

Vascular Reactivity Response to Mental Stress in Pregnant Women with Mitral Stenosis

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OBJECTIVE

To study vascular reactivity according to the analysis of blood flow and peripheral vascular resistance at rest and during mental stress in pregnant women with mitral stenosis.

METHODS

Twenty two women with mitral stenosis, 13 of whom were pregnant (PS) and 9 were non-pregnant (MIS), and 9 healthy pregnant women (NP) were studied. During gestation, 9 out of the 13 patients of the PS group required a beta-blocker (PSB) and the remaining 4 progressed without medication (PSWB). Plethysmography at rest and during mental stress analyzed muscle blood flow, peripheral vascular resistance (PVR), mean arterial pressure (MAP) and heart rate (HR) during gestation and puerperium.

RESULTS

During gestation of PSWB, muscle blood flow and HR were higher in 1.6% and 20.5% ($p = 0.05$), and PVR and MAP were lower in 19.3% and 4.4%, respectively, in comparison to the puerperium; during mental stress, the muscle blood flow increased by 55.9%, HR decreased by 30.2% and PVR and MAP were similar. In PSB, muscle blood muscle blood flow and HR were greater in 5.9% and 14.9% ($p = 0.001$) and MAP and PVR were lower in 10.3% and 9.1%, respectively, when compared to the puerperium. During mental stress, muscle blood flow and MAP increased by 69.8% and 174.1%, respectively. HR was similar and PVR decreased by 53.7%. The comparative study showed that in the NP group the muscle blood flow was higher, PVR was lower, and MAP and HR were similar in relation to the PS group, and that the PS, NP, MIS groups had a similar response to mental stress.

CONCLUSIONS

Vascular reactivity in pregnant women with mitral stenosis was preserved and the analysis of measurements showed lower values of muscle blood flow and higher values of PVR when compared to those of healthy pregnant women.

KEY WORDS

Pregnancy, mitral stenosis, vascular reactivity.

The cycle of pregnancy and puerperium provokes significant and transient cardiocirculatory changes¹ in women's bodies. As of the seventh day of fertilization², adaptations in cardiac output and peripheral vascular resistance to metabolic and hormonal demands and to uteroplacental circulation occur in order to maintain an adequate fetal development.

In light of current knowledge, variations in peripheral vascular resistance (PVR) during pregnancy are not caused only by alterations in the uterine plexus, but also by hormones such as estrogen, prolactin, and circulating prostaglandins, which are responsible for the reduction in vascular response to angiotensin³.

A decrease in the synthesis of prostaglandins or an increase in their metabolism is also known to result in an increase in vascular reactivity to angiotensin II⁴, a characteristic that is observed, for instance, in hypertensive syndromes during pregnancy⁵.

Another clinical situation that has aroused interest is the study of vascular reactivity at rest and during stress in the identification of prognostic markers in patients with congestive heart failure (CHF). In a controlled study of forearm blood flow using a plethysmograph, and of muscular reactivity using electromyography during mental stress in patients with CHF, Middlekauff et al⁶ observed a significant increase in the sympathetic activity both at rest and during mental stress when compared to healthy volunteers, as well as a reduction of PVR in both groups, although more intense in the control group.

Since we are aware of these data, it would be desirable to apply them to patients with heart diseases, given the differences in the phases of the natural history of heart diseases and PVR adaptations during pregnancy. The literature, however, lacks studies on the behavior of PVR in pregnant women with heart diseases, with emphasis on mitral stenosis, which accounts for most of the heart valve diseases in women of childbearing age and is associated with high percentages – that range from 5% to 30% - of cardiovascular complications^{7,8}, among which pulmonary congestion is the major cause of mortality.

Given the lack of knowledge on hemodynamic parameters that could correlate with the progression and prognosis of pregnant women with mitral stenosis, we chose the study on the behavior of PVR to collect information that could be applied in the daily clinical practice.

OBJECTIVE

To study the vascular response in pregnant women with mitral stenosis by analyzing muscle blood flow and PVR at rest and during mental stress.

METHODS

Thirty one women of childbearing age followed at

the outpatient service of InCor (*Instituto do Coração*) were prospectively studied. They were divided into three groups: PS group composed of thirteen pregnant women with isolated mitral stenosis; NP group composed of nine normal pregnant women; and MIS group composed of nine non-pregnant women with isolated mitral stenosis.

