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Pregnancy in patients with heart disease

Cardiopatia e gravidez

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ABSTRACT: The care of patients with heart disease has made great strides in recent decades. Despite the reduction in morbidity, pregnancy in this group represents an important cause of maternal mortality and worse fetal prognosis, even in developed countries. Obstetric follow-up of these patients needs to be individualized according to maternal risk stratification. A few randomized clinical trials have been conducted, and most are based on retrospective studies. For this article, we conducted a literature review to support the best practices in multidisciplinary care during the puerperal pregnancy cycle of patients with heart disease.

Keywords: Pregnancy; Heart diseases; Pregnancy complications, cardiovascular; Prenatal care.

RESUMO: A assistência às pacientes cardiopatas passou por enormes avanços nas últimas décadas. Apesar da queda morbidade, a gravidez nesse grupo representa importante causa de mortalidade materna e de pior prognóstico fetal, mesmo em países desenvolvidos. O acompanhamento obstétrico dessas pacientes precisa ser individualizado conforme a estratificação de risco materno. Há poucos ensaios clínicos randomizados, sendo que a maior parte das condutas é baseada em estudos retrospectivos. Neste artigo realizamos uma revisão de literatura para embasar as melhores práticas na assistência multidisciplinar durante o ciclo gravídico puerperal das pacientes portadoras de cardiopatia.

Descritores: Gravidez; Cardiopatias; Complicações cardiovasculares na Gravidez; Cuidado pré-natal.

INTRODUCTION

Gestation in women with heart disease has always been associated with high levels of maternal and perinatal morbidity and mortality. The overload imposed by the physiological hemodynamic changes of pregnancy increases the risk of clinical decompensation even in previously stable patients. Over the course of the twentieth century, improvements in clinical and obstetric care have led to favorable outcomes in most cases. Nevertheless, maternal heart disease remains one of the primary causes of maternal death both in our country and in developed countries[1,2]. Therefore, knowledge of the physiology associated with this condition and its implications for pathology should provide guiding significance for the care of patients with heart disease.

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Epidemiology

Heart diseases affects approximately 1% of pregnant women (percentages range from 0.3 to 4.2% depending on the population analyzed)[3]. In high-income countries, a reduction in rheumatic heart disease and an increase in the survival of women with congenital heart disease were responsible for the predominance of this type of disease among pregnant women[4]. Even in low- and middle-income countries, acquired diseases still predominate[2] and are associated with increased morbidity[1,5,6]. During the period from 2001 to 2005, of the 571 patients seen at the Obstetric Clinic of the *Hospital das Clínicas* (Clinics Hospital) of the University of São Paulo (USP), 45.8% were carriers of rheumatic heart disease, and 28.6% had congenital heart diseases[7].

In Brazil, Feitosa[8] reported a prevalence of heart disease in 4.2% of the pregnancies seen at *Hospital São Paulo* (Sao Paulo Hospital) between 1979 and 1998. Heart disease was responsible for 6.4% of maternal deaths in the municipality of São Paulo between 1993 and 2012[9] and 8% of the cases of maternal mortality in the State of São Paulo in 2014[10]. Other factors contribute to the increased severity of these cases, such as late motherhood and lifestyle changes (sedentary lifestyle, obesity, smoking), which in turn imply an increase in arterial hypertension and cardiovascular diseases[11-13]. Considering that maternal clinical deterioration can occur even in the late puerperium and that many cases of peripartum cardiomyopathy manifest up to 5 months after delivery, these numbers may be even higher when the cases of late maternal death are assessed[14,15].

Hemodynamic changes during pregnancy

Gestation represents a major change for all organs and systems. Progressive physiological changes allow fetal development and prepare the mother for childbirth. In healthy women, these changes usually do not present clinical repercussions, but some maternal factors may influence the adaptive capacity with regard to gestational demands[16]. Among the main maternal adaptations during gestation are cardiovascular alterations[17,18]. The patient enters a hyperdynamic state, with increases in cardiac output and heart rate, which challenges the cardiac functional reserve[19].

