Clinical research

The spectrum of adult congenital heart disease in Europe: morbidity and mortality in a 5 year follow-up period

The Euro Heart Survey on adult congenital heart disease

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Aims To describe clinical and demographic characteristics at baseline of a European cohort of adults with congenital heart disease (CHD) and to assess mortality and morbidity in a 5 year follow-up period.
Methods and results Data collected as part of the Euro Heart Survey on adult CHD was analysed. This entailed information transcribed from the files of 4110 patients diagnosed with one of eight congenital heart conditions ('defects'), who consecutively visited the outpatient clinics of one of the participating centres in 1998. The patients were included retrospectively and followed until the end of 2003 for a median follow-up of 5.1 years. Notwithstanding their overall relatively good functional class and low mortality over the follow-up period, a considerable proportion of the patients had a history of endocarditis, arrhythmias, or vascular events. There were major differences between the eight defects, both in morbidity and regarding specific characteristics. Outcomes were worst in cyanotic defects and in the Fontan circulation, but a considerable proportion of the other patients also suffer from cardiac symptoms. In particular, arrhythmias are common.
Conclusion The spectrum of adult CHD in Europe emerging from this survey is one of a predominantly young population with substantial morbidity but relatively low mortality in a 5 year period.

Introduction

The Euro Heart Survey (EHS) programme provides a structured context for gathering information on large, international, patient populations in a 'realistic' setting of actual day-to-day clinical decision making. The perspectives opened thereby are especially attractive in the field of congenital heart disease (CHD), in which scarcity of data is the norm rather than the exception. The existence of a substantial population of adults born with a cardiac defect is a relatively new phenomenon that has resulted from advances in paediatric cardiology, cardiac surgery, and other subspecialties over the past few decades. Adults with CHD are often faced with symptoms, sequelae, and complications from residual defects and interventions, including arrhythmias, congestive heart failure, endocarditis, psycho-social problems, and early death. However, epidemiological characteristics of this population, needs for care, and clinical outcome are still poorly known. In contrast to other cardiovascular diseases, not more than a few multi-centre trials have been performed and there have been no large randomized trials addressing treatment strategies. Thus, current guidelines for the management of adults with CHD are based mainly on non-randomized studies, case series, and results of consensus conferences.[1–6]

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Considering the aforementioned issues, the European Society of Cardiology has supported this survey to describe the spectrum of disease and outcomes in adults with CHD and to evaluate the role of guidelines in clinical practice. Reporting on the results of this EHS, this article describes the patient population and the manifestation of morbidity and mortality in a 5 year follow-up period.

Methods

The set-up of the study was devised and monitored by an expert committee. The existing EHS network was used for recruitment of centres and data entry. Overall data management was conducted by the staff of the Heart House in Sophia Antipolis in France.

Design of the survey

Considering the low prevalence of the various defects and low frequency of cardiovascular events, the survey was designed as a retrospective cohort study. Consecutive patients fulfilling the inclusion criteria (see what follows) were included retrospectively at their first visit to the outpatient clinic in 1998 (or else 1999 or 2000) and their follow-up data until April 2004 were recorded reviewing the medical chart. Patients were included by the local investigators.

Patients (inclusion criteria)

According to the protocol, all patients aged >17 years who had a diagnosis of one of the following eight congenital cardiac conditions ('defects') were included: cyanotic disease, Fontan circulation (i.e. status after the Fontan operation, a palliative intervention in patients with a single functional ventricle), tetralogy of Fallot, aortic coarctation (CoA), complete transposition of the great arteries (TGA), Marfan syndrome, ventricular septal defect (VSD), or secundum atrial septal defect (ASD). If more than one diagnosis applied, the diagnosis appearing first in the order in which they are listed earlier was chosen as the main diagnosis (but in the case of ASD and VSD, the more severe of the two).

Centres

Centres were identified from the lists of European hospitals with facilities for care of adults with CHD, provided by the national co-ordinators of the EHS programme, and through the Working Group on Grown-Up Congenital Heart Disease of the European Society of Cardiology. Contact persons were approached by e-mail. In addition, the survey was advertized on the EHS website and in the European Society of Cardiology's web news. Participation was on a voluntary basis and both specialized (see what follows) and non-specialized centres following a substantial population of adult patients with CHD were included.

