

# Spectrum of congenital heart defects in Croatia

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**Dilber, Daniel; Malčić, Ivan**

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## **Spectrum of congenital heart defects in Croatia**

Daniel Dilber, Ivan Malčić

Department of paediatric cardiology, University Hospital Zagreb, Croatia

Corresponding author:

Daniel Dilber

Department of paediatric cardiology

University Hospital Zagreb, Croatia

Phone number: ++385-1-2367-589

Fax:++385-1-2421-893

Email: [dilber\\_daniel@yahoo.com](mailto:dilber_daniel@yahoo.com)

1 **Abstract:**

2  
3 The aim of our study was to investigate the incidence of congenital defects in children born in Croatia during a  
4 period of 5 years, its association with extracardiac malformations, its treatment and outcome. Medical  
5 information about the patients was obtained from 14 paediatric cardiology centres that cover the whole country.  
6 Diagnosis was made by clinical findings, electrocardiography, chest X-ray, echocardiography, catheterisation or  
7 autopsy. Between October 1, 2002 and October 1, 2007, there were 205 051 live births in Croatia, 1480 of which  
8 were patients diagnosed with congenital heart disease, accounting for 0.72% of the live-born children. The  
9 distribution was made up of 34.6% children with ventricular septal defect, 15.9% with atrial septal defect, 9.8%  
10 with patency of arterial duct, 4.9% pulmonary valvar stenosis, 3.3% tetralogy of Fallot, 3.3% transposed great  
11 arteries, 3.3% aortic stenosis, 3.2% aortic coarctation, 4.3% atrioventricular septal defect and common  
12 atrioventricular orifice, 2.3% hypoplastic left heart syndrome and 8.3% other severe defects. The average age in  
13 the time of diagnoses is 70.41 days (SD 188.13), with low average time of diagnoses of severe heart defects, 9.6  
14 days, SD 32.52. Among patients, 14.5% had chromosomal defects, syndromes and/or other congenital major  
15 anomalies. During the study, 57 patients died because of cardiac anomalies or other related problems, 24 who  
16 died were operated.

17 Conclusion: The rates of specific cardiac defects and association with extracardiac malformations are generally  
18 comparable with those reported in similar studies. In spite of all problems, mortality rate of 3.85% is low but  
19 could be improved.

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21  
22 Keywords: congenital heart disease, prevalence, extracardiac anomalies, treatment  
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## 42 **Introduction**

43 Congenital heart disease are amongst the most frequent of all congenital anomalies [20]. They constitute a major  
44 cause of infant mortality and morbidity in childhood and in later adult life [25]. On the other hand, the number of  
45 adults with some form of congenital heart disease is growing rapidly as therapy becomes increasingly effective  
46 [23]. Quantification of birth prevalence and spectrum of malformations, along with analysis of past trends of  
47 management, allow for future planning of health services [7]. Congenital cardiac malformations are frequently  
48 associated with other non-cardiac congenital malformations and chromosomal anomalies. Conversely,  
49 syndromic infants constitute a substantial proportion of all children with congenital heart disease [6,11].

50 There is a wide variation between reports on prevalence of congenital heart disease and incidence of associated  
51 extracardiac malformations. Recent population-based epidemiological studies on congenital heart disease have  
52 indicated a prevalence ranging from 4 to 14 per 1000 live births. The reported incidence of associated  
53 extracardiac anomalies ranges from 7% to 45% [27-29].

54 Here, we formed a study which includes all children with congenital heart disease recognised and treated in 14  
55 paediatric cardiology centres in Croatia, born between October 2002 and October 2007.

56 The aim of this study is to describe the prevalence of congenital heart disease in live births and its association  
57 with other, non-cardiac congenital anomalies in Croatia. This study also compares its results with studies done  
58 elsewhere, and puts forward an explanation for wide variations found between studies.