Maternal plasma volume increases up to 10% between 6 and 7 weeks of gestation and increases as much as 50% around the 32nd week of pregnancy and then remains stable thereafter. The magnitude of the blood volume increase may vary according to the number of fetuses[20,21]. Peripheral vascular resistance falls in the early stages of gestation, with its nadir between 14 and 24 weeks. The primary cause of the decline in peripheral vascular resistance is peripheral arterial vasodilation, which, from the beginning of gestation, is mediated by progesterone and nitric oxide, and with the establishment of the uteroplacental circulation, there is a more pronounced drop[4,16,18].

Faced with a reduction in peripheral vascular resistance, blood pressure is reduced by approximately 10% between 7 and 8 weeks of gestation, with a progressive decrease up to 24 weeks of gestation, and then it returns to normal values close to term[16]. Among the physiological regulatory mechanisms that compensate for this decrease are the stimulation of arterial baroreceptors in the vasopressin and renin-angiotensin-aldosterone system, which, combined with resistance to the vasoconstricting action of angiotensin II, results in sodium and water retention. A consequent increase in plasma circulating volume as well as physiological maintenance of cardiac output and blood pressure also occur[18].

In response to these changes, coupled with a 20 to 30% increase in heart rate and cardiac anatomical changes, a compensatory increase in cardiac output is seen, which begins around the 7th week of gestation and increases up to 20% in the third trimester[16,17,22-24]. Cardiac output continues to increase until the end of the second trimester[25] and reaches values 30 to 50% higher than those before pregnancy; cardiac output also reaches a plateau around 32 weeks of gestation. After delivery, an additional increase in cardiac output is observed during the first few days after delivery, with a return to baseline within 24 weeks postpartum[26].

The number of fetuses also affects cardiovascular changes, and cardiac output and systolic volume in twin pregnancies may exceed 20% of the values observed in single pregnancies[23,27].

During labor, uterine contractions exert more volume overload on the maternal hemodynamic system and promote an increase in blood volume up to 500 ml and an increased cardiac output as high as 30%. Locoregional anesthesia helps ameliorate blood volume effects, stabilizes the heart rate[16,28] and reduces the maternal push (which momentarily increases the cardiac output)[29].

After delivery, large fluid reabsorption occurs within the first 24 hours, as approximately 500 liters of blood returns from the uterine circulation to the general circulation, vena cava decompression and absorption of the third space. Cardiac output increases by up to 59%, whereas ejection volume increases by 71% in the immediate puerperium[16,20,30]. In this phase, patients with cardiovascular disorders may have difficulty adapting to the increased cardiac output and may present with decompensated heart failure and/or acute pulmonary edema[31].

Influence of hemodynamic changes in pregnant women with heart disease

The previously described physiological hemodynamic changes significantly burden the cardiovascular system and may lead to severe clinical decompensation in pregnant patients with heart disease, including patients who were previously asymptomatic and those who may have difficulties tolerating the increase in preload and postload reduction associated with increases in heart rate and decreases in peripheral vascular resistance[13].

In addition, during intrapartum, the rapid increase in intravascular volume during contractions, as well as the maternal push (which is associated with increased sympathetic tone and is stimulated by pain and anxiety), are high-risk factors for the occurrence of acute pulmonary edema. Epidural anesthesia may reduce sympathetic tone, but there is a risk of transient hypotension related to peripheral vasodilation[13].

As repercussions of pregnancy on maternal heart disease depend on the etiology of the disease, the presence of surgical interventions, the presence of lesions or residual function, the type of therapy employed, the occurrence of complications or previous events and the functional condition, the clinical presentations are variable[32-34].

In a multicenter registry that included 1321 patients with heart disease between 2007 and 2011, Ruys[2] found that heart failure (13.1% of cases) was the most common complication. Maternal mortality was found to be significantly higher in patients with a New York Heart Association (NYHA) functional class of III or IV and in patients who experienced fetal death and prematurity.

In general, patients with uncorrected congenital heart defects or palliative surgeries present high obstetric and fetal risks as well as cardiac complications during pregnancy, but few lesions contraindicate gestation[4]. Obstetric, neonatal and cardiovascular complications are more prevalent in these patients[35,36] and are directly related to their cardiac function[35].

