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Clinical and echocardiographic variables associated to left atrium enlargement. Differences between genders

Variables clínicas y ecocardiográficas asociadas con dilatación de la aurícula izquierda. Diferencias entre géneros

Francisco Sánchez-Lezama,* Luis Gerardo Domínguez-Carrillo,**
Carlos Harrison-Gómez,*** Mariela Ramírez-Lagundas****

Key words:
Left atrial enlargement, echocardiography.

Palabras clave:
Crecimiento auricular izquierdo, ecocardiografía.

ABSTRACT

Introduction: Left atrium (LA) enlargement is a predictor of cardiovascular events. **Objective:** To inform clinical an echocardiographic findings related to LA enlargement in patients with normal left ventricle (LV) systolic function without valvulopathy or cardiomyopathy, and gender differences. **Methods:** Forty patients with LV ejection fraction ≥ 50% were evaluated with a complete transthoracic echocardiogram. **Results:** In the sample, 55% were female (n = 22) and 45% men (n = 18); age of 68.5 ± 36.7 years with range of 35 to 87; only hypertension was a significant risk factor. LA volume in female was 56.8 ± 36.06 mL and 73.4 ± 94.04 mL in male; the LA indexed volume was 33.31 ± 14.84 mL/m^2 BSA in women and 39.22 ± 56.56 mL/m^2 BSA in men (p = 0.05). LV concentric remodeling was found in 52.5% (n = 21) and it was the most frequent structural change; on the other hand concentric hypertrophy was more prevalent in women (p = 0.05) and the diastolic diameter of the LV showed significant difference between genders (p = 0.05). No other significant differences between genders were found in any other parameter. **Conclusions:** Systemic hypertension was the most prevalent risk factor, being more frequent in men, as well as greater extent of LA volume and diastolic diameter of LV; concentric remodeling was very frequent in both genders and LV end diastolic pressures were normal in both groups.

RESUMEN

Introducción: *La dilatación de la aurícula izquierda (AI) es un predictor de eventos cardiovasculares.* ***Objetivo:*** *Informar los hallazgos clínicos y ecocardiográficos asociados con dilatación de AI en pacientes con función sistólica del VI normal, en ausencia de miocardiopatía y valvulopatía, y las diferencias entre géneros.* ***Métodos:*** *Cuarenta pacientes con fracción de expulsión del VI ≥ 50% se evaluaron con ecocardiograma transtorácico completo.* ***Resultados:*** *En la muestra, 55% fueron mujeres (n = 22) y 45% hombres (n = 18); la edad de 68.5 ± 36.7 años con rango de 35 a 87; como factor clínico de riesgo, sólo la hipertensión fue significativa. El volumen de AI en mujeres fue 56.8 ± 36.06 mL y 73.4 ± 94.04 mL en hombres; el volumen indexado de AI fue 33.31 ± 14.84 mL/m^{2}SC en mujeres y 39.22 ± 56.56 mL/m^{2}SC en hombres (p = 0.05). La remodelación concéntrica del VI se encontró en el 52.5% (n = 21) de los casos y fue el cambio estructural más frecuente; por otro lado la hipertrofia concéntrica fue más prevalente en mujeres (p = 0.05) y el diámetro diastólico del VI mostró diferencia significativa entre géneros (p = 0.05). No se encontraron diferencias significativas entre géneros en ninguno de los otros parámetros.* ***Conclusiones:*** *En la muestra estudiada la hipertensión arterial fue el factor de riesgo más prevalente, siendo más frecuente en hombres, al igual que mayor grado de dilatación auricular y del diámetro diastólico del VI; la remodelación concéntrica resultó muy frecuente en ambos géneros y las presiones de llenado fueron normales en ambos grupos.*

* Cardiologist. Chief of Echocardiography Department. Hospital Ángeles León. México.
** Rehabilitation Medicine Specialist. Professor of Medicine School from León, Guanajuato University. México.
*** Cardiologist. Professor of Medicine School from León, Guanajuato University. México. Hospital Ángeles León.
**** Medicine Student. Medicine School from Anáhuac México Norte University. México.

