Long-term experience with the prenatal diagnosis of cardiac anomalies in high-risk pregnancies in a tertiary center

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Key words:
Arrhythmia; Congenital heart disease; Diagnosis; Echocardiography.

Background. **The aim of this study was to analyze the role of the prenatal diagnosis of cardiac anomalies in our center.**

Methods. **The data of 5540 pregnant women at risk for congenital heart disease and studied at fetal echocardiography between 1984 and 2002, with complete follow-up were retrospectively analyzed.**

Results. **There was a progressive gradual increase in the number of cases examined per year; 670 fetuses (12% of the population) had congenital heart disease, 6.3% of the milder lesions were not detected. A cardiac arrhythmia was diagnosed in 284 fetuses. Extracardiac and chromosomal anomalies were associated in 23.7 and 14.6% respectively. Recurrence of congenital heart disease was 4.1%. One hundred and seventy-four patients (26%) opted for pregnancy termination; of the 496 fetuses whose parents decided to continue with pregnancy, 10.1% died *in utero*, 33.7% postnatally and 56.2% survived. The post-surgical mortality was 30.4%. Negative prognostic factors were associated anomalies, heart failure and complex congenital heart disease. Twenty-nine out of 33 fetuses with persistent tachyarrhythmias treated *in utero* survived; fetuses with complex and isolated atrioventricular block had a 75 and 11.1% mortality.**

Conclusions. **Prenatal diagnosis was useful in the management of pregnancy and a planned birth and was life-saving in case of tachyarrhythmia.**

(Ital Heart J 2003; 4 (12): 855-864)

Received June 12, 2003; revision received September 29, 2003; accepted October 6, 2003.

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Introduction

Prenatal screening for congenital heart anomalies by means of fetal echocardiography is nowadays a part of routine fetal evaluation in specialized centers. Screening in unselected populations yields a low sensitivity and specificity, but a good diagnostic accuracy, even for complex cardiac lesions, may be achieved by specialized operators[1-12]. The clinical utility of an early diagnosis of cardiac anomalies is, however, still controversial. Ethical problems related to the decision regarding the continuation of pregnancy and impact on the future of pediatric cardiology and cardiac surgery are discussed[13-15]. It is obvious that specific conditions in each country influence both the diffusion of screening for cardiac abnormalities as well as the level of obstetrics and also the decision taken by involved families.

The purpose of this study was to analyze our experience with prenatal cardiac diagnosis, in a tertiary center, during a 17-year period, considering both the basal aspects of the screening as well as the outcome of the cases diagnosed as having cardiac problems. The data regarding the first period of our activity were reported in a previous study[2].

Methods

An organized prenatal echocardiographic diagnostic activity was started in our center in November 1984. Until December 2002, a total of 5590 pregnant women at risk for congenital heart disease was studied at fetal echocardiography. The reasons for referral were either maternal risk factors (family history of congenital heart disease, maternal diseases such as connective tissue disorders, diabetes, infections acquired in pregnancy, etc.) or fetal risk factors found at routine obstetric ultrasound scan (fetal structural malformations, amniotic fluid volume abnormalities, unexplained fetal growth retardation, non-immune fetal hydrops or a specific suspicion of a cardiac anomaly or arrhythmia). The gestational age at first examination varied between 16 and 39 weeks (median 28

weeks). About two thirds of the cases were referred from first- or second-level obstetric centers, while the cases with a familial risk were often sent by cardiologists.

The echocardiographic examination of the fetuses (using two-dimensional, M-mode Doppler and, since 1986, color Doppler techniques) was performed according to routine methodology together with a complete fetal scan. The ATL Ultramark 9 (Advanced Technical Laboratory, Bothell, Washington, DC, USA) and Acuson 128 XP/10 (Mountain View, CA, USA) machines, with 5 and 3 MHz probes, were used for fetal evaluation. Follow-up examinations were performed in those cases in which the parents decided to go ahead with pregnancy in spite of the presence of fetal cardiac anomalies. We planned these examinations according to the clinical indications, usually at 3-4 week intervals.

The analysis of the current report was aimed at the evaluation of:
1) basal aspects of the prenatal cardiac diagnostic activity (number of cases studied per year, referral factors, diagnostic precision) dividing the examined period in two: the first period 1984-1988, analyzed in a previous report[2], and the second period 1989-2002;
2) analysis of the series with congenital heart disease and of the group with arrhythmias with regard to their specific features, the presence of associated anomalies or of heart failure (defined as the presence of cardiomegaly, signs of right ventricular insufficiency, with tricuspid regurgitation and associated ascites, hydrothorax, hydropericardium or subcutaneous edema, in progression according to the entity). The outcome of the affected cases was analyzed with respect to the subgroups of cardiac pathology.