Drenthen and colleagues studied 1696 pregnancies in patients with congenital heart disease. In this cohort (*ZAHARA – ZwangerschapbijAangeborenHARtAfwijkingen*), 19.4% spontaneous abortions occurred, and 3.4% had elective abortions; follow-up was conducted in 1302 pregnancies in 714 patients[36]. Perinatal complications included premature labor (12%), fetal growth restriction (14%) and neonatal mortality (4%). Maternal complications were directly related to the presence of cyanotic heart disease ($p < 0.0001$), previous medication use ($p < 0.0001$), left ventricular outflow tract obstruction ($p < 0.0001$) and mechanical valve prosthesis ($p = 0.0014$)[36].

Valve disease (congenital or acquired) is associated with a wide spectrum of injuries and has an incidence of clinical complications of 15%; these include arrhythmias, ventricular failure and endocarditis. In general, regurgitant lesions are better tolerated, and stenoses imply more clinical repercussions throughout pregnancy due to the inability of the cardiovascular system to adapt to the increased circulating blood volume and cardiac output[29]. Therefore, previously asymptomatic patients may have symptoms triggered and/or exacerbated by pregnancy modifications[33,37].

In cases of severe mitral stenosis, there is a progressive increase in left atrial volume, with increased pulmonary capillary pressure and risk of pulmonary hypertension, overload and subsequent right ventricular failure. The increase in circulating volume during pregnancy directly implies that this mechanism and can lead to maternal cardiac decompensation[29]. In turn, in severe aortic stenosis (valvular area < 1 cm^2 and transvalvular gradient >50 mmHg), there is an increase in left ventricular preload and the possibility of ventricular hypertrophy. During pregnancy, an increased gradient (postload reduction from the decrease in peripheral vascular resistance) is also observed. The main complications that can occur during intrapartum are primarily due to the inability of the body to tolerate the preload reduction[29].

Pulmonary arterial hypertension is characterized by vascular remodeling and an elevation of the mean pulmonary artery pressure to above 25 mmHg. Patients with pulmonary hypertension are intolerant to pregnancy changes and present a very high risk of morbidity and mortality[33,37], with a greater chance of right ventricular failure and clinical deterioration, especially at the end of the second trimester and puerperium. Maternal mortality varies from 30 to 50%[38]. Cardiac output control is very important, since patients are dependent on preload, and the reduction in output may result in circulatory collapse.

The increased incidence of coronary artery disease in women of childbearing age is also notable. Acute myocardial infarction is estimated to occur in 6.2 per 100,000 births. The mortality due to acute myocardial infarction during pregnancy and puerperium reaches 11%, and the maternal risk is greatly increased if delivery is performed during the acute phase or within the first two weeks after treatment with 9% fetal loss[33].

Outflow tract obstructions (valve stenosis, obstructive asymmetric hypertrophy) and systemic ventricular dysfunction limit the increase in cardiac output and may restrict uteroplacental circulation and fetal growth[33]. Several studies have found more frequent fetal and/or neonatal complications (prematurity, fetal growth restriction, fetal death) in cardiac patients, and this risk is amplified by the presence of cardiac risk factors such as NYHA III or IV functional class, obstruction of the outflow tract, anticoagulation or cyanosis and obstetric conditions such as multiples pregnancies[14,39,40].

B-Natriuretic peptide (BNP) or its inactive portion (NT-proBNP) has been proposed as a predictor of cardiac decompensation and is a great tool for risk stratification in the early stages and during pregnancy. BNP values < 100 have a negative predictive value of 100% for the identification of cardiovascular events during pregnancy[13,41]. In a longitudinal study by Blatt et al.[41], which included 7 patients with dilated cardiomyopathy and a left ventricular ejection fraction < 45%, the NT-proBNP dosage at 30 weeks of gestation presented a better prognostic value compared with serial echocardiography.

Influence of maternal heart disease on obstetric and neonatal outcomes

Several studies relate the inadequacy of hemodynamic changes to worse obstetric and perinatal outcomes, including those of healthy pregnant women. In a prospective study, Borges et al.[42] evaluated cardiac output by echocardiogram in 22 pregnant women without pathology and observed that patients who had newborns who were small for gestational age presented cardiac outputs and left atrium diameters that were unaltered throughout pregnancy; however, these women had a 28% increase in peripheral resistance. Vasapollo et al.[43] performed a case-control study that included maternal echocardiographic evaluation in 21 patients with single gestations and growth-restricted fetuses and 21 control gestations. The study found that the group with fetal growth-restricted had lower cardiac output, a lower left ventricular ejection fraction and greater peripheral vascular resistance.