Specialized centres were defined as tertiary referral centres meeting all three of the following criteria: availability of paediatric cardiology or congenital cardiac surgery, at least one cardiologist dedicated to adult CHD, and at least 200 congenital outpatient visits per year.

Data collection and entry

Demographical and clinical data were derived from patients' medical records and entered online in a web-based electronic case record form (CRF). The CRF was developed under the auspices of the Expert Committee and data were entered by the investigators themselves or by specially trained data collection officers.

Patient data were entered anonymously, with only a number to identify the centre and another indicating the order of entry. The CRF was supplied with a software-implemented utility for automated checking of data for consistency and completeness and to ensure that values were not excessively out of the normal range.

The electronic files were managed by the data management staff at the European Heart House, who also performed additional queries in case of missing, incomplete, or 'outlying' data. The database was opened on 1 July 2003 and closed on 30 April 2004.

Data collected

The following data were collected: a general section of the CRF assessed demographic data; the use of medication; diagnostic procedures performed during follow-up; clinical baseline characteristics (such as functional status) and history of endocarditis, arrhythmias, or vascular events; pregnancies; and vital status at the end of follow-up. Arrhythmias considered were supraventricular arrhythmias and ventricular arrhythmias, but premature beats were excluded.

In separate sections devoted to the individual defects, defect-specific diagnostic findings (both quantitative and qualitative) at study entry as well as changes in the parameters assessed, which occurred during follow-up, were to be recorded. In addition, it was required to indicate which interventions (surgical or transcatheter) had been performed before study entry and during follow-up.

Data analysis

The final database was sent for analysis to the EHS adult CHD data analysis centre at the Academic Medical Centre in Amsterdam.

Statistical methods used were mainly descriptive. Categorical variables are presented as percentages and numbers: continuous variables as means (standard deviation) for normally distributed variables and as medians (interquartile range) for non-normally distributed data. Mortality in the follow-up period was analysed with the Kaplan–Meier method; the log rank test was used to test whether mortality was different among the groups, accepting a P value < 0.05 as significant. Outcomes of reproductive behaviour in women were assessed by calculating the percentages of females who had at least one full-term pregnancy before the end of follow-up. The corresponding measure for a hypothetical age-matched sample of the general Dutch population was calculated using life-tables made available by the national statistical bureau (Statistics Netherlands[7]). These provide, for each year (going back to 1950) and each age, the number of first-borns. Although this data may allow some comparisons, no hypothesis testing was performed for this measure of childbearing, as the Dutch general population was not considered to be an entirely appropriate standard. All statistical analyses were performed with the SPSS statistical software package (SPSS release 12.01).

Results

Centres

In the manner described earlier, 132 centres were identified to be interested in participating. Eighty-one centres actually started to enter patient data. One of these centres did not continue as a result of a reorganization within the hospital; another centre appeared not to have enough patients to include. Thus, ultimately 79 centres participated in 26 countries.

Population

A total of 4168 cases were included. Forty-eight of the 79 participating centres were specialized (as mentioned earlier). Details on participating centres as well as the number of patients included per country are given in the Appendix. Eighty-seven per cent of the patients were included at specialized centres.

After scrutiny of the data for completeness and consistency, 4110 patients were selected for extensive analysis. [58 cases (1.4%) were excluded].

Inclusion per defect is shown in *Table 1*. Median follow-up was 5.1 (3.6–5.7 years) years. Status after 5 years of follow-up was available for 3642 patients (89%). In 155 cases, the patients were lost to follow-up prior to 5 years (4%), whereas 306 patients had been referred to another centre (7%). In seven cases (0.2%), the relevant item indicating status in the CRF at the end of follow-up was missing.

The age distribution at baseline was strongly skewed, with most patients in their twenties or thirties (see *Table 1*). The overall median age was 27.9 (21.7–38.6) years and 79% of the patients were aged <50 years. As shown in *Table 1*, median age varied per defect, reflecting the severity of the condition. Thus, almost all (98%) Fontan and TGA patients were aged <40 vs. only half (52%) of ASD patients. The oldest patient was an 87-year-old woman with an ASD. Oldest patients in the remaining defects were aged 80 (Cyanotic defect), 57 (Fontan circulation), 72 (tetralogy of Fallot), 74 (CoA), 62 (TGA), 77 (Marfan syndrome), and 77 years (VSD).

