Long-term outcome after surgery for congenital heart disease in infancy and childhood

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Long-term outcome after surgery for congenital heart disease in infancy and childhood

De resultaten op lange termijn van chirurgische correctie van aangeboren hartafwijkingen op de kinderleeftijd

Proefschrift

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Voor Karlien,
Jurriaan en Eva

CONTENTS

CHAPTER 1

INTRODUCTION

Before the era of cardiac surgery about half of the patients born with a congenital heart defect died within the first year of life[1,2]. Survival until adulthood was very rare for patients with transposition of the great arteries (20 years survival <1%)[3], rare with tetralogy of Fallot (20 years survival <10%)[4] and although survival beyond two decades was more common for patients with atrial septal defect, ventricular septal defect and pulmonary stenosis, their life expectancy also was considerably reduced[5-9].
Cardiac surgery would change the natural history dramatically. It all started in 1939, when Robert Gross ligated a patent ductus arteriosus in a 7 year old girl. In 1941 Crafoord was the first to treat a patient with aortic coarctation surgically[10] and in 1945 Blalock, at the advice of the pediatrician Helen Taussig sutured the subclavian artery end-to-side on the pulmonary artery of a patient with tetralogy of Fallot, establishing the Blalock-Taussig shunt[11]. Brock introduced the blind valvulotomy for pulmonary stenosis in 1948[12]. Lewis became the first surgeon to do open-heart surgery: he closed an atrial septal defect with the use of total body hypothermia and inflow occlusion in 1953[13]. In the following years this technique was successfully used in patients who needed cardiac surgery for atrial septal defect, isolated valvular aortic or valvular pulmonary stenosis. However, failure was uniform when applied to patients with a more complex congenital heart defect. Lillehei was the first to perform successful open-heart surgery in patients with more complex intracardiac defects, such as ventricular septal defect, atrioventricular septal defect or tetralogy of Fallot[14]. He used cross-circulation as a technique for extracorporal oxygenation. This technique implied that the circulation of a healthy volunteer, who was lying next to the patient in the operation theatre, was used during the surgical procedure to support patient's circulation. Partly because of the potential dangers for the "donors" this technique was soon abandoned in favour of another technique that had become available, and which would become the standard for the subsequent decades: the membrane oxygenator[15,16]. This idea, discussed earlier by our countryman Kolff, allowed for extracorporal oxygenation. Thus cardiopulmonary bypass provided the surgeons sufficient time to visualize the structures in the non-beating heart to permit corrective measures[17], and so even complex cardiac malformations became eligible for surgery. In these same early postwar years cardiac catheterization was proved to be feasible, for which the pioneers Cournand, Richards and Forssman were awarded the Nobel prize in 1956. These developments both in the medical and in the surgical field were the start of one of the most impressive changes in modern medicine: instead of a *mortality* of 85% in the first two decades, the 20-years *survival* has become 85% or more nowadays[18]. This change took two or three decades, and was the result of a gradual decline of number of patients who were earlier considered inoperable and of improvements in surgical techniques and peri-operative care, which resulted in a substantial reduction of the hospital mortality of operated patients. Enthusiasm about this accomplishment was understandable and justified, but sometimes carried too far. This is reflected in the language that is commonly used for surgical procedures; if these are not evidently palliative, they are often called corrective. Stark correctly questioned this in his address to the annual meeting of the American Association for Thoracic Surgery in 1988: "Do we really correct congenital heart defects?"[19].

He defined an operation as corrective if normal function was achieved and maintained, life expectancy was restored to normal and further medical or surgical treatment was not necessary. If taken very strictly, this definition excludes all operations from being corrective, because the duration of follow-up is yet too short to ascertain a normal life expectancy. Even if it was replaced by "normal health for the duration of follow-up", Stark considered only two lesions truly correctable: persistent ductus arteriosus and atrial septal defect. Because of many sequelae that occurred after surgery in all other congenital cardiac defects, he put a question mark after all other types of "correction". This conclusion concurred with the experience of the many pediatric and the few adult cardiologists who were dedicated to the long-term care of patients after surgery for congenital heart defects[20,21].

