

Clinical Characteristics Associated with Unfavorable Outcomes in Peripartum Myocardiology

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Objective

To assess the clinical characteristics of women with a previous diagnosis of peripartum myocardiology and to study the characteristics associated with unfavorable outcomes.

Methods

Clinical, obstetric, and echocardiographic variables were studied in 12 patients with peripartum myocardiology, assessed at diagnosis and at a current appointment, when they were divided into 2 groups: FG ($n = 6$, without cardiac alterations) and UG ($n = 6$, with cardiomegaly and persistent ventricular dysfunction). The comparisons were made using the Student t test and Fisher's exact test ($P < 0.05$).

Results

At diagnosis, mean age of the patients (8 Caucasian and 4 black/non-Caucasian) was 24 ± 7.4 years, all in Functional Class IV (NYHA) and 8 reporting gestational hypertension or preeclampsia. Mean follow-up time was 25 months. Ten patients developed Functional Class I/II. Comparison between the groups demonstrated that UG had lower left ventricular ejection fractions (0.30 ± 0.05 vs. 0.58 ± 0.09 ; $P < 0.001$) and greater LV systolic diameter (58 ± 5 mm vs. 46 ± 3 mm; $P < 0.001$) at diagnosis. An unfavorable outcome was more frequent among non-Caucasian women ($P = 0.01$). In the current evaluation, UG had lower relative wall thickness (0.13 ± 0.02 vs. 0.17 ± 0.02 ; $P < 0.05$) and greater LV mass (283 ± 90 g vs. 186 ± 41 g; $P < 0.05$).

Conclusion

Patients with previous peripartum myocardiology had unfavorable outcomes associated with black race, and stronger initial cardiac alterations; a favorable outcome was associated with a reduction in myocardial mass and an increase in relative ventricular wall thickness.

Key words

heart failure, echocardiogram, gestation

Peripartum myocardiology (PPMC) is a rare form of heart failure with an unknown cause, occurring usually during pregnancy (one month before delivery) or after delivery (up to 5 months), in previously healthy women without preexisting cardiac disease. Its diagnosis is made after other causes of myocardiology have been excluded¹⁻³. The incidence is estimated at 1:3000 to 1:4000 live births, corresponding to 1000 to 1300 women affected every year in the United States².

Although it is a rare anomaly, it is important because of the high mortality rate, ranging from 18% to 56%². This variability is related to the diversity of the clinical evolution; the outcome can be complete normalization of cardiac dimensions and function or progressive ventricular failure leading to death. Even in the first case, where the left ventricle returns to normal, evidence exists that the contractile reserve is involved, and the disease may be recurrent⁴. Additionally, women with peripartum myocardiology had significantly worse evolution when compared with women with dilated cardiomyopathy diagnosed before pregnancy^{5,6}.

Risk factors related to peripartum myocardiology include multiparity, advanced maternal age (> 30 years), twins, preeclampsia, gestational hypertension, and black race². One study⁷ also considers obesity and Cesarean delivery as predisposing factors, and another study⁸ considers a history of chronic hypertension as a predisposing factor.

The prognosis of women with peripartum myocardiology may depend on normalization of size and of left ventricular function up to 6 months after delivery². Among the women with persistent left ventricular dysfunction, the cardiac mortality rate was 85% in 5 years, whereas in the group of patients with normal ventricular function, deaths from cardiovascular disease did not occur in the same time interval⁹.

Few studies in our literature describe the clinical outcome of these patients. Marin-Neto et al¹⁰ assessed 14 patients with a diagnosis of peripartum myocardiology and verified that some women presented in a hyperdynamic state with increased cardiac output. Avila et al¹¹ and Albanesi and Silva¹² reported that left ventricular function determines the prognosis of future pregnancies. A study published by Carvalho et al¹³ concluded that some echocardiographic characteristics such as increase in the final left ventricle diastolic diameter, in the acute phase of the disease, and the late appearance of symptoms, in the postpartum period, are associated with a poor prognosis.