In addition, the proportion of females differed per defect. In ASD, 67% of patients were females vs. only 39% in CoA and TGA.

Clinical characteristics at baseline

In the last column of *Table 1*, for each defect the proportion of patients displaying a certain characteristic relevant for that specific defect (mainly relating to previous interventions) is recorded.

The distribution of patients according to NYHA functional class is shown in *Table 2*. Within the group of cyanotic defects, Eisenmenger patients had a significantly lower exercise capacity compared with other cyanotic patients (proportion of patients with NYHA Class greater than I, 93.7 vs. 79.7%; $P < 0.001$). Also recorded in *Table 2* is the medical history at inclusion regarding arrhythmias, endocarditis, and vascular events. Supraventricular arrhythmias had occurred in 18% of patients vs. 5% for ventricular arrhythmias. Overall, 3% of patients were reported to have experienced endocarditis, 4% cerebrovascular accidents/transient ischaemic attacks (CVA/TIA), and 1% had a previous myocardial infarction or had undergone percutaneous transluminal coronary angioplasty or coronary artery bypass grafting (MI/PTCA/CABG), but there were important differences among

the different defects. Prevalence of systemic arterial hypertension (not shown in the table) was 4% for the group as a whole, but as high as 46% in CoA and 17% in ASD.

Follow-up: mortality

A total of 115 patients (2.8%) died during the study period. *Table 3* provides the number of patients who died of any cause (all-cause mortality) and those who died of cardiovascular causes. In addition, the table gives 5 year mortality rates and 95% confidence intervals as estimated by the Kaplan–Meier method. All-cause mortality was lowest in patients with CoA, VSD, and ASD and highest in those with cyanotic defect or Fontan circulation. The mode of death was cardiovascular in the majority of patients (82% of all deaths); cardiovascular death (as proportion of all-cause mortality) was highest in patients with cyanotic defects, Fontan circulation, tetralogy of Fallot, and VSD. The Kaplan–Meier curve (see *Figure 1*) contrasts all-cause mortality among the eight defects (log rank test, with type of defect as factor: $P < 0.0001$), depicting survival from study entry.

Follow-up: morbidity

Among patients with a follow-up of at least 3 years, the NYHA functional class worsened in 6%. In cyanotic defects and in the Fontan circulation, this occurred in 21 and 17%, respectively. In only 1% of CoA patients, the NYHA class became worse. Among ASD patients, the NYHA class improved more often than it worsened.

Pacemakers were inserted (at some time in the period from before inclusion until the end of follow-up) in 6% of patients, most frequently in TGA (22% of patients), followed by the Fontan circulation (7%) and tetralogy of Fallot (6%), and least frequently in Marfan syndrome (1%). Twenty-seven patients were given an implantable cardio-defibrillator.

Overall, 713 of 3694 patients (19%) underwent surgery or a catheter-based intervention ($n = 193$) during follow-up. A large proportion of these interventions consisted of the closure of an ASD: 293 of 504 open ASDs were closed during follow-up [of which 114 (39%) by a catheter-based technique]. Not more than 21 of these 713 patients underwent more than one procedure.

Findings regarding the number of outpatient visits and frequency of investigations are shown in *Table 4*.

Table 1 Baseline characteristics

	Inclusion (n)	Age[a]	Females (%)	Defect-specific information
ASD II	882	39 (25–52)	67	43% closed
Ventricular septal defect	628	27 (20–36)	53	44% closed
Tetralogy of Fallot	811	26 (21–34)	48	40% transannular patch repair
CoA	551	26 (21–35)	39	90% previous repair
TGA	363	23 (20–27)	39	86% atrial switch procedure
Marfan syndrome	287	29 (22–38)	50	28% previous aortic intervention
Fontan circulation	198	23 (19–28)	45	60% tricuspid atresia
Cyanotic defect	390	29 (23–37)	62	60% Eisenmenger
Overall	4110	27 (23–37)	52	

[a]Values presented are median (IQ range).

