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ASSESSMENT OF LEFT ATRIAL PHASIC VOLUMES AND FUNCTIONS DURING THIRD TRIMESTER OF HEALTHY PREGNANCY

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Abstract

Background: *Pregnancy is a physiological process associated with morphologic, hemodynamic, and functional adaptation of the heart in the transient preload and afterload changes . Ventricular volume and LA dimensions progressively increase due to increase in the volume load in the third trimester that worsens potential heart disease . Limited echocardiographic information exists on left atrium volume and function during third trimester of healthy pregnancy among Iraqi women.*

Aim: *to assess the left atrium volume and function during third trimester of healthy pregnancy.*

Methods: The study was carried out on 75 healthy pregnant women (cases) and 75 nonpregnant women (control group) , women were attended to Al-Furat Teaching Hospital from 1st of April 2022 to 30 of May 2023, comprehensive 2D echocardiographic study had been done for each one of them.

Results: *Pregnant women group showed a high significant increase in left atrial maximum volume ,left atrial minimum volume and pre-atrial volume compared to non pregnant women (41.8 ± 11.50 vs. 25.16 ± 6.04 , p<0.0001), (17.28 ± 7.76 vs. 11.77 ± 4.07 , p< 0.0001) and (8.69 ± 4.24 vs. 6.8 ± 2.93 ,p < 0.002) respectively.*

As well, the study showed that in pregnant women group there is high significant increase in left atrial reservoir ,conduit and booster function (32.94 ± 9.57 vs. 18.38 ± 4.79, p< 0.0001) , (24.26 ± 9.06 vs.13.41 ± 3.92 ,p< 0.0001) (8.58 ± 4.66 vs. 4.98 ± 2.30 , p< 0.0001) compared with control. In addition, left atial the total emptying fraction % and Active ejection fraction % significantly higher in pregnant women than the control (0.79 ± 0.08 vs. 0.73 ± 0.09, p< 0.0001), (0.49 ± 0.13 vs. 0.42±0.13 , p<0.002).

Conclusion: *In healthy pregnant women at the third trimester there is increase in left atrial volumes (maximum, minimum and pre –atrial) and enhancement in (reservoir , conduit and booster) functions by using 2-Dimensinal Echocardiography .*

Keywords: *Left atrium, left atrial phasic volumes , third trimester pregnancy*

Introduction

The word atrium is of Latin origin, and it refers to a central room of a Roman house from which one could enter several chambers [*Loukas et al., 2016*]. The left atrium is one of the heart's four chambers. It receives oxygen rich blood from the pulmonary system and pumps this blood into the left ventricle which then returns it to the systemic circulation [*Gray,2005*]. The left atrium (LA) is crucial in car-

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diovascular function not only as a mechanical contributor, elastic reservoir, and primer for left ventricular filling, but also as an essential component in intravascular volume management via the synthesis of atrial natriuretic peptide. Althoughleft atrium diameter in the parasternal long-axis view has been routinely employed,left atrium volume is a more forceful marker for predicting events thanleft atrium areas or diameters [*Galiuto et al., 2011*].

General anatomical features of the left atrium:The left atrium, a cuboidal-shaped chamber near the base of the heart, is the most posterior of all the cardiac chambers. The superior wall of the left atrium is near the junction of the pulmonary trunk and the right pulmonary artery. The left atrium connects to the base of the left ventricle anteroinferiorly and to the left at the mitral valve orifice. Furthermore, when the coronary sinus and the great cardiac vein are viewed externally, they are located inferior and on the posterior wall of the left atrium, filling the left atrioventricular sulcus [*Whiteman et al., 2019*]. Although smaller, the left atrium is muscular and thicker than its right atrium [*Gray,2005*]. Its wall is punctured by the openings of the pulmonary veins proximally, left atrial appendage laterally, and the mitral valve distally (Figure. 1) [*Whiteman et al., 2019*]. Transmurally, the thickness of the musculature of the left superior wall ranges from 3.5 to 6.5 *mm*, while the lateral wall thickness approximates between 2.5 and 4.9 *mm*. The myocardial fibers of the walls are made of one or more alternating layers with marked sectional variations in thickness [*Ancona et al., 2014*] .