Repercussions of maternal heart disease on perinatal outcomes also depend on the type of heart disease, the clinical manifestations and the type of medication used[44]. Retrospective and prospective studies of pregnancies in women with heart disease show that the occurrence of perinatal events is significantly increased in these cases[45-47] and that this risk is increased by the presence of cardiac and obstetric risk factors[48]. The main independent factors that negatively influence perinatal prognosis are anticoagulation, cyanosis, NYHA functional class III or IV, multiple gestations, systemic ventricular outflow tract obstruction, metallic valve prosthesis and smoking[48,49].

Siu[49] observed prematurity in 15% and perinatal mortality in 10% of the cases. In a series of 571 patients who were followed at the HCFMUSP Obstetric Clinic (61% with acquired heart diseases), we observed fetal death in 1.2%, fetuses that were small for gestational age in 28% and prematurity in 22.4% of cases[7], and the distribution of low-birthweight fetuses was similar between different etiologies. The main factor that influenced prematurity was the maternal functional class (25% with functional class I/II vs. 41% with functional class III/IV)[7].

Gelson et al.[40] performed a prospective cohort study with 331 cardiac patients and 662 controls and found that the weight percentile of the newborns of the mothers with heart disease was lower ($p < 0.001$) and that the risk of perinatal complications was higher (34% vs. 15% OR: 2.9, $p < 0.001$). In a multivariate analysis, myocardial dysfunction was the factor that was associated with perinatal adverse effects[40].

In a retrospective study by Ouyang et al.[50] in 2010, 112 pregnancies in 65 women with congenital heart defects of functional class 1 or 2 were analyzed; adverse obstetric events were found in 32.6% of patients, and the most frequent was preterm delivery.

To study placentation in women with congenital heart disease, in 2013, Pieper et al.[35] performed a prospective multicenter study of 209 pregnant women with congenital heart disease and 70 pregnant women without pathologies, and no patients with uncorrected cyanotic heart disease were included. They performed a Doppler velocimetric assessment of the uterine and umbilical arteries at 20 and 32 weeks of gestation and found an association between the evaluation of cardiac function on the Doppler echocardiogram and serum NT-proBNP. Among the clinical characteristics, functional class worsening occurred only in patients with heart disease, of whom 10% had cardiovascular events. The pre-gestational and 20-week parameters related to the change in umbilical artery resistance were right ventricular function ($p = 0.002$), altered NT-proBNP levels ($p = 0.085$) and systemic ($p = 0.001$) or pulmonary ($p = 0.045$) valve regurgitation. Obstetric events occurred in 58.9% of patients with congenital heart disease vs. 32.9% in healthy patients ($p < 0.005$), and assisted vaginal deliveries were also more prevalent (47.4% vs. 25.7%, $p = 0.001$). In cardiac patients, the increase in umbilical artery resistance at 32 weeks was related to obstetric events ($p = 0.049$), younger gestational age at delivery (38.3 vs. 39.7 weeks, $p < 0.005$), lower birth weight (3036 g vs. 3578 g, $p < 0.005$) and more frequent Apgar scores < 9 at the 10th minute (8.7% vs. 0%, $p = 0.009$). Those authors concluded that placental flow parameters are altered in patients with congenital heart disease and suggest that this factor may imply a higher incidence of obstetric complications in this group[35].

Risk assessment

For risk stratification, we must account for the physiological hemodynamic changes during pregnancy and cardiac pathologies with a high mortality rate. Risk stratification will determine the frequency of clinical reassessment during pregnancy and will also assist in labor, choice of delivery type and postpartum evaluation.

