


# Accuracy of Prenatal Diagnosis of Congenital Cardiac Malformations

## Acurácia do diagnóstico pré-natal de cardiopatias congênitas

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### Abstract

**Objective** To evaluate the accuracy of the diagnosis of fetal heart diseases obtained through ultrasound examinations performed during the prenatal period compared with the postnatal evaluation.


**Methods** A retrospective cohort study with 96 pregnant women who were attended at the Echocardiography Service and whose deliveries occurred at the Complexo Hospitalar Santa Casa de Porto Alegre, in the state of Rio Grande do Sul, Brazil. Risk factor assessment plus sensitivity and specificity analysis were used, comparing the accuracy of the screening for congenital heart disease by means of obstetrical ultrasound and morphological evaluation and fetal echocardiography, considering  $p < 0.05$  as significant. The present study was approved by the Research Ethics Committee of the Institution.

**Results** The analysis of risk factors shows that 31.3% of the fetuses with congenital heart disease could be identified by anamnesis. The antepartum echocardiography demonstrated a sensitivity of 97.7%, a specificity of 88.9%, and accuracy of 93% in the diagnosis of congenital heart disease. A sensitivity of 29.3% was found for the obstetric ultrasound, of 54.3% for the morphological ultrasound, and of 97.7% for the fetal echocardiography. The fetal echocardiography detected fetal heart disease in 67.7% of the cases, the morphological ultrasound in 16.7%, and the obstetric ultrasound in 11.5% of the cases.

**Conclusion** There is a high proportion of congenital heart disease in pregnancies with no risk factors for this outcome. Faced with the disappointing results of obstetric ultrasound for the detection of congenital heart diseases and the current unfeasibility of universal screening of congenital heart diseases through fetal echocardiography, the importance of the fetal morphological ultrasound and its performance by qualified professionals is reinforced for a more appropriate management of these pregnancies.

### Keywords

- ▶ fetal heart disease
- ▶ fetal echocardiography
- ▶ morphological sonography

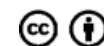
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**Resumo**

**Objetivo** Avaliar a acurácia do diagnóstico de cardiopatias congênitas obtidos por meio das ecografias realizadas durante o pré-natal comparativamente à avaliação pós-natal.

**Métodos** Estudo de coorte retrospectivo com 96 gestantes atendidas no Serviço de Ecocardiografia cujos partos ocorreram no Complexo Hospitalar Santa Casa de Porto Alegre, RS, Brasil. Utilizou-se a avaliação de fatores de risco e a análise de sensibilidade e especificidade, comparando-se a acurácia do rastreamento de cardiopatia congênita por meio da ecografia obstétrica, da avaliação morfológica e da ecocardiografia fetal, considerando-se como significativo um  $p < 0,05$ . O referido estudo foi aprovado pelo Comitê de Ética em Pesquisa da Instituição.

**Resultados** A análise de fatores de risco demonstra que 31,3% dos fetos com cardiopatia congênita poderiam ser identificados pela anamnese. As ecografias anteparto possuem sensibilidade de 97,7%, especificidade de 88,9% e acurácia de 93,0% no diagnóstico da cardiopatia congênita. Ao se analisar cada tipo de ecografia separadamente, encontrou-se sensibilidade de 29,3% para a ecografia obstétrica, de 54,3% para ecografia morfológica, e de 97,7% para ecocardiografia fetal. A ecocardiografia fetal definiu a cardiopatia fetal em 67,7% dos casos, a ecografia morfológica em 16,7%, e a ecografia obstétrica em 11,5%.

**Conclusão** Demonstra-se uma elevada proporção de cardiopatia congênita em gestações sem fatores de risco para esse desfecho. Frente aos resultados desanimadores da ecografia obstétrica para a detecção de cardiopatias congênitas e na atual inviabilidade de rastreamento universal de cardiopatias congênitas por meio da ecocardiografia fetal, reforça-se a importância da ecografia morfológica fetal e sua realização por profissionais qualificados para esse fim de forma a permitir o manejo mais adequado destas gestações.