Left atrium Function: The main mechanical function of the left atrium (LA) is to facilitate and modulate the filling of the left ventricle (LV) with blood returning from the lungs. This is accomplished during LV systole as a reservoir for the inflow volume from pulmonary veins, as a conduit during early LV diastole transferring blood stored in the atrium, and from the pulmonary veins, to the LV, and finally, as a booster pump that enhances LV end-diastolic filling [*Galiuto et al., 2011*]. Althoughleft atrium assessment has been proven to be very useful in many cardiovascular diseases, the assessment ofleft atrium function is complex due to a variety of reasons as geometrical assumptions, as theleft atrium shape is not as simple due to the presence of theleft atrium appendage, confluence of pulmonary veins, and the interatrial septum .Sinceleft atrium varies during the cardiac cycle, temporal sampling is recommended when precise evaluations of dimensional changes are required. So no other imaging technique, except

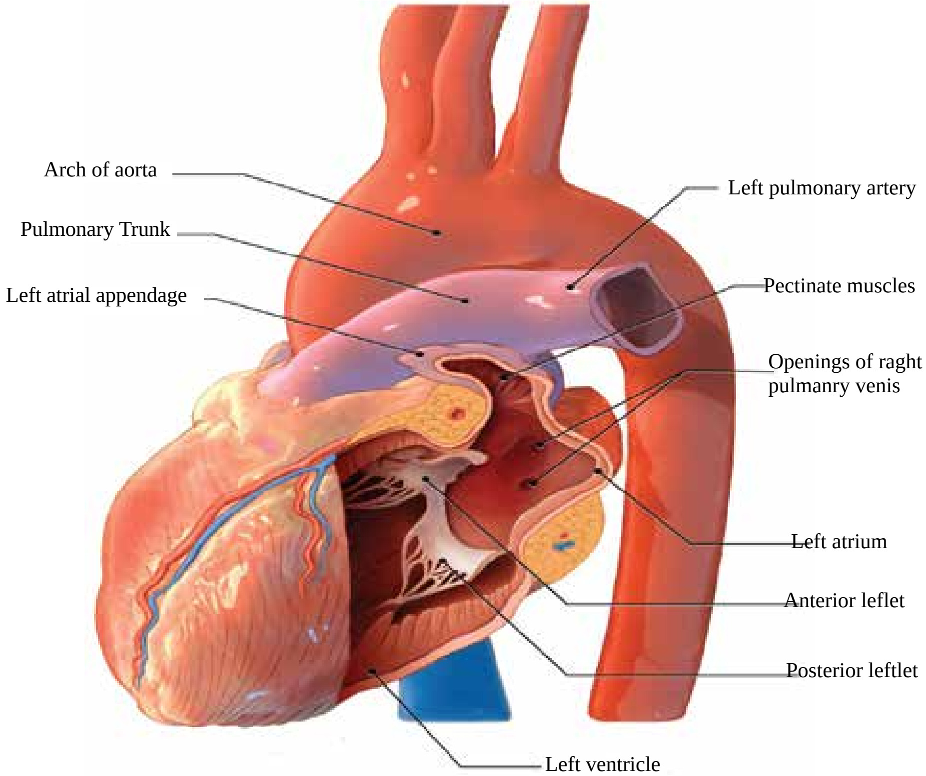

Figure 1. *Attributes of the left atrium (Illustration by Brandon Holt ©2019 , provided under CC-BY–NC–ND) [Whiteman et al., 2019].*

echocardiography, can be used as a gold-standard for the evaluation ofleft atrium dynamic changes even the cardiac magnetic resonance) insufficient for the assessment of fast changes inleft atrium dimensions, especially when irregular and fast rhythms are present [*Galiuto et al., 2011*].

When the mitral valve (MV) is closed during LV systole and isovolumic relaxation, theleft atrium acts as a distensible **reservoir**, accommodating blood flow from the pulmonary veins and storing elastic energy generated by systolic descent of the mitral annular plane in the form of pressure. During early LV diastole, the elastic energy is returned facilitating early LV filling [*Galiuto et al., 2011; Todaro et al., 2012*]. Then theleft atrium behaves as a conduit that starts with MV opening and terminates beforeleft atrium contraction allowing passive emptying during early ventricular diastole and diastasis . Finally, at end-diastoleleft atrium is also a muscular pump (**booster**), which operates depending on its own pre-load according to the Frank– Starling mechanism, which contributes to maintaining adequate LV end-diastolic volume by actively emptying [*Galiuto et al., 2011; Todaro et al., 2012*]. Understanding each of these roles is critical for correctly determining phasic variations in dimensions and flow patterns into and out of the left atrium during the cardiac cycle in both normal and diseased hearts (Figure 2).