P. Engelfriet et al.

Table 2 History of morbidity and functional status at baseline

	Endocarditis	CVA/TIA	MI/CABG/PTCA	Supraventricular arrhythmias	Ventricular arrhythmias	NYHA I	NYHA II	NYHA III/IV
ASD II	0 (3/879)	4 (36/876)	2 (16/880)	28 (243/861)	2 (16/861)	59 (504/825)	30 (257)	11 (91)
VSD	7 (44/621)	2 (14/622)	1 (5/626)	9 (56/617)	3 (18/617)	76 (472/619)	19 (118)	4 (29)
Tetralogy of Fallot	4 (33/810)	4 (32/807)	1 (5/806)	20 (159/796)	14 (115/796)	69 (551/793)	24 (189)	6 (53)
CoA	2 (11/547)	1 (6/545)	1 (4/546)	4 (21/547)	2 (9/547)	81 (441/543)	15 (84)	3 (18)
Transposition	1 (4/361)	6 (20/359)	0 (1/360)	26 (95/362)	2 (7/362)	67 (244/362)	27 (96)	6 (22)
Marfan syndrome	2 (5/284)	1 (4/285)	1 (2/286)	8 (23/281)	2 (6/281)	79 (223/282)	19 (54)	2 (5)
Fontan circulation	2 (3/198)	12 (23/198)	0 (0/198)	45 (90/198)	0 (0/198)	40 (78/193)	51 (98)	9 (17)
Cyanotic defect	6 (22/386)	10 (37/384)	0 (1/385)	16 (58/374)	6 (22/374)	12 (45/172)	44 (172)	44 (170)
Overall	3 (125/4086)	4 (172/4076)	1 (34/4088)	18 (745/4036)	5 (193/4036)	63 (2558/4031)	26 (1068)	10 (405)

All values are percentage followed by a fraction with frequency in the numerator and the number of patients with sufficient data to evaluate the item (k/n) in the denominator. In the last two columns only the numerators are given, as the rows of the last three columns sum to 100%.

CVA, cerebrovascular accident; TIA, transient ischaemic attack; MI, myocardial infarction; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; NYHA, New York Heart Association functional class.

Outpatient visits, expressed as the number of visits per patient-year, showed that a patient visited the outpatient clinic approximately three times per 2 years. Transthoracic echography was the most frequent type of diagnostic procedure, and its use did not vary very much among the different defects. Transoesophageal echocardiography was used most frequently in ASD. Magnetic resonance imaging was used most frequently in CoA and relatively infrequently in Marfan syndrome. Holter monitoring was used most often in Fontan circulation, tetralogy of Fallot, and TGA.

Use of medication (>3 months at some time during follow-up) is specified for β-blockers, diuretics, anti-arrhythmic agents, and anti-thrombotics in *Table 5*, which also indicates the proportion of patients not using any kind of chronic medication.

Pregnancy

Finally, *Table 6* displays the proportion of females who had at least one full-term pregnancy ever by the end of follow-up. Also displayed in the same table are the corresponding figures for an age-matched sample of the general Dutch population (see Methods).

Discussion

The spectrum of adult CHD in Europe emerging from this survey is one of a predominantly young population with substantial morbidity but relatively low mortality in a 5 year period. The majority of patients have no or only mild functional limitations. However, there are major differences between the eight congenital heart conditions studied, both in severity and regarding specific characteristics. Outcomes are worst in cyanotic defects and in the Fontan circulation, but a considerable proportion of patients in the group of 'milder' defects also suffer from cardiac symptoms.

To our knowledge, this is the first study reporting on the functional status of a large group of patients and a range of different defects. It is encouraging that the majority of patients did not have severe functional limitations. More than 60% of patients were in NYHA class I and only a small proportion of patients were in class III or IV. Cyanotic defects and the Fontan circulation are obviously among the most severe congenital heart conditions, as was also reflected in the mortality rates. Cyanosis due to an intractable right–left shunt is a multi-system disorder with a chronic and progressive course.[8] More than half of the cyanotic patients had Eisenmenger syndrome, for which a high mortality has been reported.[9] Follow-up studies of patients who underwent a Fontan operation have also shown high mortality rates.[10] In a recent study it was found that, of 36 patients followed-up for a mean of 10 years, 28% had died.[11]

In contrast to these defects with prominent systemic effects, mortality was low at the other end of the spectrum. In particular, the mortality data on ASD indicate that some of the older studies overestimated mortality.[12,13]