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INTRODUCTION

It is well recognized that left atrium (LA) enlargement is a marker of LV diastolic filling impediment and a potential predictor of adverse cardiovascular outcomes such as atrial fibrillation, stroke, congestive heart failure, and cardiovascular death.1 It has been shown that aging alone does not independently contribute to LA enlargement, in fact, it is well known that LA enlargement reflects diverse pathophysiologic processes, and as previously stated, associated with excess morbid cardiovascular outcomes. Our focus is exclusively on left atrial structure and function in non-valvular cardiomyopatic disease and its potential as an additive risk factor, and in the near future disclose if therapeutic favorable modifications in LA structure and function will translate in improved cardiovascular outcomes.[2] LA mechanical function can be described by three different phases of the cardiac cycle: a) during ventricular systole and isovolumetric relaxation, the LA functions as a pool that receives blood from pulmonary venous return and stores potential energy in pressure form; b) during ventricular diastole, the LA operates as a duct or canal transferring blood into the left ventricle (LV) after mitral valve is opening via a «suction» effect in early diastole and pressure gradient later during «plateau» or diastasis and through which blood flows from the pulmonary veins into the left ventricle; c) the LA contraction increases LV filling and contributes to stroke volume by approximately 20 to 30%. LA enlargement carries important clinical information.[3,4] Left atrial volume is superior to LA diameter as a measure of LA size, and should be incorporated into routine clinical echocardiographic evaluation because it does have important prognostic implications and helps guide therapy. Based on data stated above, we conducted this study in 40 patients with LA enlargement but normal LV systolic function without valvular disease or cardiomyopathy in order to inform clinical and echocardiographic findings, and associated gender differences.

METHODS

We included in our study forty consecutive patients with an enlarged LA in echocardiographic study, 22 females and 18 males. All patients with normal LV ejection fraction (≥ 50%) were included and those with valvular heart disease and/or cardiomyopathy were excluded. All studies were performed by a cardiologist board certified in echocardiography. Conventional measurements in M-mode echocardiography, two-dimensional, pulsed, continuous, color and tissue Doppler reports were performed using either a Phillips echocardiograph model iE33 or a Phillips Sonos echocardiograph 5500, using 1-3 MHZ multifrequency transducer, with special emphasis on structure and size of left atrium. The cutoff point to determine de LA as enlarged was 29 mL/m^2 of body surface area. Demographic profiles findings and measurement were recorded. Variables obtained were: age, sex, smoking, history of hypertension, diabetes mellitus, dyslipidemia; left ventricle diastolic diameter (LVDD), left ventricle systolic diameter (LVSD), posterior wall thickness (PWT), LV ejection fraction (LVEF). Specific measurements were: LV end-diastole thickness/radius ratio (T/R), which was obtained by M mode echo measurement: posterior wall thickness x 2/diastolic diameter; normal value was established in < 0.42. Left ventricular mass, calculated by M-mode using the following equation:[4] $1.04 \times (0.8 \times ([LVDD + IVST + PWT]^3 – [LVDD]^3)) + 0.6$; normal value was considered < 95 g/m^2 BSA in women and < 115 g/m^2 BSA in men. According to this, four different ventricular geometry were considered: a) normal (normal mass and normal T/R ratio); b) concentric remodeling (normal mass and increased T/R ratio); c) concentric hypertrophy (increased mass and increased T/R ratio) and d) eccentric hypertrophy (increased mass and normal T/R ratio).

Left atrial volume, which was obtained by the biplane Simpson method in apical 2- and 4-chamber views using the built-in software of the machine. For this purpose, LA areas were manually traced at end-systole in apical four- and two-chamber views, ensuring that there was no foreshortening of the LA. Automatic volume calculation was performed using the software for the modified Simpson's disc summation method in the echo machine. LA volume was indexed to body surface area and expressed as LA volume index (mL/m^2 BSA). Normal value of left atrium volume was < 29 mL/m^2 BSA in the apical four chamber view, using a 1-2 mm sample volume, pulse wave (PW) Doppler cursor is placed between the mitral leaflet tips during diastole. From the mitral inflow profile the E wave was measured. The average of early septal and lateral diastolic velocities (e') were measured by tissue Doppler imaging from the apical four-chamber view. The E/e' ratio was calculated and a value ≥ 15 was considered as indicative of high LV filling pressures. Data analysis was done using SPSS 17, student t test and Fisher exact test were applied whenever applicable.

RESULTS

Sample consisted of 40 patients *(Table 1)*, 55% were females (n = 22) and 45% males (n = 18); the average (mean) age and standard deviation (SD) for the first was 68.5 ± 36.7 years with range of 35 to 87 years; for the second one it corresponded an mean and SD of 63 ± 40.08 years and range of 20 to 88 years. A higher average age (5 years) was found in the female gender but the presence of left atrial enlargement was observed in this sample at an earlier age in the male with a difference of 15 years.