59

## 60 **Materials and methods**

61 Congenital heart disease was defined as „a gross structural abnormality of the heart or intrathoracic great vessels  
62 that is actually not potentially of functional significance [26]. We excluded functionless abnormalities of great  
63 veins, but included congenital arrhythmias and cardiomyopathies. We excluded patent ductus arteriosus as a  
64 single defect in preterm infant before three months because it is more often based on abnormal physiology rather  
65 than on a structural abnormality [13,21,22], we excluded patent foramen ovale with the tiny left-to-right shunt in  
66 the first year of life because of high rate of spontaneous closure [13,14], we excluded isolated partial anomalous  
67 pulmonary venous connection because it is rarely reported in reports of the incidence of congenital heart  
68 disease[13], mild pulmonic stenosis if the systolic gradient across the valve is under 20 mmHg if showed no  
69 progression with time. We also excluded bicuspid aortic valve and mitral valve prolapse and mitral  
70 incompetence as isolated congenital lesion because they are not usually reported in the other studies of incidence  
71 in this pediatric population [13,14]. For the purpose of this study we excluded abnormalities of coronary arteries,  
72 pericardium and AV fistule, aortic arch branch abnormality and vascular ring. We included aortic stenosis if a  
73 flow velocity in the ascending aorta exceeded 2 m/s. Information about the patients was obtained from medical  
74 records from 14 paediatric cardiology centres that cover the whole country. Diagnosis of congenital heart disease  
75 was made by clinical findings, electrocardiography, chest X-ray, echocardiography, catheterisation or autopsy.  
76 All cases of congenital heart disease were coded according to European Paediatric Cardiac Code (EPCC) [8].

77 When a patient had more than one lesion, we considered the defect that required treatment, or the one that caused  
78 the greatest hemodynamic effect, to be the main malformation.

79 For the purpose of this study, we define “severe” congenital heart defects as the following 12 conditions:  
80 hypoplastic left heart syndrome (HLHS), single ventricle, tricuspid atresia, common arterial trunk, interrupted  
81 aortic arch, pulmonary atresia without ventricular septal defect, complete transposition of great arteries (TGA),

82 double outlet right ventricle (DORV), atrioventricular septal defects and common AV junction (AVSD), totally  
83 anomalous pulmonary venous connection (TAPVR), tetralogy of Fallot, and Epstein's malformation of tricuspid  
84 valve [27].

85 For the purpose of this study, a syndrome was defined as „a recognised pattern of congenital abnormalities  
86 whose unique combination of features sets it apart from other patterns [18]. Syndromes were subdivided into  
87 recognised chromosomal anomalies and recognised non-chromosomal syndromes or sequences. A malformation  
88 was defined as „a permanent change produced by intrinsic abnormality of development in a body structure  
89 during prenatal life“[18]. Malformations were subdivided into major and minor malformations following  
90 guidelines set out by EUROCAT (European Registers of Congenital Anomalies and Twins) [1]. Only major  
91 malformations were included.. Chromosomal analyses were made by using high-resolution banding and  
92 fluorescence in situ hybridization.

93 The study was set up according to the EUROCAT registries principles to cover congenital heart disease in case  
94 of late fetal deaths following prenatal diagnoses of cardiac disease, livebirths and stillbirths [1,20]. Early fetal  
95 deaths or spontaneous abortions are not covered by the study.

96 All children with congenital heart disease born to Croatian residents between October 1st 2002 and October 1st  
97 2007 were included. Information on patients born during five years study and with the diagnoses of congenital  
98 heart defect of 745 through 747 according to the ninth revision, Q20 through Q28 of the tenth revision of the  
99 International Classification of Disease, and from 01.01.01 through 09.29.31 according to the European Paediatric  
100 Cardiac Code – The Short List [8], was obtained during the period of study, from medical records from 14  
101 paediatric cardiology centres that cover the whole country. The patients and their diagnoses were organised as  
102 age cohorts according to the age of birth, with patients and their diagnoses belonging to the year of birth,  
103 whenever diagnoses was made.

104 We also obtained access to autopsy reports and death certificates of those patients who had died. All pregnant  
105 women in Croatia are offered prenatal ultrasonic screening in the nineteenth week of gestation, and they are  
106 referred for specialized fetal echocardiography if an abnormality is suspected from the four chamber view  
107 obtained at that visit, or if there are other fetal or maternal factors for increased risk. We collected the data  
108 obtaining approval for the study from the ethical committee of the University Hospital of Croatia A resident was  
109 considered to be anyone who had lived in Croatia for one year or more.