Predictors of maternal cardiac risk

Numerous studies have been performed that aimed to identify and stratify the risk of these patients. Among

them, we can highlight data obtained by the cohort, prospective and multicenter CARPREG study performed by Siu et al.[49] in pregnant women with heart disease. Out of the patients included in this study, 75% of the women had congenital disease and 25% had acquired disease, whereas those with mitral valve prolapse without insufficiency were excluded. The frequency of cardiovascular complications during pregnancy was 13%, half of which occurred during childbirth; the primary complications were heart failure and arrhythmias. Three deaths were recorded. In this study, four predictors of maternal complications were defined: NYHA functional class (FC) >II before pregnancy; cyanosis; moderate to severe left ventricular dysfunction (ejection fraction (EF) < 40%); obstruction of the left heart (mitral valve area < 2 cm^2, aortic valve area < 1.5 cm^2, mean pulmonary artery pressure gradient >30 mmHg) and history of cardiovascular events (thromboembolism, arrhythmias, infective endocarditis, heart failure). The estimated risk of complications during pregnancy in patients with heart disease, with no predictive factor described above, was 5%; with 1 factor, the risk was 27%, and with 2 factors, the risk was 75%.

Another risk classification used was described by the World Health Organization (WHO), which, with the collaboration of international family planning programs and through the systematic review of the literature, prepared documents that recommend the most appropriate method of contraception in women with heart disease and that define the risks of pregnancy in this population[51-53]. This risk classification was further divided into four categories:

- **Class 1**: Risk of morbidity and mortality similar to those of the general population. Cardiac pathologies include the following: valvopathies with mild lesions, corrected congenital heart disease without sequelae (for example, atrial communication, patent ductus arteriosus), mitral valve prolapse and the presence of isolated ventricular extrasystoles. Cardiologic monitoring during pregnancy may be limited to one or two visits;

- **Class 2**: Slightly increased risk of maternal morbidity and mortality. In this category we find the following: corrected tetralogy of Fallot, uncorrected septal defects and most arrhythmias. Cardiology monitoring is recommended in each trimester;

- **Class 2-3**: Depending on individual circumstances, patients may be class 2 or 3. The risk is increased if additional risk factors or a combination of conditions are present. For example, the risk of pregnancy in a woman with moderate mitral and aortic insufficiency and mildly altered ventricular function will be class 3. Examples of this class are as follows: mild ventricular dysfunction, hypertrophic cardiomyopathy, Marfan syndrome without aortic dilatation, mild to moderate ventricular dysfunction, severe pulmonary stenosis and prior peripartum cardiomyopathy without residual ventricular dysfunction;

- **Class 3**: Significantly increased risk of maternal morbidity or mortality. Examples of this category are the following: mechanical heart valve prostheses, corrected transposition of large vessels, uncorrected aortic coarctation, bicuspid aortic valve with ascending aorta with a diameter of less than 45 mm, cyanotic heart disease and other complex congenital heart diseases. These women require pre-conception counseling and care during the prenatal period and during delivery, with monthly cardiologic evaluation. Inpatient hospitalization may be required for clinical observation and compensation;

- **Class 4**: High morbidity and mortality, and therefore, pregnancy is contraindicated; in case of pregnancy, therapeutic abortion should be proposed. If the pregnancy continues, care should be similar to that of class 3 patients. The conditions included in this category are as follows: pulmonary hypertension due to any cause, severe systemic ventricular dysfunction, grade III-IV heart failure or an ejection fraction less than 30%, peripartum cardiomyopathy in a previous pregnancy with ventricular dysfunction, Marfan syndrome with aortic dilatation greater than 40 mm and severe aortic stenosis.

Predictors of fetal risk

Women with heart disease have higher rates of fetal and neonatal complications than the general population, and the most frequent are fetal growth restriction, prematurity, intracranial hemorrhage and fetal death.

The study by Siu et al.[49] found an incidence of 20% of neonatal complications, and intrauterine growth restriction and prematurity were the most frequent. The predictors of these complications were the same as those mentioned for maternal risk, in addition to the use of anticoagulants, twin pregnancy, smoking and maternal age less than 20 years or greater than 35 years. In the ZAHARA study[36], the independent predictors of obstetric risk were mechanical prosthetic devices, cyanotic heart disease, use of cardiovascular medication prior to pregnancy and noncardiological factors (smoking and twinning). It is interesting to note that, in these studies, the presence of pulmonary hypertension was not a predictor of obstetric or cardiac complications probably because it is underrepresented in the studied population (European and Canadian). In the study by Ruys[2] (ROPAC – *the Registry on Pregnancy and Cardiac disease*), which comprises a multicenter registry of 28 countries including many developing countries (where pulmonary hypertension is more prevalent), it was observed that pulmonary hypertension was an independent factor of precocious heart failure in pregnancy (before the 30th week); this may have led to more preterm deliveries.

