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ORIGINAL ARTICLE

Parents' request for termination of pregnancy due to a congenital heart defect of the fetus in a country with liberal interruption laws

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ABSTRACT

Objectives: This study aimed to evaluate the prenatal rate of congenital heart defects (CHDs) and the frequency of termination of pregnancy (TOP) due to a CHD, depending on the severity of the defect and concomitant diseases of the fetus.

Methods: The data were assessed retrospectively between 2002 and 2017. Ultrasound examination was performed mostly in the second trimester. For analysis, the CHDs were divided into three groups of severity and three groups of fetus impairment.

Results: A total of 40,885 fetuses underwent echocardiography. The CHDs were detected in 1.0% (398/40,885) and were an isolated anomaly in 69% (275/398). Forty-nine percent (197/398) of families decided to TOP. In all groups of severity, the rate of TOP rose linearly when comparing isolated defects and cases with associated morphological and genetic impairments. The TOP was significantly dependent on the associated anomalies in patients with the most correctable defects ($p < .001$) and the severity of CHDs in isolated cases without any other impairment ($p < .001$).

Conclusion: The parents' decision to terminate increased with the severity of the defect and the associated anomalies of the fetus. The parents were mostly influenced by the associated anomalies when the CHD was correctable, and genetic factors played a more important role than morphological ones.

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KEYWORDS
Congenital heart defect; fetal echocardiography; screening; termination of pregnancy

Introduction

Congenital heart defects (CHDs) are the most frequently observed congenital defects in the human population [1], representing up to 40% of all congenital malformations [2]. The etiology of CHDs is complex, as genetic and environmental factors play a part [3]; however, multifactorial and unclear influences prevail and have led to a multifactorial hypothesis regarding the etiology [4]. The prevalence of CHDs is typically reported as 6–8 cases per 1000 live births [5], but the number varies in different studies from 4/1000 to 50/1000 cases [6].

Most CHDs can be detected prenatally [7]. In the Czech Republic, ultrasound examination of the fetal heart (fetal echocardiography) is performed during prenatal screening for CHDs by a gynecologist, pediatric cardiologist, or geneticist. With the improving quality of the ultrasound screening of CHDs and earlier examination in the first trimester [8], the number of diagnosed heart defects has increased. If a pathology is suggested, the workup will include further evaluation of extracardiac anomalies and additional genetic testing. The parents are always fully informed and have the option to continue or terminate the pregnancy [9]. In the Czech Republic, the pregnancy is possible to terminate by gestational age 24 weeks when either chromosomal or structural abnormality is present, and this country has a high incidence of termination of pregnancy (TOP). Unfortunately, with the increasing success of prenatal diagnostics, the number of TOP due to a CHD of the fetus also rises. The TOP decision of parents is not only influenced by the finding of the defect but also by its severity and the associated genetic or morphological anomalies of the fetus.

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Here, we attempted to analyze these factors and understand the decisions of parents regarding the future course of pregnancy when a CHD is diagnosed. Therefore, the aim of the study was to evaluate the prenatal rate of CHDs and to assess the frequency of TOP due to a CHD, depending on its severity and concomitant diseases of the fetus.

Materials and methods

This study is a case series from the Department of Pediatric and Prenatal Cardiology, University Hospital Ostrava, Czech Republic, a tertiary center. The unique aspect of this tertiary center is that all pregnant women from the tertiary center monitored area have been referred for a fetal echocardiography performed by pediatric cardiologist instead of a routine ultrasound screening of CHDs in the second trimester performed by a gynecologist. The data were assessed in a 16-year retrospective study performed between 2002 and 2017.

A total of 40 137 pregnancies underwent fetal echocardiography mostly between the 18th and 22nd week of pregnancy. In high-risk pregnancies, fetal echocardiography examination was performed at the gestational age of 16 weeks, and a follow-up control fetal echocardiography examination was performed before the gestational age of 24 weeks. When CHD was diagnosed, the fetus was thoroughly examined for the presence of extracardiac anomalies by a fetal–-maternal specialist and the performance of invasive prenatal procedure (transabdominal amniocentesis) to assess a fetal karyotype was always recommended. When parents decided to proceed with the pregnancy, the fetal hemodynamics and well-being were properly monitored during by pediatric cardiologist and fetal–maternal specialist during antenatal care. All newborns with CHDs were delivered at specialized center (University Hospital Motol, Prague and University Hospital Ostrava) and were followed by a pediatric cardiologist until 18 years of age. In cases when the pregnancy was terminated, autopsy was always performed in the presence of a pediatric cardiologist. The data were updated continuously, including analyses from genetic reports. This study was reviewed by the Institutional Review Board and approved by the local Ethics Committee (No. 229/2018).

