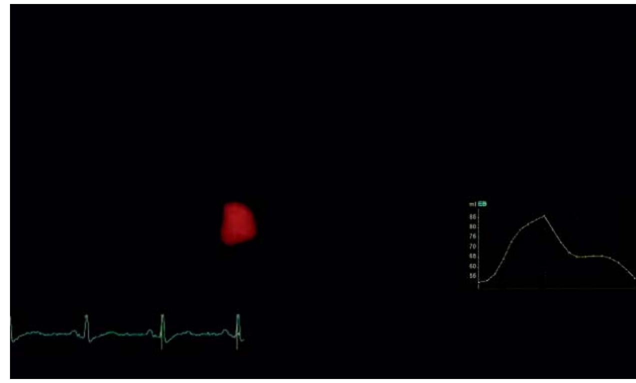

Figure 4. 3D echocardiographic evaluation of left atrium-the 3D LA reconstructed volume.

2D speckle tracking is a new echo technique that analyses myocardium deformation with no angle dependency (a nondoppler method)[11,12].

Apical four chamber and two chamber views during breath hold were obtained, with a stable ECG recording. Good quality recordings were needed, allowing reliable delineation of myocardial tissue. The settings were made for obtaining an adequate temporal and spatial resolution, with recording of three consecutive heart cycles, using a narrow sector, with optimization of visualizing LA cavity and a frame rate set between 50 and 80 frames per second. LA endocardial border was manually traced in endsystole in both apical views and an epicardial surface tracing was generated by the system, creating the region of interest (ROI) of 6 segments in each apical view. The software also generates strain curves for each atrial segment, throughout the entire cardiac cycle. LA strain has a typical pattern - a