In the series of patients analyzed in the ROPAC study[2,54] a relationship between the WHO classification and

the maternal and perinatal events was observed (Table 1). It was observed that the occurrence of adverse events was more intense according to the class to which the patients belonged.

Table 1 - distribution of maternal and perinatal events according to the WHO risk categories

	TOTAL	WHO class I	WHO class II	WHO class III	WHO class IV	P
Maternal mortality	1%	0	1%	1%	4%	0.086
Maternal hospitalization	26%	13%	18%	36%	66%	< 0.001
Cardiac insufficiency	12%	1%	6%	19%	57%	< 0.001
Cesarean sections	41%	27%	37%	49%	60%	< 0.001
Postpartum hemorrhage	3%	0	1%	5%	11%	< 0.001
Childbirth < 37 weeks	15%	9%	15%	17%	30%	< 0.001
Fetal death	2%	0	1%	3%	6%	0.001
Neonatal death	1%	1%	0	0	0	0.5
Newborn mean weight (grams)	3010	3109	3074	2925	2735	< 0.001
N	1321	241	514	504	53	-

SOURCE: Adapted from Ruys et al.[54]

We must also remember that pregnant women with congenital heart defects are at higher risk of having children with heart disease. The risk of congenital heart disease in the general population is 0.8 to 1% and is as high as 12% when one of the parents has heart disease. In specific cases, the risk may reach 50% in cases of DiGeorge, Marfan and Noonan syndromes, or in cases of hypertrophic cardiomyopathy (familial form)[39,44,45].

Prenatal assistance

The team of care for pregnant cardiac patients should be multidisciplinary and should be composed of obstetricians, cardiologists, anesthesiologists, pediatricians, nurses, psychologists, nutritionists, physiotherapists and social workers who are able to provide care for this population. Preferably, this assistance should be performed in a tertiary or quaternary care center. It is assumed that the initial evaluation should be performed as early as possible, and during this initial consultation, we should make the patient aware of the foreseeable risks of pregnancy and the importance of guidance follow-up and frequent follow-up.

As recommended by national[55,56] and international[52] guidelines, the local protocols[34] are as follows:

• Maternal weight control: It is important to minimize cardiac overload so that no excessive weight gain occurs, and occasionally, a low sodium diet may be recommended to control water retention;

• Rest: This recommendation will depend on the functional capacity of the heart according to the NYHA classification, which notes that the classification may be misleading since many patients may unconsciously reduce their physical effort within the limits of their dysfunction and deny any disability;

• Avoid smoking;

• Iron supplementation: Carefully evaluate the need for iron replacement, as anemia increases cardiac work;

• Detection and early treatment of infections (infectious processes also increase cardiac work);

• Cardiovascular drug therapy: Therapy should be re-evaluated by adjusting the dose and substituting drugs that may impair the inception of disease, such as oral anticoagulants (in the period of embryogenesis), angiotensin II converting enzyme inhibitors, angiotensin II receptor blockers and hydantoinates. Statins and spironolactone are also contraindicated; the use of warfarin should be judicious and should be reserved for patients with mechanical valve prostheses or chronic atrial fibrillation with high thrombotic risk. Amiodarone should be avoided (because of the risk of neonatal hypothyroidism) and should be used only for severe arrhythmias that do not respond to other drugs. Virtually all other cardiovascular medications can be administered if the benefit outweighs the potential risk;

• Prevention of rheumatic disease: This is indicated in patients with rheumatic valvulopathy. Benzathine penicillin should be administered – 1,200,000 IU every 21 days throughout gestation to decrease the risk of new rheumatic events during this period;

• Prophylaxis for bacterial endocarditis (infective endocarditis – IE): Although antibiotic prophylaxis for IE is questioned in uncomplicated obstetric procedures, we recommend this measure since complications or contamination cannot always be anticipated in the daily

practice of obstetrics. Antibiotic prophylaxis is indicated before post-abortion curettage, vaginal deliveries, cesarean sections and invasive obstetric procedures, in moderate- to high-risk patients for IE (valvulopathy, women with valve prosthesis, complex congenital heart disease or systemic-pulmonary surgical shunts or any patient with a history of IE), according to the scheme below:

o Intravenous administration of 2 g of ampicillin and 1.5 mg/kg gentamicin (up to 120 mg) prior to the procedure – in cases of allergy to penicillin and derivatives, 1 g of vancomycin intravenously (diluted in 100 ml of saline solution, infuse in one hour);

o For dental procedures, endoscopy, and procedures in infected tissues, 2 g of amoxicillin orally, one hour before the procedure – in case of allergy to penicillin derivatives, 600 mg of clindamycin or 500 mg of azithromycin.