#### 110 **Statistics**

111 For relevant findings, we primarily used descriptive statistics. Ninety-five percent confidence intervals for rates  
112 were calculated using binomial distribution. Means and standard deviations were calculated for continuous  
113 variables. Significance of difference in congenital heart defects distribution by gender was tested by multiple  
114 logistic regression. To measure association for categorical variables Pearson's Chi square test was used. Official  
115 Croatian publications were used to obtain total live birth from October 1st 2002 to October 1st 2007. All data  
116 were collected in File Maker pro 5, and then exported to the Microsoft Office Excel. For statistical analysis we  
117 used Statistical Package for Social Sciences 13.0 (SPSS Inc., Chicago, IL, USA).

#### 118 **Results:**

119 From October 1st 2002 to October 1st 2007, there were 205 051 live births. Congenital heart disease had been  
120 diagnosed in 1480 children, 700 girls (47%) and 780 boys (53%), giving a prevalence of 0.72%. The yearly  
121 incidence varied from 8.14 ‰ of live-born children in 2002 to 6.59‰ in 2007 (Table 1).

122 Ventricular septal defect was the most common heart defect, diagnosed in 513 children, accounting one third of  
123 the total number (34.6%). Atrial septal defect was diagnosed in 235 children (15.9%), 145 had patency of arterial  
124 duct (9.8%), 73 pulmonary valvar stenosis (4.9%), 49 tetralogy of Fallot (3.3%), 49 transposed great arteries  
125 (3.3%), 49 aortic stenosis (3.3%), 47 aortic coarctation (3.2%), 64 had atrioventricular septal defect and common  
126 atrioventricular orifice (4.3%), 34 had hypoplastic left heart syndrome (2.3%), 26 with cardiomyopathy (1.8%),  
127 73 rhythm disturbances (4.9%), and 123 (8.3%) with other severe defects (excluding hypoplastic left heart  
128 syndrome, atrioventricular septal defects, tetralogy of Fallot and transposition of great arteries). Table 2. lists the  
129 distribution of the specific lesions and gender of the patients. For coarctation of aorta (OR 2.17, CI 1.15-4.09,  
130  $p<0.05$ ) and aortic stenosis (OR 1.89, CI 1.03-3.47,  $p<0.05$ ) the ratio was significantly increased in favour of  
131 males, and for the atrial septal defect (OR 1.32, CI 1.0-1.75,  $p=0.05$ ) the ratio was significantly increased in  
132 favour of females.

133 Table 3 shows prevalence of defects during the study period with significantly increasing trend ( $p<0.05$ )  
134 observed only for coarctation of aorta. For the purpose of reduction of potential bias by the number of patients  
135 who could be diagnosed later in live, years 2006 and 2007 were excluded from the study of changing prevalence  
136 of specific defects, with calculated statistical significance as a deviation from the rectangular distribution only  
137 for the period 2003-2005.

138 The average age in the time of diagnoses is 70.41 days (SD 188.13), with median age of 4 days (Q1-Q3: 1-37),  
139 with average time of diagnoses of severe heart defects, 9.6 days (SD 32.52) and median age of 1 day (Q1-Q3: 0-  
140 4). Prenatal diagnoses was made in 3% of all children. No case of late fetal death or abortion due to severe  
141 cardiac disease were documented during the study.

142 Of all 1480 patients with congenital cardiac malformations, 215 (14.5%) had associated non cardiac anomalies  
143 (Table 4). Of these, 50.2% had chromosomal defects, 14.4 % syndromes and 35.3% other major congenital  
144 anomalies (Table 5). Down syndrome accounted for 89.8% of all chromosomal anomalies, with a birth  
145 prevalence of Down syndrome associated with cardiac anomaly of about 0.47/1000 live births. The most  
146 common non-chromosomal syndrome was diGeorge syndrome with a proportion of 35.5%, followed by  
147 Williams-Beuren, Noonan, Ivemark, Alagille and other (Table 5). Syndromes are divided according to the most  
148 frequent genetic basis of development [29,31]. The most common major non-cardiac malformations were  
149 gastrointestinal anomalies.

150 The most common cardiac anomaly associated with Down syndrome is atrioventricular septal defect, with a  
151 percentage of 41.2 %.