The diagnosis of the presence or absence of a cardiac anomaly was compared with the postnatal follow-up data or with the *postmortem* diagnosis, directly by some of us in case of delivery in our hospital, otherwise by means of questionnaires sent to the families or by telephone interview. The minimum interval for the conclusive cardiological postnatal diagnosis was 6 months of age (in order to exclude minor cardiac defects). By June 2003, follow-up data had been obtained for 5540 cases.

Results

Basal aspects of the screening. There was a gradual increase in the number of new cases studied per year: 447 cases were examined in the first period and 5143 cases since then; the trend is shown in figure 1. Accordingly, there was an increase in the number of cases diagnosed annually as having a cardiac anomaly.

In both periods there was a large number of cases referred for fetal risk factors (50% that increased to 63% during the second period). The number of cases referred for a family history and maternal diseases did not significantly differ, while a specific referral for a suspicion of a cardiac anomaly increased from 6 to 24% in the second period, with a mean of 15%.

The median age at the time of diagnosis of a congestive heart disease was 28 weeks of gestation (30 weeks during the first period and 26 weeks during the second one). An early diagnosis before 24 weeks of gestation was made in 59.7% of cases (402/670), but only in 17% of cases during the first period (14/80). This percentage increased to 65.8% (388/590) during the second period.

Table I compares the frequency of single referral factors in the general population and in the series with congenital heart disease. It is evident that the prevalence of congenital heart disease was higher among cases referred for fetal risk factors (especially among those with extracardiac anomalies or sent for a specific suspicion of a cardiac abnormality). Twenty one percent of the population screened was referred for familial risk factors; the overall recurrence rate of congenital heart disease was 4.1% (47/1131), but these cases constitute 8.3% of the series with congenital heart disease.

Frequency of congenital heart disease in the population. A fetal diagnosis of congenital heart disease was made in 635/5540 cases (11.5%). There were other 35 cases in whom minor types of congenital heart disease such as small ventricular o atrial septal defects were diagnosed after birth, from a few days up to 6 months of age (6.3% of cases with false negative fetal diagnosis). A total of 670 cases (12% of the population with a

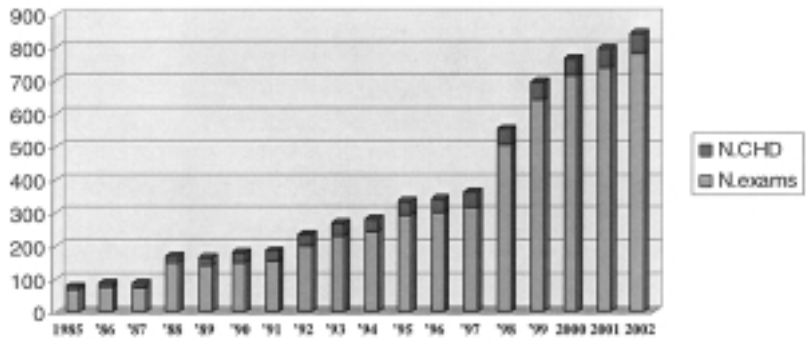

Figure 1. *Number of exams (new cases) and of cases with congenital heart disease (CHD) studied at fetal echocardiography per year (1985-2002).*

Table I. Frequency of single referral reason in the total referred population and in the series with congenital heart disease (CHD).

Referral factor	General population (%)	Series of CHD (%)
Anamnestic risk factors		
Familiarity for CHD	21	8.3
Familiarity for ECA/CA	3	1
Maternal disease/infections/drugs	10	2
Fetal risk factors		
Non-immune hydrops fetalis	2	15
Fetal ECA	16	23
Fetal CA	5	3
Retarded fetal growth	8	8
Poly/oligohydramnios	2	6
Fetal arrhythmias	20	5
Suspicion of CHD at obstetric echography	15	32

CA = chromosomal anomaly; ECA = extracardiac anomaly.

known follow-up) was therefore affected with congenital heart anomalies and these cases were considered for the global analysis. Fetal congenital heart disease was diagnosed in 635 of the 670 cases in whom it was finally documented (sensitivity 94.8%).

Frequency of fetal arrhythmias. Cardiac arrhythmia was present in 284 fetuses with or without structural cardiac anomalies (5.1% of the population studied). An extrasystolic arrhythmia was diagnosed in 220 cases: 39 had tachyarrhythmias [6 an episodic supraventricular tachyarrhythmia, 21 persistent supraventricular tachyarrhythmias (of whom 9 with heart failure) and 11 with atrial flutter (of whom 6 with heart failure]. Twenty-five cases had complete atrioventricular block, associated with congenital heart disease in 16 and isolated in 9 (in the presence of maternal connective tissue disease or of anti-Ro, anti-La antibodies).

