

Doppler Echocardiographic Assessment of Pregnant Women with Chronic Arterial Hypertension

Nádia Cristiane de Mattia, Regina Lúcia Barbin, Vera Therezinha M. Borges,
José Carlos Peraçoli, Beatriz B. Matsubara

Botucatu, SP - Brazil

Objective - To assess structural and functional cardiac changes in asymptomatic pregnant women with chronic arterial hypertension (CAH).

Methods - One hundred pregnant women with CAH underwent conventional Doppler echocardiography. The Student *t* test was used to compare them with 29 normotensive pregnant women (NT) in their third gestational trimester.

Results - Systolic (SBP; mmHg) and diastolic (DBP; mmHg) blood pressure values were higher ($p < 0.001$) in the CAH pregnant women (SBP: 139 ± 19 and DBP: 92 ± 18) as compared with those of the NT group (SBP: 112 ± 10 and DBP: 74 ± 9). A significant enlargement of the left atrium (4.10 ± 0.48 cm vs 3.6 ± 0.3 cm; $p < 0.001$) and of the left ventricular normalized mass (59.6 ± 19.7 g/cm^{2.7} vs 41.9 ± 3.4 g/cm^{2.7}; $p < 0.001$) was observed. Cardiac output (CO, L/min) and systolic volume (SV, mL) were significantly higher in the CAH group (CO: 6.0 ± 1.54 vs 4.9 ± 2.1 , $p < 0.01$; SV: 77.3 ± 19.8 vs 56.5 ± 25.8 , $p < 0.001$).

Conclusion - Chronic hypertensive pregnant women have structural and functional cardiac changes that justify routine cardiologic assessment, even in the absence of cardiopulmonary symptoms.

Key words: myocardial hypertrophy, ventricular function, volume overload

Pregnancy is a physiological condition in which chronic blood volume overload occurs and causes adaptive heart modifications. The increase in blood volume may reach 70% compared with that in the pregestational condition. This volume increase begins in the first gestational weeks and, around the 26th week, reaches a significant amount¹.

During pregnancy, a number of hemodynamic changes occur to allow an adequate supply of oxygen and nutrients to the fetus and the maternal tissues, whose metabolism is modified by the new physiological situation². Of the changes observed, the increase in cardiac output is the most important. A reduction in blood pressure is also observed in the first trimester, and it is maintained constant until the delivery. A reduction in peripheral resistance occurs because of the vasodilating action of the gestational hormones, mainly progesterone. In addition, a significant reduction in afterload occurs, mainly secondary to opening of arteriovenous shunts in the placenta³.

This way, the cardiovascular changes characteristic of gestation cause a reduction in blood pressure². Because of these changes, patients with chronic arterial hypertension (CAH) frequently have a reduction in their blood pressure levels during pregnancy, eliminating the need for antihypertensive medication. Usually, the gestational complications depending on CAH do not relate to left ventricular dysfunction⁴.

In hypertensive pregnant women, installation of a new hemodynamic condition is observed: the transition from a situation of pressure overload to that of volume overload.

Clinically, chronic hypertensive pregnant women also have a drop in blood pressure levels in the first half of the gestational cycle⁵. In the second gestational half, a more resistant uterus-placental circulation may develop due to a poor physiological adaptation of the decidua, leading to a reduction in blood offer to the fetus. In this condition, blood pressure levels are believed to increase due to an imbalance in the production of thromboxane and prostacyclin with a disproportional increase in the first².

Faculdade de Medicina de Botucatu - UNESP
Mailing address: Beatriz B. Matsubara – Faculdade de Medicina de Botucatu – UNESP - Depto de Clínica Médica – Rua Rubião Júnior, S/Nº - 18618-000 – Botucatu, SP, Brazil – E-mail: beatrizm@fmb.unesp.br
English version by Stela Maris C. e Gandour

Advances in the characterization of the cardiovascular changes have facilitated the diagnosis and follow-up of pregnant women with heart disease. Echocardiography allows the evaluation of pregnant women because it is a noninvasive procedure, with no maternal-fetal risks, and is sensitive enough to detect minor structural and functional cardiac changes⁶.