152 Of the 1480 children born during the period of study, 430 needed an operation. Among 553 cardiac surgeries  
153 performed, 202 were done in two institutions in Croatia and 351 were done in 7 institutions abroad. Case  
154 complexity was analysed using both the Aristotle Basic Complexity Score and the Risk Adjustment for  
155 Congenital Heart Surgery methodology, The methodological details of each system are described in the  
156 respective references [17,19] The average complexity for cardiac procedures done in Croatia according to the  
157 Aristotle Basic Complexity Score (ABC score) was 6.1 and the average complexity for procedures done abroad  
158 according to the Aristotle Basic Score was 9.2 with statistically significant difference ( $p<0.001$ ). The average  
159 complexity for cardiac procedures done in Croatia according to the RACHS-1 methodology was 2.2 and the  
160 average for procedures done abroad according to the RACHS-1 methodology was 3.1 with statistically  
161 significant difference ( $p<0.001$ ). Among 202 procedures done in Croatia, death occurred after 10 procedures

162 with mortality rate at discharge of 5 %, on the other hand, among 351 procedures done abroad death occurred  
163 after 14 procedures with calculated mortality rate at discharge of 4%. During the study 57 children died, 24  
164 children who died were operated, other died because of a cardiac anomaly or other related problems. Mortality  
165 related to congenital cardiac defects was thus 3.85 %.

166

167 **Discussion:**

168 Early studies of the incidence of congenital heart disease produced low incidence of about 4 per 1000 live births,  
169 but this figure has been rising steadily until recently when incidences of 12 to 14/1000 live births, or higher,  
170 have been reported in the literature [2,3,6,7,10,13,14, 23,28,33]. Older studies were hampered by lack of non-  
171 invasive diagnostic technique, with mild lesions diagnosed on clinical grounds only, some mild lesions may not  
172 have been included if spontaneous resolution occurred on follow-up with disappearance of clinical signs. On the  
173 other hand, improving diagnostic capability with colour Doppler echocardiography has allowed more confident  
174 diagnoses of minor lesions and increased the number of diagnoses of small degrees of aortic stenosis, pulmonary  
175 stenosis and atrial septal defects. There are also, more reasons for a low incidence, a few studies were restricted  
176 to infancy and so missed some patient who present later in life, some studies bases their data on the results of  
177 foetal echocardiography in populations, these studies will not detect patients with a small ventricular or atrial  
178 septal defects, an abnormal patent ductus arteriosus or many with coarctation of aorta. In certain communities  
179 the increasing use of foetal echocardiography also leads to abortion and can substantially reduce the incidence of  
180 specific lesions or the total incidence. By contrast, high incidences were found in those studies that examined all  
181 or almost all newborns, because they detected large numbers of small ventricular septal defects, foramen ovale  
182 apertum, tiny arterial ducts or other trivial lesions. If studies includes bicuspid aortic valves, isolated lobar  
183 anomalous pulmonary veins connection, so called pulmonary or aortal stenosis with gradient across the valve  
184 less than 20 mmHg, the prevalence should be increased by 20/1000 live births.

185 Actual prevalence of congenital heart disease for the five years period in Croatia is 7.2 per 1000 live births and is  
186 comparable with similar studies. The rates of specific cardiac defects in our study are generally comparable with  
187 those reported from the Baltimore-Washington study by Ferencz et al and from EUROCAT registry [1,6,7]. As  
188 expected, the most frequent diagnosis was ventricular septal defect, followed by atrial septal defect, patent  
189 arterial duct, pulmonary stenosis, and atrioventricular septal defects. These five diagnoses accounted for more  
190 than 60% of all cases.