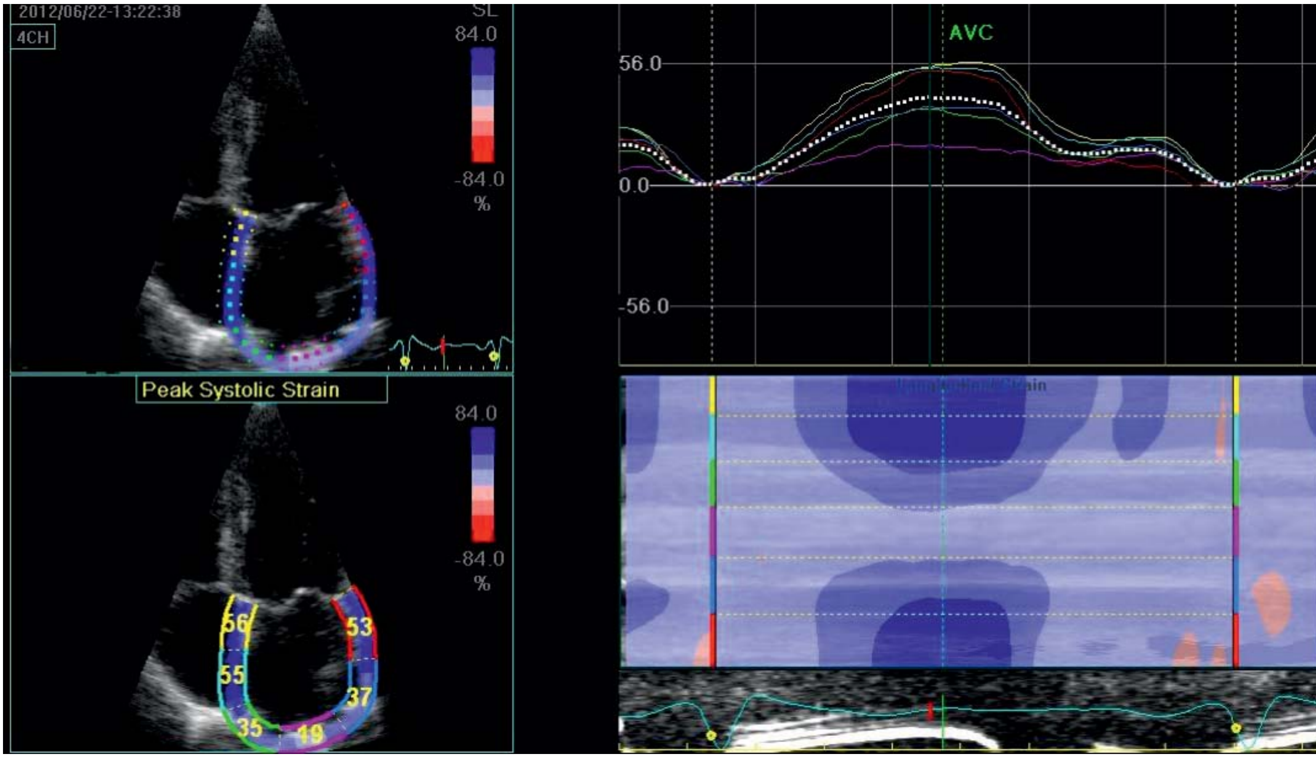

Figure 5. Assesing left atrial strain in apical 4c view.

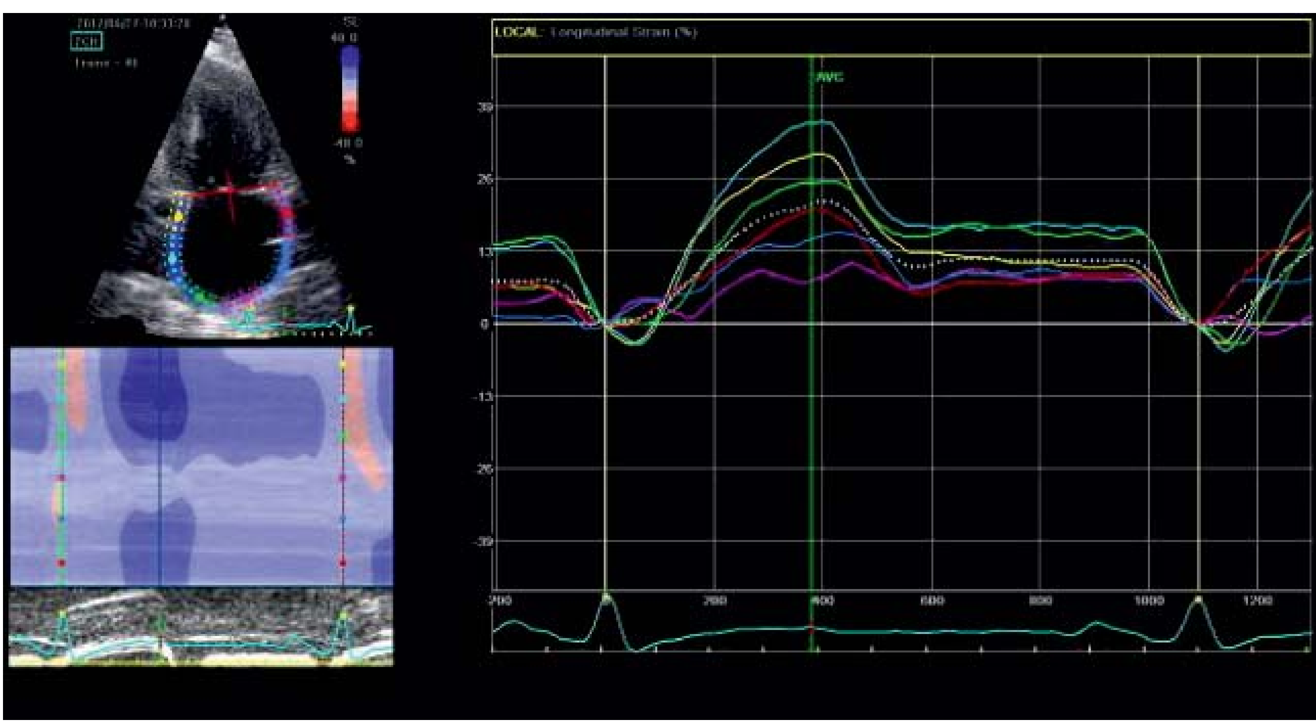

Figure 6. Assesing left atrial strain in apical 2c view.

high positive wave at the end of ventricular systole (PALS) followed by two distinct descending phases in early diastole and late systole (PACS). The mean measurements for each view was automated generated as a separate white curve. Global PALS and PACS was calculated by averaging the 12 LA segments.