Diagnostic precision and problems. As mentioned above, out of the series with congenital heart disease, there were 35/670 cases (6.3%) with a false negative diagnosis. An incomplete or imprecise diagnosis was made in 28/670 cases (4.2%).

The more commonly missed pathology was ventricular septal defect (usually small muscular defects found after birth) and small atrial septal defects found obviously only after birth; other missed diagnoses included one mild form of tetralogy of Fallot, one case of transposition of the great arteries seen at 18 weeks of gestation, a few cases of mild pulmonary stenosis, bicuspid aortic valve and 3 cases of aortic coarctation, one complicated with massive hydrops. The diagnosis was incomplete in the cases with isomerism and with complex congenital heart anomalies, where we could not precisely define all cardiac features.

Major diagnostic difficulties arose in the cases examined during the third trimester that showed an excessively large right ventricle in comparison to the normal standard values for gestational age[16], with an otherwise normal left ventricle and aortic arch and a large foramen ovale (19 cases): a diagnosis of a probable future postnatal atrial septal defect ostium secundum was made in some of them, when the foramen ovale exceeded 8 mm in diameter; in others the evolution toward a mild form of aortic coarctation was hypothesized. After birth 13 of these cases showed a mild-to-moderate atrial septal defect ostium secundum, exceeding the habitual transient features of a small patency of the foramen ovale and still unchanged and hemodynamically significant at 6 months of age; 6 infants had a mild kinking of the aortic isthmus, without any significant transisthmic gradient.

Severe aortic coarctation was usually diagnosed on the basis of a markedly dilated right ventricle; in some cases the isthmic narrowing was clearly visible only later on (at 25-28 weeks of gestation).

Characteristics and outcome of the series with congenital heart disease. Table II shows the frequency of the single groups of congenital heart disease, with their relative outcome. In this analysis we also included, as a group 8, cases with idiopathic non-immune hydrops (a condition which does not constitute an anatomic cardiac lesion), because of their characteristic features of cardiac involvement (enlargement of the right heart sections and tricuspid regurgitation) and relevant impact that we wanted to analyze. Figure 2 shows the distribution of single congenital heart lesions in the series, with an evidently higher frequency of more complex anomalies. In our series we had a relatively large number of cases diagnosed as having ventricular septal defects and others in which a diagnosis of a probable future atrial septal defect was made during the third trimester screening (as reported above).

Association with chromosomal and extracardiac anomalies (Fig. 3). Out of 670 fetuses with congenital heart disease, 98 (14.6%) had chromosomal anomalies (38

Table II. Subdivision of the series of fetuses with cardiac anomalies according to pathology and respective outcome.

Group of CHD	No. cases	TP	IUD	Postnatal death	Alive)
AV defect	99	33 (33.3%)	10 (10.1%)	36 (36.4%)	20 (20.2%)
Isolated	56				
Complex	43				
Anomalies of the AV connections	146	57 (38.8%)	9 (6.1%)	48 (32.4%)	33 (22.25%)
UVH	31				
HLV	68				
TrA	32				
Eb/NEb	15				
Anomalies of the V-A connections	116	35 (30.2%)	5 (4.3%)	26 (22.4%)	50 (43.1%)
Tetralogy of Fallot	33				
Pulmonary atresia + VSD	11				
Pulmonary atresia + intact septum	2				
Truncus	10				
TGA	20				
CTGA	8				
DORV	32				
Shunts	122	19 (15.6%)	8 (6.6%)	11 (9%)	84 (66.7%)
VSD	88				
ASD2	34				
Anomalies of the great vessels	72	9 (12.5%)	1 (1.4%)	17 (23.6%)	45 (62.5%)
CoA	42				
AS	10				
PS	20				
Anomalies of the myocardium	50	9 (18%)	7 (14%)	16 (32%)	18 (36%)
DCM	6				
Myocarditis	11				
HCM	33				
Miscellaneous	42	8 (19%)	0	8 (19%)	26 (61.9%)
Tumors	12				
IFNI	22	4 (18.2%)	10 (45.5%)	5 (22.7%)	3 (13.6%)
Total	670	174 (26%)	50 (7.5%)	167 (24.9%)	279 (41.6%)

AS = aortic stenosis; ASD2 = atrial septal defect ostium secundum; AV = atrioventricular; CoA = coarctation of the aorta; CTGA = corrected transposition of the great arteries; DCM = dilated cardiomyopathy; DORV = double outlet right ventricle; Eb = Ebstein tricuspid valve dysplasia; HCM = hypertrophic cardiomyopathy; HLV = hypoplastic left ventricle; IFNI = idiopathic fetal non-immune hydrops; IUD = intrauterine death; NEb = non-Ebstein tricuspid valve dysplasia; PS = pulmonary stenosis; TA = truncus arteriosus; TGA = transposition of the great arteries; TP = termination of pregnancy; TrA = tricuspid atresia; UVH = univentricular heart; V-A = ventriculo-arterial; VSD = ventricular septal defect.