Systemic arterial hypertension was the most prevalent risk factor for LA enlargement in our study, present in 57.5% of the total cases (n = 23); no statistically significant differences were found in the other risk factors: smoking occurring in 25% of cases, diabetes mellitus in 15%, and dyslipidemia in 27.5%. Hypertension was more frequent in men compared to women (72% vs 45%), (p = 0.05).

Regarding the echocardiographic findings *(Table 2)*, the LA volume in women showed a X and SD of 56.8 ± 36.06 mL; in men 73.4 ± 94.04 mL; the indexed volume was 33.31 ± 14.84 mL/m^2 BSA in women (mild dilation) and 39.22 ± 56.56 mL/m^2 BSA in men (moderate dilation), this was statistically significant. Also, there was a statistically significant difference in LV diastolic diameter between women and men: 41.38 ± 11.31 mm vs 47.38 ± 8.45 mm, respectively (p = 0.05). No statistically significant differences were found between genders in any of the other parameters studied.

In the evaluation of the left ventricular filling pattern, using the pulsed Doppler inflow and mitral annular Doppler tissue velocity, it is worth noting that the E/e' ratio was less than 12 cm/s which translates normal filling pressures, and no gender differences were found in E wave and e' wave, as well as in E/e' ratio.

Respect to LV structural changes, hypertrophy was observed in 30% of the cases, with statistically significant difference in favor of the female gender with 8 cases (36.3%) against 4 in the male (22.2%) (p = 0.05).

Concentric remodeling was the most common LV hypertrophic pattern observed in the sample studied occurring in 52.5% of the cases (n = 21), no difference was found between genders; the pattern of normal ventricular geometry was found in 17.5% of the total patients studied. Presence of atrial fibrillation

Table 1: Demographic data and risk factors in 40 patients with left atrium enlargement.

Age	Female 22 (55%) 68.5 ± 36.7 R: 35-87 n (%)	Male 18 (45%) 63 ± 40.08 R: 20-88 n (%)	p	Total 40 (100%)
Smoking	5 (22.7)	5 (27.7)	NS	10 (25.0)
HBP	10 (45.4)	13 (72.2)	0.05	23 (57.5)
DM	3 (13.6)	3 (16.6)	NS	6 (15.0)
Dyslipidemia	5 (22.7)	6 (33.3)	NS	11 (27.5)

HBP = high blood pressure; DM= diabetes mellitus; R = range.

Table 2: Ecahocardiographic findings in 40 patients with left atrium enlargement and its distribution by gender.

	Female 22 (55%)	Male 18 (45%)		
	Mean ± SD	Mean ± SD	p	Total 40 (100%)
LVDD	41.38 ± 11.31 R: 33-49	47.38 ± 8.45 R: 42-54	0.05	—
LVSD	24.13 ± 13.43 R: 16-35	28.27 ± 7.77 R: 22-33	NS	—
IVS	11.31 ± 3.67 R: 8.6-13	12.10 ± 6.50 R: 8.2-17.4	NS	—
PW	9.94 ± 2.33 R: 8.7-12	10.81 ± 3.39 R: 8.2-13	NS	—
EF	71% ± 0.09 R: 63-77	68% ± 0.11 R: 58-74	NS	—
SF	44 ± 0.30 R: 31-74	40 ± 0.16 R: 30-53	NS	—
LAV	56.8 ± 36.06 R: 42-93	73.4 ± 94.04 R: 49-182	0.05	—
Indexed LAV	33.31 ± 14.84 R: 33-54	39.22 ± 56.56 R: 29-109	0.05	—
E wave	78.76 ± 41.71 R: 55-114	72.46 ± 48.79 R: 42-111	NS	—
e'wave	7.91 ± 10.74 R: 5.1-20.3	8.41 ± 5.16 R: 5.8-13.1	NS	—
E/e'	10.32 ± 9.68 R: 4.3-18	8.01 ± 7.07 R: 5-15	NS	—
Atrial fibrillation	1 ± 4.50	3 ± 16.60	0.05	4 10
Concentric hypertrophy	8 ± 36.30	4 ± 22.20	0.05	12 30
Normal	3 ± 13.60	4 ± 22.20	NS	7 17.5
Concentric remodeling	11 ± 50.00	10 ± 55.50	NS	21 52.5

LVDD = left ventricle diastolic diameter; LVSD = left ventricle systolic diameter; IVS = interventricular septum; PW = posterior wall; EF = ejection fraction; SF = shortening fraction; LAV = left atrial volume; SD = standard deviation; R = range.

