

Prenatal diagnosis of six major cardiac malformations in Europe – A population based study

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Aim. To present data on prenatal diagnosis of six major cardiac malformations in low-risk European populations.

Methods. Data from 12 Eurocat registries on congenital malformations. All registries have multiple sources of information and use the same methods of data collection and coding. The six cardiac malformations included were hypoplastic left heart, tricuspid atresia, single ventricle, Tetralogy of Fallot, transposition of great arteries and common A-V-canal.

Results. There were significant differences in the proportion of cases diagnosed prenatally, with the highest detection rate in France (91% for single ventricle in Paris) and the lowest detection rate in countries without prenatal ultrasound screening (no cases diagnosed prenatally in the Danish registry area). Prenatal detection rate was significantly higher for the three malformations affecting the size of the ventricles (hypoplastic left heart, tricuspid atresia, single ventricle) compared to the other three malformations (46% versus 24%, $p < 0.001$). Time of diagnosis was late, with only one third diagnosed before 24 weeks of gestation. The risk of fetal death seems to be low.

Conclusion. There are significant regional differences in prenatal detection rate of major cardiac malformations in Europe.

Key words: cardiac malformations; population based; prenatal diagnosis

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Infants with congenital heart defects (CHD) have a wide spectrum of lesions, ranging from small

Abbreviations:

CHD: congenital heart disease; ICD: International Classification of Diseases; BPA: British Paediatric Association; GA: gestational age; IA: induced abortions.

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asymptomatic defects to malformations with a very high mortality (1). With ultrasonography it is possible to diagnose major cardiac defects prenatally by means of the four-chamber view (2, 3). Prenatal diagnosis enables decisions to be made to continue the pregnancy, ensuring delivery in hospitals with pediatric cardiology expertise or to terminate the pregnancy. The sensitivity of prenatal ultrasound screening for CHD in low risk populations is reported from 14% to 45% in three studies using comparable methods (population based, retrospective, one week follow up in livebirths) (3–5). In the Eurofetus study, which is the largest prospective study in low risk populations including all pregnant women having at least one ultrasound performed, prenatal detection rate of cardiac mal-

formations was 28%, and for major cardiac malformations 39% were seen prenatally (6).

Here we will present data on prenatal diagnosis of six specified major cardiac malformations from 12 European population-based registries of congenital malformations. The registries include data of all pregnancies with malformations whether prenatal ultrasound examination is performed or not. Prenatal screening recommendations may differ between regions.

Material and methods

The study is based on routinely collected data from 12 Eurocat registries of congenital malformations. The geographically defined populations and the methods of case ascertainment of Eurocat are described elsewhere (7). The registries are

based on multiple sources of information, including hospital records, birth and death certificates and post mortem examinations, and also information about livebirths, fetal deaths with GA \geq 20 weeks and induced abortions after prenatal diagnosis of malformations. Malformations are coded according to ICD/BPA 9.

Prenatal ultrasound screening for congenital malformations was routinely performed in all but two registry areas (Groningen and Funen County). Recommended GA at ultrasound screening is seen in Table I. In France and Spain three ultrasound investigations (one in each trimester) were offered to each pregnant woman: two mainly for biometric purposes and one screening for congenital malformations in the second trimester. In Glasgow one ultrasound was routinely performed in the first trimester of pregnancy while investigations in the sec-

Table I. Registries included in the study, number of births and number of cases with six major cardiac malformations 1990–94 and the official recommendation for gestational age (GA) at ultrasound screening (US) for congenital malformations in the registry areas

Country	Total no. of births	Total no. of cases (% of total cases)	Recommended GA for US screening for congenital malformations
Paris	F 183,049	348 (25%)	19–22
Strasbourg	F 67,294	133 (9%)	19–22
Bouche-du-Rhone	F 114,099	173 (12%)	19–22
Glasgow	GB 60,931	107 (8%)	First trimester
Belfast	GB 128,185	67 (5%)	16–18
Asturias	E 36,742	42 (3%)	(18)–20
Basque Country	E 80,293	133 (9%)	(18)–20
Tuscany	I 91,475	102 (7%)	20–22
Antwerp	B 33,070	46 (3%)	18–24
Hainaut	B 65,282	93 (7%)	18–22
Groningen	NL 97,298	141 (10%)	No screening
Funen County	DK 29,559	32 (2%)	No screening
Total	987,277	1417	