We do not have in our work a study on the clinical aspects and outcomes of patients with a diagnosis of peripartum myocardiology.

diopathy. Thus, the objectives of the present study were to assess clinical characteristics of women with a previous diagnosis of the disease and to assess the characteristics associated with unfavorable outcomes.

Methods

All women included in the study met the diagnostic criteria of Demakis et al⁹; these were 1) development of heart failure in the last month of pregnancy or 5 months after delivery, 2) absence of a determinable cause for heart failure and 3) absence of apparent heart disease before the last month of pregnancy. All the procedures were approved by the Ethics Committee of the Institution, OF.37/2002-CEP.

In the period from 1994 to 2002, 14 cases of peripartum myocardiopathy were diagnosed at Hospital das Clínicas, and retrospectively assessed through evaluation of medical charts and updated clinical evaluations, conducted after the patient was included in the study called current evaluation. Two patients were not present at the appointment and were excluded from the study. In the only death, we have regarded as the "current evaluation" that information recorded in the chart after the event. All patients that were present at the last evaluation gave their written consent. All medical evaluations were performed by cardiologists.

During clinical evaluation, the following variables were recorded: a) obstetric variables: obstetric history, gestational age at delivery, weight variation during gestation before diagnosis, type of delivery, obstetric complications, vitality and maturity of the newborn; b) clinical and demographic variables: race, age, weight, height, symptoms, Functional Class, heart rate, and blood pressure at diagnosis and in the current evaluation, together with the medication in use, outcome, and personal and familial history.

Doppler-echocardiographic examinations that were attached to the chart and performed in the echocardiography laboratory were analyzed, in the physical therapy diagnosis section at Hospital das Clínicas. Patients underwent a new examination, at the current evaluation. The analysis included the following variables obtained in the first and last examinations performed: a) morphometric variables obtained from the M-mode echocardiogram: left atrium (LA) size, left ventricle diastolic (LVd), and systolic (LVs) diameters and left ventricle mass (LVM); $LVM = [(2PPd + LVd)^3 - LVd^3] \times 1.05$, where PPd and LVd are respectively wall thickness and left ventricle cavity diameter at diastole. Relative thickness of ventricular wall was also assessed (PPd/LVd); b) functional variables: percentage of LV diameter variation (% Δ D), ejection fraction (EF), cardiac output (CO), ejected volume during systoles (VS), and E/A ratio, corresponding to the ratio between the peak velocity of the transmitral flow in the rapid ventricular filling (E) phases and atrial contraction (A).

After the current evaluation, patients were divided into 2 groups, according to clinical outcome in the follow-up period: 1) patients with favorable outcomes, that is, patients with normal cardiac function and morphology, with EF > 0.56, % Δ D > 26%, AE \leq 38mm and LVD \leq 56mm, in the current evaluation; and 2) patients with unfavorable outcomes, with dilation and persistent left ventricle dysfunction.

Mean values were calculated with the respective standard deviation for each variable assessed. When the variable's distri-

bution was not normal, medians and interquartile ranges were calculated. Comparison between the 2 groups of patients was performed using the Student *t* test and Fisher's exact test. The association between the relative thickness of the myocardial wall and ejection fraction was assessed using Spearman's correlation coefficient. The significance level adopted was $P < 0.05$.

Results

The patients' clinical and obstetric variables are found in table I. Mean age was 24 ± 7.4 years (range, 15 to 36) at diagnosis. Ten patients were in their first or second pregnancy, and 8 underwent Cesarean delivery. Of the patients with unfavorable outcomes, 4 were black, whereas all the patients of the group with favorable outcomes were Caucasian ($P < 0.05$). The median follow-up was 25.5 months, and 75% were followed-up for at least 15 months.