(AF) was observed in one woman and in 3 men, a finding with statistically significant difference.

DISCUSSION

Echocardiography is one of the most important non-invasive methods that allow a simultaneous and continuous recording of LA size and volume.[5] There are three main volumetric measurements: the maximum volume, which occurs just before the mitral opening (max LA vol.), the minimum volume, at the time of mitral closure (min LA vol.), and the average volume, before the P wave (average LA vol.). This measurement is indexed by the body surface, considering the maximum normal value of 28 mL/m² BSA.[6] In a previous report of a Mexican population, cardiac chambers dilation was identified in 371 (27.79%, from a total of 1,335 patients), from these LA enlargement was seen in 242 cases (65.13%).[7] In the current study we assessed people with normal LV ejection function, without valvular heart disease and/or cardiomyopathy.

The size and function of the LA largely reflects the global function of the circulatory system, especially the diastolic function of the left ventricle, being a true biomarker of the latter and therefore its modifications turn out to be a marker of risk of cardiovascular events.

Physiologically, the LA acts as a reservoir for the volume of the pulmonary venous return, maintains it during its contraction and the LV isovolumetric relaxation period. When the mitral valve opens, it transfers its contents to the LV, due to pressure gradients initially, later by means of its contraction it does so actively immediately before the start of the LV systole, determining the final diastolic volume. Therefore, the LA acts as a reservoir (40%), as a conduit (35%) and as a pump (25%), and the transition between the almost continuous flow of the pulmonary circulation and the intermittent flow of the LV filling depends on it.[8] Different pathological conditions can alter the normal physiology of LV filling and conduce to structural alterations. Not infrequently the volume status of the LA will be modified, since during the proto-diastole, the relaxation failure is associated with a decrease in the function of the duct and an increase in the reservoir and contraction phases due to a decrease in the atrial-ventricular gradient. As the diastolic dysfunction is accentuated, the contribution of the conduit mechanism increases significantly while those of the reservoir and contraction decrease considerably.

Echocardiography is an excellent method to study LV filling dynamics, and as such, the magnitude of the first transmitral E wave represents the ventricular filling in the early diastole, which is a combined effect of the passive function of LA and active LV (suction), and is an index of LV relaxation. The E wave is decreased early in the LV relaxation failure. The deceleration time of the E wave (from the maximum speed to the velocity 0) is another element that assesses the ventricular relaxation and that is prolonged if the relaxation is abnormal. The transmitral A wave magnitude is frequently used to evaluate the contractile function of LA and is related to ventricular distensibility.[9] Wave A becomes more prominent as LV filling pressures increase. The E/A ratio describes the atrial contribution to filling the ventricle. On the other hand, the correlation and similarity between waves of tissue Doppler (TD) signals in the middle or lateral mitral annulus to those of the atrial walls make TD invaluable in the study of LV filling. The e' wave of the mitral annulus correlates with the maximum velocity of the transmitral flow, and the atrial fraction of the LV filling is diminished during atrial dysfunction. The relationship between the E waves of the mitral filling and the e'wave of the mitral annulus (E/e') also reflects the filling pressures of LV and they are codependents.

In our echocardiography laboratory, diastolic dysfunction is the second most frequent finding among 1,440 patients evaluated with 30.7% of the cases.[7] Nevertheless in this current study of patients with the LA enlargement that excluded patients with valvular heart disease, cardiomyopathy and/or LV systolic dysfunction, there are other factors related to left atrial enlargement, commonly systemic hypertension, also a less compliant cardiovascular system, and the gross structural and histological changes associated with it such as fibrosis, importantly mediated by neuro-adrenergic system activation, including renin-angiotensin-aldosterone and adrenergic system.[10]

Currently, other technologies are available to evaluate the repercussion in LA structure and function.[11] Tissue Doppler (TD) is one of the echocardiographic methods for studying atrial function. With the sample volume located in one of the LA walls, a velocity versus atrial myocardial time curve is generated, either in real time or as a result of the post-processing of a color TD image.[12] This has also been found with Doppler, which shows an increase in the phase of active emptying (atrial contraction), which compensates for the decrease in the passive emptying phase. The decrease in ventricular compliance (for example associated with age or hypertrophy) produces an increase in the left atrial pressure in order to maintain the filling of the LV. The secondary increase in wall tension of LA results in atrial myocardial stretch, dilation, and increased contractility according to the