• Inhibition of preterm labor: Initially, we must determine whether labor is being caused by cardiac decompensation. Often, with improvement in the clinical condition and tissue perfusion, the contractions reduce and may even cease. In cases of low functional reserve and flow obstructions (valve stenosis, moderate or severe ventricular dysfunction), the use of tocolytics is contraindicated due to the risk of worsening the cardiovascular condition. In other situations, atosiban can be used judiciously and always in places with intensive care (due to the risk of acute pulmonary edema associated with tocolysis and the use of corticosteroids for fetal lung maturation).

• Corticosteroid therapy for fetal lung maturation: may cause blood volume overload and may precipitate or worsen heart failure. This therapy should not be used routinely. It is recommended that this be used judiciously and always in a hospital environment with adequate clinical support[34].

• Prevention of thromboembolism: The cardiological situations that most frequently require anticoagulant therapy in pregnancy are mechanical prostheses, atrial fibrillation, history of thromboembolism, intracavitary thrombus, congestive heart failure (CHF), risk of arterial or venous thrombosis and risk of pulmonary embolism.

The most appropriate anticoagulation regimen in patients with mechanical valve prostheses has not yet been established. Alternative proposals have been considered, and the most accepted is the following[34,44]:

o First trimester: use subcutaneous heparin (maintain APTT twice that of baseline value) or low molecular weight heparin – 1 mg/kg every 12 h. In this case, monitoring the heparin activity (or antiXa between 0.6 and 1.0) is recommended;

o From the 13th to the 36th week of gestation, use oral anticoagulant (dosing according to the International Normalized Ratio (INR)), maintain INR = 2.5 to 3.5. The control of oral anticoagulants should be more frequent during pregnancy due to the increase in the procoagulant factors during pregnancy and also due to the risk of fetal hemorrhage in cases of high INR;

o Between the 34th and 36th weeks, return to heparin and schedule delivery. During labor induction, use intravenous heparin and stop the infusion when the patient goes into labor. Reintroduce heparin 6 to 12 hours postpartum;

o In the puerperium, transition to oral anticoagulants as soon as is safe with respect to perioperative bleeding by suspending heparin (regular or low molecular weight) when the INR is in the appropriate range.

In cases of atrial fibrillation, there is a tendency to adopt the same behavior, although no studies on pregnant women have been published. In the other cited cases, low molecular weight heparin (or even regular heparin) may be used in prophylactic or therapeutic doses (discuss case by case with the cardiology team).

Complementary examinations: Complementary examinations should be requested for the diagnosis and follow-up of patients with heart disease; these include rheumatic function tests, electrocardiogram, echocardiogram and others as required by each clinical situation.

Cardiac procedures*:* If indicated, electrical or medical cardioversion and even pacemaker implantation may be performed. Valvuloplasty and cardiac surgery, when necessary, should be performed between 13 and 28 weeks, which is a more favorable period for the mother and the fetus. Due to the high risk of fetal and maternal morbidity, surgery during pregnancy is recommended only for cases that are refractory to clinical treatment.

Scheduling of follow-ups*:* The management depends on the severity of the cardiac injury. WHO class 3 and 4 patients may require more frequent returns or even prolonged hospitalizations for maternal clinical surveillance and fetal vitality.

Birth and puerperium care

Decisions regarding the time of resolution of pregnancy and mode of delivery in women with heart disease are still a subject of debate in the literature[57,58]. The timing of delivery will depend on maternal and fetal conditions. In patients without hemodynamic repercussions and good fetal evolution, term should be reached, and a spontaneous labor is preferred. In patients in the WHO class 3 group, such as those with more severe disease and greater hemodynamic repercussions, it is recommended that delivery be anticipated (from the 37th week). Labor induction may be indicated for fetal reasons (growth restriction, for example), for maternal reasons (worsening of clinical conditions) or to provide better logistical and therapeutic support in some cases (anticoagulant management, availability for intensive care in the puerperium)[34]. In the cases of patients with significant

clinical repercussions, such as heart failure refractory to clinical treatment, delivery will be indicated, regardless of gestational age[34,52,56].