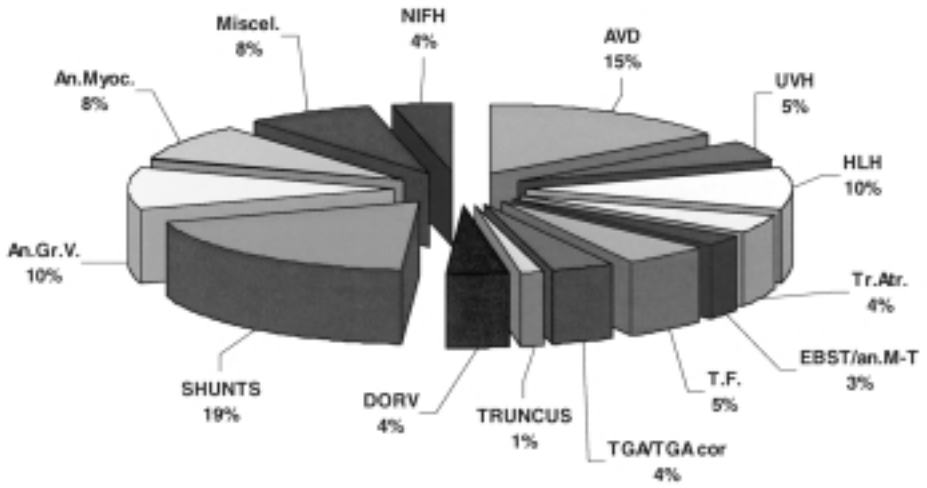

Figure 2. *Subdivision of the series according to the type of cardiac anomaly. An.Gr.V. = anomalies of the great vessels/semilunar valves; An.Myoc. = anomalies of the myocardium; AVD = atrioventricular defect; DORV = double outlet right ventricle; EBST/an.M-T = Ebstein/anomalies of the tricuspid-mitral valve; HLH = hypoplastic left heart; Miscel. = miscellaneous; NIFH = non-immune fetal hydrops; TF = tetralogy of Fallot; TGA/TGA cor = transposition of the great arteries/corrected; Tr.Atr. = tricuspid atresia; UVH = univentricular heart.*

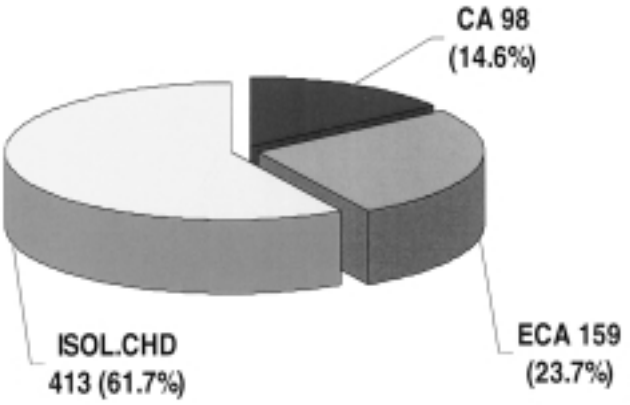

Figure 3. *Subdivision of the series according to the associated chromosomal (CA) and extracardiac anomalies (ECA). ISOL.CHD = isolated congenital heart disease.*

cases had trisomy 21, 32 trisomy 18, 7 trisomy 13, and 20 other anomalies) and 159 (23.7%) had associated extracardiac anomalies. Among the fetuses with extracardiac anomalies there were also cases with features of cardiac hypertrophy, hypertrophic cardiomyopathy, with an increased thickness of the cardiac walls with respect to the normal standard values[16]; this was usually observed in association with renal or central nervous system malformations. There were also other 3 fetuses with a pattern of dilated cardiomyopathy and associated extracardiac anomalies.

Signs of heart failure were present in 96 fetuses (14.3%). Table III summarizes the frequency of chromosomal and extracardiac anomalies and of heart failure per single groups of cardiac defects.

Twenty-four fetuses (3.6%) were twins.

Arrhythmia was associated with congenital heart disease in 32/670 fetuses: extrasystoles in 14 cases, supraventricular tachycardia in 2 (short episodes associated with an extrasystolic arrhythmia in one case of atrioventricular defect and a persistent form in another case with features of left ventricular dilated cardiomyopathy) and atrial flutter in a fetus with cardiomyopathy in a diabetic mother; 16 fetuses had a third degree atrioventricular block associated with a congenital heart anomaly (Table IV).