For the purpose of this study, and to understand the TOP decision of the parents, three groups of CHDs were defined, based on severity and management (Table 1). Cases with complex cardiac abnormalities were classified according to the dominant heart lesion. The authors used their knowledge regarding the postnatal course of heart defects and the outcomes from their management in the Czech Republic [10]. Group A consisted of defects that are, despite possible critical manifestations, mostly managed with a primary surgical correction or catheterization, without any further significant complications; however, reoperation or recatheterization is possible. In this group, residual findings tend to be less significant and are mostly well tolerable. Group B included defects that can be managed with a single procedure to achieve a primary correction of the defect. However, these defects are associated with certain clinical complications (hypoxic events, arrhythmias, late progression of residual findings) and a higher probability of reoperation or recatheterization; yet, the biventricular circulation is preserved. Group C included defects that always require a repeated surgical procedure and only achieve single-ventricle circulation. Overall, it was possible to conclude that Group A had the most correctable defects, with the best outcomes; Group B defects were of moderate severity; and Group C had the most severe defects, with the most complicated course and future single-ventricle circulation. These groups were subsequently analyzed in relation to the associated morphological or genetic abnormalities of the fetus, and the heart defects were classified into the following groups: isolated, if a normal karyotype was present and there was no extracardiac malformations; abnormal karyotype, if there was a chromosome aberration present, with or without extracardiac malformations; and associated malformations, if extracardiac malformations were observed, with a normal karyotype [11].

Table 1. Classification and definition of CHD groups and abbreviations.

Group A: probable primary correction, biventricular circulation	
AVSD	Atrioventricular septal defect
VSD	Ventricular septal defect
CoA	Coarctation of aorta
TGA	Transposition of the great arteries
PS	Pulmonary stenosis
AS	Aortic stenosis
IAA	Interruption of the aortic arch
Group B: surgery/repeated surgery, possible complications, biventricular circulation	
TOF	Tetralogy of Fallot
DORV	Double outlet right ventricle
PAVSD	Pulmonary atresia with ventricular septal defect
EBST	Ebstein's anomaly
CAT	Common arterial trunk
CTGA	Corrected transposition of the great arteries
Group C: multiple surgeries, single-ventricle circulation	
HLH	Hypoplastic left heart syndrome
TA	Tricuspid atresia
SV	Single ventricle
PAIVS	Pulmonary atresia with intact ventricular septum
MA	Mitral atresia

TABLE 2. Prenatally diagnosed CHDs and their association with genetic and morphological impairments, from 2002 to 2017.

CHD	*N*	Isolated (%)	Chromosomal aberration (%)	Extracardiac anomalies (%)
Group A				
AVSD	63	19 (30)	34 (54)	10 (16)
VSD	36	27 (75)	7 (19)	2 (6)
CoA	28	19 (68)	6 (21)	3 (11)
TGA	31	28 (90)	0 (0)	3 (10)
PS	27	25 (92)	1 (4)	1 (4)
AS	23	22 (96)	0 (0)	1 (4)
IAA	3	1 (67)	2 (33)	0 (0)
Group B				
TOF	35	17 (49)	14 (40)	4 (11)
DORV	23	17 (74)	4 (17)	2 (9)
PAVSD	11	8 (73)	2 (18)	1 (9)
EBST	10	10 (100)	0 (0)	0 (0)
CAT	10	5 (50)	4 (40)	1 (10)
CTGA	4	2 (50)	0 (0)	2 (50)
Group C				
HLH	52	45 (86)	4 (8)	3 (6)
TA	13	10 (77)	3 (23)	0 (0)
SV	13	8 (61)	1 (8)	4 (31)
PAIVS	12	8 (67)	0 (0)	4 (33)
MA	4	4 (100)	0 (0)	0 (0)
Total	398	275 (69)	82 (21)	41 (10)

The abbreviations used are defined in Table 1.