Studies carried out with pregnant women with CAH have shown a significant increase in myocardial mass as compared with that of normotensive pregnant women (NT) with no indicators of change in left ventricular geometry. Supranormal systolic function, characterized by systolic function indices slightly higher than the mean of the general population, and probable subclinical diastolic dysfunction have been reported⁶.

Despite these characteristics, routine assistance for pregnant women with CAH, asymptomatic from the cardiopulmonary point of view, does not include systematic cardiological evaluation. Systemic arterial hypertension is a disease that potentially causes structural and functional cardiac changes that are well defined in the literature⁷. In addition, pregnancy, as a volume overload condition, causes already known morphological and functional cardiac changes¹. Therefore, it would seem reasonable to suppose that the association of these 2 conditions would have more drastic repercussions on the heart than pregnancy alone would.

The present study aimed at assessing morphological and functional cardiac changes in pregnant women with CAH as compared with NT pregnant women.

Methods

All procedures were approved by the committee on ethics in research of the Hospital das Clínicas of the Medical School of Botucatu – UNESP.

The study comprised 100 chronic hypertensive patients followed up in the prenatal clinics of the Hospital das Clínicas of the Medical School of Botucatu. The diagnosis of CAH was based on the criterion established by the III Brazilian Consensus on Arterial Hypertension⁸: permanently elevated blood pressure levels above the normal limits, systolic blood pressure > 140mmHg or diastolic blood pressure > 90mmHg, or both, when blood pressure is measured with proper methods and conditions.

During pregnancy, all patients in the study underwent at least 1 echocardiographic examination, whose indication was based on the clinical diagnosis of arterial hypertension independent of cardiopulmonary complaints.

The results were compared with those of a group of 29 healthy normotensive pregnant women (NT group) followed up at the prenatal clinics of the same institution. These patients had no congenital or acquired heart diseases and came voluntarily for the echocardiographic evaluation during the third gestational trimester.

All patients underwent standard clinical and obstetric evaluation according to the routine of the service.

Doppler echocardiographies were performed from 8 to

11 AM by the same echocardiography specialist, the patients being well fed and in a calm environment with controlled temperature of 25°C. During the procedure, the patients remained in the left lateral decubitus position with the head elevated at 30°. A 1-dimensional image was obtained with the pointer directed by the 2-dimensional image in the parasternal short-axis view. The following measurements were recorded⁹: left chamber dimensions, ventricular septum thickness, and left ventricular posterior wall thickness.

Based on the analysis of blood flow through the left ventricular outflow tract obtained in the apical position, systolic volume (SV; mL) and cardiac output (CO; L/min) were calculated. Still in the same position, the diastolic flow through the mitral valve was recorded for the analysis of the following diastolic function indices: maximum velocity of rapid ventricular filling (E wave; cm/s), maximum velocity of ventricular filling during atrial contraction (A wave; cm/s), and the E/A ratio.

At the end of the examination, with the patient in the left lateral decubitus position, blood pressure was measured in the left upper limb with the mercury sphygmomanometer, and the value obtained corresponded to the arithmetic mean of 3 measurements.

Based on the mathematical formulas below, the following variables were calculated: cardiac output (CO; L/min), left ventricular mass (LVM; grams)¹⁰, relative left ventricular mass (LVMr; g/m^{2.7})¹¹, relative wall thickness of the left ventricle (Hd/LVDD)¹², ejection fraction (EF; %)¹³, and percentage variability of the ventricular diameter (%<D; %)⁹.

Cardiac output: $CO = SV \times HR$, where SV is systolic volume (mL), and HR is heart rate (bpm).

Left ventricular mass: $LVM = \{[(VSd + PWd + LVDD)^3 - LVDD^3] \times 1.04\} - 13.6$, where VSd and PWd are the diastolic thickness of the ventricular septum and of the left ventricular posterior wall (cm), respectively, and LVDD is the left ventricular diastolic diameter (cm).