Outcome of the cases with congenital heart disease. Out of 670 cases, 174 (26%) and 60% of those with an early diagnosis opted for termination of pregnancy: 44 with associated chromosomal anomalies, 53 with extracardiac anomalies and 77 with serious isolated congenital heart disease.

Among the 496 fetuses that continued pregnancy 50 (10.1%) died *in utero*; 167 (33.7%) died postnatally and 279 (56.2%) survived. Out of 96 fetuses with heart

Table III. Frequency of extracardiac (ECA) and chromosomal anomalies (CA) and of heart failure (HF) per group of congenital heart disease (CHD).

Group of CHD	ECA (%)	CA (%)	HF (%)
Isolated AV defect	16.7	59.2	16
Complex AV defect	11.7	16.3	10
Anomalies of the AV connections	18.5	0.7	17.5
Anomalies of the V-A connections	22.2	21.4	2.4
Shunts	27.6	18.7	5
Anomalies of the great arteries	16.7	11.1	8.6
Anomalies of the myocardium	46	8	35.9

AV = atrioventricular; V-A = ventriculo-arterial.

Table IV. Subdivision of fetal arrhythmias.

Type of arrhythmia	No. cases	HF	IUD	ND	Alive
Extrasystole	220				
Supraventricular	190	–	–	–	190
Complex*	30	–	–	–	30
Tachyarrhythmias	39				
Episodic SVT	6	–	–	–	6
Persistent SVT	21	9	1	1	19
Atrial flutter	12	6	–	3	9
Total AV block	25				
Isolated (SLE, LLAC, anti-Ro)	9	3	1	–	8
Complex (AVD, UVH, cTGA, PS)	16	9	4	8	4

AV = atrioventricular; AVD = atrioventricular defect; cTGA = corrected transposition of the great arteries; HF = heart failure; IUD = intrauterine death; LLAC = lupus-like anticoagulant syndrome; PS = pulmonary stenosis; SLE = systemic lupus erythematosus; SVT = supraventricular tachycardia; UVH = univentricular heart. * supraventricular and ventricular.

failure, only 13 survived (13.5%). In 96 cases with ductus-dependent congenital heart disease the delivery was planned in a cardiac surgery center in order to optimize the postnatal treatment.

Thirty-two infants underwent invasive procedures (Rashind septectomy, pulmonary and aortic valvuloplasty and pacemaker implant). Two infants with complete atrioventricular block associated with an atrioventricular defect died after pacemaker implantation due to advanced hydrops; 20 of them were subsequently operated.

One hundred and sixty-one infants underwent first step cardiac surgery (palliative procedures or correction of defects such as coarctation): 46 cases (28.6%) died perioperatively and 5 infants (3.1%) died later on of endocarditis, cardiac arrest or other conditions; 27 infants underwent second step cardiac surgery (1 died) and 6 underwent third step cardiac surgery (1 died). The total postsurgical mortality was 31.75% (51/161 infants). Table V illustrates the surgical mortality in different periods; it is evident that in the more recent years the surgical mortality was significantly reduced; however, it should be borne in mind that the Norwood procedure (associated with a very high mortality) was recently performed in a smaller number of cases.

The overall mortality was 32.4% for the whole series and 43.7% for those cases in which pregnancy was continued (217/670 cases). It was higher in the presence of chromosomal or extracardiac anomalies (Fig. 4) and in cases of heart failure. Antifailure maternal-fetal treatment with digoxin was attempted in 23 cases, without any substantial effect in all but 2 cases. The mortality was higher in more complex cardiac defects (anomalies of the atrioventricular connections and myocardial disease, as shown in table II). Figures 5 and 6 show the trend of mortality *in utero* and postnatally, for each of the cardiac defects.

A total of 279 infants survived (41.6% of the whole series and 56.2% of those cases in whom pregnancy was continued) and they are now aged 16 months-15 years (median 5.4 years).

The survival rate was higher for isolated congenital heart disease and for less complex cardiac defects (shunts, and in the group of anomalies of the great vessels; Table II and Fig. 4).

Types of fetal arrhythmias and relative outcome (Table IV). Fetuses with extrasystolic arrhythmias and episodic supraventricular tachyarrhythmia did not require specific treatment and were born alive with tran-

Table V. Surgical mortality.

Period	No. cases	Perioperative mortality	No. late deaths	Norwood first step mortality	Total mortality
1985-1996	61	27 (44.3%)*	2	7/9 (77.7%)	29/61 (47.9%)
1997-1999	44	9 (20.5%)**	1	2/4 (50%)	10/44 (22.7%)
2000-2002	56	10 (17.8%)***	2	1 case died	12/56 (21.4%)
Total	161	46 (28.6%)§	5	10/14 (71.4%)	51/161 (31.7%)

* all first step cardiac surgery; ** 8 first step, 1 second step cardiac surgery; *** 9 first step, 1 third step cardiac surgery; § 42 first step, 1 second step, 1 third step cardiac surgery.