Table 3. Decision to terminate the pregnancy after prenatal diagnosis.

CHD	*n*	Termination (%)	Delivery (%)
Group A			
AVSD	63	43 (68)	20 (32)
VSD	36	5 (14)	31 (86)
TGA	31	7 (23)	24 (77)
CoA	28	8 (29)	20 (71)
PS	27	1 (4)	26 (96)
AS	23	6 (26)	17 (74)
IAA	3	3 (100)	0 (0)
Group B			
TOF	35	14 (40)	21 (60)
DORV	23	12 (52)	11 (48)
PAVSD	11	8 (73)	3 (27)
EBST	10	3 (30)	7 (70)
CAT	10	10 (100)	0 (0)
CTGA	4	3 (75)	1 (25)
Group C			
HLH	52	42 (81)	10 (19)
TA	13	12 (92)	1 (8)
SV	13	5 (38)	8 (62)
PAIVS	12	12 (100)	0 (0)
MA	4	3 (75)	1 (25)
Total	398	197 (49)	201 (51)

The abbreviations used are defined in Table 1.

Results presented in other tables are listed in the same order of CHDs as in Table 1. The CHDs in individual groups are ordered according to their incidence in the observed population, in descending order.

The data obtained were stored and processed using Microsoft Excel. The same program was used for descriptive statistics and chart generation. Results are presented in tables as numbers and percentages. The chi-squared test was used to compare variables. The level of significance α for the probability of a type-I error (p or *p* values) was set at .05 for all tests. Analyses were performed using IBM SPSS software v. 24.

Results

Basic evaluation

A total of 40 885 fetuses (40 137 pregnancies) underwent fetal echocardiography between 2002 and 2017. CHDs were detected in 1.0% (398/40 885) of fetuses and were an isolated anomaly in 69% (275/398). In 21% (82/398) of cases, a concomitant genetic disorder was diagnosed and 10% (41/398) of cases had other extracardiac malformations, with a normal karyotype. Table 2 presents a detailed listing of all prenatally diagnosed cases of CHDs and their individual genetic and extracardiac abnormalities. The highest frequency of genetic abnormalities was associated with atrioventricular septal defects, with Down syndrome representing 45% of all genetic pathologies. In general, trisomy 21, 18, and 13 and the 22q11 deletion (DiGeorge syndrome) were responsible for 81% of all genetic abnormalities. More than 30% of the genetic abnormalities was found in common arterial trunk, interruption of the aortic arch, and tetralogy of Fallot. During the monitored period, we did not observe any cases of genetic disorder associated with Ebstein's anomaly, aortic stenosis, pulmonary atresia with intact ventricular septum, transposition of the great arteries, and corrected transposition of the great arteries. The most common extracardiac anomalies associated with heart defect in fetuses with normal karyotype were

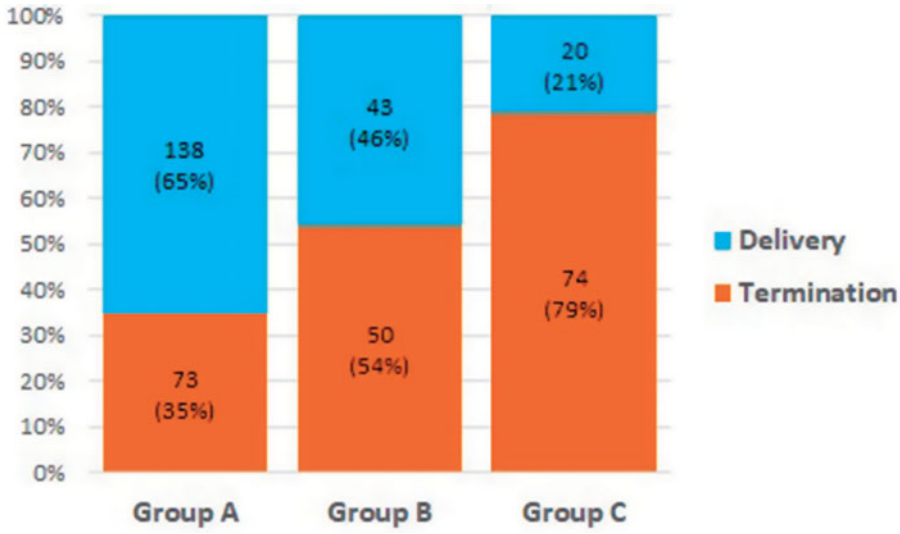

Figure 1. Dependence of TOP on the severity of the defect.

gastrointestinal and urogenital tracts malformations and limb deformities.