Eight patients presented with gestational hypertension or pre-eclampsia (PE). According to New York Heart Association classification (NYHA), 100% were in Functional Class IV at diagnosis, undergoing treatment for heart failure with digitalis, furosemide, and angiotensin converting enzyme inhibitors. No difference was found between the therapeutics adopted for the 2 groups of patients. In the current evaluation, 8 out of the 12 patients were in Functional Class I, 2 were in Functional Class II, and 2 were in Functional Class IV. According to this distribution, all patients with favorable outcomes were in Functional Class I.

One patient died suddenly on admission for treatment of congestive heart failure; she was a 17-year-old Caucasian girl, with a single gestation, and she died 2 months after diagnosis; made 5 months after delivery.

Table II presents the average between the respective standard deviation for echocardiographic variables of the 12 patients, at diagnosis, and in the current evaluation. Comparison between the variables was not performed, because of the great heterogeneity of the time interval between the evaluations, in the cohort. Direct and significant association between the relative ventricular wall thickness and the indicator of systolic function obtained in the current evaluation was observed (fig. 1).

In table III, the age, heart rate, and cardiac output at the 2 times and in the 2 groups considered are presented. The only statistical difference between the groups was the cardiac output obtained at diagnosis (FG: 4.3 ± 0.8 l/min vs. UG: 3.1 ± 0.8 l/min; $P < 0.05$).

In figures 2 to 4, the echocardiographic variables obtained in the 2 groups are presented, at diagnosis and in the current evaluation. At diagnosis, the favorable group was comparable to the unfavorable one regarding the increased dimensions of left cardiac chamber (fig. 2, A and B). In the time interval between the evaluations, a more expressive reduction was seen in these dimensions in the patients with favorable outcomes with a significant difference between the groups. From diagnosis, systolic performance was worst in the group with unfavorable outcomes (fig. 3, A and B), reflected in the increased left ventricle systolic dimension (58 ± 5 mm and 46 ± 3 mm, $P < 0.001$), and in the decreased ejection fraction (0.30 ± 0.05 and 0.58 ± 0.09 , $P < 0.001$). Figure 4 demonstrates the left ventricle mass values and relative ventricular wall thickness. At diagnosis, the 2 groups were comparable regarding left ventricle mass and relative ventricular poste-

**Table I - Clinical and obstetric variables (individual values)**

Race	Age (years)	Obstetric History	Follow-up Time (months)	Outcome	Gestational Problems	Type of delivery	Current CF
W	36	G2P2MOC1	47	F	GH	Cesarean Delivery	I
W	34	G4P3M1C3	24	F	PE; APE	Cesarean Delivery	I
W	24	G1P1MOCO	27	F	APE; GH	Normal	I
W	24	G1P1MOC1	60	F	GH; PE	Cesarean Delivery	I
W	26	G2P2M1C1	14	F	GH; PE	Cesarean Delivery	I
W	20	G2P2MOC1	3	F	GH	Cesarean Delivery	I
B	27	G2P1M1C1	118	U	GH	Cesarean Delivery	I
P	15	G1P1MOCO	17	U	---	Normal	IV
W	17	G1P1MOC1	2	U	---	Cesarean Delivery	IV
W	15	G3P3MOCO	43	U	---	Normal	II
B	33	G2P2MOC2	24	U	GH	Cesarean Delivery	II
P	18	G3P3MOC2	112	U	---	Normal	I
M	24	---	40.9	---	---	---	---
SD	7.4	---	38.6	---	---	---	---

M - mean; SD - standard deviation; ID - identification; W - white; B/P - black/non-Caucasian; G - number of gestations; P - parity; M - number of miscarriages; C - number of Cesarean deliveries; F - favorable outcome; U - unfavorable outcome; GH - gestational hypertension; PE - preeclampsia; PAE - pulmonary acute edema; FC - functional class (NYHA).