Relative left ventricular mass: $LVMr = LVM / \text{height}^{2.7}$.

Relative wall thickness: $Hd/LVDD = [(VSd + PWd) / 2] / LVDD$.

Ejection fraction: $EF = (LVDD^3 - LVSD^3) / LVDD^3$, where LVSD is the left ventricular systolic diameter (mm).

Percentage variability of the ventricular diameter: $\%dD = [(LVDD - LVSD) / LVDD] \times 100$.

The means of the variables obtained in the 2 groups were compared with the Student *t* test, adopting the significance level of $p < 0.05$. The statistical software used was Statistica 5.0 for Windows (1995).

Results

In the CAH group, 22 patients were nulliparous, 25 primiparous, and 53 were multiparous; in the NT group, 5 patients were nulliparous, 23 were primiparous, and the 5 remaining were multiparous (fig. 1).

Table I and figure 2 depict some clinical variables of the pregnant women in both groups. A statistically significant difference between the groups was observed in regard to

age. The mean age of the patients in the CAH group was 31.5 ± 7.2 years and in the NT group 26.9 ± 3.5 years ($p < 0.001$). Figure 2 depicts the distribution of the patients at different age brackets. Most chronic hypertensive pregnant women (41%) were 31 to 40 years old, while the NT pregnant women were 21 to 30 years old. Body weight was greater in the hypertensive women with a mean of 79 ± 19.1 kg versus 67.5 ± 22.6 kg, observed in the normotensive women ($p = 0.007$).

Systolic and diastolic blood pressure values were also greater in the CAH group as compared with those in the NT group. A mean systolic blood pressure of 139 ± 19 mmHg was observed in the hypertensive pregnant women and of 112 ± 9.5 mmHg in the normotensive ones ($p < 0.001$). The

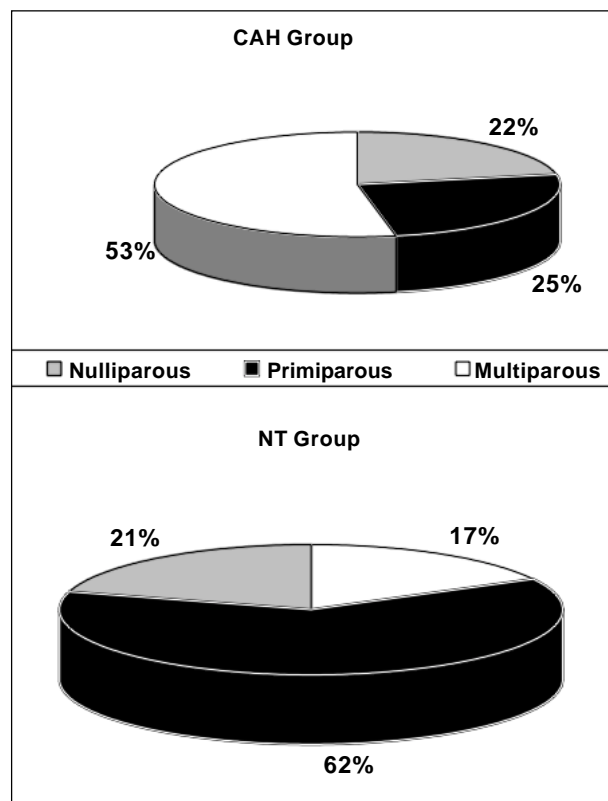


Fig. 1 – Graph representation of the proportions relative to parity in the pregnant women studied. Multiparas predominated in the group of patients with chronic arterial hypertension (CAH group) while primiparas predominated in the control group (NT group).

Group	Age (years)	Height (m)	Weight (kg)	SBP (mmHg)	DBP (mmHg)	HR (bpm)
NT	26.9 ± 3.5	1.54 ± 0.16	67 ± 22.6	112 ± 9.5	74 ± 9.3	86 ± 13
CAH	$31.5 \pm 7.2^*$	1.55 ± 0.07	$79 \pm 19.1^{**}$	$139 \pm 19^*$	$92 \pm 17.6^*$	$77 \pm 12^{***}$

SBP and DBP - systolic and diastolic blood pressure, respectively; HR- heart rate; (*) $P < 0.001$ vs NT, Student t test; (**) $P = 0.007$ vs NT, Student t test; (***) $P = 0.002$ vs NT, Student t test.