Termination of pregnancy without other risk factors for the fetus

In our study, 49% (197/398) of families decided to terminate the pregnancy due to the CHD. The pregnancies were terminated between the 12th and 24th week of pregnancy (median 20). The resulting courses of pregnancies for individual types of defects are presented by group and type of CHD in Table 3. In group A, 35% (73/211) of families decided to terminate the pregnancy, compared with 54% (50/93) in Group B and 79% (74/94) in Group C. The decision to terminate the pregnancy depended on the severity of the defect ($p < .001$) with the TOP percentage linearly increasing with the severity (Figure 1). Parents chose TOP in 100% of cases with pulmonary atresia with intact ventricular septum, common arterial trunk, and interruption of the aortic arch. In addition, the following defects of the heart were associated with a high rate of TOP (70–90%): tricuspid atresia, pulmonary atresia with intact ventricular septum, hypoplastic left heart syndrome, mitral atresia, and corrected transposition of the great arteries. Most (68%) pregnancies with an atrioventricular septal defect were terminated as were 40–50% of pregnancies with fetuses with defects such as the tetralogy of Fallot, double outlet right ventricle, and single ventricle.

Termination of pregnancy and extracardiac diseases

We separately assessed the influence of associated genetic and morphological anomalies, which may lead to extracardiac impairment of the fetus, on the parents' requests to terminate the pregnancy due to CHDs. In summary, TOP was performed for 41% (114/275) of fetuses with isolated CHDs, 59% (24/41) of fetuses with CHDs with a morphological anomaly and normal karyotype, and 72% (59/82) of fetuses with confirmed genetic pathologies associated with the CHD. The distribution of the associated anomalies and their relation to the TOP in individual groups are presented in Figure 2. The overall rate of CHDs in individual groups are reported in Table 4.

The relationships between TOP and extracardiac pathologies and the defect severity were analyzed in two ways. First, associated anomalies were always assessed according to the CHD groups (Figure 3). In all CHD groups (Groups A, B, C), the TOP proportion increased linearly when comparing isolated defects with genetic impairments. The TOP proportion significantly depended on the associated anomaly in Group A ($p < .001$). In addition, when the CHDs were ordered from isolated to morphological anomalies to genetic anomalies, there was a significant linear trend in Group A ($p < .001$); while, Groups B and C showed slight linear trends that were not significant. We also used a reverse analysis of the CHD significance and the individual impairment of the fetus. Again, the TOP percentage rose with the increasing severity of the CHD in all groups of fetal impairment. The TOP incidence significantly depended on the degree of the defect in isolated CHDs ($p < .001$), with a clear significant linear trend ($p < .001$). A linear trend was also observed cases with genetic and morphological impairments; however, no dependency was confirmed.

Both analyses showed that in cases with correctable CHDs and presumed minor residual effects, the