Table II - Means and respective standard deviation of the echocardiographic variables obtained at diagnosis and in the current evaluation

	Initial evaluation	Current evaluation
LA (mm)	42.7 ± 5.33	38.1 ± 5.57
LVd (mm)	63.6 ± 3.97	57.6 ± 8.43
LVs (mm)	52.0 ± 7.5	42.2 ± 10.9
PPd/IVd	0.12 ± 0.02	0.15 ± 0.03
LVM (g)	259.1 ± 33.6	234.2 ± 83.6
EF	0.44 ± 0.16	0.58 ± 0.22
%ΔD	18.3 ± 8.4	27.2 ± 11.9
E/A	1.65 ± 0.73	1.60 ± 0.61

LA - left atrium dimension; IVd - left ventricle (LV) diastolic diameter; LVs - LV systolic diameter; PPd/IVd - LV wall relative thickness; LVM - LV mass; EF - ejection fraction; %ΔD - ventricular diameter variation; E/A - ratio between rapid ventricular filling peak velocity (E) and peak velocity during atrial contraction (A).

rior wall thickness. In the current evaluation, a decreased left ventricular mass was observed, together with greater left ventricular posterior wall thickness in the group of patients with unfavorable outcomes (fig. 4, A and B).

Doppler and echocardiographic variables of diastolic function (tab. IV) were comparable in the 2 groups with peripartum myocardio

Discussion

The 12 cases presented in this study are clinically relevant, because of the low incidence of the disease. In fact, the studies published in the literature on the theme also have a similar cohort^{5,7-14}. It is important to point out the 47 cases diagnosed in 7 years, in a medical service in Haiti, by Fett et al³, with no reasons for this high incidence.

The mean age of our patients at diagnosis was lower than that found in the literature, which is 30 years of age or older^{2,5,7}. When they were divided into 2 groups according to clinical evolution and echocardiography, no significant difference was found in their mean age, contrary to the study of Carvalho et al¹³, in

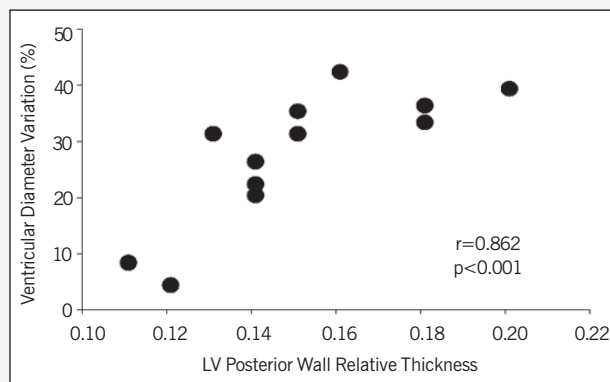


Fig. 1 - Association between the ventricular diameter variation and the relative LV posterior wall thickness, obtained in the current evaluation. The values of the Spearman's correlation are presented together with the result of the statistical test.

which women from the group with unfavorable outcomes were older. Our population was also different from that of the literature concerning race and parity, because the majority was Caucasian (64.3%), in the first or second pregnancy, at diagnosis. The literature generally assumes as risk factors, black race, multiparity and twins^{2,5,7,9,14}. All of our black patients had unfavorable outcomes, and they accounted for 67% of the group with unfavorable outcomes, also reported by Carvalho et al¹³. Ford et al⁸ studied a population of patients very similar to ours regarding mean age at the onset of the disease, race, and the percentage of nulliparous women compared with the total number of women assessed, and they have observed an outcome index greater than that reported in the literature. The authors have attributed these findings to the fact that these were young women, with low parity and no comorbidities. Therefore, we considered it important to assess separately those patients with favorable outcomes and those with unfavorable outcomes.