All patients were in functional class (FC) I/II, according to the New York Heart Association (NYHA), and had a sinus rhythm recorded by the electrocardiogram (ECG). Those with mitral stenosis used penicillin G benzathine at prophylactic dose for rheumatic disease and had a mitral valve area lower than 1.5 cm², as estimated by Doppler echocardiogram (ECHO). In the NP and PS groups, the study started between sixteen and 24 weeks of gestation. All received thorough information on the protocol and gave their written informed consent before the beginning of the study. The study was approved by the Ethics Committee for Analysis of Research Projects (CAPPesq) of the Clinical Board of *Hospital das Clínicas* and of *Faculdade de Medicina da Universidade de São Paulo*.

The exclusion criteria were: age under eighteen or above forty years; NYHA-FC IV; atrial fibrillation, concomitant structural heart lesion; past history of thromboembolism, peripheral vascular disease or pulmonary disease; high blood pressure, diabetes mellitus and smoking.

Clinical protocol - The patients underwent a monthly medical assessment when the NYHA-FC was analyzed, at the third trimester of pregnancy and at the puerperium in the groups of pregnant women, and at the first medical visit in the MIS group. The following events were considered clinical endpoints: congestive heart failure, thromboembolic accident, cardiac arrhythmia, and infective endocarditis. Electrocardiograms and Doppler echocardiograms were performed at admission to the protocol with the purpose of studying changes in heart rhythm and measurements of mitral valve area (MVA), calculated by the pressure half-time method.

Hemodynamic protocol - The hemodynamic parameters studied were: forearm muscle blood flow and peripheral vascular resistance, mean arterial pressure and heart rate recorded at rest and during mental stress and in two stages for the PS and NP groups, that is, between the 28th and 32nd weeks of gestation and in puerperium, and, for the MIS group, only at admission to the protocol.

The muscle blood flow was assessed non-invasively, using the venous occlusion plethysmography method with the left arm elevated. A silastic tube containing mercury and connected to a low-pressure transducer and to a plethysmograph (Hokanson AG-101) was placed around the arm at 5 cm of the humerus-radius joint. The wrist cuff was inflated to a suprasystolic level for one minute prior to the measurement takings and at 15-s intervals, whereas the upper-arm cuff was inflated above venous pressure for seven to 8 s. The peripheral vascular resistance (PVR) was

calculated using the ratio between mean arterial pressure (mmHg) and muscle blood flow (ml/min/100 ml) in the forearm, as follows: $PVR = MAP \text{ (mmHg)} / \text{Blood Flow (ml/min/100 ml)}$.

During plethysmography a mental stress test was performed with colors (Stroop color-word test), in which the participant should name out loud and fast the color of words that are printed in incompatible colors. This procedure was performed for 3 min of resting period (baseline), and followed by 4 min of color test (stress). At the end, each participant was asked about the level of difficulty of the color test, according to the levels of difficulty previously established: 0 = not stressing; 1 = little stressing; 2 = stressing; 3 = very stressing; and 4 = extremely stressing.

Mental stress (MS) behavior was assessed by the difference between the mean of the baseline phase and the value obtained at the first minute of mental stress, considered in our study as the test peak value: $MS = \text{Mean of Baseline (MB)} / \text{first moment of mental stress (M1)}$.

Systolic blood pressures (SBP), diastolic blood pressures (DBP) and mean (MBP) were continuously measured during the test with a cuff connected to an Ohmed 2300 Finapres monitor, and the heart rate (HR) was obtained in a computer-recorded electrocardiographic tracing, all analyzed in specific programs (AT/CODAS).

Statistical analysis - Calculation of means and standard deviation, analysis of variance (ANOVA) for the comparison between groups (PS, NP, MIS) and phases (pregnancy and puerperium), analysis of covariance (ANCOVA) for the comparison of stress behavior parameters (mean of baseline minus value at the first moment of stress) for the following factors: groups, phases and their interaction, and further independent t- tests, and paired t-test for the comparison between group differences (two by two) and between behavior differences during pregnancy and puerperium were used, respectively. The SPSS - Statistical Package Social Science Version 8.0 (1997) was used in these analyses, at a significance

level of 0.05.

RESULTS

Case series analysis - During gestation, nine out of the thirteen patients of the PS group had therapeutic indication for beta-blocker due to deterioration of FC; therefore, the PS group was subdivided into two distinct subgroups: PSB composed of nine pregnant women on beta-blocker (propranolol at a daily dose ≤ 80 mg), and PSWB composed of four pregnant women not receiving a beta-blocker.