Table II+III. Regional differences in prenatal diagnosis and induced abortions for six major cardiac malformations, 1990–1994. Total number of cases in each registry, proportions detected prenatally and resulting in induced abortions (IA)

Table II	Hypoplastic left heart			Tricuspid atresia			Single ventricle		
	Total	% prenat.	% IA	Total	% prenat.	% IA	Total	% prenat.	% IA
Paris	70	89	74	23	83	39	33	91	79
Strasbourg	20	65	30	12	83	17	9	78	33
Bouche du Rhone	35	57	46	13	85	62	13	77	77
Glasgow	16	13	0	2	0	0	12	0	0
Belfast	21	0	0	3	0	0	10	20	0
Asturias	6	0	0	4	0	0	6	0	0
Basque Country	19	26	11	11	27	0	11	45	9
Tuscany	18	33	6	7	14	0	9	22	0
Antwerp	11	9	9	10	20	10	1	0	0
Hainaut	20	40	5	9	0	0	5	20	20
Groningen	22	9	0	16	13	6	4	25	25
Funen	9	0	0	1	0	0	1	0	0
Total	267	45%	30%	111	43%	19%	114	51%	37%

Table II+III. Regional differences in prenatal diagnosis and induced abortions for six major cardiac malformations, 1990–1994. Total number of cases in each registry, proportions detected prenatally and resulting in induced abortions (IA)

Table III	Transposition			Tetralogy of Fallot			Common A-V-canal		
	Total	% prenatal	% IA	Total	% prenatal	% IA	Total	% prenatal	% IA
Paris	66	64	27	57	60	30	99	30	26
Strasbourg	27	52	15	26	31	0	39	18	8
Bouche du Rhone	37	46	35	42	29	10	33	30	30
Glasgow	36	6	3	20	15	6	21	0	0
Belfast	13	15	8	11	9	9	9	22	0
Asturias	12	0	0	7	43	0	7	0	0
Basque Country	41	5	2	16	6	0	35	14	3
Tuscany	31	3	3	20	10	0	17	12	0
Antwerp	9	22	22	11	18	9	4	0	0
Hainaut	15	13	13	25	16	8	19	5	5
Groningen	62	10	6	35	11	3	2	50	50
Funen	9	0	0	8	0	0	4	0	0
Total	358	25%	13%	278	27%	10%	289	20%	15%

ond trimester of pregnancy was performed only on indication. All registry areas permitted termination of pregnancy due to severe fetal malformations. Late termination of pregnancy (GA >24 weeks) was only allowed in France.

The six cardiac malformations examined were hypoplastic left heart syndrome, single ventricle, tricuspid atresia, transposition of great arteries, tetralogy of Fallot and common AV-canal. Only malformations coded with the specified code were included. ICD/BPA 9 has no specified code for hypoplastic right heart, and therefore the diagnosis tricuspid atresia was selected as it is always associated with right ventricular hypoplasia.

The study period was 1990–94 and covered a total number of 987,277 births.

Results

Total number of births and number of cases from each registry are shown in Table I. Tables II and III show the number of cases, the proportion of cases diagnosed prenatally, and the proportion of induced abortions for the six selected CHD. For malformations affecting the size of the ventricles (Table II) prenatal detection rate was 46% while

Table IV. Time of diagnosis for prenatally diagnosed cases of major cardiac malformations

	GA known	< 23 weeks	23–32 weeks	>32 weeks
Hypoplastic left heart	110	40	50	20
Tricuspid atresia	44	15	18	11
Single ventricle	55	20	27	8
Transposition	81	30	41	10
Tetralogy of Fallot	65	20	31	14
Common A-V-canal	55	20	27	8

prenatal detection rate for the three malformations in Table III with normal size of the ventricles was 24%. This difference is highly significant ($p < 0.001$). Prenatal identification of the six cardiac malformations both total and for each malformation was significantly higher in France compared to the other countries ($p < 0.01$).

The time of diagnosis for the prenatal identified cases of CHD was late (Table IV) despite the fact that ultrasound screening programs for malformations are usually performed between 16 and 22 weeks of gestation. Thirty-five percent were diagnosed before 23 weeks of gestation, 47% between 23–32 weeks and 17% of more than 32 weeks.

In this survey, there were a total of 1,417 cases with the selected six cardiac malformations of which only 56 were fetal deaths with GA ≥ 20 weeks (Table V). Thus, after 20 weeks of gestation, the risk of fetal death with the six selected cardiac malformations appears to be low.