**Palavras-chave**

- ▶ cardiopatia fetal
- ▶ ecocardiografia fetal
- ▶ ecografia morfológica

**Introduction**

Congenital cardiopathies are the most frequent malformations related to morbidity and mortality during infancy.<sup>1</sup> They present an incidence estimated at between 6 and 12 in each 1,000 newborns.<sup>2</sup> The treatment of these malformations represents the highest hospital cost for congenital diseases in first world countries.<sup>1</sup> Half of the incidence is formed by “minor” cardiopathies, considered not severe, being easily corrected through interventional catheterization or surgery, and the other half by “major” cardiopathies, defined as those that need surgical intervention in the first year of life, being responsible for more than 50% of the deaths due to congenital anomalies during infancy.<sup>3</sup> A study conducted by Moons et al<sup>4</sup> describes an incidence of 8.3% in newborns and stillborns with a gestational age  $\geq 26$  weeks and without chromosomic alterations.<sup>4</sup>

The indications for fetal echography are intimately related to the recognition of possible etiologic factors and of risk groups for congenital cardiopathy.<sup>2,3</sup>

A vast number of factors is associated with the augmented risk of the presence of a congenital cardiopathy, such as family history of cardiopathy, maternal diseases and/or fetal conditions. The main indication for echocardiographic fetal evaluation is the suspicion of structural abnormality in the obstetric echography, which performs the diagnosis of fetal

cardiologic anomalies in between 40 and 50% of the cases. Other factors, such as a metabolic disorder in the mother or a family history of congenital cardiac disease are also reasons to perform the specific screening exam.<sup>2</sup> In addition, the effects of environmental exposures to elements such as lithium, alcohol and cigarette smoke may compromise the development of the vascular system that, according to animal-based hemodynamic studies performed on vitelline and placental circulations, had demonstrated a relationship with changes in normal heart and vascular development.<sup>5</sup>

In the course of the last decade, there was an increase in the prevalence of congenital cardiopathy diagnosed during prenatal period, especially due to the improvement of obstetric screening.<sup>6</sup> The diagnosis of congenital cardiopathy during prenatal is considered beneficial for the neonate, allowing the preparation of the team and the immediate delivery of the newborn to specialized pediatric medical assistance, therefore decreasing the morbidity that occurs because of metabolic alterations, acidosis, hypoxemia, and target organ damage, besides preventing major emotional trauma in the parents, providing them with enough time to understand the disease and with a clear and real idea of the prognosis of the fetus.<sup>7</sup>

Considering the importance of the prenatal cardiac diagnosis, our study has the objective to evaluate the accuracy of

echography scans performed during prenatal period in relation to the outcomes found as neonatal cardiopathies.

## Methods

This is a study of a retrospective cohort with pregnant women attended at the Irmandade Santa Casa de Porto Alegre (ISCMPA, in the Portuguese acronym), in the Echocardiography Service at the Santo Antônio Hospital, in Porto Alegre, state of Rio Grande do Sul, Brazil, between March 2013 and December 2015, with data collected from electronic records. The study was approved by the ethics committee of the Institution/Brazil Platform, under the supervision of the Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA, in the Portuguese acronym) (protocol n° 1375733), accepted in November 2015.

The study group comprised fetuses with altered exams, in which were included all cases of fetal cardiopathies diagnosed during the period covered by the research, amounting an initial sample of 148 cases. Obstetric or morphological ultrasound was performed before the fetal echocardiography, and there was no influence of the echocardiography on the obstetric or morphological ultrasound in the diagnosis of congenital cardiac malformation. The exclusion criteria were births outside the maternity of the hospital, twin gestations, and stillborn fetuses, with 52 cases excluded. Only the newborns who underwent neonatal exams in the hospital were included. Neonatal echocardiography was considered the gold standard for congenital cardiopathy. The final sample comprised 96 expecting women in the study group. Other 90 pregnant women were included to form the control group, who underwent fetal echocardiography with normal results, to evaluate accuracy. The fetal and neonatal echocardiography exams were performed by pediatric specialists in fetal and neonatal echocardiography in the institution. Other obstetric and morphologic exams came from several places, such as clinics and public and private hospitals.