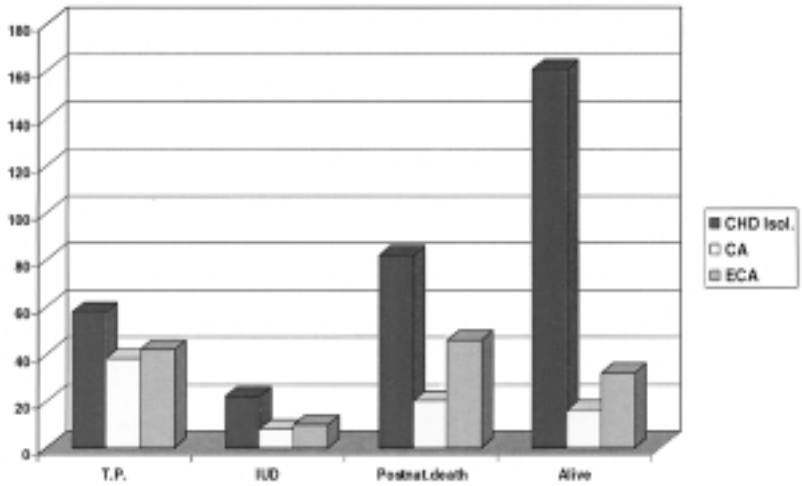

Figure 4. *Outcome in fetuses with isolated congenital heart disease (CHD) and associated with extracardiac (ECA) and chromosomal anomalies (CA). IUD = intrauterine death; TP = termination of pregnancy.*

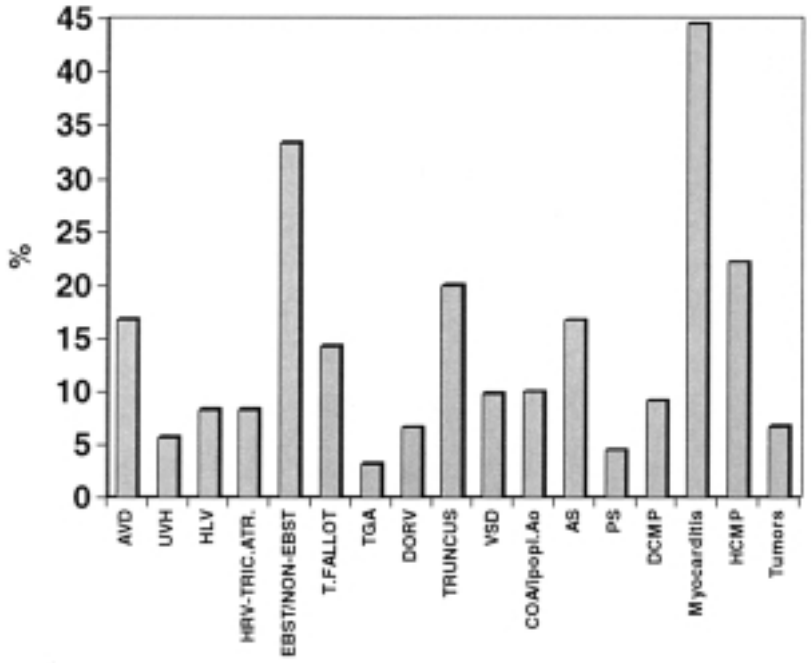

Figure 5. *Intrauterine mortality in single types of congenital heart disease (percentage of cases continuing pregnancy). AS = aortic stenosis; AVD = atrioventricular defect; COA = coarctation of the aorta; DCMP = dilated cardiomyopathy; DORV = double outlet right ventricle; EBST/NON-EBST = Ebstein/non-Ebstein anomalies; HCMP = hypertrophic cardiomyopathy; HLV = hypoplastic left ventricle; HRV = hypoplastic right ventricle; PS = pulmonary stenosis; TGA = transposition of the great arteries; TRIC.ATR = tricuspid atresia; UVH = univentricular heart; VSD = ventricular septal defect.*