Just as the studies of other authors^{3,8,14,15}, the diagnosis of peripartum myocardium, in most cases, was performed in the postpartum period, especially one month after the end of the gestation. The high index of cases of hypertension induced by gestation and preeclampsia (71.4%) in the patients from our service were also in accordance with reports in the literature. No statistical significance existed regarding the occurrence of gestational hy-

Table III - Age, heart rate (HR) and cardiac output (CO) of the patients with peripartum cardiomyopathy assessed in the initial (i) and current (a) moment. Mean and respective standard deviations are presented

	Age (years)	HRi (bpm)	HRa (bpm)	COi (l/min)	COa (l/min)
GF	27 ± 6	112 ± 19	74 ± 14	4.3 ± 0.8	4.3 ± 0.7
Gu	21 ± 7	110 ± 20	87 ± 24	3.1 ± 0.8*	3.2 ± 1.3

GF and GU - favorable and unfavorable; *P < 0.05 vs GF.

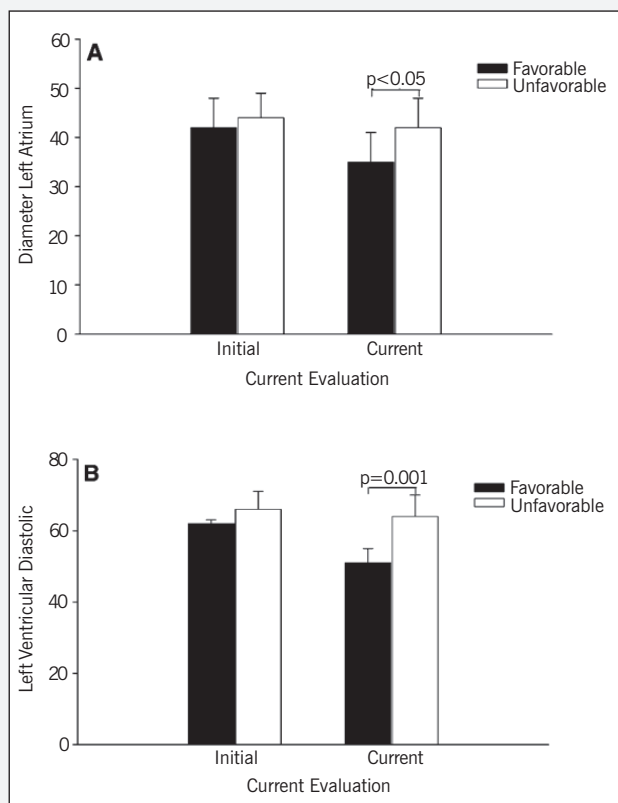


Fig. 2 - Mean and respective standard deviations of the left atrium dimensions (LA, panel A) and of the left ventricle during diastole (LVd, panel B), obtained in the initial and current evaluation, for the groups with favorable and unfavorable outcomes (Student *t* test).

pertension and the outcome of patients; this factor is not regarded in the literature as a defining factor for the prognosis of patients with the disease. Up to the moment, the mechanism involved in the physiopathology of peripartum myocardopathy that can explain its association with gestational hypertension or preeclampsia remains unknown.

In our study, 8 patients evolved with clinical improvement and Functional Class I, and only 6 patients had indicators of normal function and morphology on resting conventional echocardiography, indicating a favorable outcome. This result is also in accordance with results in the literature, which reports a good outcome in 50% of the cases^{2,5,9,12,15}.

The patients in the group with unfavorable outcomes had cardiac output lower than those from the other group at diagnosis, although their mean values were normal, even in Functional Class IV. It is possible that at that time, cardiac output was maintained through tachycardia. In both groups, the cardiac output observed was similar to that assessed at diagnosis. However, heart rate in