Regarding the mode of delivery, there is a trend towards a liberal indication of cesarean sections in this population (even without evidence) due to the fear of hemodynamic changes related to labor and delivery[58]. However, in cesarean sections, there is a greater risk of blood loss, infections and thromboembolic phenomena, which should be considered at the time of its indication. Except for a few situations, the delivery route is indicated by obstetric conditions[52,56,58]. Cesarean section indications for cardiac reasons are reserved for patients at risk of aortic dissection (coarctation of the aorta, or Marfan syndrome with ascending aorta diameter greater than 40 mm), and in patients under oral anticoagulation at the time of delivery (due to the risk of fetal cerebral bleeding due to the plastic phenomena of delivery). The relative indications of cesarean section are severe aortic stenosis, recent myocardial infarction, severe pulmonary hypertension and decompensated heart failure. In these cases, maternal risks, duration of delivery, available resources and fetal condition should be considered[34,56,58].

Neuraxial analgesia promotes a reduction in hemodynamic overload due to labor and is recommended in all patients with heart disease and should be indicated early[16,28]. During labor, the patient should be kept in a lateral position (to facilitate venous return) or in a high decubitus position[34]. Fluid administration should be reduced and monitored, especially during induction, due to the antidiuretic effect of oxytocin[52,55]. Maternal monitoring should be careful, with cardiac auscultation, pulmonary auscultation, control of diuresis, cardioscopy and oximetry, and blood pressure monitoring. In cases of greater hemodynamic instability, intra-arterial pressure control may be used; currently, monitoring with central catheters is rarely indicated[29,59]. At the time of the expulsive period, abbreviation with forceps or a vacuum-extractor is recommended in patients with hemodynamic repercussions to avoid the cardiac output oscillations related to the pushes. The risk of bleeding is increased during delivery in patients with heart disease, especially in those receiving anticoagulants, those who are cyanotic and those with pulmonary hypertension. Strict hemostasis and caution regarding uterine hypotonia are recommended. The use of ergot alkaloids and bolus oxytocin is contraindicated, and when more uterotonic agents are needed, rectal misoprostol is preferred[34,52,56].

Locoregional analgesia is widely recommended for vaginal deliveries, while general anesthesia may be indicated in cesarean sections in patients with limited hemodynamic reserve, depending on the maternal clinical condition, the urgency of the procedure and the experience of the anesthesiologist. Regardless of the route of delivery, neuraxial anesthesia is contraindicated in patients treated with anticoagulants. Peripartum anticoagulation management aims to reduce anesthetic risks and maternal bleeding. Heparin should be suspended from 12 to 24 hours before the procedure (depending on the dose used) and reintroduced up to 12 hours after delivery[34].

In the puerperium, more attention is required, as approximately two-thirds of maternal deaths related to heart disease occur in this period[8]. The increase in blood volume in the first days after delivery may precipitate clinical decompensation in addition to the risks associated with the occurrence of anemia, thromboembolism and infection. The patients should receive intensive care within the first 24 or 48 hours after delivery, and discharge must be delayed. Antithrombotic prophylaxis should be considered in all patients with heart disease, even those who did not use it prior to delivery, because of the increased risk of thromboembolism in the puerperium. The adjustment to the drug therapy is initially achieved in a hospital environment, which has more options; therapy consists of converting enzyme inhibitors and angiotensin II receptor blockers (allowed in this phase, even in nursing mothers) and more liberal use of diuretics. Discharge will be allowed only once the patient has stabilized[34,52,55,56]. In the late puerperium, appropriate contraception should be recommended for that period depending on the clinical condition of the patient.

In summary, gestation in a patient with heart disease represents a hemodynamic challenge, with important maternal and perinatal repercussions. Adequate care avoids more serious complications and should be offered by a multiprofessional team in places with adequate resources and should aim to reduce the morbidity and mortality of the maternal-fetal binomial.

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