RESULTS

Baseline characteristics

The frequency of female gender was higher in group 1 (65%) comparative to the arrythmia group (43.4%.)

Age (59.5y+-12 vs 67.2y+-8, p=0.003) and the mean time of HTN diagnosis (42 mo+-6 vs 80 mo+8, p=0.007) were significantly higher in group 2; the other cardiovascular risk factors (smoking, dyslipidemia) were similar as prevalence.

Table 2 summarizes general characteristics of the two groups.

All the echocardiographic parameters were age and sex-matched.

2D LA volumes and emptying fractions

All LA volumes (LAVmax, LAVmin, LAVpreA) and indexed values were greater in atrial fibrillation group, with high significance (for all p<0.0001). Also, we found significant lower emptying fractions (active, passive and global) in group 2, proving a more advanced dysfunction in hypertensive patients with atrial fibrillation.

3DLA volumes and emptying fraction

As it was expected, 3D volumes and emptying fractions were also more affected in group 2. In comparison with 2D values, 3D volumes and emptying fractions were lower, but with no statistical significance.

LA strain-PALS and PACS

The positive peak atrial strain values (mean for 12 atrial segments) were significantly higher in the first group (26.1% versus 15.7%, p<0.0001), while the peak contraction strain was lower in the first group, but without any statistical relevance.

Table 2. General characteristics

	Group 1 N=46	Group 2 N=23	P
Age (years)	59.5±12.9	67.2±8.6	0.003
Gender			
Female	30(65.2%)	10(43.4%)	NS
Male	16(34.8%)	13(56.6%)	
BSA, m^2	1.85±0.2	1.8±0.2	NS
BP			
systolic	140.6±16.5	147.9±18.6	NS
diastolic	85.38±8.3	86.07±8.8	NS
Time from HTN dgn (months)	42	80	P=0.007
Smoking	8(17.3%)	5(21.7%)	NS
Dyslipidemia	16(34.7%)	6(26.0%)	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); BSA=body surface area; BP=blood pressure; dgn=diagnosis.

Table 3. LA size phasic volumes

	Group 1 N=46	Group 2 N=23	P
LAV preA(ml)	42.7±10.3	59.9±14.9	<0.0001
LAV preA(ml/m^2)	23.1±5.9	36.3±8.1	<0.0001
LAV max(ml)	61.4±14.5	86.7±23.1	<0.0001
LAV max(ml/m^2)	33.2±7.9	48.2±10.2	<0.0001
LAV min(ml)	26.6±9.5	47.1±15.4	<0.0001
LAV min(ml/m^2)	14.4±5.3	26.2±6.41	<0.0001
LA ant-post diam	39.2±4.5	43.6±6	0.02
LA longitudinal diam	50.1±5.8	57.4±8.4	<0.0001
LA transversal diam	41.1±3.6	47±3.9	<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); 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

	Group 1 N=46	Group 2 N=23	P
LA active EF biplane	38.4±10.9	27.7±8.2	<0.0001
LA passive EF biplane	30.6±9.8	24.1±9	0.023
LA total EF biplane	57.5±8.7	45.4±7.4	<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. LA 2D and 3D volumes and global EF

	Group 1 N=46	Group 2 N=23	P
2D LAV max (ml/m^2)	33.2±7.9	48.2±10.2	<0.0001
3D LAV max (ml/m^2)	30.1±8.4	47.1±10	<0.0001
2D LAV min (ml/m^2)	14.4±5.3	26.2±6.41	<0.0001
3D LAV min (ml/m^2)	16.2±5.6	30.1±3	<0.0001
2D LA EF	57.5±8.7	45.4±7.4	<0.0001
3D LAEF	46.16±7.7	36.09±5.9	<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); LA=left atrium; EF=emptying fraction.

Table 6. Peak systolic atrial strain (average of 12 atrial segments)

	Group 1 N=46	Group 2 N=23	P
PALS (%)	26.1±7.4	15.7±5.6	<0.0001
PACS (%)	-16.4±-0.16	-15.3±0.1	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); PALS=peak atrial longitudinal strain; PACS=peak atrial contraction strain.