191 Compared with Baltimore-Washington study, the rate for patent arterial duct was slightly greater, the possible  
192 reason might be excluding patent ductus arteriosus as a single defect in preterm infant before three months, but  
193 inclusion of tiny patent arterial duct with can be incidental finding in hemodynamically normal heart. Some  
194 studies based on echocardiography have shown that in the term infant the ductus arteriosus is almost always  
195 closed by four to seven days after birth [21,22,30], studies done a few days after birth will have recorded a larger  
196 number with a „so called“ patent arterial duct. The rate for atrioventricular septal defect is 4.3%, mean  
197 percentage with regards to reports from other registries with rates from 1.34% to 7.4% [6,33]. Incidence of  
198 atrioventricular septal defects varies in accordance with the age of the involved mothers due to fact that the  
199 Down syndrome is more common in mothers who are more than 34 years old, and atrioventricular septal defects  
200 are very frequent in those with Down syndrome [5,13]. Because termination of pregnancy is performed if  
201 trisomy 21 is discovered, the incidence of atrioventricular septal defects is likely to decrease [13,23]. In Croatia,



202 the official religion is Roman-Catholic and termination of pregnancy is illegal, so prenatal diagnoses and  
203 growing proportion of pregnant women in which foetal echocardiography was done, have no important influence  
204 to prevalence of congenital heart defects. Early fetal deaths or spontaneous abortions, according to the literature,  
205 are not at present covered by registration system, although they may be of great interest for the study of  
206 congenital malformations [20]. Due to the fact that spontaneous abortions and illegal abortions are not  
207 systematically reported and because of potential proportion of illegal abortions because of prenatal diagnoses of  
208 cardiac heart disease, estimated number of unknown cases could remain high [20].

209 The total rates for the 12 severe defects selected did not vary significantly between the studies [27,28]. We  
210 counted rhythm disturbances in our current analysis, mostly paroxysmal supraventricular tachycardia and  
211 neonatal bradycardia together with congenital atrioventricular block, because of recognized proportion of 4.9%  
212 of all congenital heart diseases in our study.

213 During the five years of study, prevalence of congenital defect as well as the prevalence of specific diagnoses  
214 changed in total number. If we look at the prevalence throughout the study, it is possible that prevalence is  
215 higher than in 2006 and 2007 due to fact that some children with congenital heart disease born in last years of  
216 study have not yet been diagnosed and the number may still rise. The prevalence might also rise because of the  
217 fact that some children born in 2007 years and followed up as foramen ovale will be included in the number of  
218 children with congenital heart disease as atrial septal defects at the age of 12 months. Increasing trend of  
219 coarctation of aorta might be due to continuous improving of early diagnoses.

220 For all the cardiac defects, the average sex ratio was 1/0.9. The proportion of males and females is similar to  
221 reports from other studies [6,27,28]. There were significantly high sex ratios in the groups with left sided  
222 opstruction anomalies, aortic stenosis and coarctation of the aorta.

223 The average time of diagnoses shows that most patients with congenital heart disease are now diagnosed during  
224 infant period, with low average time of diagnoses of severe heart defects, near period of discharge from hospital.  
225 Potential factor leading to early detection of congenital heart disease could be due to the fact that Croatia is a  
226 small country, access to medical specialist is good, detection and follow up of patients is fairly centralised and  
227 provided in tertiary medical centres. For these reasons, we think that Croatian population can provide accurate  
228 information on the incidence of congenital heart disease, as well as the age of diagnoses.

229 Patients with cardiac defects often have other congenital anomalies, chromosomal defects and syndromes. The  
230 proportion of comorbidity is between 4-45% depending on many factors [4,6,9-11,20,24,27,28,33]. The  
231 prevalence of congenital heart disease associated with chromosomal anomalies depends on the maternal age  
232 profile in the country, the proportion of chromosomal cases diagnosed prenatally followed by termination of  
233 pregnancy. The percentage of chromosomal defects and other anomalies depends on methodology, such as  
234 differing inclusion criteria for both congenital heart disease and syndromes and malformation [13]. The  
235 increased number of minor defects is diluting the proportion of other anomalies [33]. Distribution of congenital  
236 heart disease associated with non-cardiac malformation is higher in autopsied children reaching percentage of 45  
237 % [12,32]. Here we find 215 children (14.5%) with recognised non-cardiac anomalies. Of these, 50.2% had  
238 chromosomal defects, 14.4 % syndromes and 35.3% other congenital major anomalies. Heritable syndromes can  
239 also be grouped by genetic abnormalities on chromosomal abnormalities, microdeletions, and gene mutations or  
240 by developmental similarities on group associated with situs and looping defects, syndromes with cardiofacial

241 (branchial arch) abnormalities, VACTERL, syndromes with intracardial flow disturbances, sy Noonan,  
242 connective tissue disorders, metabolic genetic syndromes.