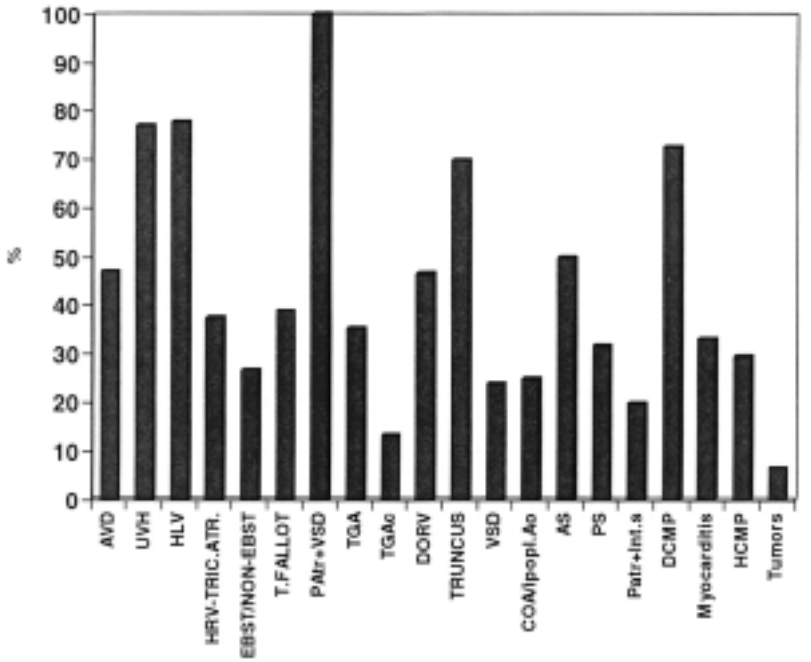

Figure 6. *Postnatal mortality in single types of congenital heart disease (percentage of cases continuing pregnancy). AS = aortic stenosis; AVD = atrioventricular defect; COA = coarctation of the aorta; DCMP = dilated cardiomyopathy; DORV = double outlet right ventricle; EBST/NON-EBST = Ebstein/non-Ebstein anomalies; HCMP = hypertrophic cardiomyopathy; HLV = hypoplastic left ventricle; HRV = hypoplastic right ventricle; PAtr = pulmonary atresia; PS = pulmonary stenosis; TGA = transposition of the great arteries; TGAc = corrected transposition of the great arteries; TRIC.ATR = tricuspid atresia; UVH = univentricular heart; VSD = ventricular septal defect.*

sient rhythm problems only. Among 33 fetuses with persistent tachyarrhythmias, maternal-fetal treatment was indicated in 29; digoxin was used as a first choice drug, associated in 2 cases with verapamil and in 5 with flecainide; in 2 cases three drugs were used. Intrauterine rhythm control was achieved in 19/29 fetuses treated (65.5%); digoxin alone was effective in 13 (44.8%), with a better response in non-hydropic fetus-

es. Five fetuses with hydrops died, 1 *in utero* and 4 after a preterm delivery due to premature rupture of membranes[17].

Out of a total of 25 cases with complete atrioventricular block, 12/16 cases with associated congenital heart disease (75%) and 1/9 (11.1%) with isolated block died. Survival was better in cases with isolated block and in those with less complex congenital heart disease.

Discussion

The composition of our series with congenital heart disease corresponds to the reports of other groups, as for a higher frequency of complex congenital heart anomalies and a higher frequency of the association of congenital heart disease with extracardiac and chromosomal anomalies in comparison to the postnatal data[1-3,18-21]. This fact is partly due to the referral reasons and partly to a high intrauterine loss of fetuses with complex cardiac defects or multiple malformations.

Our series with congenital heart disease however shows some peculiarities: the median age at the time of diagnosis of the cardiac anomaly was rather high in this population, with about 40% of the cases with congenital disease diagnosed during the late second or third trimester. This fact explains a larger number of cases with minor cardiac anomalies such as ventricular septal defects (difficult to detect at an earlier stage of pregnancy) and also the increased frequency of cases with an abnormal right ventricular prevalence seen in the third trimester. In some of the latter cases we made a diagnosis of a probable future atrial septal defect because of the finding of a larger foramen ovale than the normal standard; these cases actually presented the features of a moderately sized atrial septal defect after birth and still at 6 months of age. Other cases with an abnormal right ventricular prevalence showed mild aortic coarctation/kinking after birth. Some cases with small ventricular or atrial septal defects were diagnosed only after birth (at the 6-month clinical evaluation). However, there was an increase in the number of cases with an early diagnosis, within 24 weeks of gestation, in the second period of the analysis (obtained in 65.8% of cases).

We have also observed a rather frequent association of hypertrophic cardiomyopathy, of a secondary form, with extracardiac anomalies (renal or central nervous system malformations) or with metabolic disorders. This fact may be attributable to the frequent referral for these maternal or fetal conditions to our center, but has already been reported in the literature[18,22]. Fetuses with associated renal problems frequently presented with an increased arterial pressure after birth. The outcome of our series confirms the experience of other groups: the fetal and postnatal mortality of fetuses with associated extracardiac or chromosomal anomalies or in cases with heart failure was high. This is in accordance with the findings of other authors[1,3,18-21], all of whom indicated these conditions as negative prognostic factors. It is well known that some heart defects, which predispose to valvular insufficiency (such as atrioventricular septal defect, Ebstein anomaly or truncus arteriosus) or those with an impaired myocardial contractility, expose the fetus/infant to the early development of heart failure and have a poor prognosis[19-25]. In fact, heart failure was more frequent among those fetuses affected by myocardial disease, atrioventricular defects and anomalies of the tricuspid valve with a high perinatal loss. An equally high mortality has been reported by many authors for tachyarrhythmias complicated by hydrops and complete atrioventricular block[26,27]. In our series, the fetuses with isolated block or the cases associated with more simple cardiac anomalies had a better survival.