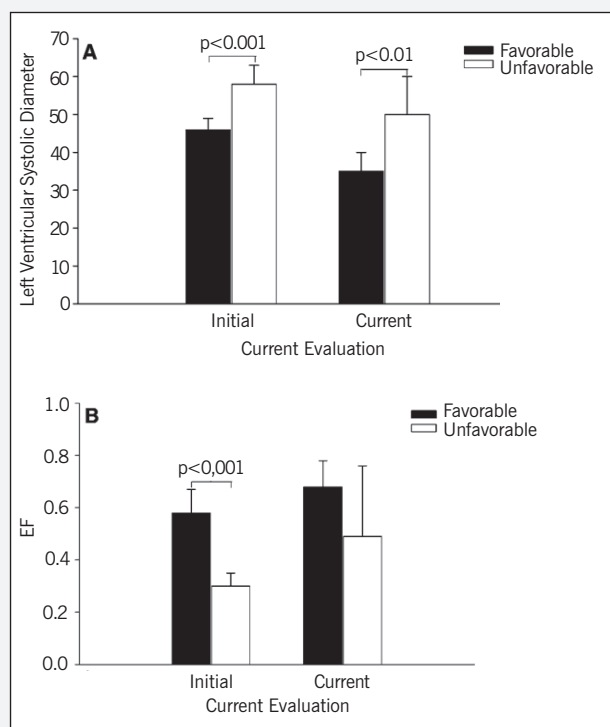


Fig. 3 - Means and standard deviations of the left ventricle systolic dimension (LVs, panel A) and of the ejection fraction (EF, panel B), obtained in the initial and current evaluation, for the groups with favorable and unfavorable outcomes (Student *t* test).

the last evaluation was smaller, indicating an increase in the ejected volume, in accordance with the clinical improvement observed. Another point that should be emphasized is that the patients had a decrease in heart rate during the period they were observed regardless of the outcome, probably because of the treatment.

According to the echocardiographic values obtained at diagnosis cardiomegaly was not marked, although the patients were in Functional Class IV (NYHA), reinforcing the acute feature of the picture. Early examination in the onset of the disease may also justify the difference in the clinical picture of the 12 patients, and the not so significant decrease of the initial ejection fraction and the initial % Δ D. With acute aggression, any reduction of the ejection may lead to a sudden increase in residual volume in the cavity. If the chamber is not adapted to this increased volume, a disproportionate increase in the ventricular filling pressure would occur. Thus, the pulmonary congestion is disproportionately more intense than the reduction of the ejection fraction and the % Δ D. In fact, dyspnea at rest, and the signs of pulmonary congestion are predominant in the initial clinical picture.

Current evaluation demonstrated ejection fraction and % Δ D with mean values slightly lower than those considered normal, 0.56 and 26%, respectively. These results suggest that, despite the apparent good clinical outcome, cardiac damage persisted in many patients. At diagnosis, the group with unfavorable outcomes had slightly increased left ventricle diastolic dimensions, with only a statistical tendency compared with the other group (P = 0.065); however, they also had increased left ventricles and reduced ejection fractions. Our observations are in accordance with those in the study of Carvalho et al¹³, who found a strong association between increased values of ventricular diastolic dimension and poor prognosis when dividing patients according to their clinical outcome. Probably

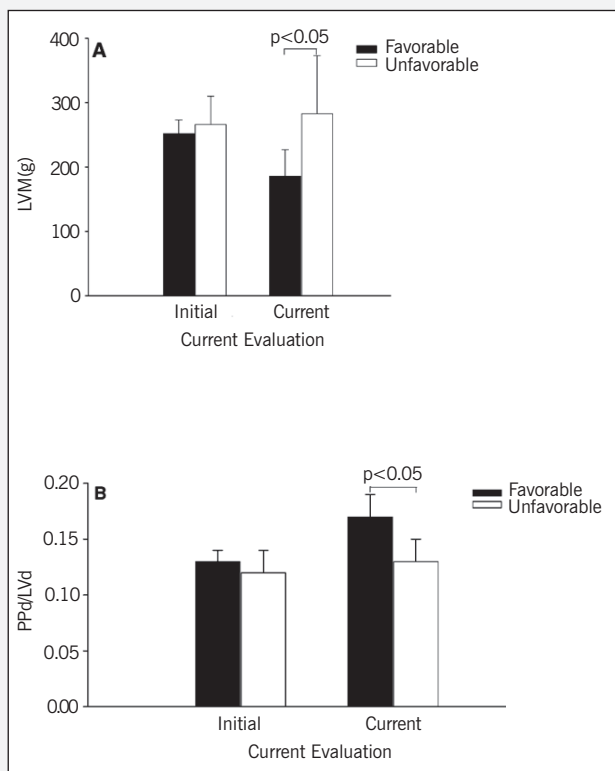


Fig. 4 - Means and standard deviations of the left ventricle mass (LVM, panel A) and the ventricular wall relative thickness (PPd/LVd, panel B), obtained in the initial and current evaluation, for the groups with favorable and unfavorable outcomes (Student *t* test).