The description and comparison between groups regarding ages and echocardiographic measurements taken at the beginning of the study showed that age in the MIS group was higher than in the NP (Table 1). The analysis of NYHA-FC verified that the nine pregnant women of the NP group remained in FC I/II during gestation and puerperium; among the nine patients of the PSB subgroup, seven progressed to FC III during the study and one patient of the MIS group, the remaining of the PSWB subgroup and of the MIS group remained in FC I/II throughout the study. The statistical analysis between echocardiographic variables was performed only between the groups with mitral stenosis, that is, PS and MIS. Complications such as thromboembolism, infective endocarditis or pulmonary congestion were not recorded during the study.

Comparative analysis of hemodynamic parameters in the groups and subgroups at rest and during stress

Group of normal pregnant women (between gestation and puerperium) - At rest, a significant difference was observed for the following variables: muscle blood flow – which increased by 21.3% ($p = 0.003$); PVR – which decreased by 31.3% ($p = 0.023$), and HR – which increased by 13.1% ($p = 0.018$) during gestation, whereas MAP remained similar in the two study phases (Table 2). During the stress phase, an increase by 34.4% ($p = 0.489$) and 348% ($p = 0.048$) in muscle blood flow and MAP, respectively, was verified during gestation, whereas a reduction in PVR by 42.9% ($p = 0.280$) was observed during puerperium, and HR was similar in both study phases (Table 2).

Table 1 – Comparative analysis of ages and echocardiographic measurements

Groups	PSB	PSWB	NP	MIS	p
N° patients	9	4	9	9	
Age (years)	30.7 ± 1.1	28.3 ± 1.7	27.0 ± 1.3	35.0 ± 1.6	< 0.01
MVA (cm ²)	1.2 ± 0.1	1.4 ± 0.1	3.4 ± 2.1	1.3 ± 0.2	ns
MG (mmHg)	11.5 ± 0.9	9.0 ± 1.1	-	9.2 ± 0.9	ns
SPRV (mmHg)	57.7 ± 9.3	41.6 ± 7.2	18.6 ± 0.9	42.6 ± 2.7	ns
LA (mm)	50.6 ± 1.8	45.3 ± 3.2	29.8 ± 0.8	50.0 ± 1.9	ns
EF%	68.9 ± 0.7	70.7 ± 1.8	71.3 ± 1.2	71.0 ± 1.1	ns

Age (mean and standard deviation); MVA- mitral valve area; MG- mean gradient of mitral transvalvular flow; SPRV- systolic pressure in right ventricle; LA- left atrium; EF- left ventricular ejection fraction; p- statistical significance; ns- non significant. The statistical analysis of echocardiographic measurements was performed between the PSB, PSWB and MIS groups.



Table 2 – Comparison of hemodynamic parameters of the NP group during pregnancy and puerperium at rest and during stress

Parameters	Pregnancy	Puerperium		% variation	p value
		At rest			
Flow	2.86 ± 0.12	2.25 ± 0.18		21.3 ↑	0.003
PVR	30.89 ± 2.09	40.55 ± 4.33		31.3 ↓	0.023
MAP	85.92 ± 3.78	86.04 ± 4.59		0.1 ↓	0.750
HR	84.23 ± 3.28	73.19 ± 3.34		13.1 ↑	0.018
During stress					
Flow	1.35	1.07		34.4 ↑	0.489
PVR	-5.91	-11.35		42.9 ↑	0.280
MAP	12.23	2.38		348.0 ↑	0.048
HR	6.52	6.25		8.4 ↑	0.917

↑ increase and ↓ reduction, during pregnancy in relation to puerperium; p- statistical significance value; Flow- expressed in ml/min/100 ml; MAP- mean blood pressure in mmHg; HR- heart rate in beats per minute; PVR- peripheral vascular resistance in mmHg/ml/minute/100 ml.

Subgroup of mitral stenosis without use of beta-blocker (gestation and puerperium) - At rest, the muscle blood flow increased by 1.6% (p = 0.866), and HR by 20.5% (p = 0.057), whereas PVR and MAP had a reduction by 19.3% (p = 0.647) and 4.4% (p = 0.119), respectively, in relation to the puerperium. During stress, there was an increase in muscle blood flow by 55.9% (p = 0.118) and HR by 30.2% (p = 0.228), and PVR and MAP were similar in both study phases (Table 3).