Since the end of the 1960's hundreds of studies have been published on sequelae after surgery for all types of congenital cardiac malformations. The emphasis on the problems long-term after surgery was logical, but also had an untoward effect. Reviewing the literature one might get the impression that the overall long-term result of cardiac surgery for this patient group is not good. Consequently, employment prospects and insurability of patients operated upon for a congenital cardiac defect are poor[22]. However, it should be realised that virtually all studies focus on specific problems in selected patients groups. Data on the prevalence of sequelae after cardiac surgery, on which a judgement on the health condition of the entire operated population should be based, are rare, because there are amazingly few studies (if any) based on consecutive series of patients who were prospectively followed for years after surgery and who were regularly thoroughly examined. There are a few retrospective follow-up studies in which a very large proportion of a consecutively operated group of patients participate, but these studies are performed by means of telephonic interviews or written questionnaires[23-26]. Although very useful for evaluation of symptomatic sequelae and medical or surgical intervention, these studies are not designed to detect asymptomatic sequelae, and therefore give no reliable picture (too optimistic) of the postoperative cardiac status. Only meticulous examination of (a representative sample of) the complete population of operated patients will provide a reliable picture of their cardiac status, including prevalence of asymptomatic sequelae. Ideally not only the cardiac status should be examined, but also the psychosocial functioning of these patients, in order to get an integral impression how patients fare long-term after cardiac surgery at young age. The outcome of such a study would be of importance not only for patients and physicians, but also for employers, insurance companies and health-care planners.

This was the rationale behind the retrospective follow-up study of all patients operated upon in Rotterdam, which, as a unique feature, would report both the health status of the entire group of operated patients and their psychosocial functioning.

All patients who underwent open-heart surgery for a congenital cardiac malformation in Rotterdam between 1968 and 1980, and who were younger than 15 years of age at the time of the operation were included in the follow-up study. The year 1968 was chosen as starting point because in this year cardiac surgery was started in the Dijkzigt Hospital, and 1980 was chosen as end point to have at least 10 years of follow-up. The follow-up started in 1989 with the retrieval of the current status (alive or dead) and the current address of the patients through the Dutch local registrar's system. Once traced, every survivor received a letter explaining the study and inviting him/her to come to Rotterdam to undergo extensive medical and psychological testing.

The total study population comprised 734 patients, of whom 102 (14%) had died at the time of the follow-up study, 25 (3%) had left abroad and 18 (2%) were untraceable. Of the remaining 589 patients, 498 (85%) took part in the psychological part of the study and 445 (76%) took part in the medical part. The results of the five largest diagnosis groups (atrial septal defect, ventricular septal defect, tetralogy of Fallot, transposition of the great arteries and pulmonary stenosis; together 86% of the study population) are discussed in chapters 2 to 6. Chapter 7 provides an overview of the differences and the similarities of the outcome of the 5 diagnosis groups. Each of the following 9 remaining diagnostic groups (aortic stenosis, discrete subaortic stenosis, primum type atrial septal defect, complete atrioventricular septal defect, pulmonary atresia, tricuspid atresia, total abnormal pulmonary venous drainage, truncus arteriosus, and miscellaneous) comprised too few patients to allow analysis and conclusions that could be considered representative for these groups. Therefore these patients were left out of the presentation of the medical part of the results of this study. Chapters 8 and 9, which must be considered as an addendum to the actual thesis, concern results of the psychological part of the study. The psychosocial functioning of young adults is discussed in chapter 8 and behavioural and emotional problems in children and adolescents in chapter 9. Chapter 10 contains the general discussion. Chapter 11 gives a summary of the contents of the chapters.
The study was initiated and supervised by prof.dr. John Hess, head of the division of Pediatric Cardiology and prof.dr. Frank Verhulst, head of the department Child Psychiatry. The study was conducted by dr. Elisabeth Utens, clinical psychologist, drs. Folkert Meijboom, pediatric cardiologist and mrs. Willie Chevalier-De Jager, secretary.