Table IV - Doppler and echocardiographic variables of the diastolic function of the patients with peripartum myocardopathy in the initial (i) and current (a) evaluation with the mean and respective standard deviation

	E/Ai	E/Aa	Ei (cm/s)	Ea (cm/s)	Ai (cm/s)	Aa (cm/s)
GF	1.43±0.88	1.52±0.55	87±32	78±26	71±25	53±13
GU	1.92±0.46	1.59±0.70	79±7	71±21	42±13*	52±18

GF and GU - favorable and unfavorable outcome; E/A - ratio between transmitral flow peak velocity in the rapid ventricular filling phase (E) and duration of atrial contraction (A); *P < 0.05 vs. GF.

one of the factors involved; is that the heart with lower dilation enables the maintenance of less increased levels of right and left ventricular afterload, with more suitable systolic performance, and preserved systemic flow, with greater conditions of tissue perfusion¹⁰. Other authors^{16,17} observed that, among the clinical, echocardiographic, hemodynamic, or histologic characteristics assessed in the beginning of the picture, only the left ventricle systolic function

was associated with a poor outcome. The normalization of heart size in up to 6 months is also mentioned as being associated with a favorable outcome of peripartum cardiomyopathy⁹.

Considering all the patients, left ventricle mass values observed on admittance indicated that hypertrophy was already present in the first evaluation. This is an interesting result because we have considered that the examination was performed too early, in the evolution of the pathology, days after the onset of the symptoms. The presence of hypertrophy in this initial period suggests that some kind of stimulus for hypertrophy must have been occurring before the onset of symptoms. Whether this stimulus was humoral or mechanical (hypertension) or physiologic due to pregnancy is impossible to know. In the current evaluation, the patients with unfavorable outcomes had left ventricle mass greater than that in those patients with favorable outcomes. This result suggests that the patients with good evolution had hypertrophy regression, whereas the other patients remained with this alteration.

From the evaluation of relative ventricular wall thickness, we were able to suggest that the first examination reflected ventricular dilation, with eccentric remodeling of the cavity. This is one of the reactive mechanisms in the acute phase of heart failure to increase the ventricular capacity in a situation of increased volume¹⁸. Thus, the greater PPd/LVd value in FG compared with UG, in the current evaluation, was interpreted as a sign of adaptation and return of the original left ventricle geometry. Significant direct association was observed between the relative wall thickness and ventricular ejection index. This result suggests that the geometry of the chamber plays an essential role in cardiac performance. This assumption is reinforced by the lack of significant association between the myocardial mass or ventricular dimension and systolic function indicators. The loss in ejection was associated with disproportional growth of the cavity volume, uncompensated by myocardial hypertrophy. This unbalanced situation leads to preload and postload increase with the development of heart failure¹⁸. The relative thickness of the wall, at diagnosis, was not a variable that would indicate a favorable or unfavorable outcome of the patients.

With the analysis conducted so far, we may conclude that peripartum myocardopathy has severe clinical repercussions, in the series of cases studied, with favorable outcomes in only 50% of the cases. When the patients were subdivided according to the type of outcome, it was possible to conclude that the unfavorable outcome of peripartum myocardopathy is associated with black race, and cardiac morphologic and functional alterations, more increased since the beginning of the clinical picture, and the favorable outcome is associated with myocardial mass reduction and relative ventricular wall thickness increase.

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