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ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Fetal echocardiography – 25 years of experience in Serbia

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SUMMARY
Introduction/Objective Congenital heart diseases are the most common congenital anomalies. The objective of the study was to determine reliability, specificity, and sensitivity of fetal echocardiography in detection of congenital heart diseases in a referral center for fetal echocardiography.
Methods We analyzed 14,500 fetal echocardiography exams (FEC) between 1991 and 2014, performed in two tertiary centers.
Results The average maternal age at the time of diagnosis was 32 years. The mean gestational age at the time of diagnosis was 25.9 weeks. The most common indications for FEC were suspicious abnormal cardiac findings in obstetrical screening sonography (50.6%). Among 9,055 examined fetuses, pathological finding on the fetal heart was found in 638 cases. The most common congenital heart diseases were structural anomalies of the fetal heart in 81%, of which 13.3% were fetuses with hypoplastic left heart syndrome and 11.2% with ventricular septal defect. Of all fetuses with diagnosed congenital heart defect, 46.2% were born alive and had good postnatal prognosis, while 2.7% died *in utero*, and 10.6% died in the early neonatal period. Pregnancy was terminated in 40.4% of fetuses with severe congenital heart defect. Sensitivity of the diagnostic procedure in our study was 95.9%, and specificity was 99.9%.
Conclusion Our study proves that FEC is a reliable, informative diagnostic tool in detecting congenital heart defects with high specificity and sensitivity. With multidisciplinary approach, it provides an optimal time window for improving perinatal outcome.
Keywords: prenatal diagnosis; congenital heart defect; perinatal outcome; fetal echocardiography

INTRODUCTION

Congenital heart diseases (CHD) are among the most common congenital anomalies, with incidence 4–13 per 1,000 newborns [1]. Early prenatal diagnosis is considered essential because it allows early intervention. Fetal echocardiography as a diagnostic procedure was introduced between 1970 and 1980 [2, 3]. With the advancement of technology and interdisciplinary approach, prenatal diagnosis of CHD with fetal echocardiography has resulted in a decrease of morbidity and mortality of these patients [4, 5].

The aim of this study was to analyze recent trends in the indications of fetal echocardiography and to evaluate the reliability of fetal echocardiography as a method for prenatal diagnosis of CHD at a tertiary referral center in Belgrade, Serbia.

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METHODS

We analyzed the fetal echocardiography databases form Clinic of Gynecology and Obstetrics, Clinical Centre of Serbia and University Children`s Hospital in Belgrade in the period from 1991 to 2014, and reviewed the medical records of 9,055 fetuses from 8,838 pregnancies (217 multiple gestations). We divided all findings into normal and abnormal ones and then analyzed the abnormal findings. The clinical data we collected for this retrospective study were gestational age at the time of diagnosis, maternal age at the time of diagnosis, indications, results of fetal echocardiography, and perinatal outcome. Fetal echocardiography was performed by an experienced perinatology specialist and a pediatric cardiologist.

Indications

We classified indications for fetal echocardiography among the diagnosed CHD into five categories: abnormal cardiac findings at obstetric ultrasonography, extracardiac findings at obstetric screening, maternal risks, familial risks, and teratogenic risk factors.

Fetal echocardiography results and the postnatal outcome in fetuses with congenital heart disease

All results were classified into normal and abnormal. All abnormal results were divided into three subclasses: structural anomalies, arrhythmias, and structural anomalies with arrhythmias.

Structural anomalies were then stratified into fife subclasses: valvular/obstructive abnormalities of the left/right heart [hypoplastic left heart syndrome (HLHS), aortic stenosis, coarctation of the aorta, stenosis and atresia of the mitral valve / stenosis and atresia of the pulmonary valve, atresia and dysplasia of the tricuspid valve and Mb. Ebstein], shunt lesions [atrial septal defect (ASD), ventricular septal defect (VSD), atrioventricular septal defect (AVSD), total anomalous pulmonary venous return (TAPVR)], complex abnormalities (tetralogy of Fallot with or without agenesis of the pulmonary valve, complete transposition of the great arteries, double outlet right ventricle, common pulmonary artery), cardiomyopathy, and rare anomalies.