Notwithstanding the fact that, in general, functional class was relatively good, a considerable proportion of patients had a history of major morbidity at baseline, in particular, arrhythmias, endocarditis, or a stroke/TIA. It is clear that the course of CHD is marked by arrhythmias in a substantial

Table 3 Mortality

	n	Number of deaths		5 year mortality	
		Cardiovascular	Non-cardiovascular	Kaplan-Meier estimate (%)	95% CI (%)
ASD II	882	5	4	1.1	0.3, 1.9
VSD	628	6	2	1.6	0.5, 2.7
Tetralogy of Fallot	811	8	3	1.3	0.5, 2.1
CoA	551	2	1	0.7	0.0, 1.4
TGA	363	9	0	3.0	1.0, 4.9
Marfan syndrome	287	3	2	1.7	0.0, 3.3
Fontan circulation	198	12	4	8.2	4.0, 12.3
Cyanotic defect	390	44	10	12.6	9.1, 16.0
Overall	4110	89	26	3.0	2.4, 3.5
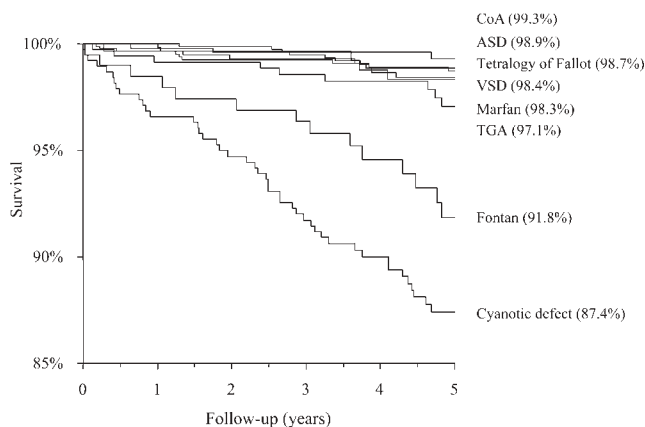
Figure 1 Kaplan–Meier survival curves for the eight defects.

part of the patient population. Arrhythmias are the most frequent cause of hospitalization.[14] We found that supraventricular arrhythmias occurred in at least one of every five patients, whereas one of every 20 patients experienced ventricular arrhythmias. Differences in prevalence of arrhythmias between the defects roughly reflect the different pathological arrhythmogenic substrates. Arrhythmias are known to be a frequently encountered problem in TGA, Fontan circulation, and tetralogy of Fallot. In TGA, the extensive damage to the atria which results from the atrial switch procedures, is believed to be responsible for atrial fibrillation/flutter, sinus node dysfunction [sick sinus syndrome occurred in 17% of the patients (not shown in the table)], and atrioventricular conduction abnormalities (7%, not shown).[15] Ventricular arrhythmias are especially common in Fallot patients, as is confirmed by our data. ASDs and the concomitant volume overload of the right atrium also frequently cause arrhythmias. In a group of patients selected for surgery, Gatzoulis et al.[16] found a prevalence of 19%. Unfortunately, operative closure introduces a new substrate for arrhythmogenicity, and in patients with closed ASD the incidence is still high. It is hoped that catheter-based closure will reduce the occurrence of rhythm disturbances. Because of the relative novelty of this technique, in our cohort, only a minority of patients had undergone such closure at the time of inclusion. However, for the closure of the ASD during follow-up, already in nearly half (39%) of the cases, a catheter-based method had been used.

Defects associated with the highest endocarditis risk include unclosed VSDs, repaired tetralogy of Fallot, and cyanotic conditions.[17,18] The prevalence of a history of endocarditis in cyanotic patients in our cohort (6%) was higher than that reported in previous studies (e.g. Daliento et al.[9] found 3.7% in their cohort). Moreover, in contrast to earlier reports, cases of endocarditis did occur in Fontan circulation and TGA corrected by Mustard repair. Although endocarditis might be slightly over-represented in our cohort because of the manner of selection of the patients for this survey (see what follows), this large-scale study shows that endocarditis remains an important complication.