Termination of pregnancy in cases with severe congenital heart disease was chosen in our series by a lower percentage of cases than that reported by other authors: 25% of the overall series, but 59% of those with an early diagnosis; in two thirds of cases associated anomalies were present. The percentage of couples who opt for termination of pregnancy varies in different reports, being influenced by the peculiar ethical and religious customs of different countries.

The overall survival of our series was slightly better than in some other reports[3,18]; this fact is partly due to the composition of our series, which also included less severe cardiac anomalies.

In our experience, fetuses with ductus-dependent lesions did not present problems during fetal life, with the exception of 2 cases with aortic coarctation who developed heart failure. In this group of defects the clinical utility of prenatal diagnosis is certainly higher, giving an opportunity to organize a planned delivery in a specialized cardiac surgery center and thus increase the probability of a better surgical outcome *quoad vitam*. The postsurgical mortality was still high in our series; however, during the last years there was an evident decrease, thanks to the improvement in surgical techniques; on the other hand, we have to point out that operations such as the Norwood procedure, which are associated with the highest mortality[28], are being performed less often during the last years (due to increasingly frequent preference of couples for the termination of pregnancy in these cases). There is still controversy regarding the benefits of prenatal diagnosis in terms of a better survival and surgical outcome[15,29]. However, recent studies indicate a better outcome in cases with a prenatal diagnosis as compared to those diagnosed postnatally[29-34].

The diagnostic accuracy achieved by our group concerning screening in high-risk pregnancies was comparable to that of other reports[4,5,7,9,11], with a good sensitivity. It is well known that some cardiac anomalies such as ventricular septal defects might not be detected

and we feel that this limit should be explained to the couple. An incomplete diagnosis of minor associated cardiac lesions usually does not play an important role in the management of the cases. In case of an abnormal prevalence of the right heart sections with respect to the normal standard values for gestational age, we found it rather difficult to correctly evaluate the fetuses during the third trimester echocardiography. This problem has also been pointed out by others, and at times it is only at the postnatal evaluation that the cardiac situation is correctly assessed. Future atrial septal defects, duct patency or mild aortic coarctation cannot be always excluded[35,36].

Having analyzed the screening activity for congenital heart disease throughout a long period, we can conclude that some aspects changed only slightly: referral to our center is still prevalent for fetal risk factors and, mainly, for associated extracardiac or chromosomal anomalies, which is explained by an intense activity of our tertiary center in global prenatal diagnosis. Our activity increased throughout the years both in terms of the number of new cases examined per year and of the cases diagnosed as having a congenital heart disease. Besides, there certainly was a significant increase in the number of cases diagnosed earlier, within 24 weeks of gestation. In our context, however, specific referral for a suspicion of a cardiac anomaly increased only from 6 to 24%, which is still a low percentage that should be improved at the obstetric level (increasing the general knowledge and skill of obstetricians in the ultrasound examination of the fetal heart).

Studies regarding fetal heart screening, based on the 4-chamber view, in low-risk pregnancies in two other Italian regions[8,12] showed a still rather low overall sensitivity, but a higher specificity for major heart defects.

Considering the relatively low prevalence of the heart defects detected, screening of congenital heart disease in cases with a positive family history might seem to be poorly productive. However, our data and a previous analysis by our group show a higher recurrence rate of congenital heart disease with respect to the literature and, specifically a high recurrence of serious anomalies such as a hypoplastic left heart syndrome, atrioventricular defect, tetralogy of Fallot or hypertrophic cardiomyopathy[37,38]. Exclusion of a major cardiac problem is very important from the psychological and emotional points of view for these families.

The detection and a precise diagnosis of fetal arrhythmias are truly fundamental, mainly in tachyarrhythmias in which an early diagnosis and a successful treatment are life-saving. Fetuses with congenital heart block may benefit from prenatal diagnosis, mainly in terms of the management of pregnancy. A specific treatment with steroids or inotropes may be useful in these cases[39].

In conclusion, our analysis shows a good prenatal diagnostic sensitivity achieved in our center, but still a rather low detection rate of cardiac anomalies at the obstetric level. Despite the severe prognosis of cases with complex heart defects, we feel that an early prenatal diagnosis should be offered to the couple so as to allow for a more conscious management of pregnancy.

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