Perinatal outcome and treatment options were analyzed according to the obtained data for each class of diagnosed CHD.

Statistics

The obtained data was presented descriptively, by percentage and indicators of diagnostic accuracy: sensitivity and specificity.

RESULTS

Indications

The most common indication for fetal echocardiography was an abnormal cardiac finding in obstetric screening in 323 pregnancies (50.6%). The second most common indication was abnormal extracardiac finding in obstetric screening (245 pregnancies – 38.4%). Positive family history was an indication for 41 pregnant women (6.4%). Maternal risk factors were indications in 26 (4%) and teratogenic factors in three (0.4%) cases.

Fetal echocardiography results in fetuses with congenital heart disease

Among the 9,055 pregnancies, CHD was diagnosed in 638 (7.2%) cases.

Of 638 fetuses with CHD, structural anomaly was found in 515 (81%) cases. Valvular/obstructive abnormalities of the left heart were found in 106 (20.1%) fetuses: HLHS in 70 (13.3%), coarctation of the aorta in 22 (4.1%), atresia of the mitral valve in eight (1.5%), and aortic stenosis in six (1.1%) cases.

Valvular/obstructive abnormalities of the right heart were found in 95 (18%) fetuses: pulmonary artery atresia in 32 (6.0%), pulmonary artery stenosis in 15 (2.8%), tricuspid valve atresia in 15 (2.8%), tricuspid valve dysplasia in 16 (3.0%), and M. Ebstein in 17 (3.2%) cases.

Shunt abnormalities were found in 123 (23.3%) fetuses: ASD in 16 (3%), VSD in 59 (11.2%), AVSD in 46 (8.7%), and TAPVR in two (0.4%) cases.

Complex CHD were found in 158 (29.9%) fetuses: T. Fallot in 30 (5.6%), T. Fallot and agenesis of pulmonary valve in nine (1.7%), univentricular heart in 29 (5.5%), common truncus arteriosus in 10 (1.9%), double outlet right ventricle in 46 (8.7%), transposition of the great arteries (TGA) in 29 (5.5%), and L-TGA in five (0.9%) cases.

Cardiomyopathy was found in 13 (2.5%) and rare anomalies in 33 (6.2%) fetuses.

Isolated arrhythmia had 110 (17%) fetuses. Structural anomaly with arrhythmia was found in 13 (2%) fetuses.

Perinatal outcome in fetuses with congenital heart disease

Among 638 fetuses with CHD, 295 (46.2%) were born alive and survived the neonatal period. The highest survival rate was noticed in fetuses with arrhythmias (33.5%) and shunt anomalies (24%). Of the total number of diagnosed CHD, the most common anomalies among live-born children were isolated VSD (6.5%), TGA (3.3%) and T. Fallot (2.9%).

In utero, lethal outcome occurred in 17 fetuses (2.7%). The most common structural anomaly in fetuses from this group was HLHS (11.8%).

In the early neonatal period, 68 children (10.6%) died. The highest mortality rates were in cases of cardiomyopathy (30.8%) and obstructive lesions of the left heart (21.7%).

Pregnancy was terminated in 258 (40.4%) cases with CHD.

Sensitivity and specificity of fetal echocardiography

Prenatally, 26 neonates with CHD were not diagnosed (12 with VSD, four with stenosis of the pulmonary artery, one T. Fallot with agenesis of the pulmonary artery, one with atresia of the pulmonary artery with VSD, three with critical coarctation of the aorta, one with critical stenosis of the aorta in twin pregnancy, one with TGA, two with TAPVR**,** and one with aortic-pulmonary septum).

In seven fetuses prenatally diagnosed with CHD, the diagnosis was not confirmed postnatally.

Sensitivity of the procedure in our group was 95.2%, and specificity was 99.91%.