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CHAPTER 2

LONG TERM FOLLOW-UP (9-20 YEARS) AFTER SURGICAL CLOSURE OF ATRIAL SEPTAL DEFECT AT YOUNG AGE

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ABSTRACT

To assess the cardiac status long term after surgical closure of atrial septal defect (ASD) at young age, 104 out of 135 children who were consecutively operated (aged 0 to 14 years) in our institution between 1968 and 1980, took part in a follow-up study and underwent a complete cardiological examination. The mean follow-up was 14.5 ± 2.8 years. Most (87%) judged their health as good or very good. At physical examination all patients were in good health. Ninety three patients (89%) were in sinus rhythm. Echocardiography demonstrated that right ventricular dilatation was present in 27 patients (26%), of whom 2 had a residual atrial septal defect. Bicycle ergometry revealed that 88 patients (88%) had a normal exercise capacity. Both supraventricular and ventricular arrhythmias were seen in 67% of the patients on 24 hour ambulatory Electrocardiogam, but only 3 patients (3%) had received antiarrhythmic medication, and 4 patients (4%) had needed a pacemaker. In the group of patients with right ventricular dilatation the exercise capacity and prevalence of arrhythmias did not differ significantly from those in the group with a normal sized right ventricle. The outcome in patients with a secundum type defect was not different from that of patients with a sinus venosus type defects. The finding of anatomical, functional, or electrophysiological abnormalities was not associated with a longer duration of follow-up. These findings indicate that the functional cardiac status long term after surgical closure of ASD is generally good, irrespective of the presence of anatomical or electrophysiological sequelae. The future clinical significance of arrhythmias which are now asymptomatic, and persisting right ventricular dilatation in this patient group remains to be determined.

INTRODUCTION

Surgical closure of ASD has been performed since 1952[1,2]. If patients were operated upon in childhood, long term survival has proven to be not different from that of an age and sex matched control population[3-5]. Since precocious death is no longer the most important outcome, quality of life has become a major issue. Questions to be asked in this respect are: do they feel healthy, are they restricted in physical activity, are there substantial residual abnormalities? Sinus node dysfunction, right ventricular dilatation, pulmonary hypertension and left ventricular dysfunction are mentioned as sequelae in earlier reports[3-10]. However, reports on the incidence of sequelae in consecutive series of patients who were operated at young age are not available. To provide patients, employers, physicians and healthcare workers more insight into the occurrence and

clinical significance of sequelae, we studied the long term "objective" and "subjective" well being in a consecutive series of patients who underwent open heart surgery, with use of cardiopulmonary bypass, for closure of an ASD at young age.

PATIENTS

All 135 patients with secundum type ASD or sinus venosus type ASD who had undergone primary surgical repair in our institution between 1968 and 1980 and who were < 15 years of age at the time of the operation were included in the present study. Seventy-six patients (56%) were female, and 59 were male (44%). A secundum type ASD was present in 105 patients, and a sinus venosus type ASD in 30 patients. Mean age at the time of the operation was 7.5 ± 3.5 years (range 0 to 14). After a mean follow-up of 14.5 ± 2.8 years (range 9 to 20) 104 patients (77%) participated in the follow-up study: 80 patients with a secundum type ASD, and 24 patients with a sinus venosus type ASD. Sixty patients were female (58%) and 44 were male (42%). The mean age at the time of the follow-up study was 21.8 ± 4.8 years (range 10 to 33).

METHODS

Baseline characteristics. In order to obtain baseline data on all 135 patients, the preoperative clinical findings, (including cardiac catheterisation), data on surgical technique and postoperative course were collected. The pre- and peri-operative data of the patients who participated in the follow-up study were compared with those who refused to participate.

Follow-up Procedures and Measurements. Using the local registrars' offices 128 patients (95%) could be traced and were found to be alive. They received a letter in which the background and the objective of the study was explained, with an invitation to participate. A total of 104 patients (77%) agreed to participate. All 104 underwent a complete cardiological examination, which included an interview, physical examination, standard 12-lead electrocardiogram, echocardiography (M-mode, 2-D echo, pulsed-,continuous wave-, and colour flow Doppler), bicycle ergometry and 24 hour ambulatory electrocardiography (24 hour electrocardiogram) at the out-patient clinic of our institution between November 1989 and April 1991.

A part of the interview consisted of a standardized questionnaire from the Continuous Quality of Life Survey of the Dutch population by the Netherlands Central Bureau of Statistics (data not published)[11].

In the *standard 12-lead electrocardiogram,* the presence of a right bundle branch block was defined as a RSR' pattern of the QRS complex with a duration of at least 0.12 seconds, with R'> R in V_1. Right ventricular hypertrophy was defined as a heart axis between 90 and 180 degrees in the frontal plane, and in V_1 R or R' > 5 mm with R or R'> S in the absence of a right bundle branch block. First degree atrioventricular block was considered to be present if atrioventricular conduction time > 0.20 seconds.

Echocardiography was performed with a Toshiba SSH 160-A or a Vingmed CFM 700. Left ventricular dimensions were compared with normal values corrected for sex and body weight. A shortening fraction of the left ventricle < 0.30 was considered as decreased. Since reliable echocardiographic criteria for right ventricular dilatation or hypertrophy are not available, the presence of these features was judged independently by 2 experienced investigators.