The energy stored by the left atrium during ventricular systole is released after mitral valve opening, considerably adding to LV stroke volume during the left atrium reservoir phase. The left atrium conduit phase spans early LV filling and diastasis. left atrium contractile phase performance depends on preload, afterload, intrinsic contractility, and electromechanical coupling. Echocardiography has become the established method for non-invasive evaluation of this triphasic nature [*Todaro et al., 2012*]

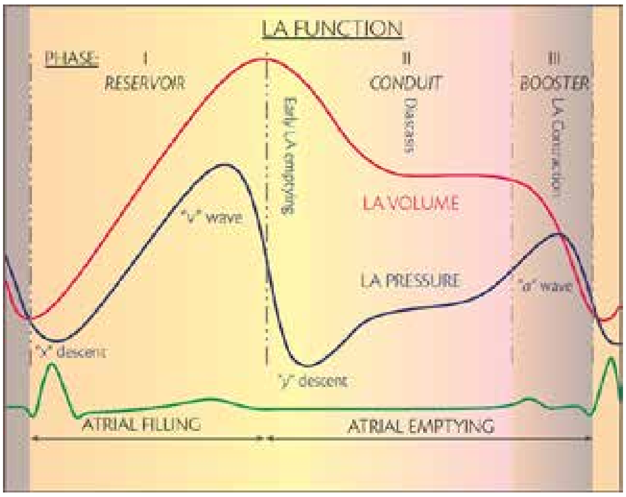

Figure 2. *Left atrial function. Schema indicating the phases of LA function, volume, and pressure changes over the cardiac cycle [Galiuto et al., 2011]*

During pregnancy ,the morphologic, hemodynamic, and functional adaptation of the heart in the transient preload and afterload are changing. Increasing the volumetric load and decreasing peripheral resistance during pregnancy have been well documented in previous publications [*Osman et al., 2017*] .

The increase in the volume load in the third trimester worsens any potential heart disease. Previous studies demonstrated changes in LV function during pregnancy, particularly diastolic function. left atrium structural and functional changes are indicators of LV diastolic dysfunction [*Song et al.,2015*]. However, although there are many publications about maternal heart adaptation during pregnancy [*Melchiorre et al.,2012 ;Ouzounian et al.,2012*]. left atrium functions and their relevance to other cardiovascular adaptation findings have not been adequately addressed [*Tasar et al., 2019*]

Methods:

The study samples collected from Gynecological consultation unit in Al-Furat Teaching Hospital at Al-Najaf Governorate from the beginning of April 2022 till end of March 2023. The Study group included 75 healthy pregnant woman at third trimester of age (18-40 years old) and 75 healthy non pregnant young women of the same age as control group. All women were subjected to thorough medical history and physical examination to exclude other conditions as clinical evidence or previous history of any organic cardiac disease, renal disease, thyroid disease, severe anemia, diabetes, hypertension, and on any chronic medication or smoking. The height (*cm*) and weight (*kg*) are obtained by means of measuring tape and digital weight scale respectively. Calculation of body mass index is carried out as: Weight (*kg*) / Height (m^2) for each one [*Addo et al ., 2010*]. ECG , Abd U/S : to calculate gestational age, have been recorded. All individual participants in the study gave their informed consent.

Echocardiographic analysis: A complete 2DE was performed in all women , using a commercially available Vivid E9 ultrasound machine (GE Healthcare, Horten, Norway) equipped with 2.5 *MHz* S5-1 transducer. ECG leads were placed over the chest and women were examined in the left lateral decubitus position to bring the heart forward to the chest wall and lateral to the sternum, with dimmed light room as recommended by the American society of echocardiography. The LV diastolic parameters were measured from the apical four-chamber view using pulsed-wave Doppler at the level of the mitral orifice included early (E) and late (A) transmitral flow velocities and the ratio of early to late velocities (E/A). The average of peak early diastolic velocities at septal and lateral of mitral annular (E') assessed by pulsed-wave tissue Doppler, and the E/E' ratio to estimate LV filling pressure [*Lang et al.,2015*].