DISCUSSION

Identification of congenital heart defects is important because they are the most common congenital anomalies, and in 50% they are the leading cause of neonatal deaths [6, 7]. Pregnant women with increased risk for giving birth to a child with CHD require more detailed evaluation of the fetal heart, as well as those with high risk for aneuploidy based on the combined screening [8, 9]. Theoretically, most congenital heart defects can be diagnosed prenatally and suspicion for them can arise at the recommended routine evaluation of fetal anatomy in the second trimester.

In a study from 1997 conducted in Belgrade, basic indications were family history in 42.6% of the cases, maternal infection in the first trimester (11.5%), maternal diabetes (9.6%), and indirectly suspected cardiac anomaly because

of the clinical manifestations of polyhydramnios or fetal arrhythmia (28.4%) [10]. In 2004, Friedberg reported that the most common indication were family history of CHD (23%) and maternal diabetes (18%). Obstetrical ultrasound indicating CHD accounted for only 13% [11]. Obstetric screening has only recently found an even greater prevalence of cardiac abnormalities.

Our results show that approximately half of all fetal echocardiographic exams have been performed because of abnormal cardiac findings at the obstetric screening (50.6%). The next common indication was the extracardiac finding at obstetric screening (38.44%). Other indications were familial (6.41%), maternal (4.06%), and teratogenic risk factors (0.47%).

Prenatal diagnosis of CHD allows parents to receive information on the diagnosis, the further course of pregnancy, and possible treatment before or after birth, which makes it easier for them to make a decision whether to continue the pregnancy or to terminate it earlier.

In our investigation that included 9,055 fetuses, CHD was diagnosed in 638 of cases. The incidence of CHD was 7.2%. This percentage is significantly higher than the incidence of CHD in the general population, because it is the population of pregnant women with increased risk for the development of fetal CHD. It is noticed that the prevalence of newborns with CHD is persistent over the last 15 years [12].

The most frequent were valvular obstructive lesions of the left heart, isolated in 201 (38.1%) cases, and associated with other anomalies in a total of 310 (58.7%) cases. The most common of obstructive abnormalities were the hypoplasia of the left heart, diagnosed in 70 (66.3%) cases, and pulmonary artery atresia (5.94%).

Isolated shunt lesions were diagnosed in 123 (23.3%) cases and associated with other anomalies in a total of 221 (41.7%) cases. Prenatal shunt and valvular lesion ratio is 1.6:1, and it does not correlate to the postnatal ratio, which is 1.3:1. Thus, our results correspond to those in the literature, where this ratio is 1.2–1.4:1 [13, 14]. Those findings are understandable, considering specific characteristics of fetal circulation.

Prenatally diagnosed complex CHD reduces neonatal morbidity and mortality. Out of the total number of diagnosed CHD, 295 (46.2%) newborns survived the fetal and neonatal period. These children had hemodynamically stable anomalies with a relatively favorable prognosis. The higher survival rate was noted in the group of children with isolated VSD (6.5%), TGA (3.3%), and T. Fallot (2.9%). There were no survivals in the group with hypoplastic left heart (0/70).

Lethal outcome *in utero* occurred in 17 fetuses (2.7%). The incidence of intrauterine fetal death in the group of fetuses with CHD was 2.7% (17/638). Supraventricular tachycardia with heart failure was the leading cause of intrauterine demise in 35.3%, followed by HLHS in 11.8%.

In the early neonatal period, 68 children died (10.6%). The highest mortality rate was among the neonates with cardiomyopathy (30.8%) and obstructive lesions of the left heart (21.7%). In our country, the prognosis of these pregnancies is unfavorable due to limited treatment options (e.g. heart transplantation), so the choice of treatment is usually reduced to palliative care.

The pregnancy outcome after the CHD diagnosis depends on many factors, but the most important one is certainly the type of defect, its prognosis, and its impact on the quality of life.