The proportion of patients with a history of stroke/TIA in the Fontan patients of our cohort was large compared with what has been reported in the literature,[19,20] although a recent study found a cumulative incidence of thromboembolic events of 25% in a 10 year (mean) follow-up period.[11] It should be noted, however, that the events in some of our cases might have taken place before the Fontan procedure. In theory, the Fontan repair should remove one important cause of thromboembolism, namely an open connection between the right and left sides of the heart (at least in Fontan procedures without a surgically created fenestration). In contrast, supraventricular arrhythmias are frequent after repair (discussed earlier), whereas some types of Fontan operations introduce synthetic conduits in the circulation. Moreover, the Fontan circulation is known to be associated with abnormalities in the coagulation profile, which may lead both to thromboembolism and bleeding complications.[21] The issue of anti-coagulant medication in Fontan patients therefore remains an important dilemma in their clinical management.

The high prevalence of a history of stroke/TIA (10%) among the cyanotic patients is noteworthy in the light of somewhat conflicting reports in the literature. Perloff et al.[22] followed 112 patients with cyanotic disease for a total of 748 patient-years without observing a single stroke. In contrast, Ammash and Warnes[23] found that 13.6% of a group of 162 patients had a history of a cerebrovascular event. Daliento et al.[9] reported that 7.9% of their Eisenmenger patients had experienced a stroke. Apart from changes in the composition of the blood, which result from hypoxemia (hyperviscosity, microcytosis), interplay with other risk factors such as hypertension and atrial fibrillation appears to play a role in the increased frequency of cerebrovascular events in this group of patients. Also bleeding events occurred often. In our group,

Table 4 Follow-up evaluation: clinic visits and investigations

	Outpatient visits (visits/ patient-year)	TTE (visits/100 patient-year)	TEE (visits/100 patient-year)	MRI (visits/100 patient-year)	Holter (visits/100 patient-year)
ASD II	1.45	77	14	<1	14
VSD	1.14	60	4	1	9
Tetralogy of Fallot	1.42	66	4	5	23
CoA	1.27	63	3	13	5
TGA	1.52	76	3	4	30
Marfan syndrome	1.37	87	6	2	6
Fontan circulation	1.92	88	8	5	33
Cyanotic defect	1.86	68	3	3	18
Overall	1.44	71	6	6	16

TTE, transthoracic echocardiography; TEE, transoesophageal echocardiography; MRI, magnetic resonance imaging; Holter, Holter monitoring.

Table 5 Use of medication

	No drugs	Diuretics	Beta-blocking agents	Ace-inhibitors	Anti-arrhythmics	Anti-thrombotics		
						Coumarins	Aspirin	Other anti-platelets
ASD II	42 (367/880)	20 (177)	18 (160)	18 (161)	11 (100)	21 (182/879)	17 (146)	1 (10)
VSD	64 (403/625)	11 (69)	12 (73)	15 (95)	4 (23)	9 (58/624)	4 (27)	0 (3)
Tetralogy of Fallot	56 (455/808)	14 (115)	17 (137)	13 (101)	12 (98)	11 (87/809)	7 (57)	1 (8)
CoA	42 (234/551)	11 (58)	38 (210)	22 (120)	3 (15)	11 (58/550)	5 (28)	1 (3)
TGA	43 (157/363)	16 (58)	17 (62)	33 (119)	12 (45)	18 (67/363)	7 (24)	1 (2)
Marfan syndrome	13 (38/287)	9 (25)	72 (208)	14 (41)	5 (14)	33 (92/283)	2 (6)	0 (1)
Fontan circulation	10 (20/198)	37 (73)	26 (51)	39 (77)	36 (71)	61 (120/198)	19 (38)	1 (1)
Cyanotic defect	23 (88/389)	37 (143)	11 (44)	16 (63)	17 (67)	23 (88/385)	18 (70)	2 (9)
Overall	43 (1762/4101)	18 (718)	23 (945)	19 (777)	11 (433)	18 (752/4091)	10 (396)	1 (37)

Values are percentage followed by numbers in parentheses. In the first column the denominator of the fraction (k/n) indicates the number of cases for which data on drug use were available. Use of anti-thombotics was assessed separately. Use of medication means the use of drugs for at least 3 months at any time prior to the end of follow-up.

the percentage of patients with bleeding problems was almost equal to that of patients suffering from thrombotic complications.

Hypertension did not seem to play an important role in the patients of this survey, except in the case of CoA. In fact, hypertension is a serious consequence of CoA and prevention of its complications is a major principle of management. The fact that in our cohort almost half of the CoA patients were hypertensive is not exceptional. The relatively high prevalence of hypertension among ASD patients is probably partly due to the higher age of this group, but a role for pathophysiological mechanisms cannot be excluded.