The study compared the diagnosis obtained through fetal echography with the final diagnosis determined after birth, obtaining through these analyses the accuracy of the ultrasonography for diagnosing congenital cardiopathy, as well as evaluating the frequency and the type of alterations that were found.

The estimates of the sample size were calculated using the software WinPEPI (Programs for Epidemiologists for Windows), version 11.43 (Brixton Health, Llanidloes, United Kingdom, Wales), and were based on studies by Wald et al (2007)<sup>8</sup> and by Durand et al (2015).<sup>9</sup> For a confidence level of 95%, and an error margin of 10%, the minimum necessary total of 96 exams was obtained.

The data analysis was made in IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp, Armonk, NY, USA). The quantitative variables were described by average and standard deviation (SD) or by median and interquartile range, and the qualitative variables through absolute and relative frequencies. The incidence was identified, with a confidence interval (CI) of 95% for the estimation of the population and sensibility for each specific type of identified congenital

anomalies, analyzing the accuracy according to the image method that was used, either a conventional obstetric echography or a morphologic study, evaluating the agreement between the diagnostic methods through the kappa coefficient. The association among the variables was evaluated by the Pearson chi-squared test. Values of  $p < 0.05$  were considered statistically significant.

## Results

Considering the analysis of risk factors, 20.8% of the evaluated expectant mothers were of advanced maternal age, of which 8.4% presented diabetes mellitus, while 2.1% presented an obstetric or familial history of cardiopathy. As to the moment of diagnosis, the cardiopathies were identified in the second trimester of the pregnancy in 35.4% of the cases, and in the third trimester in 64.6% of the cases. There was an association with other non-cardiac malformations in 30.2% of the cases. In 17.7% of the cardiopathy cases, the pregnant women suffered from diabetes mellitus (DM), considering that, of these, 17.6% were type I; 29.4% suffered from DM type II, and 52.9% suffered from gestational DM. The association between DM and other non-cardiac malformations was not significant. ► **Table 1** demonstrates the characteristics of the study group according to the risk factors in which the echocardiography was performed. From the 96 cases studied, 35 evolved to death after birth, bearing in mind that 82.9% of these deaths were caused by the cardiopathy. Among the patients that passed away, the cardiopathies were complex, the majority with multiple cardiac malformations (31%), hypoplasia of the left ventricle (17.2%), and great vessels transposition (13.7%).

Our study showed a sensitivity of 97.7%, a specificity of 88.9%, and an accuracy of 93.0% in the diagnosis of congenital cardiopathy during the prenatal period. Ninety-six percent of the pregnant women of the study underwent at least one obstetric echography, but only 36.5% underwent a morphological echography. While analyzing each type of echography separately, we found a sensitivity of 29.3% for the obstetric echography, of 97.7% for the morphologic echography, and of 97.7% for the fetal echocardiography ( $p < 0.05$ ).

**Table 1** Characteristics of the study group according to the risk factors in which the echocardiography was performed

Risk factors	n (%)
Advanced maternal age	20 (20.8)
Diabetes	17 (17.7)
DM 1	(17.6)
DMG	(52.9)
DM 2	(29.4)
Cardiopathy in the family	2 (2.1)
Neonatal mortality	35 (36.5)
Associated non-cardiac malformation	29 (30.2)

Abbreviations: DM1, diabetes mellitus type 1; DM2, diabetes mellitus type 2; DMG, gestational diabetes mellitus.