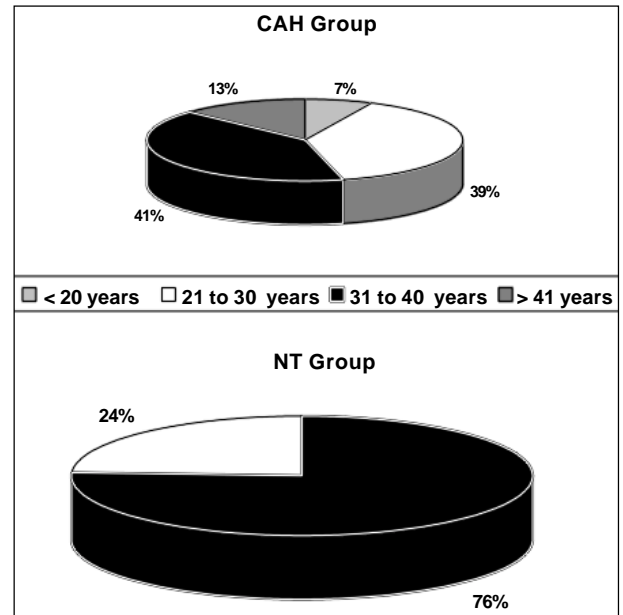


Fig. 2 - Graph representation of the proportions relative to age bracket in the pregnant women studied. Most hypertensive patients (CAH group) were older than 30 years, while most normotensive patients (NT group) were between 21 and 30 years old.

mean diastolic blood pressure in the CAH group was 92 ± 18 mmHg, and, in the NT group, it was 73.6 ± 9.3 mmHg ($p < 0.001$). In the CAH group, 45 patients were not taking antihypertensive medication, or were doing it in an irregular way; 30 were on monotherapy with a diuretic or a-methyldopa; and the remaining were on monotherapy with a beta-blocker or a calcium channel blocker or were taking a combination of drugs. Only 1 patient was taking an angiotensin-converting enzyme inhibitor.

Heart rate in hypertensive pregnant women was significantly lower than in the normotensive ones (77 ± 12 bpm vs 86 ± 13 bpm, $p = 0.002$).

Table II shows the cardiac structural variables obtained on echocardiography of pregnant women in the CAH and NT groups.

A significant increase in the left atrium and in the left ventricular diastolic diameter was observed in the CAH group as compared with the measurements in the NT group. Left ventricular systolic diameter was similar in both groups, which had a mean diastolic thickness of the ventricular septum equal to that of the posterior wall, whose value was greater in the CAH group (0.93 ± 0.14 cm) as compared with that in the NT group (0.77 ± 0.1 cm).

The mean left ventricular mass was 201 ± 61 g in the CAH group, and 134.5 ± 28.7 g in the NT group ($p < 0.001$); the mean left ventricular mass corrected to height^{2.7} (LVMr) was 59.6 ± 19.7 g/m^{2.7} in the CAH group, and 41.9 ± 3.4 g/m^{2.7} in the NT group ($p < 0.001$).

The relative wall thickness of the left ventricle during diastole (Hd/LVDD) was 0.37 ± 0.06 in the CAH group and 0.32 ± 0.01 in the NT group ($p < 0.001$), indicating concentric hypertrophy.

Table II - Structural cardiac variables obtained on echocardiography of the NT group and the CAH group. Means and their respective standard deviations are shown.