Subgroup of mitral stenosis on beta-blocker (gestation and puerperium) - at rest, the muscle blood flow increased by 5.9% (p = 0.857), and MAP and PVR decreased

by 10.3% (0.531) and 9.12% (0.922), respectively, during gestation; however, a significant increase in HR by 14.9% (p = 0.001) was observed during gestation. During stress, the muscle blood flow increased by 69.8% (p = 0.436), HR was similar, and PVR decreased by 53.7% (p = 0.576), and MAP increased by 174.1% (p = 0.571) (Table 3).

Group of mitral stenosis non-pregnant women (during stress and at rest) : a significant increase by 75.3% (p = 0.001) in muscle blood flow, by 3.8% (p = 0.011) in MAP, and by 20.5% (p = 0.001) in HR, as well as a reduction by 38.1% (p < 0.0001) in PVR were observed during stress in relation to rest (Table 4).

Table 3 – Comparison of parameters of the PSWB and PSB subgroups during pregnancy and puerperium at rest and during stress

Phase	Pregnancy		Puerperium		% variation		p value	
	PSWB	PSB	PSWB	PSB	PSWB	PSB	PSWB	PSB
At rest								
Flow	2.3 ± 0.5	2.2 ± 0.3	2.2 ± 0.5	2.0 ± 0.2	1.6 ↑	5.9 ↓	0.866	0.857
PVR	39.7 ± 4.6	43.1 ± 5.6	47.4 ± 15.6	46.9 ± 6.8	19.4 ↑	9.1 ↓	0.647	0.922
MAP	82.5 ± 4.1	81.6 ± 5.2	86.1 ± 4.6	90.0 ± 2.8	4.4 ↑	10.4 ↑	0.119	0.531
HR	86.6 ± 2.8	81.6 ± 4.4	68.8 ± 6.4	71.0 ± 5.2	20.6 ↓	14.9 ↓	0.057	0.001
Stress								
Flow	1.61	1.07	0.71	0.63	55.9 ↑	69.8 ↓	0.118	0.436
PVR	- 12.07	- 13.23	- 11.91	- 8.61	1.3 ↓	53.7 ↓	0.979	0.576
MAP	6.44	4.33	6.10	1.58	5.3 ↓	174.1 ↓	0.753	0.571
HR	8.27	2.71	10.7	2.60	30.2 ↑	4.2 ↓	0.228	0.847

↑ increase and ↓ reduction, during pregnancy in relation to puerperium; p- statistical significance value; Flow: expressed in ml/min/100 ml; MAP- mean arterial pressure in mmHg; HR- heart rate in beats per minute; PVR- peripheral vascular resistance in mmHg/ml/minute/100 ml.

Table 4 – Measurements taken at rest and during stress in the MIS group

Group	Flow (ml/min/100ml)	PVR (mmHg/ml/min/100ml)	MAP (mmHg)	HR (bpm)
Baseline	2.39 ± 0.23	39.45 ± 3.00	88.74 ± 4.03	73.84 ± 2.46
M1	4.19 ± 0.55	24.41 ± 2.82	92.16 ± 4.73	88.97 ± 4.70
Stress	1.80	-15.04	3.42	15.13
% variation	↑ 75.31	↓ 38.12	↑ 3.85	↑ 20.49
p value	0.001	0.0001	0.011	0.001

Stress- (Baseline-M1); M1- first minute stress; Baseline- mean of three minutes of stress %I = stress percentage; p- significance.

Comparative analysis of hemodynamic parameters between groups and subgroups

Between subgroups of pregnant women with mitral stenosis on beta-blocker (PSB) or not (PSWB) - At rest, similar results of muscle blood flow, PVR, and MAP variables, and a mild increase in HR in the PSWB group ($p = 0.490$) were observed during gestation, whereas the subgroups were similar during puerperium. During stress, an increase in HR ($p = 0.490$) was observed in PSWB, however it was not significant (Table 3).

Between the NP group and PSB and PSWB subgroups - At rest, the increase in muscle blood flow was higher in the NP group ($p = 0.045$) in relation to the two subgroups during gestation (Figure 1A); a reduction in PVR, more significant in the NP group ($p = 0.059$) was observed (Figure 1B); and no difference was observed in MAP and HR between the groups and subgroups studied (Figures 1C and 1D). In puerperium, the groups and subgroups were similar as regards the parameters analyzed (Figure 1A, 1B, 1C, 1D).