It should be noted that the manner in which patients were selected for this survey has introduced a bias towards a more severe range of morbidity. This is especially apparent when we consider the number of interventions performed. Thus, the fact that almost 40% of ASD patients underwent an intervention (mostly closure of their defect) is, of course, due to the inclusion of most patients in specialized, often tertiary referral centres. In contrast, the frequency of interventions in adults with CHD underscores the need for staff with sufficient training and expertise. In our cohort, a considerable proportion of patients had pacemakers, which should alert

us, again, to the prominence of (often complex) rhythm disturbances. More than 20% of our sample of TGA patients had a pacemaker inserted.

The use of medication is, to some extent, another indicator of morbidity, although some drugs are prescribed for prophylaxis. We found that more than half of the patients were on some form of chronic medication. Among Fontan patients, only 10% did not use drugs. However, even among ASD patients, a significant proportion of patients did use drugs. The types of drugs used, of course, largely reflect the prevalence of particular forms of morbidity among the different defects. The high proportion of Fontan patients using anti-thombotics and anti-arrhythmic agents are a case in point. The use of anti-arrhythmic agents and anti-thrombotics was more frequent than in previously reported studies.[16] In line with current guidelines, a large proportion of Marfan patients prophylactically used β-blockers.[24] The use of diuretics was especially high among patients who are at risk for right-sided decompensation, in particular, patients with Fontan circulation, among cyanotic patients and, in our sample, also ASD patients. It is noteworthy that, even though the use of aspirin and coumarins is not generally recommended in cyanotic disease,

Table 6 Percentage of females with at least one full-term pregnancy ever by the end of follow-up

	Ever pregnant		General Dutch population[a]
	%	n (observed)	%
ASD II	50	(232/462)	46
VSD	40	(111/281)	38
Tetralogy of Fallot	36	(129/354)	36
CoA	40	(76/191)	38
TGA	30	(41/137)	33
Marfan syndrome	36	(50/137)	42
Fontan circulation	2	(2/88)	31
Cyanotic defect	18	(42/238)	43
Overall	36	(683/1888)	40

Expected percentages have been calculated for an age-matched sample, with age at the end of follow-up as reference.

[a]Data for the Dutch population were derived from tables provided by Statistics Netherlands.

almost one out of every five cyanotic patients was using one of these drugs.

The data on frequencies of diagnostic procedures and out-patient visits provide an indication of the intervals at which patients are actually being screened as part of regular follow-up and of 'the amount of care' an adult CHD population of a certain size needs. The issue of organization of care and planning of future needs of this rapidly growing population is one of the central concerns in the evolution of the adult CHD discipline.

The age distribution of this population implies that most women are in their reproductive age. As this survey was not designed to assess the reproductive history of the female patients in an exhaustive manner, the pregnancy data collected were summarized into a simple measure. Considering merely the proportion of females with at least one full-term pregnancy, it seems that, in the case of the less severe defects, childbearing is not very much affected by the presence of the defect. It is remarkable, and testimony to the success of the management of CHD, that, after correction, TGA still allows a substantial proportion of women to bear children.[25] This is very different when cyanosis is present or when there is only one functional ventricle. It should be noted that, generally, pregnancy is strongly advised against in these conditions.[26,27] How CHD affects childbearing and vice versa is obviously an important and complicated issue that requires more extensive research.

Finally, the demographic characteristics of our study population are largely consistent with what is known at present. The observation that the population is relatively young is in line with the fact that only after the major improvements in cardiac paediatric surgery in the middle of the previous century did the majority of patients begin to survive into adulthood. It is also apparent that patients with more severe conditions with a high mortality, in particular, the Fontan circulation and cyanotic defects, are even younger. Contrasts in the proportion of females among patients with the different defects can largely be traced to the differences in prevalence of the conditions at birth,[28] which suggest that mortality in the various defects is not gender-related.

Limitations

One of the problems in studying adult CHD is the large number of different lesions and clinical situations one may encounter. In designing this survey, a compromise had to be accepted between attempts at being comprehensive and the necessity to limit the amount of data collected. Therefore, it was decided to restrict the survey to eight of the most common congenital conditions. However, even under this restriction, in order to keep the CRF 'manageable', limitations had to be observed regarding the amount of detail with which clinical characteristics and medical history could be assessed.