Variable	NT group	CAH group
LA (cm)	3.6 ± 0.3	4.1 ± 0.5*
LVDD (cm)	4.8 ± 0.3	5.1 ± 0.5**
LVSD (cm)	3 ± 0.1	3.1 ± 0.5
VSD (cm)	0.77 ± 0.1	0.93 ± 0.14*
PWd (cm)	0.77 ± 0.1	0.93 ± 0.14*
LVM (g)	134.5 ± 28.7	201 ± 61.1*
LVMr (g/m ^{2.7})	41.9 ± 3.4	59.6 ± 19.7*
Hd/LVDD	0.32 ± 0.01	0.37 ± 0.06*

LA- left atrium; LVDD- left ventricular diastolic diameter; LVSD- left ventricular systolic diameter; VSD- thickness of the ventricular septum during diastole; PWd- thickness of the left ventricular posterior wall during diastole; LVM- left ventricular mass; LVMr- relative left ventricular mass; Hd/LVDD- ratio between the mean wall thickness and the ventricular diameter during diastole; (*) P=<0.001 vs NT, Student *t* test; (**) P=0.006 vs NT, Student *t* test.

Table III shows the systolic function variables. The mean of the percentage variability of the ventricular diameter (% dD) was 38.8±5.6% in the CAH group, and 37.4±1.5% in the NT group (p>0.05). The mean ejection fraction was 0.77±0.06 in the CAH group, and 0.75±0.02 in the NT group (p>0.05).

The mean cardiac output was 6±1.5 L/min in the CAH group, and 4.9±2.1 L/min in the NT group (p<0.01). The systolic volume was 77.3±19.8 mL in the CAH group, and 56.5±25.8 mL in the NT group (p<0.001).

Table IV shows the diastolic function variables. The maximum velocity of rapid ventricular filling (E) was 82±22cm/s in the CAH group, and 74±19 cm/s in the NT group (p = 0.07). The mean final diastolic velocity (A) was 63±17 cm/s in the CAH group, and 53±10 cm/s in the NT group (p = 0.003). The ratio between the initial and final diastolic velocities (E/A) was the same for both groups.

Discussion

This study showed that the cardiac changes in pregnant women with CAH were significant as compared with those found in normotensive pregnant women.

It should be emphasized that the pregnant women in both groups underwent echocardiography at different gestational ages. The NT group was systematically assessed

Table III - Systolic function variables obtained with Doppler echocardiography in patients in the NT and CAH groups. Means and their respective standard deviations are shown.

Group	%DD (%)	EF	CO (L/min)	SV (mL)
NT	37.4 ± 1.5	0.75 ± 0.02	4.9 ± 2.1	56.5 ± 25.8
CAH	38.8 ± 5.6	0.77 ± 0.06	6 ± 1.5*	77.3 ± 19.8*

% DD- percentage variability of the ventricular diameter; EF - ejection fraction; CO - cardiac output; SV - systolic volume; (*) P=<0.001 vs NT, Student *t* test.

Table IV - Diastolic function variables obtained with Doppler echocardiography in patients in the NT and CAH groups. Means and their respective standard deviations are shown.

Group	E (cm/s)	A (cm/s)	E / A
NT	74 ± 19	53 ± 10	1.4 ± 0.3
CAH	82 ± 22	63 ± 17 *	1.4 ± 0.5

E- initial diastolic velocity; A- final diastolic velocity; E/A- ratio between E and A; (*) P=0.003 vs NT, Student *t* test.

during the third gestational trimester, when the cardiac changes induced by the increased blood volume characteristic of pregnancy were maximum. On the other hand, the chronic hypertensive pregnant women assessed during any gestational age showed these changes in different degrees of development. Therefore, differences between the 2 groups may have been underestimated. Nevertheless, the option to keep the chronic hypertensive pregnant women assessed during the first and second gestational trimesters in the study aimed at not missing important information on this group, because almost 40 patients would have been eliminated if only those undergoing echocardiography during the third gestational trimester were considered.

The significantly higher age and body weight found in the CAH group were expected. This may be explained by the incidence of primary arterial hypertension, which most of the time begins during the third decade of life, and, therefore, pregnant women with CAH are older than normotensive pregnant women¹⁴.