Between the NP and MIS groups and PSWB and PSB subgroups - (puerperium data) the groups were similar both at rest and during stress for muscle blood flow (Figure 2A), PVR (Figure 2B), MAP (Figure 2C), and HR (Figure 2D) parameters. The analysis of covariance

of the parameters in the first phase of mental stress compared with those at rest in the NP group and PSWB and PSB subgroups in gestation and puerperium phases showed a significant difference as regards muscle blood flow ($p = 0.006$), PVR ($p = 0.003$); MAP ($p < 0.001$) and HR ($p < 0.001$).

DISCUSSION

The improvement of knowledge on the physiological aspects of pregnancy and their interaction with the hemodynamic behavior of heart diseases has contributed to the reduction in maternal morbidity and mortality during the cycle of pregnancy and puerperium.

In mitral stenosis, the alarming percentage of 86% of deterioration from class I/II to class III/IV during the second and third trimesters of gestation, as reported by Ávila et al⁷, shows the clinical importance imposed by cardiocirculatory overload resulting from hemodynamic alterations during pregnancy.

These data clearly show that pregnancy is a potential factor for clinical deterioration of the mitral lesion during its natural history. Thus, the identification of prognostic variables such as age, functional class, atrial fibrillation, CHF, acute pulmonary edema, pulmonary hypertension, right ventricular overload, and valve area has contributed to the risk stratification of pregnant women with mitral stenosis^{8,9}.

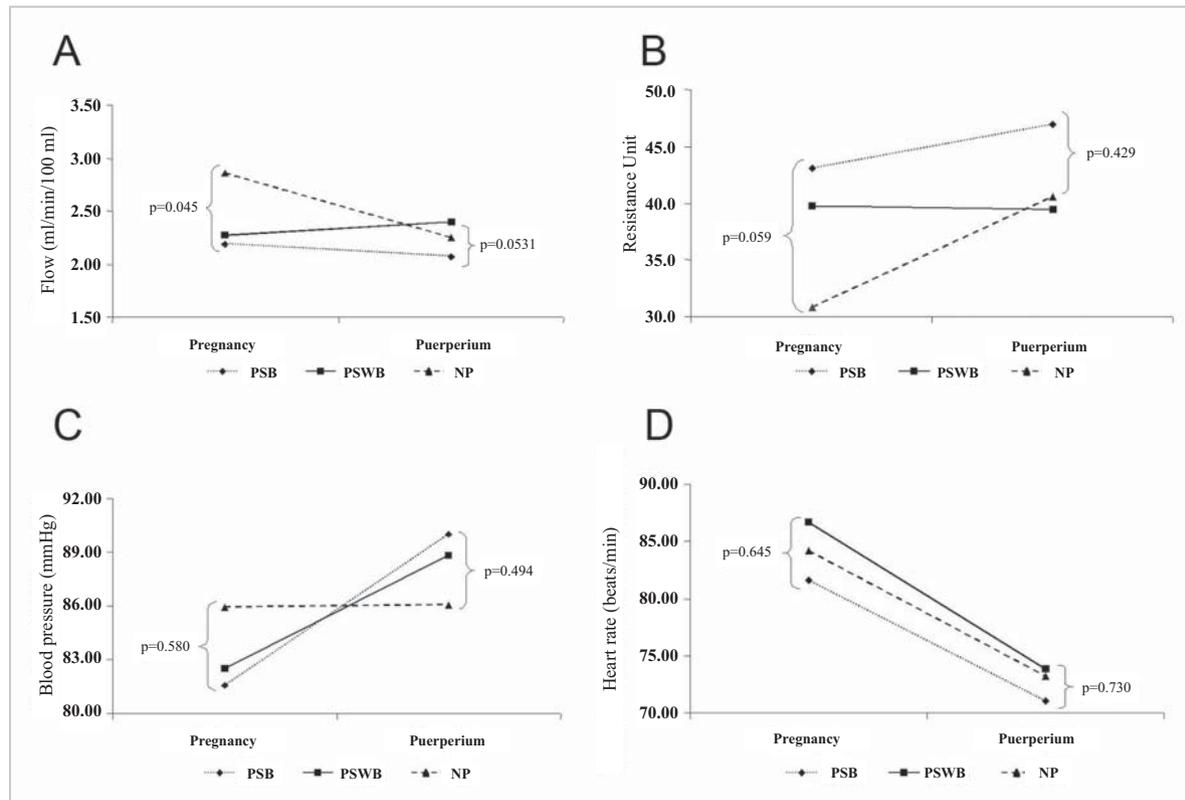


Fig. 1 – Comparison of variables between pregnancy and puerperium at rest, between the PSB and PSWB subgroups and NP group. MS - mental stress; PSB- pregnant woman with mitral stenosis using beta-blocker; PSWB- pregnant woman with mitral stenosis not using beta-blocker, and NP- normal pregnant woman; Flow- ml/min/100 ml; MAP mmHg; PVR mmHg/ml/minute/100; HR- beats/minute.