Left atrium measurments:

2D biplane method : The antero-posterior diameter, as measured by M-mode or 2D echocardiography, is no longer considered to be an accurate measure of the real left atrium dimension. For these reasons, the American Society of Echocardiography, together with the European Association of Echocardiography, recommend measuring left atrium volumes using either an ellipsoid model or the Simpson's method in four- and two-chamber apical view [*Todaro et al., 2012*].

After tracing the left atrium cavity areas, the measurement software package automatically calculates the left atrium volume according to or using the area–length formula (Figure 3)[*Kühl et al., 2004*]:

$$\text{LA volume (mL)} = \frac{0.85 \times (A_4 \times A_2)\text{C area})}{\text{Length}}$$

Modified biplane Simpson's rule or area–length method

1. By using 2 orthogonal planes of the left atrium (usually A4C and A2C views)
2. Obtaining the best image quality, optimizing sector width and place focal zones distally for better lateral resolution in the far-field and increasing gain just to the point on which image drop-outs in the atrial walls have disappeared.
3. To achieve maximum left atrium size, avoid left atrium foreshortening (differences in length measured from the two orthogonal planes should be equal or less than 5*mm*).
4. Selecting adequate frames for measurement. End-systolic frame (just before mitral valve opening, end of T wave on ECG) for maximum left atrium volume

Figure 3. *Pre-atrial contraction volume (preA) , measured at the onset of the P-wave on an electrocardiogram (A); minimal left atrial (LA) volume (LA min), measured at the closure of the mitral valve in end diastole (B); and maximal LA volume (LA max), measured just before the opening of the mitral valve in end-systole (C)* [*Todaro et al., 2012*].

5. left atrium area border planimetry , the inferior border should be the mitral annular plane and endocardial tracing should exclude atrial appendage and pulmonary veins
6. Long axis left atrium: orthogonal to mitral annulus plane from its midpoint to superior margin of left atrium ∗

∗ As small discrepancies are acceptable, the most common option is to average the two lengths from the 4-chamber and 2-chamber views [*Kühl et al., 2004*]

Left atrium passive volumes consist of (Figure 3):

- Maximal left atrium volume (LAmax), obtained from an end-systolic frame measured just before the opening of the mitral valve in end-systole.
- Minimal left atrium volume (LAmin), obtained from an end-diastolic frame just before mitral valve closure; and
- Preatrial contraction volume (V=LApreA), obtained from the last frame just before mitral valve reopening as the result of left atrium contraction at the onset of the P-wave on an electrocardiogram (ECG).

Left atrium active volumes are:

- LA reservoir volume (LA max* LAmin)
- LA conduit volume (LV total stroke volume-left atrium reservoir volume)
- LA passive emptying volume (LA max- LA preA)

Left atrium contractile volume (LA preA – LA min) [*Todaro et al., 2012*].

LA reservoir function was assessed by: Left atrium (total emptying volume) , calculated as LA max—LA min

LA conduct function was assessed by: passive emptying volume or (LA strok volume) calculated as LA max -LA pre-A

LA booster pump function was assessed by: active atrial stroke volume, calculated as LA pre-A - LA min;

Total emptying fraction (EF)= Total emptying volume /LA max

Passive EF=Passive emptying volume/LA max

Active EF= active emptying volume /pre-A [*Song et al.,2015*]

Statistical analysis:

Conducting using SPSS 18. Data analyzed as per group I (total: n=75) compared with a control group (total: n=75). Calculation of mean, standard deviation and standard error of mean was done. Study groups are compared using independent T test. Probability value p of < 0.05 considered to be significant ($\alpha=0.05$)

RESULTS:

The instances that influence left atrium volumes are age, sex, height, and weight [*Eshoo et al.,2009; van Grootel et al., 2018*] and because the study population were matched by age and sex , so to address these possible changes, left atrium volumes were indexed to BSA. In our study, no differences have been found between the indexed & original measures of all left atrium volumes after correcting for BSA.

In the current study , the conventional echocardiographic data are demonstrated in Table (1) when compared pregnant women and control groups, we observed an enlarged left atrium volumes (Max, Min and Pre-A) and increased left atrium reservoir , conduit and booster function. The value of left atrium emptying fraction significantly increased as well as the left atrium active and passive ejection fraction in the pregnant women. In addition , the mitral E/A ratio showed significant difference among the two groups and the mitral E/E' ratio increased in pregnant women group as well.

TABLE 1.

Left atrium volumes (Mean±SD) in pregnant and nonpregnant group of women.