Obesity and overweight are highly prevalent in the population with arterial hypertension. Although this association has not been well clarified, several mechanisms have been reported in the literature associating obesity and systemic arterial hypertension¹⁴. Fat mass increase has been implicated in the genesis of insulin resistance, which could explain the epidemiological findings of the increased risk for systemic arterial hypertension in the obese. In addition, obese patients have increased plasma renin activity, because the increase in the interstitial pressure in the renal medullary region causes tubular and vascular compression, leading to a drop in the renal tubular hydrostatic pressure. Because of a compensatory mechanism, the renin-angiotensin system is activated to maintain the tubular flow, therefore elevating blood pressure. Therefore, overweight and obesity are considered etiological factors for the occurrence of CAH^{14,15}.

The blood pressure levels observed in the CAH group were not so high, but they were significantly higher than those found in the NT group. The fact that pregnancy may cause lower blood pressure levels is well known. Vasodilation subsequent to the action of placental hormones and their contraregulating actions causes a drop in peripheral resistance. In addition, placental fistulas open, the uterus-placental flow increases, and a reduction in the renin-angiotensin-aldosterone system action occurs. In fact, preg-

nancy has been reported to have a beneficial effect on the blood pressure levels of patients with CAH, which may reach values considered within the normal limits for the general population. However, this blood pressure drop does not reduce the greater obstetric risk in this group⁴.

The lower heart rate observed in chronic hypertensive pregnant women may have been caused by the antihypertensive medication, although most patients were taking medication on an irregular basis or were taking no medication at all. Approximately 30% of the patients were taking medication that interfered with heart rate, such as central action inhibitors and beta-blockers.

A mean 14% increase in the left atrium (LA) was observed in the CAH group as compared with the control group. Considering that in this group the greatest LA value observed was 4.3cm, this could be considered a borderline value of physiological increase. Considering this limit, we observed that 33 patients in the CAH group had an increase in LA. This variability may be due to the increased blood volume of these patients or may correspond to a preexisting alteration secondary to CAH.

Although, the mean LVDD was significantly greater in the CAH group as compared with that in the NT group, the values were within the limits considered normal for the general population⁹. The mean difference of 3 mm was considered irrelevant.

Significant left ventricular hypertrophy occurred in the CAH group with a mean 49% increase in the left ventricular mass as compared with that of the control group. Even normalizing the variable, the increase persisted. Hypertrophy was secondary to the combined increases in ventricular wall thickness and ventricular diameter. Considering that many of these patients (37%) were in the first or second gestational trimester, we suspect that this difference has been underestimated.

The option to use a ventricular mass index normalized for height²⁷ was based on the report by Wachtell et al¹⁶, who analyzed several forms of normalization of left ventricular mass and concluded that the best factors of normalization are those that correct the index by height and body surface. Normalization for height and not for body weight was chosen, because weight gain during pregnancy occurs in a heterogeneous way and may lead to errors in the final result. It is worth noting that some type of myocardial mass normalization should be adopted to make the diagnosis of hypertrophy more reliable.

In our case series, the myocardial hypertrophy observed in the CAH group was of the concentric type, because a significant increase in the Hd/LVDD ratio occurred, indicating that the increase in wall thickness was proportionally higher than the increase in ventricular cavity diameter. Of all variables analyzed, this was the one that showed the most drastic difference as compared with that in the control group. These results do not agree with those reported by other authors who found myocardial hypertrophy with no ventricular geometry change in pregnant women with CAH⁶. An aspect to be highlighted is that this study does not al-

low conclusions about the mechanisms involved in the pathophysiology of the most evident myocardial hypertrophy observed in the CAH group. This means that it is not possible to define whether this hypertrophy corresponds to a preexisting alteration secondary to chronic blood pressure overload, or whether these patients respond more intensely to the neurohumoral stimuli characteristic of pregnancy. This approach deserves further study.