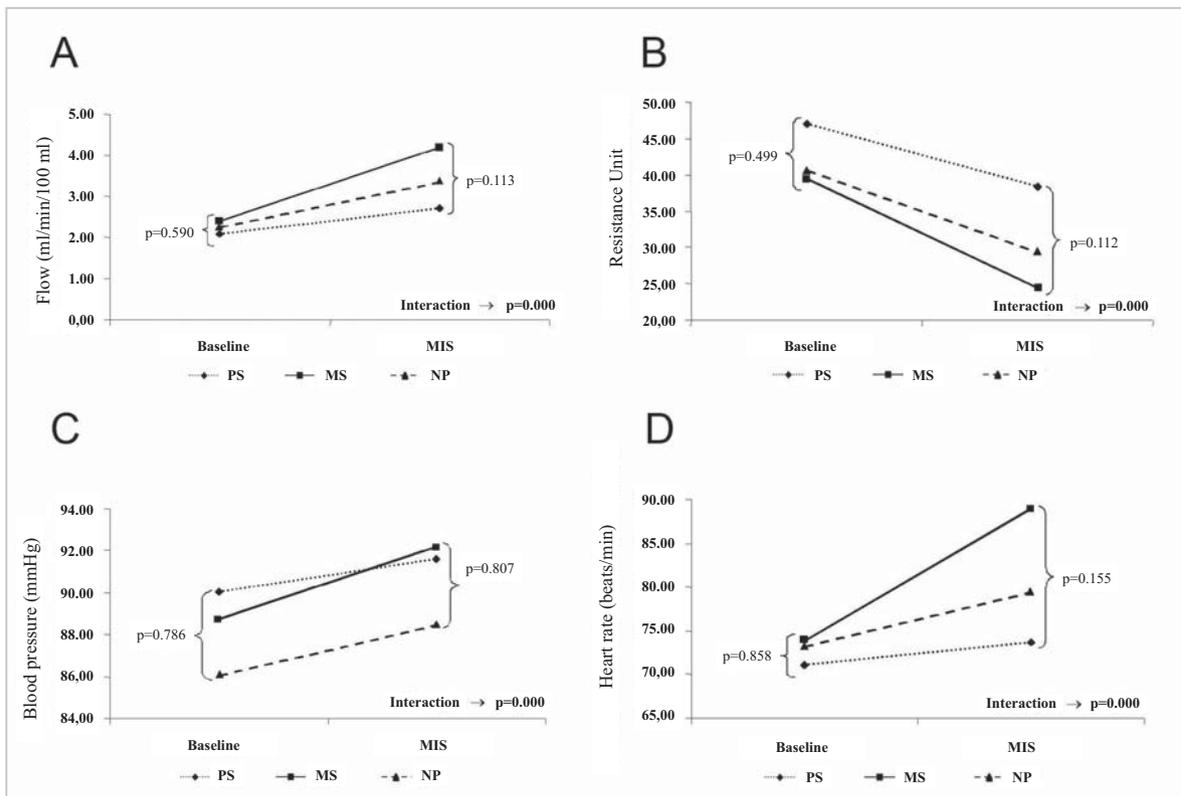


Fig. 2 – Comparison of variables at rest and during stress between the PS, MS and NP groups in puerperium. MS - mental stress; PS - pregnant woman with mitral stenosis; MIS - non-pregnant woman with mitral stenosis; and NP - normal pregnant woman; Flow- ml/min/100 ml; MAP mmHg; PVR mmHg/ml/minute/100; HR- beats/minute.

The continuing search for prognostic factors encouraged us to study hemodynamic parameters during pregnancy as compared to post-partum in women with mitral stenosis, with the objective of obtaining clinical and laboratorial support, for a better knowledge of possible complications in this group of pregnant women.

Thus, we included the group of normal pregnant women (NP) and of women with mitral stenosis (MIS) with the purpose of giving support to the analysis of the method used and of the gestation component in the binomial heart disease and pregnancy.

This study considered a period of clinical course - thus subject to therapeutic decisions - and not only a moment of study performance. Thus, the treatment dynamics of each case cannot be predicted in a prospective protocol and its application determined the subdivision of the PS group into two subgroups according to the need or no need of beta-blockers, due to deterioration of the clinical course and/or severity of the valve lesion.