**Table 2** Characteristics of study group according to cardiopathies identified in newborns

Cardiopathies identified in newborns	n (%)
Multiple cardiac malformations	21 (21.9)
Hypoplastic left heart syndrome	14 (14.5)
Transposition of the great vessels	11 (11.5)
Tetralogy of Fallot	9 (9.4)
Atrioventricular septal defect	7 (7.3)
Pulmonary valve atresia	4 (4.2)
Hypoplastic right heart syndrome	4 (4.2)
Aortic stenosis	2 (2.1)
Ebstein anomaly	2 (2.1)
Hypertrophic cardiomyopathy	2 (2.1)
Others*	9 (9.4)
Normal**	11 (11.4)

\*Others include one case for each of the cardiac pathologies listed below: coarctation of the aorta, constriction of ductus arteriosus, cardiac tumor, ventricular septal defect, pulmonary stenosis, left isomerism, atrioventricular block, common arterial trunk, Taussig-Bing anomaly; \*\* Congenital heart disease was not confirmed after birth (5 constriction of ductus arteriosus, 4 ventricular septal defect, 1 coarctation of the aorta and 1 hypertrophic cardiomyopathy).

The fetal echocardiography contributed to the diagnosis of the cardiopathy in 67.7% of the cases, the morphologic echocardiography in 16.7%, and the obstetric echocardiography in 11.5% of the cases. The most frequent prenatal diagnosed pathologies were multiple cardiac malformations (18.8%), major vessels transposition (11.5%), hypoplasia of the left ventricle (11.5%), tetralogy of Fallot (9.4%), atrioventricular septum defect (7.3%), and constriction of the arterial canal (6.3%). **Table 2** demonstrates the characteristics of the study group according to the cardiopathies identified in the postnatal echocardiography.

## Discussion

Nowadays, the indications to perform a fetal echocardiography are restricted to some situations considered of risk. However, the prenatal diagnosis of cardiopathies is of paramount importance to enable a better monitoring of the fetus, allowing to plan the birth of the cardiopathic fetus in a center of reference, improving the survival of the newborn.<sup>1-3,10-14</sup> Studies have shown that there is a better survival rate after the surgical correction of the cardiopathy when the diagnosis of the anomalies is performed during the pregnancy instead of during the postnatal period.<sup>15,16</sup> There is proof of a decrease in costs considering the necessity of transportation to the intensive care unit (ICU) and the plan to use prostaglandin, which is highly utilized for opening the arterial canal.<sup>17</sup> Other possible advantage comprises the prevention of trauma in parents who need time to understand the physiopathology of the disease and its outcome.<sup>7</sup>

Among the risk factors of congenital cardiopathy, advanced age of the mother, use of medication, maternal or familial

cardiopathy stand out. Our study shows that a high proportion of congenital cardiopathy cases detected in the prenatal period is diagnosed in women who do not present the known risk factors.<sup>7</sup> This finding corroborates to the performance of fetal echocardiographic exams for the general population of pregnant women despite the evidence yet insufficient to include this conduct during prenatal period.<sup>18</sup>

The importance of the prenatal diagnosis is also shown in the number of newborns that went to the neonatal ICU (87%), plus the necessity of surgery (50%), allowing a better organization before the birth when the diagnosis is already known.<sup>1</sup>

Obstetric echocardiography is not considered the ideal exam for detecting cardiopathies because a large number of cases is not detected through this exam.<sup>19</sup> The low rate of detection of cardiopathies in obstetric ultrasounds is found in other revisions, as cited by Khoo et al<sup>20</sup> in their Australian study, in which the detection of cardiac malformation in the obstetric exam was of 22.5%, considering that, in this study, 96% of the patients underwent at least one obstetric echocardiography. This same conclusion was reached in the United States, in Ohio, where the rates of cardiac anomalies detection were < 50% with obstetric echocardiography.<sup>21</sup> Previous studies emphasize the importance of routine fetal tracking for cardiopathy through fetal echocardiography due to the fact that this exam is more sensitive and specific,<sup>1-8,11-14,22-26</sup> which is in line with what has been found in our study, in which the sensitivity of fetal echocardiography was superior to other ultrasounds.