Several studies have shown¹⁷ that obesity may be an independent stimulus for myocardial growth, even in the presence of normal blood pressure levels. Although obesity represents a smaller impact on cardiac hypertrophy as compared with elevated blood pressure levels, obesity and arterial hypertension were observed to act synergistically on myocardial hypertrophy^{18,19}. Although pregnant women in the CAH group had body mass greater than those in the NT group, our study did not aim at classifying these patients as obese or overweight, and, therefore, conclusions about the influence of obesity and overweight in the changes found could not be drawn. Maybe, if the patients were classified according to their body masses, more reliable conclusions could be drawn regarding the extent to which weight increase caused the changes found.

Obesity and salt and water retention caused by activation of the renin-angiotensin-aldosterone system, conditions to which our CAH group was submitted, are well known to increase cardiac output. In addition, the physiological changes characteristic of pregnancy can also increase cardiac output as early as the sixth gestational week^{1,2}. Assuming that chronic hypertensive pregnant women have a left ventricle adapted to work in a regimen of higher blood pressure and that pregnancy reduces blood pressure levels, we can conclude that the left ventricle behaves hemodynamically in the CAH group²⁰.

The increase in blood volume activating the Frank-Starling mechanism, the increase in ventricular mass, the reduction in afterload, and the stimulation of the sympathetic autonomic nervous system could justify the improvement in cardiac performance reflected in the increased systolic volume and cardiac output. Therefore, the supra-normal function in chronic hypertensive pregnant women may be due to both the improvement in contractility and the favorable variabilities in load under which the ventricle operates. Myocardial contractility is a complex intrinsic property difficult to be quantified *in vivo*. However, in situations of hemodynamic overload, when compensated hypertrophy occurs with no significant structural change, such as myocardial fibrosis, an improvement in the contractile function has been described²¹.

At present, no explanation exists for the absence of variation in the ejection fraction and in the percentage variability of the ventricular diameter (% dD). These indices were expected to indicate the same changes found in cardiac output. It is worth noting that other authors²², who used M-mode echocardiography to assess the ventricular function of normotensive pregnant women, were also not able to show variations in systolic function based on

ejection fraction and % <D indices, although cardiac output and systolic volume were increased. Therefore, we interpreted these indices as not sensitive enough to show variation and that the indices derived from flow analysis on left ventricular ultrasonography (cardiac output and systolic volume) are more useful for assessing pregnant women.

The analysis of diastolic function was limited to the study of the maximum velocities of early ventricular filling (E) and during atrial contraction (A) and also to the ratio between these 2 velocities (E/A). Recent studies^{23,24} discussing diastolic function assessment on Doppler echocardiography have recommended that other additional indicators should be used to increase the method's sensitivity for detecting changes in this phase of the cardiac cycle. Therefore, some patients with this dysfunction may have gone undiagnosed. However, it is worth noting that the assessment used in this study is widely reported in the literature and the most commonly used in echocardiographic laboratories.

The isolated observation of the increase in A velocity in the patients in the CAH group as compared with that in control patients has no significance in identifying diastolic dysfunction in these patients. In fact, in addition to the significant increase in A, a statistical tendency indicating an increase in E velocity was also observed. The elevated

cardiac output in pregnant women in the CAH group may explain that finding. The E and A velocities in the transmitral diastolic flow are directly related to the pressure gradient between the atrium and the ventricle. Therefore, in a situation of increased blood volume, the venous return to the left atrium may also be considered increased. Consequently, a physiological increase in blood pressure occurs in the atrial chamber. In the absence of left ventricular dysfunction, the diastolic pressure in this chamber is assumed to remain low, resulting in a slightly increased transmitral diastolic gradient with an also higher flow velocity. This way, considering only the structural changes described, chronic hypertensive pregnant women have no diastolic dysfunction. However, although the analysis of the mean values show no difference in the E/A ratio between the groups, 22 patients in the CAH group had inversion of the E/A ratio (E/A<1), ie, an E value lower than the A value, while no patient in the NT group had the change. Therefore, the frequency of diastolic dysfunction in this group of patients should not be overlooked.

In conclusion, chronic hypertensive pregnant women have structural and functional cardiac changes that justify routine cardiac assessment, even in the absence of cardiopulmonary symptoms.

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