In fact, we observed that seven out of the nine patients in the subgroup of pregnant women with mitral stenosis who required beta-blocker (PSB) progressed to FC III and had a mean valve area of 1.2cm². These data are consistent with those of Ávila et al⁷ study, that significantly showed a distinct progression of gestation at these limits, that is: mitral valve area greater than 1.2 cm for FC III and lower than this value for FC IV.

The literature lacks studies on the hemodynamic behavior of mitral stenosis and its correlation with clinical aspects during pregnancy. The use of invasive methods available in practice limited the acquisition of knowledge on the behavior of peripheral vascular resistance and muscle blood flow and their associations with diseases during pregnancy.

However, non-invasive methods have now been broadly used. Ultrasonography and the venous occlusion plethysmography method are easy and quick to perform at a low cost and have contributed to the study of the endothelial function and vascular reactivity in different clinical situations, including pregnancy^{10,11}.

Edouard et al¹², using the plethysmograph, verified variations in venous tone and blood viscosity of the lower extremities in nine normal pregnant women, when the first and the third trimesters of gestation were compared to the period of three to six months after delivery.

In the present study, the 31% reduction in PVR of normal pregnant women (NP) in relation to the puerperium is consistent with the data verified by Clark et al¹³, who used the thermodilution technique and pulmonary artery catheterization in ten normal primiparous pregnant women and observed a 21% reduction in PVR in the third trimester of gestation, when compared with the period between the 11th and 13th week after delivery.

The mechanisms of arteriolar dilation during pregnancy have been attributed to estrogenic components^{3,4}, to prolactin and to the increase in circulating prostaglandin levels (PGE2 and PGI2), a substance that is responsible for the reduction in vascular response to angiotension. Recently, alterations in vascular tone during pregnancy have been shown to be possibly attributed, in part, to changes in the synthesis of vasoactive substances derived from the endothelium, especially the endothelin which is theoretically able to mediate the synthesis of prostaglandins and the nitric oxid which has been related to vasodilation during pregnancy¹⁴⁻¹⁶.

PVR also decreased by 19% and 9% during pregnancy of the subgroups with mitral stenosis (PSWB and PSB), respectively, not very differently from the puerperium; however, the values were lower than the percentage of 31% of normal pregnant women. This different PVR behavior at rest in pregnant women with mitral stenosis may be attributed to an abnormal state of vascular response at rest due to the low cardiac output or to an inadequate response to mechanisms of vasodilation during pregnancy.

Similar data were published by Sakai et al¹⁷, who, using a plethysmograph, demonstrated that the severity of pre-eclampsia in pregnant women with high blood pressure was related to an inadequate vascular response, increase in peripheral vascular resistance and reduction in peripheral vascular muscle blood flow.

In face of these results, it is reasonable to assume that diseases such as arterial hypertension or mitral stenosis can interfere with vascular reactivity during pregnancy, predisposing to an abnormal PVR response at rest.

The muscle blood flow increase by 21% in normal pregnant women (NP), when compared to the post-partum, corroborates Dorup et al's data¹⁸, who reported a 26% increase in peripheral muscle blood flow in normal pregnant women in the first trimester, and 46% at the end of gestation in relation to non-pregnant women, as assessed by ultrasonography.

The finding of a small increase by 1.6% and 5.9% in blood muscle blood flow in pregnant women of the subgroups of pregnant women with mitral stenosis (PSB and PSWB respectively), in turn, supports the hypothesis that mitral stenosis may be included in the special group of diseases that modify vascular response to muscle blood flow during pregnancy. Vascular muscle blood flow reduction was also observed to occur in both subgroups, that is, the one with beta-blocker (PSB) and the other without beta-blocker (PSWB).

The significant increase in HR verified during gestation in relation to puerperium in the groups studied is consistent with previous reports¹⁹ that have demonstrated a progressive increase in HR, from the fourth week of gestation up to term. The initial changes in HR seem to be related to the production of chorionic gonadotrophin,

and the late changes to cardiocirculatory alterations that accompany the fetal and placental development.

HR variation between gestation and puerperium was higher (20.6% versus 14.8%) in the subgroup without beta-blocker (PSWB) as expected; however it was not significant probably due to the limited sample size.

Brooks²⁰, assessing the sensitivity of baroreflexes in the control of heart rate in the hearts of pregnant rabbits, evidenced an increase in baseline sympathetic activity during gestation and, additionally, a reduced action of the parasympathetic nervous system on the heart. Anyway, the similarity of HR between the group of normal pregnant women (NP) and the subgroup (PSB) that had more severe characteristics of mitral stenosis in our case series corroborates the benefit of beta-blockers in mitral stenosis for the control of HR in pregnancy.