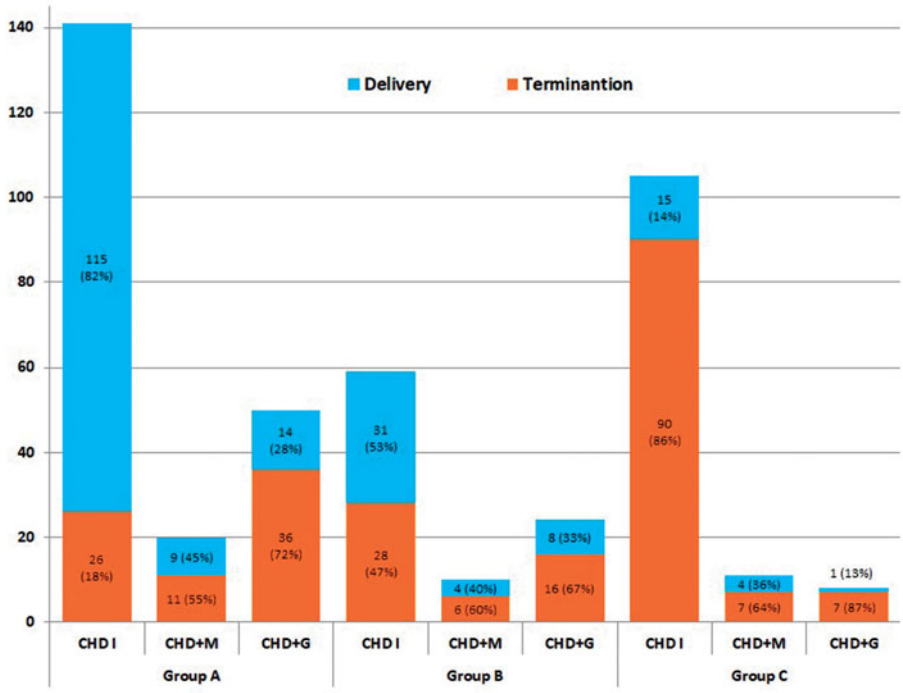

Figure 2. TOP according to the significance of the defect and associated anomalies (I-isolated, M-extracardiac malformation with normal karyotype, G-concomitant genetic disorder).

Table 4. Termination of pregnancy, in relation to genetic and morphological pathologies.

CHD		Termination *n* (%)			Delivery *n* (%)		
	n	CHD I	CHD + G	CHD + M	CHD I	CHD + G	CHD + M
Group A							
AVSD	63	9 (21)	26 (60)	8 (19)	10 (50)	8 (40)	2 (10)
VSD	36	3 (60)	2 (40)	0 (0)	24 (77)	5 (16)	2 (7)
TGA	31	6 (86)	0 (0)	1 (14)	22 (92)	0 (0)	2 (8)
CoA	28	2 (25)	5 (62)	1 (13)	17 (85)	1 (5)	2 (10)
PS	27	0 (0)	1 (100)	0 (0)	25 (96)	0 (0)	1 (4)
AS	23	5 (83)	0 (0)	1 (17)	17 (100)	0 (0)	0 (0)
IAA	3	1 (33)	2 (67)	0 (0)	0 (0)	0 (0)	0 (0)
Group B							
TOF	35	6 (43)	8 (57)	0 (0)	11 (52)	6 (29)	4 (19)
DORV	23	7 (58)	3 (25)	2 (17)	10 (91)	1 (9)	0 (0)
PAVSD	11	6 (74)	1 (13)	1 (13)	2 (67)	1 (33)	0 (0)
EBST	10	3 (100)	0 (0)	0 (0)	7 (100)	0 (0)	0 (0)
CAT	10	5 (50)	4 (40)	1 (10)	0 (0)	0 (0)	0 (0)
CTGA	4	1 (33)	0 (0)	2 (67)	1 (100)	0 (0)	0 (0)
Group C							
HLH	52	36 (86)	4 (9)	2 (5)	9 (90)	0 (0)	1 (10)
TA	13	10 (83)	2 (17)	0 (0)	0 (0)	1 (100)	0 (0)
SV	13	3 (60)	1 (20)	1 (20)	5 (62)	0 (0)	3 (38)
PAIVS	12	8 (67)	0 (0)	4 (33)	0 (0)	0 (0)	0 (0)
MA	4	3 (100)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)
Total	398	114 (58)	59 (30)	24 (12)	161 (80)	23 (11)	17 (9)

The abbreviations used are defined in Table 1. I: isolated, G: concomitant genetic disorder, M: extracardiac malformation with a normal karyotype.

decision of parents regarding the TOP was significantly influenced by extracardiac morphological or genetic impairments of the fetus, with a genetic impairment considered more important than a morphological one. Among the moderate and severe defects, further impairment of the fetus, despite the linearly increasing trend, did not play a significant role in decisions regarding TOP. In cases with an isolated CHD, the parents' decision about TOP was influenced by the degree of severity of the defect. The severity did not play an important role in cases with other impairments of the fetus. The smallest TOP percentage, 18% (26/141), was observed in Group A, that is, in cases with correctable defects, without associated pathologies. The largest percentage of terminations, 87% (7/8), was in Group C, ie in cases with complicated defects and associated genetic diseases.