243 Delineation of association by developmental events may clarify the etiology of congenital heart disease. Well-  
244 designed family studies could identify individuals at increased risk and provide a scientific basis for genetic  
245 counselling of at-risk families [29].

246 Surgery was performed on 29% of all infants with congenital heart disease. Out of 553 cardiac surgeries  
247 performed, 202 were done in Croatia and 351 were done abroad. Among children who were operated, during the  
248 study, 24 died, giving the all-cause mortality in patients who underwent cardiac surgery of 5.6 %. As it could be  
249 seen after stratification for complexity, majority of complex operations, is still performed in medical centers  
250 abroad. Of all 1480 children with congenital heart disease, during the period of study 57 died (3.85%) because  
251 of heart or other related reasons. Although mortality rate is near reports from other more developed centers [15],  
252 it is not satisfying, especially having in mind that majority of complex surgery procedures is still performed in  
253 centers abroad. Improvements in the medical care of patients with congenital heart disease, including early  
254 diagnoses, diagnostic procedures, neonatal care, intensive care units was not followed by advance in surgical  
255 development. Further analysis should reveal potential problems and additional improvement in the care of  
256 children with congenital heart disease will further diminish the mortality of this common group of congenital  
257 disorders [14].

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## Tables

Table 1. Prevalence of congenital heart disease in Croatia from October 1st 2002 to October 1st 2007

Time period	Live-born children	Children with CHD <sup>a</sup>	Prevalence (per 1000 live-born)
1.10-31.12.2002	9704	79	8.14
2003	39 668	314	7.92
2004	40 307	289	7.17
2005	42 492	314	7.39
2006	41 446	277	6.68
1.1-1.10.2007	31 434	207	6.59
1.10.2002-1.10.2007	205051	1480	0.72

<sup>a</sup> congenital heart disease

Table 2. Distribution of congenital heart defects and the ratio of males and females in children born in Croatia from 1st 2002 to October 1st 2007

Congenital heart disease	Number	(%)	Male/Female
Ventricular septal defect	513	(34,6)	1/0.97
Atrial septal defect	235	(15,9)	1/1.14
Patent arterial duct	145	(9,8)	1/1.16
Pulmonary valvar stenosis	73	(4,9)	1/0.97
Tetralogy of Fallot	49	(3,3)	1/0.78
Transposed great arteries	49	(3,3)	1/0.58
Aortic stenosis	49	(3,3)	1/0.48
Coarctation	47	(3,2)	1/0.42
Atrioventricular septal defect	64	(4,3)	1/1.2
Hypoplastic left heart syndrome	34	(2,3)	1/0.62
Cardiomyopathy	26	(1,8)	1/0.86
Rhythm disturbances	73	(4,9)	1/0.59
Severe heart defect (excluding TF <sup>a</sup> , HLHS <sup>b</sup> , AVSD <sup>c</sup> , TGA <sup>d</sup> )	123	(8,3)	1/0.73
Total	1480	(100,0)	1/0.90

<sup>a</sup> tetralogy of Fallot, <sup>b</sup> hypoplastic left heart syndrome, <sup>c</sup> atrioventricular septal defect and common AV junction,