Although non-significant, MAP had a tendency to a reduction during pregnancy in the groups studied when compared to puerperium, consistent with longitudinal studies that have verified a decrease in systemic blood pressure from the beginning to the half time of gestation²¹, particularly at the expense of diastolic pressure and further elevation close to pre-gestational values by term.

Rubler et al²² did not verify significant differences in MAP between pregnant and non-pregnant women at several gestational ages. Controversy on MAP variations during pregnancy may be related to variations in manual measurements in which BP may be underestimated because of the absence of the fifth Korotkoff sound resulting from the hyperkinetic state, and also because of influences of the patient posture.

The similarity found in hemodynamic parameters at rest between the groups and subgroups of pregnant women in the post-partum and those of the patients with mitral stenosis supports the idea that pregnancy represents a transient risk of hemodynamic maladaptation; however, it seems not to interfere in the natural history of the disease.

Another aspect of the originality of this study was the assessment of the response to mental stress of pregnant women with mitral stenosis. The stress tests stimulated in laboratory may be seen as a strategy for investigation of the influence of environmental factors on the development of cardiovascular diseases.

The behavior of vascular reactivity during stress may represent a pathogenic mechanism in the development of diseases, that is, a marker of the autonomic central nervous system in the control of the cardiovascular system, or it may demonstrate the alterations of vascular compliance in individuals prone to diseases in the future.

Atterhog et al²³, using mental stress tests (Stroop color-word test), cold pressor test and isometric handgrip, studied cardiovascular and sympathetic responses in



thirteen healthy men and twelve asymptomatic men with primary electrographic abnormalities of ventricular repolarization and demonstrated higher variations of plasma levels of noradrenalin and adrenalin, of increase in blood pressure (BP) and HR in the group with electrographic abnormality.

The present study, which is perhaps the pioneer in the utilization of mental stress in mitral valve disease, showed a significant variation in all hemodynamic parameters during the test in the group of non-pregnant women with mitral stenosis (MS), similar to those recorded in normal individuals²⁴.

This behavior is different from that of patients with heart failure whose situation is characterized by vasoconstriction at rest and abnormal vasodilation response during physical or mental stress.

Negrão et al²⁵ showed that both at rest and during stress test muscular blood muscle blood flow and reflex vasodilation response are reduced in patients with heart failure, and that the impaired endothelium-mediated vasodilation may not be the major cause of vasoconstriction at rest, and it should be attributed to other mechanisms, such as alterations in the cholinergic and nitric oxide response.

It is reasonable to hypothesize that the adaptation mechanisms of mitral stenosis do not interfere in peripheral vascular reactivity; that is, the endothelium-dependent sympathetic response, at least in adapted patients, is preserved under stress stimulus unlike in other situations where endothelial injury is present, such as those with low cardiac output due to ventricular dysfunction or atherosclerotic ischemic disease^{26,27}.

In the SOLVD study²⁸, the analysis of noradrenalin and renin levels showed higher values in the group of symptomatic patients with ventricular dysfunction (ejection

fraction lower than 35%) in relation to the asymptomatic patients, suggesting that the neurohormones with a vasoconstrictor effect predominate in relation to those with vasodilator effect in patients with a poorer prognosis.

During pregnancy, studies on vascular reactivity during mental stress are limited to cases of pre-eclampsia, among which we should point out Woisetschlager's²⁹, who, when assessing the changes in blood pressure and elevation in heart rate, demonstrated an exacerbation of vascular reactivity in pregnant women with pre-eclampsia when compared to normal pregnant women.

In the present study, the similarity between vascular reactivity during stress in gestation and in the post-partum – a period that is not under the influence of gestational hormones, shows that sympathetic and endothelium-dependent responses are preserved both in normal women and in those with mitral stenosis, whether pregnant or not.

The limitation of this study is due to the small number of patients in the subgroups of pregnant women with mitral stenosis according to the need for treatment with a beta-blocker. However, the literature lacks original information, particularly concerning the behavior of vascular reactivity in pregnant women with mitral stenosis.

We concluded that the vascular response to mental stress, as measured by plethysmography, is preserved in pregnant women with mitral stenosis. Additionally, we observed higher values of PVR and lower values of blood muscle blood flow in comparison with healthy pregnant women.

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