Discussion

Heart defects are the most frequently observed morphological anomalies in the human population [12]. The prevalence usually ranges between 6 and 18 cases per 1000 live births [13,14]. These numbers may reach 30/1000 when taking into consideration bicuspid aortic valves and 75/1000 live births when considering all insignificant CHDs, including minor septal defects [6]. Most CHDs are prenatally detectable. Ultrasound examination of the fetal heart (fetal echocardiography) is a very precise method for detecting cardiac malformations and produces excellent results when performed by an experienced physician [16,17]. The fetal echocardiography examination has a high specificity and sensitivity for detection of significant CHDs; however, detection of insignificant defects is limited [18].

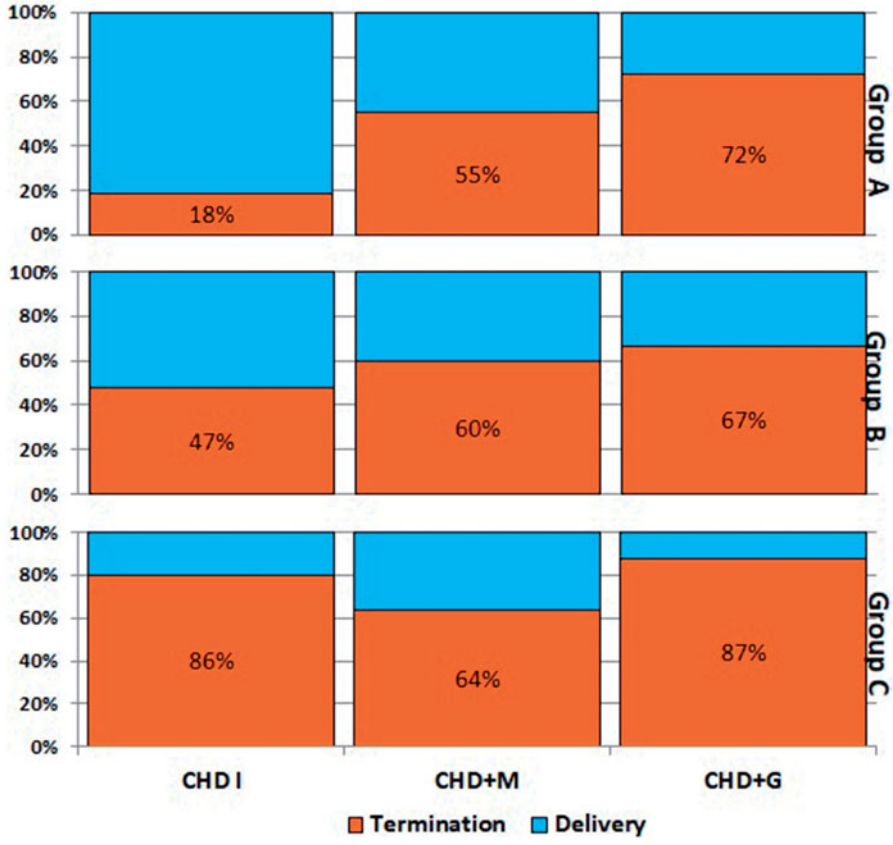

Figure 3. TOP according to concomitant anomalies and CHD severity (I-isolated, M-extracardiac malformation with normal karyotype, G-concomitant genetic disorder).

The parents of the fetus can decide to continue with or terminate the pregnancy when a defect is detected. The main findings of this study are as follows: (i) the cardiac defect was observed as an isolated finding in most cases and there was an association with extracardiac malformations and a genetic pathology in one-third of cases; (ii) parents of the fetus decided to terminate the pregnancy after a CHD was diagnosed in half the cases; (iii) the decision to terminate is partially associated with concomitant genetic and extracardiac abnormalities; and (iv) concomitant anomalies of the fetus affect the TOP decision, most significantly in cases of surgically-correctable CHDs.