Discussion

Our study shows large variation in the prenatal detection rate for major cardiac malformations. Two explanations, however, must be considered when

Table V. Total number of cases with cardiac malformations compared to number of fetal deaths with gestational age ≥ 20 weeks

	Total	Fetal deaths
Hypoplastic left heart	267	11
Tricuspid atresia	111	6
Single ventricle	114	5
Transposition	358	13
Tetralogy of Fallot	278	11
Common A-V-canal	289	10

comparing the results. Firstly, the Eurocat form includes only the time of diagnosis for the first malformation identified in infants with multiple malformations. For such cases it is not known whether it was the cardiac or the extracardiac malformations that were diagnosed prenatally. Half of the cases with common A-V-canal have Down syndrome and 20% of all cases with CHD have associated malformations (1). However, this problem is similar for all registries. Secondly, even complex CHD may not be diagnosed within the first week of life. Some registries include only cases diagnosed before one week of age, while others include cases diagnosed up to several years after birth. By comparing registries with different time of follow-up, data from registries including late diagnosed cases may give rise to a lower percentual prenatal detection rate for this reason. As both Bouche-du-Rhone and Strasbourg registries include late diagnosed cases, short follow-up is not the explanation for the higher detection rate in France.

We can conclude that there are major regional differences in the prenatal detection rate of cardiac malformations with the highest detection rate in France and the lowest rate in countries without routine ultrasound screening (Denmark and The Netherlands). The higher prenatal detection rate in France cannot be explained by a later GA at ultrasound screening for congenital malformations (Table I). We think that the difference is explained by a more specialized level of ultrasound investigations in France. The difference between France and the other European countries concerning prenatal diagnosis and terminations of pregnancy has been known by the Eurocat Network for many years (7) and is documented for other groups of malformations in several publications (8, 9).

We find a highly significant difference in prenatal detection between malformations affecting the size of the ventricles and malformations with normal size of the two ventricles. In the Eurofetus study (6) prenatal detection rate for these six malformations ranged from 21% for transposition of great arteries to 46–58% for each of the other five malformations. The number of cases in each group is much smaller than in our study. For transposition of great arteries, the malformation can only be diagnosed by ultrasound if the outflow tract is visualized, while the other malformations can be seen by the four-chamber view.

It is generally agreed that there is a high risk of fetal death in pregnancies with CHD (10, 11). This study seems to indicate that the risk of fetal death for fetuses with these six cardiac defects is low. The diagnosis of CHD in fetal deaths is only possible by post-mortem examination. The proportion of post-mortem examinations among fetal deaths in

the Eurocat populations is not known and therefore our results should be interpreted with caution. The knowledge of the risk of fetal death is important, when counseling the parents after prenatal diagnosis of CHD and therefore further studies evaluating the risk of fetal deaths with CHD are needed. It is known that the prognosis for the fetuses is profoundly affected by the presence of associated major malformations or karyotype anomaly (10). Therefore, it is important to consider other malformations in the fetus before counseling the parents.

In pediatric cardiology there is a tradition for comparing prevalence data of CHD in livebirths (1, 12). Due to the large difference in the number of induced abortions (Tables II + III), it is necessary to include not only livebirths but also fetal deaths and induced abortions when comparing prevalence between different countries.

Only one-third of the cases in this study were diagnosed before 24 weeks of gestation, which is the limit for termination of pregnancy in most countries. For the remaining two-thirds, as a result of prenatal diagnosis, the mothers can be transferred to a hospital with pediatric cardiology service. In theory outcome of especially ductus-dependent CHD should be better if the malformations are diagnosed before birth and treatment can be planned before start of symptoms. Until now, it has not been possible to show benefit of prenatal diagnosis for liveborn infants with CHD (13, 14) and it seems difficult at prenatal echocardiography to predict if the fetus after birth will be ductus-dependent (15).

Surgical treatment by a Fontan type procedure can now be offered to many children with univentricular hearts (hypoplastic left heart, tricuspid atresia and single ventricle) with an acceptable mortality. Although most children have a high quality of life during the early postoperative years, cardiac failure will eventually occur after 10–30 years ultimately leading to consideration of cardiac transplantation (16–18).

Therefore, after prenatal diagnosis of isolated complex cardiac malformation with only one functional ventricle, the parents are faced with a very difficult decision whether to continue or to terminate the pregnancy.

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