Termination of pregnancy may be an option in cases of complex heart defects known to have poor prognosis (HLHS) which could be diagnosed at the level of screening, but also in anomalies showing significant deterioration during repeated prenatal checks. In our study, termination of pregnancy was done in 258 (40.4%) cases after the diagnosis of CHD had been reached. All the fetuses had complex heart defects, and some also had chromosomal aberrations or extracardiac anomalies. In Serbia, termination of pregnancy for medical indications is legally defined and is not limited by the gestational age.

The sensitivity of fetal echocardiography in our study was 95.9% and specificity was 99.9%. The positive predictive value was 95.9% and the negative predictive value was 99.9%. These values were correlated with the results obtained from large global studies. The sensitivity is around 42%, and specificity is approximately 98%. The positive predictive value of echocardiography is about 90%, and negative predictive value is 93% [15].

The rate of detection in tertiary institutions is around 85–95% [16]. The largest discrepancies are related to the atrioventricular morphology and outlets of the great arteries. Our study shows that high accuracy rate could be achieved by the obstetrician if the sonographer is experienced and preferably trained by the pediatric cardiologist specialized in fetal echocardiography.

CONCLUSION

In our study, 26 neonates with CHD were not diagnosed prenatally (12 with VSD, four with stenosis of the pulmonary artery, one with T. Fallot with agenesis of pulmonary artery, one with atresia of the pulmonary artery with VSD, three with critical coarctation of the aorta, one with critical stenosis of the aorta in trigeminal pregnancy (in one of the triplets), one with TGA, two with TAPVR**,** and one with aortic-pulmonary septum). In seven fetuses, diagnosis made prenatally was not confirmed postnatally. False positive fetal echocardiography findings are rare, making the specificity of this method high, with over 90%. The most frequent false positive diagnoses were VSD and coarctation of the aorta.

Our study proves that fetal echocardiography is a reliable, informative diagnostic tool in detecting congenital heart defects with high specificity and sensitivity. With multidisciplinary approach, given the fact that Serbia is still a country in transition, with limited options for the treatment of congenital heart defects, it provides optimal time window for improving perinatal outcome.

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Фетална ехокардиографија – 25 година искуства у Србији

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САЖЕТАК

Увод/Циљ Урођене срчане мане су најчешће конгениталне аномалије.

Циљ рада је био да се утврде поузданост, специфичност и сензитивност феталне ехокардиорафије у постављању дијагнозе урођених срчаних мана.

Методе Анализирано је 14.500 феталних ехокардиографских прегледа (ФЕК) у периоду 1991–2014. године, који су вршени у у два терцијална центра.

Резултати Просечна старост трудница у тренутку постављања дијагнозе је била 32 године. Просечна гестацијска старост плода у тренутку постављања дијагнозе је била 25,9 недеља. Најчешћа индикација за ФЕК је била сумња на урођену срчануману у току рутинског прегледа (50,6%). Од укупно 9.055 фетуса патолошки налаз на срцу је дијагностикован код 638 фетуса. Најчешће урођене срчане мане су биле структурне аномалије код 81% фетуса, од којих су 13,3% били фетуси са хипоплазијом левог срца и 11,2% фетуси са вентрикуларним септалним дефектом. Од свих фетуса код којих је дијагностикована урођена срчана мана, 46,2% је рођено живо и имало добру постнаталну прогнозу, 2,7% је имало леталан исход *in utero*, а код 10,6% је леталан исход наступио у неонаталном периоду. Прекид трудноће је извршен код 40,4% фетуса са тешким урођених срчаним манама. Сензитивност ФЕК у нашој студији је износила 95,9%, а специфичност 99,9%.

Закључак ФЕК је поуздана, информативна дијагностичка процедура урођених срчаних мана, са високом сензитивношћу и специфичношћу. ФЕК уз мултидисциплинаран приступ пружа оптимални период за постављање дијагнозе и побољшање перинаталног исхода.

Кључне речи: пренатална дијагноза; урођене срчане мане; перинатални исход; фетална ехокардиографија