In the present study, the rate of CHDs was 1% among prenatally examined fetuses, and 21% of the cases with a CHD had chromosomal aberrations, which corresponds with the results of other studies [20,21], and 10% suffered from a CHD with another extracardiac pathology, but a normal karyotype. The highest frequency of genetic abnormalities was associated with atrioventricular septal defects (54%), with a dominance of Down syndrome [22–25]. The presence of a chromosomal aberration was mostly observed as an isolated cardiac pathology [26,27]. Down syndrome was the most common followed by DiGeorge syndrome, which is most frequently seen with tetralogy of Fallot [28]. Trisomy 18 was the third most frequent chromosomal pathology and is most frequently associated with septal defects; in our case, this condition was mostly observed prenatally with atrioventricular septal defects. Trisomy of other autosomes in relation to a CHD is rare and viable mostly in a mosaic form. Turner syndrome, which is the most frequently observed chromosomal aberration in females, was associated with coarctation of the aorta and hypoplasia of the left heart. During the monitored period, there were no cases of Ebstein's anomaly, pulmonary atresia with an intact ventricular septum, transposition of the great arteries, or corrected transposition of the great arteries associated with genetic abnormalities. Although, some CHDs have a low rate of genetic abnormalities and the patient may not be karyotyped; therefore, some genetic pathologies may be overlooked [29]. For these defects, possible genetic causes have been studied and causal mutations examined [30,31], but despite improvements in the detection and interpretation, complications of phenotype heterogeneity and incomplete penetration are still possible [32].

According to Czech legislation, parents can decide about termination or continuation of pregnancy when

a significant defect is diagnosed prenatally. In the Czech Republic, the findings (fetal echocardiography, follow-up ultrasound examinations, screening, genetic testing) are assessed by a geneticist. In various registers, the rate of TOP varies between 0 and 50% depending on the CHD diagnosis [33]. The Czech Republic has one of the highest TOP rates in the world, along with countries in Western Europe. During our study period, 49% of families decided to terminate the pregnancy after a CHD was prenatally diagnosed. Generally speaking, without further studies of associated anomalies, the decision to terminate increased with the rising severity of the heart defect. The TOP decisions significantly differed in cases of CHDs that would require single-ventricle circulation and repeated postnatal surgical interventions. These procedures are associated with a higher morbidity and mortality [34] compared with heart defects that require one-time surgery and a biventricular solution. The decisions of the parents were similar to other studies [35,36]. In this study, we have found TOP for ventricular septal defects, however, all these CHDs were associated with extracardiac anomalies.

Another factor affecting the TOP is early diagnostics. We prefer the period between the 18th and 22nd week of pregnancy for CHD screening, when the visibility and yield of the examination are best [37]. It is also possible to offer early fetal diagnostics in cases of pregnancies burdened with risk factors [38–40]. First-trimester screening of CHDs is possible, and significantly influences the spectrum of CHDs and leads to a higher number of terminated pregnancies [41]. Early fetal diagnostics of significant defects result in TOPs in more than 70% of cases.

It is not only the severity of the CHD that influences the decision of parents concerning TOP, associated anomalies of the fetus also come into play [29,42]. Overall, there was a significant difference in the prenatal detection rate and the proportion of induced abortions between cases of isolated CHDs and CHDs associated with chromosome anomalies, multiple malformations, and syndromes. The authors attempted to analyze the relation between individual groups and TOPs. The rate of TOP was smallest for cases with surgically-correctable defects, without any other concomitant impairment. However, the rate of TOP in isolated CHDs was 41% on average, and in other studies performed elsewhere, the TOP rate reached around 20% for isolated CHDs [43]. Despite the exclusion of extracardiac pathologies, the TOP rate for cases with isolated defects requiring univentricular correction reached 86%. The highest TOP rate was observed, as expected, in cases with univentricular CHDs associated with a genetic impairment, and this finding corresponds with other observations [33].

Generally speaking, the aim of prenatal diagnostics is to further examine fetal pathologies and provide counseling. When appropriate, it is also recommended to use illustrations of the defect during the explanation [44]. The parents are properly instructed about the type of defect, and they decide about continuation or termination of the pregnancy themselves. It is also necessary to plan the delivery of the newborn with a defect, together with appropriate postnatal care at a corresponding center. The knowledge of a CHD prior to birth may decrease the morbidity and mortality for certain types of critical and significant heart defects [45]. The presence of a defect in the family has not only medical concerns, but also social and economical issues.

In conclusion, in the observed region, one half of the families decided to terminate the pregnancy if a CHD was detected prenatally. The parents' decision to terminate increases along with the severity of the defect and associated anomalies of the fetus. The associated anomalies influence the parents most in cases of surgically-correctable CHDs, and genetic factors play a more important role than morphological ones.

Disclosure statement

No potential conflict of interest was reported by the authors.

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