Despite the recommendation of the American Institute of Ultrasound in Medicine<sup>27</sup> for sonographic cardiac screening examination including four-chamber view, left and right ventricular outflow tracts, the report of the sonographic examination should also document the nature of eventual technical limitations, such as increased maternal abdominal wall thickness. We are not sure how the sonographic cardiac screening examination was performed, if it included in fact four-chamber view and ventricular outflow tracts. In general, obstetric echocardiography has a summarized description of the ultrasound report. This data is important because it actually expresses the real way how the description of the sonographic cardiac screening is obtained in the majority of the obstetric exams in the daily assistance, which, in spite of its evolution in the last decade, it is still far from the ideal.

Our observation is similar to what has been reported in a recent article that concludes that, despite revised obstetrical guidelines highlighting the importance of outflow tract imaging, referrals and prenatal diagnosis of these types of critical congenital heart disease remain low. Education of obstetrical sonographers and practitioners who perform fetal anatomic screening is vital to increase referrals and prenatal detection of critical outflow tract anomalies.<sup>28</sup>

In the present study, differently from international studies, the cardiac malformation diagnosis in most cases was obtained in the third trimester, which was possibly a reflex of the health conditions in our region, where echocardiography is performed later on, as well as the pregnancy diagnosis, also making it difficult the access to tertiary services.

The detection rates of cardiopathies in routine obstetric exams are low. However, fetal echocardiography is a

sensitive and specific tool for the detection of these pathologies. Based on these findings, we stress the importance of a detailed fetal morphological exam in an audited service, with properly trained echographers enabled to ratify the fetal echocardiography whenever facing an unsatisfactory exam during the prenatal evaluation, in order to facilitate the optimization in the rate detection of congenital fetal cardiopathies, enabling the handling of these cases.

Despite the limitations arising from a retrospective study and the limited sample, the present study has among its strengths the adherence to the inclusion criteria, so that it allowed the integral monitoring, in a longitudinal study, of the evaluation of the risk factors, and in obtaining the definitive diagnosis with the birth of children in a reference hospital in the South of the country. The fetal echocardiography screening can be used in the evaluation of low-risk fetuses examined as part of the routine prenatal care, enabling a more accurate diagnosis of cardiac defects. Knowing that the risk of cardiopathy of the population in general is of ~ 1%, there would be an indication for fetal echocardiography, considering the favorable cost-benefit, in all situations when the absolute risk is higher than this amount, according to the following subdivision: high risk when the absolute risk is estimated > 2%, low risk when the absolute risk is estimated between 1 and 2%, and absence of risk when the absolute risk is < 1%, without indication for fetal echocardiography in the last case.<sup>2</sup>

In addition, according to updated guidelines, a fetal echocardiogram should be performed if congenital heart defect is suspected, if the normal four-chamber and outflow tract views cannot be obtained at the time of screening, or if recognized risk factors indicate an increased risk of congenital cardiac anomalies.<sup>29</sup>

## Conclusion

In conclusion, based on the results shown in the present study, we highlight the limitation of screening based on a strategy of risk factor evaluation for congenital cardiopathy to indicate fetal echocardiography, as well as discouraging results of exclusive monitoring through obstetric echography, becoming morphological echography a better option with eventual complementation by mean of fetal echocardiography, in face of unsatisfactory results obtained in the revision of fetal anatomy in a way that allows the adequate management of these gestations.

### Contributors

Pinheiro D. O., Varisco B. B., Silva M. B., Duarte R. S., Deliberali G. D., Maia C. R., Jiménez M. F., and El Beitune P. designed the study, analyzed and interpreted the data, wrote the article and approved the final version of the manuscript for publication.

### Conflicts of Interest

The authors have no conflicts of interest to declare.

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