Echocardiographic variable	Pregnant (n=75)	Control (n=75)	P value
LA Max	41.8±11.50	25.16±6.04	0.0001
LA Pre-A	17.28±7.76	11.77±4.07	0.0001
LA Min	8.69±4.24	6.8±2.93	0.002
LA reservoir function	32.94±9.57	18.38±4.79	0.0001
LA conduit function	24.26±9.06	13.41±3.92	0.0001
LA booster function	8.58±4.66	4.98±2.30	0.0001
Total emptying fraction	0.79±0.08	0.73±0.09	0.0001
Passive LA EF%	0.58±0.14	0.53±0.10	0.026
Active LA EF%	0.49±0.13	0.42±0.13	0.002
Mitral Valve E/A	1.25±0.32	1.4±0.4	0.036
E/E´	6.93±1.81	6.3±1.2	0.01

Notes: *SD: standard deviation, LA :left atrium, Max: maximum, Pre-A: pre- atrial , Min: minimum, EF: ejection fraction, E/A : E peak early diastole transmitral wave velocity / A peak late diastole transmitral wave velocity, E´ the average of peak early diastolic velocities at septal and lateral of mitral annular.*

DISCUSSION

Left atrium function plays a central role in maintaining optimal cardiac output , increased left atrium volume may be accompanied by a progressive impairment in left atrium function and both may precede symptom development and adversely affect prognosis [*Mustafa et al., 2009*]. In addition, the left atrium also acts as a volume sensor with the atrial wall releasing natriuretic peptides in response to stretch, generating natriuresis, vasodilatation, and inhibition of the sympathetic nervous system and renin-angiotensin-aldosterone system [*Chinali et al.,2005*] .

It is well known that the total blood volume increase significantly during pregnancy resulting in the expansion of the left atrium volume , in normal pregnancy, the left atrium is remodeled to meet special hemodynamic and metabolic needs [*Ye et al., 2021*]

Left atrium ***reservoir function:*** LA act as a chamber to conserve blood return from the pulmonary vein and to store energy in the form of pressure during LV systole. left atrium reservoir function is determined by left atrium myocardial contraction and relaxation and mitral annulus displacement during left ventricular contraction [*Song et al., 2015*]. In this study , left atrium reservoir function was increased because both; the decrease in LV compliance and increasing heart rate had a negative influence on left atrium emptying. left atrium began to adaptively enlarge to maintain adequate LV filling and satisfy increasing cardiac output [*Song et al., 2015*].

Left atrium conduit function: Left atrium as a conduit to allow the blood to drift into the LV from the pulmonary vessel during LV diastole. left atrium conduit function is reciprocally related to reservoir function but by necessity is closely related to LV relaxation and compliance [*Okamatsu et al., 2009*]

But the study results showed that the conduit function increased , this results are differs from that of *Song et al* , in (2015) who found a decrease in the left atrium conduit function during pregnancy , may be because the study also showed high E/A and E/ E´ values that reflect good LV relaxation ; the main determinant of conduit function [*Andersen et al., 2017*].

A booster pump function: LA is primarily act as the active pump to maintain LV filling during left atrium systole. Booster function reflects the magnitude and timing of atrial contractility and it not only dependent on atrial preload stretch (LA pre-A) but also on (atrial afterload) which is represented by LV end-diastolic pressure [*Anwar et al., 2007; Wakami et al., 2009*], in the current study ,enhanced left atrium booster function might be due to that left atrium contractility is a response to increasing of left atrium preload according to the Frank-Starling mechanism [*Anwar et al., 2007*] and is still in a compensatory state during normal pregnancy. The enlargement of the left atrium and the increase in left atrium emptying fraction are adaptive measure to maintain normal LV filling pressures and consequently LV stroke volume [*Matsuda et al., 1983*]

CONCLUSION:

The demonstration that have been found is the left atrium volume increase during pregnancy and left atrium (reservoir , conduit and booster pump) functions are enhanced during pregnancy. Most likely this is occurs as a compensatory response aids in the preservation of cardiac output in pregnant women. Even if there are no comorbidities at the time of booking, cardiovascular changes in pregnant women should be considered in their assessment and management over the antenatal period.

Limitations of the study: Because most pregnant women become tired during their echocardiographic examination, the operator must act quickly to alleviate them before they become fatigued. Moreover, the study could not ascertain the true baseline findings of the patients before their conception as the participants were selected in their third trimester.

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