<sup>d</sup> transposition of great arteries

Table 3. Prevalence of defects during the period of study

N		Year of birth										p*		
		2002		2003		2004		2005		2006			2007	
		N <sup>a</sup>	(%)	N	(%)	N	(%)	N	(%)	N	(%)		N	(%)
513	VSD <sup>b</sup>	30	(38)	112	(35.7)	97	(33.6)	102	(32.5)	92	(33.2)	80	(38.6)	0.570
145	PDA <sup>c</sup>	7	(8.9)	34	(10.8)	36	(12.5)	30	(9.6)	24	(8.7)	14	(6.8)	0.756
235	ASD <sup>d</sup>	5	(6.3)	50	(15.9)	54	(18.7)	48	(15.3)	46	(16.6)	32	(15.5)	0.832
73	PS <sup>e</sup>	6	(7.6)	15	(4.8)	10	(3.5)	17	(5.4)	12	(4.3)	13	(6.3)	0.598
49	Tetralogy of Fallot	3	(3.8)	7	(2.2)	10	(3.5)	16	(5.1)	7	(2.5)	6	(2.9)	0.148
49	TGA <sup>f</sup>	7	(8.9)	12	(3.8)	10	(3.5)	8	(2.6)	7	(2.5)	5	(2.4)	0.670
49	Aortic stenosis	5	(6.3)	10	(3.2)	11	(3.8)	7	(2.2)	6	(2.2)	10	(4.8)	0.629
47	Coarctation	1	(1.3)	3	(1.3)	8	(2.8)	18	(5.7)	14	(5.1)	3	(1.4)	0.002
64	AVSD <sup>g</sup>	1	(1.3)	19	(6.1)	13	(4.5)	15	(4.8)	12	(4.3)	4	(1.9)	0.551
34	HLHS <sup>h</sup>	0	(0.0)	4	(1.3)	7	(2.4)	10	(3.2)	4	(1.4)	9	(4.3)	0.276
26	Cardiomyopathy	3	(3.8)	6	(1.9)	4	(1.4)	6	(1.9)	4	(1.4)	3	(1.4)	0.779
73	Rhythm disturbances	6	(7.6)	16	(5.1)	8	(2.8)	18	(5.7)	16	(5.8)	9	(4.3)	0.135
123	Severe heart defect	5	(6.3)	26	(8.3)	21	(7.3)	19	(6.1)	33	(11.9)	19	(9.2)	0.554
1480	Total	79	(100)	314	(100)	289	(100)	314	(100)	277	(100)	207	100	0.506

\*statistical significance: deviation from the rectangular distribution for the period 2003-2005, <sup>a</sup>number of patients, <sup>b</sup>ventricular septal defects, <sup>c</sup>patent arterial duct, <sup>d</sup>atrial septal defect, <sup>e</sup>pulmonary stenosis, <sup>f</sup>tetralogy of Fallot, <sup>g</sup>atrioventricular septal defect and common AV junction. <sup>h</sup>hypoplastic left heart syndrome

Table 4. Number of infants with identified extracardiac anomaly according to cardiac defect type

Congenital heart defect	Extracardiac anomaly		
	Yes	No	Percentage in number of defects
Ventricular septal defect	40	473	7.8
Atrial septal defect	29	206	12.3
Patent arterial duct	13	132	9
Pulmonary valvar stenosis	6	67	8.2
Tetralogy of Fallot	10	39	20.4
Transposed great arteries	6	43	12.2
Aortic stenosis	4	45	8.2
Coarctation	9	38	19.1
Atrioventricular septal defect	43	21	67
Hypoplastic left heart syndrome	6	28	17.6
Cardiomyopathy	4	22	15.4
Rhythm disturbances	4	69	5.5
Severe heart defects (excluding TGA <sup>a</sup> , TF <sup>b</sup> , AVSD <sup>c</sup> , HLHS <sup>d</sup> )	41	82	33.3
Total	215	1265	14.5

<sup>a</sup>transposition of great arteries, <sup>b</sup>tetralogy of Fallot, <sup>c</sup>atrioventricular septal defect and common AV junction, <sup>d</sup>hypoplastic left heart syndrome

Table 5. Distribution of congenital heart defects accompanied by syndromes, chromosomal anomalies and other major congenital anomalies.

<i>A. Chromosomal anomaly</i>	Percentage (%)
Down syndrome	45.1
Turner syndrome	2.8
Edwards syndrome	1.4
Patau syndrome	0.9
Total	50.2
<i>B. Syndrome</i>	
Microdeletions	
Di George	5.1
Williams Beuren	2.8
Conotruncal face sy	0.9
Gene mutations	
Noonan	1.4
Ivemark	1.4
Allagile	0.5
Ellis van Creveld	0.5
Jeune	0.5
Klippel-Trenaunay-Weber	0.5
VACTERL	0.9
Total	14.4
<i>C. Other congenital defects</i>	
Gastrointestinal tract	8.4
Cleft palate and/or lip	5.6
Anomalies of head and face	5.6
Neurological and developmental defects	4.7
Genito-urinary tract	4.2
Multiple congenital defects	4.2
Anomalies of other thoracic organs	1.4
Haematological disease	1.4
Total of other congenital defects	35.3
Total	100