Frank-Starling law. This law has been confirmed by studies carried out with tissue Doppler that directly measures the maximum speed (Va) in the various segments of the LA. In fact over 60 years of age, the speed of the walls of LA are significantly higher than in younger people. Based on the TD color image, other modalities can be derived for both global atrial examination (tissue tracking and tissue synchronization imaging), for segmental atrial study (strain and strain rate or velocity of the deformation). In the strain and strain rate,[13] which study myocardial deformation, the contraction of the fibers shows that the shortening and distension of the atrial walls are discordant in terms of the direction of the signal when it is compared to the same signals in the ventricular walls during ventricular contraction.[14] Strain function is better indicator of segmental function than tissue Doppler, both in the ventricle and in the atrium, since it is not influenced by the traction exerted by the neighboring segments, which may affect the TD.[15]

LA function in atrial fibrillation has particular importance due to its effect on morbidity and mortality.[16,17] It has been observed that the onset of this arrhythmia is accompanied by decreased atrial compliance and increased pressure in LA.[18] With the use of strain in the atrial walls, it has been found that the deformation is absent in this arrhythmia. This may reflect decreased walls distensibility, which is related to the depression findings of the reservoir and duct phases, and the absence of the contractile phase. Left atrial volume is a more robust marker of cardiovascular events than LA area or diameter in subjects with sinus rhythm. The predictive utility of LA size for cardiovascular events in AF is poor, irrespective of the method of LA size quantitation.[1] Auricular «stunning» after cardioversion is known to last for weeks and is associated with thromboembolic risk. In chronic cardioverted patient with AF, the gradual recovery of the contractile function on the first four weeks has been demonstrated. In this study 4 patients, which represents 10% of the sample had atrial fibrillation.

When the present study is related with other reports, Baekkevar et al[19] found that when LA dimensions are compared between genders, the only difference is a higher upper normal level of max right atrium (RA) volume index than max LA volume index among males. Weihao et al[20] reports that atrial dimensions and volumes are generally larger in males in healthy Chinese adults; but in the Katayama et al report that, although the LA volume is similar between males and females, the LA volume index is significantly higher in females than in males in study of 380 patients (205 females and 175 males).[21]

In relation to the presence of hypertension (the main clinical factor found in the sample of this study), the Miyoshi et al report demonstrated that alterations in LA structure and function are mainly associated with LV diastolic and systolic dysfunction respectively in preclinical patients with hypertension, also when there are obesity and hypertension is well known to result in heart failure with preserved ejection fraction.[22] Therefore, it is clinically important to clarify the mechanisms of further deterioration of LA and LV interaction in asymptomatic patients when both problems coexist.[23]

Due to the above, and despite the fact that the patient is asymptomatic, if systemic hypertension is diagnosed for the first time, or the patient is already receiving treatment for it, echocardiographic control is essential to assess the structure, volume and size of the LA, such as possible regression of LA enlargement with established treatment.[24]

Current echocardiographic and Doppler techniques allow to detect and classify the degrees of diastolic left ventricular function. The latter works better with symptomatic patients and more advanced disease, so the early diagnosis of clinical diastolic dysfunction remains a problem not yet solved for current cardiology. The study of the left atrium is probably one of the links that allows us to understand these mechanisms.

One of the limitations of this communication is that it has a small number of cases, so the findings should be replicated by studies with greater amplitude to corroborate the findings.

CONCLUSIONS

In this studied sample of patients with left atrium enlargement, systemic hypertension was the most frequent risk factor and was more frequently observed in men. About the echocardiographic findings, the left atrium volume and the diastolic diameter of left ventricle were more important in male gender, and the concentric remodeling of the left ventricle was the most frequent morphological change. It was expected to find increased in the left ventricle filling pressures, but the results are the opposite, so it could be possible a light or incipient diastolic dysfunction, perhaps evident only during exercising or any other stress situations, which would lead to transient end LV diastolic pressures increasing. Other possibility could be that left atrial enlargement represents the initial stage of some kind of cardiomyopathy. This is why cardiologists should always pay attention when a patient is reported with left atrial enlargement and other imaging methods could be necessary in order to enhance diagnostic accuracy.

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Correspondence to:

Dr. Francisco Sánchez Lezama
E-mail: sanchezlezama@angelesleon.com