Participation was on a voluntary basis and data entry was done by the investigators on the basis of available patient records. Thus, missing data constitute an unavoidable aspect that might be a source of bias.

The vast majority of patients included in the survey were being treated on a regular basis at a specialized centre for adult CHD. Hence, the sample is to be considered as a 'clinical' sample and, as such, not entirely representative of the whole population of adults with CHD. For example, the fact that a larger proportion of ASD patients (11%) were in NYHA class III/IV than Fontan patients (9%) is largely due to the method of patient selection. Many ASD patients were included in the centres to which they were referred for intervention. This is also illustrated by the improvements in NYHA functional class over the follow-up period, which are largely the result of interventions.

Conclusions

This EHS offered a unique opportunity to gain insight into the spectrum of adult CHD throughout Europe. Its successful completion has demonstrated the feasibility of large-scale international studies in adult CHD and indicates that the discipline has become broadly established, catering to the needs of an expanding relatively young population. With more than 4000 patients included, the data presented here form an important supplement to the currently available information that is largely derived from single institutions and a small number of patients with particular defects. The findings of this study confirm that morbidity is high and emphasize the importance of specialized care for the adult born with a heart defect.

Acknowledgements

Appendix: organization of the survey

Expert Committee: Barbara Mulder (Survey Chairperson), The Netherlands; Eric Boersma, The Netherlands; Luciano Daliento, Italy; Michael Gatzoulis, United Kingdom; Rafael Hirsch, Israel; Harald Kaemmerer, Germany; Folkert Meyboom, The Netherlands; Philip Moons, Belgium; Erwin Oechslin, Switzerland; Jana Popelová, Czech Republic; Erik Thaulow, Norway; Ulf Thilén, Sweden; Jan Tijssen, The Netherlands.

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Clinical vignette

Aortic atresia, interrupted aortic arch type C perfused by bilateral arterial duct

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A non-syndromatic, 4.2 kg male newborn was admitted to the hospital at 24 h of age because of grunting and pale colour. Suspecting cardiogenic shock, prostaglandin infusion was initiated with prompt improvement of the clinical condition.

Echocardiography revealed a complex congenital heart disease. There was an unbalanced atrioventricular septal defect with a small left ventricle. There were bilateral superior caval veins, the left draining to the coronary sinus. The pulmonary veins drained to a collecting vessel which connected to the right atrium near its junction with the right superior caval vein. The aortic valve is atretic with a very small ascending aorta (AoA).

Catheterization showed a complex form of interrupted aortic arch with a peculiar relationship to the pulmonary arteries. The aortic arch was interrupted between the brachiocephalic trunk (BCT) and the left common carotid artery (LCCA). Blood supply to the very hypoplastic AoA and coronary arteries was provided by a right arterial duct (RAD), connecting the right pulmonary artery (RPA) and the BCT. This was nicely shown by retrograde injection of the right radial artery (Panel A). Through a left arterial duct (LAD), the descending aorta (AoD) was perfused as well as the distal part of the aortic arch (Panel B). Panels C and D show all great arteries and their relationship. Of particular interest is a sharp angle at the origin of the BCT and the LCCA, suggesting fibrous continuity of the arch rather than complete interruption.

A bilateral duct is a rare find. In this case of interrupted aortic arch and aortic atresia, blood supply to the coronary arteries depended on the patency of the RAD. Constriction of ductal tissue in the first hours after birth resulted in cardiac ischaemia and an early presentation with cardiogenic shock. Considering the complexity of the malformation, no further therapy was offered.

Panel A. Retrograde injection in the right radial artery. Blood supply to the AoA from the RPA through the RAD and BCT.

Panel B. Injection in the AoD. Blood supply to the AoD and distal aortic arch, with LCCA and left subclavian artery, was provided by an LAD.

Panel C. Injection in the LAD. LAD supplying the AoD and the distal arch. Right aortic arch supplying AoA. Fibrous continuity of arch (arrow) suggested by sharp angle at the origin of the BCT and the LCCA (LPA, left pulmonary artery).

Panel D. Schematic representation of great arteries. Interrupted line, presumed fibrous continuity of aortic arch.