FOLLOW-UP

Ten patients has at least an episode of atrial fibrillation in the 12 months of follow up, three patients from group 1 as a first episode of AF (representing 6.7%) and seven from the second group (30% from the group population) had at least a recurrence of AF, from which two of them remained in atrial fibrillation rhythm. None of the subjects had new onset stroke the 12 months follow up.

DISCUSSION

Assessing LA function has a recognized role in prognosis and risk stratification[8,13]. LA structural remodeling is a stable indicator of diastolic LV dysfunction and high filling pressures[14,15] that we commonly find in hypertensive patients. Progressive changes in LA structure leads to fibrosis, which represents a favorable milieu for arrhythmia. So, analysis of LA function can help us to detect the hypertensives at risk of atrial fibrillation. In many studies it was concluded that LA enlargement is an independent factor for atrial fibrillation appraisal[16-18], but, in the same time, atrial dilatation can be seen as a result of AF. There is an interdependency between the two factors. The increase overload in left atrium (as seen in hypertensives) leads to expansion of the left atrium myocardium, enhancing its reservoir and contractile function to a critical point, after which the emptying fraction starts to decline (Franck Starling law). The structural impairment leads to electrical disturbation, that influences the myocardial contraction sequence increasing also the structural alteration.

Guidelines strongly recommend the echocardiographic measurement of LA maximal volume(measured in apical four chamber view, indexed for BSA). LAVI has proved its value in clinical practice, being an established marker for assessing prognosis in general population[19]. Though most studies investigated LAVmax, lately also LAV min proved to be an accurate parameter for adverse outcomes, as for paroxysmal atrial fibrillation[20]. Several studies have showed reproducibility and feasibility of 3D echocardiography in detecting structural and functional changes in LA, adding a low interobserver variability in comparison with traditional echocardiography[21,22]. Though it is not a method used on a large scale, normal ranges for 3D maximal and minimal volume and LAEF were defined, with a LAEF low value limit at 45%[23]. Our results were similar with those presented in literature and we also found a good correlation with 2D results.

Atrial fibrillation aggravates all LA function: reservoir, conduit and contractile function[24,1]. In some studies, LA passive emptying function was found increased in patients with hypertension and atrial fibrillation comparative to hypertensive in sinus rhythm[25]. The explanation was that the recoil function of left atrium is altered in atrial fibrillation, creating increased LA pressure and an early increase in passive emptying function. In our study the passive LA emptying function was lower in atrial fibrillation group, but with lower statistical relevance compared to the differences of the other LA functions in the two groups.

The contractile function of LA was disturbed in our study in both hypertensives groups, with a higher alteration in atrial fibrillation group. At first, LA tries to compensate decreased LV filling by increasing its contractile function and in some studies the contractile function of LA was enhanced compared to normotensives. With progression of the hypertension and enlargement of LA, contractile function tends to deteriorate; also the electrical disorder, as FA, affects the contractile sequence resulting in more reduced LA active emptying[18]. This was proven not only by volumetric measurements, but also through speckle tracking appreciation of atrial myocardial deformation[26,27]. LA booster pump function appreciated by PACS was decreased in hypertensives with atrial fibrillation versus without AF, as expected, because of a more advanced remodeling atrial process. Some studies have used the echocardiographic assessment of LA function to predict recurrence of atrial fibrillation. The best predictors were peak atrial strain, as a measure of atrial reservoir capacity[28,29].

In our study we found also that the hypertension period duration is important and can be considered an underlying precipitating factor for atrial fibrillation. On the other hand, the long term effects of hypertension (and not only the atrial fibrillation) could explain the differences in LA volumes and function.

LIMITATIONS

The small number of patients in both groups and the heterogeneity of the hypertensives(all classes of hypertension, that were treated with different drug combinations) represent some limitations of this study.

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 in the AF group comparing to the other group might have influenced the results.

CONCLUSIONS

Deterioration of left atrial function is frequently seen in HTN, but dysfunction is higher when atrial fibrillation occurs, suggesting a more advanced process of atrial remodeling and fibrosis. Hypertensives should be closely monitored and evaluated for detection of left atrial dysfunction. Echocardiography-2d assessment and the novel methods as speckle tracking and 3D echocardiography proved to be a reliable method for evaluation of LA remodeling.

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