Exercise capacity was assessed by symptom-limited bicycle ergometry with stepwise

increments of workload of 20 Watts per minute. Exercise capacity was compared to that in normal individuals corrected for age, sex, and body length[12]. Exercise capacity < 85% of the predicted value was considerded to be decreased.

Ectopic ventricular activity recorded during the 24 hour electrocardiogram was considered to be abnormal if monoform premature ventricular contractions were observed in a frequency > 30 beats during any single hour, if premature ventricular contractions were multiform, or if they presented as doublets or ventricular tachycardia. Short ventricular tachycardia was defined as at least 3, but not more than 10, repetitive excitations originating from a ventricle with a rate >120 beats per minute.

Sinus node dysfunction was assessed using the criteria proposed by Kugler[13]. Arrhythmias were defined to be symptomatic if antiarrhythmic medication was prescribed, cardioversion had been applied, or pacemaker implantation had been necessary.

The study was approved by the local Medical Ethical Committee.

Data Analysis. Data are presented as mean values and standard deviation, unless indicated otherwise. The Chi-square and Fisher's exact test were used for the comparison of discrete variables. The Student t-test was used to compare continuous variables. The level of significance was chosen at $p < 0.05$.

Tests were performed for the total group of patients, as well as separately for the secundum type ASD and the sinus venosus type group. Results of the total group of patients will be presented, unless significant differences were found between these 2 sub-groups.

Table I **Demographic data, data of pre-operative cardiac catheterisation and surgical data**

	ASD II	sinus venosus type defect	total
number of patients	105	30	135
male	39 (37%)	20 (67%)	59 (44%)
female	66 (63%)	10 (33%)	76 (56%)
CARDIAC CATHETERISATION			
QP-QS ratio	2.3:1 (0.6:1-7.4:1)	2.4:1 (1.4:1-4.0:1)	2.3:1 (0.6:1-7.4:1)
peak syst. press. PA (in mm Hg)	26 ± 7 (8-50)	26 ± 6 (15-48)	26 ± 7 (8-50)
PAPVD	4 (4%)	23 (77%)	27 (20%)
SURGICAL DATA			
age at operation (in years)	7.6 ± 3.6	7.4 ± 3.5	7.5 ± 3.5
complete CPB	100 (95%)	30 (100%)	130 (96%)
direct closure	102 (97%)	0 (0%)	102 (76%)
closure with patch	3 (3%)	30 (100%)	33 (24%)

QP-QS ratio = ratio systemic flow - pulmonary flow; PA = pulmonary artery; PAPVD = partially abnormal pulmonary venous drainage; CPB = cardiopulmonary bypass

RESULTS

Pre- and peri-operative data. The essential baseline data of 135 patients are presented in Table I. The surgical procedure was performed with complete cardiopulmonary bypass and hypothermia in 130 patients (96%), and inflow occlusion was used in 5 patients. Cardioplegia was used since 1976 in 8 patients (7%). There were no peri-operative deaths. Nine patients had transient supraventricular tachycardia in the early postoperative period; none of these patients had atrial flutter or fibrillation, and none of them received anti-arrhythmic therapy.

A comparison of the baseline characteristics of the 104 participants with the 31 non-participants revealed no significant differences with regard to their pre-operative status (clinical symptoms, electrocardiogram, shunt size, pulmonary artery pressure), age at operation, year of operation, and postoperative course.

Medical history and physical examination. When questioned about their current general health (on a scale of "very good", "good", "moderate", "not good", or "bad"), 90 patients (87%) considered their health as good or very good, and 14 patients (13%) as moderate. None judged it as not good or bad. This health assessment is not significantly different from that of the normal Dutch population. Additional medical or surgical treatment after the first operation had been necessary in 8 patients (8%). Reoperation because of a substantial residual ASD was performed in 1 patient. Symptomatic supraventricular arrhythmia had been present in 6 patients (6%), of whom 3 were treated medically for periods of atrial flutter or fibrillation, and 3 needed pacemaker implantation 2 to 4 years after the primary operation because of symptomatic bradycardia due to sinus node dysfunction. These 6 patients all had experienced transient supraventricular arrhythmias during the immediate postoperative period. In 1 patient a complete atrioventricular block, already present pre-operatively, necessitated pacemaker implantation 1 day after the closure of the ASD. Ninety three patients (90%) had been discharged from routine outpatient clinical follow-up a few years after surgery. At physical examination all patients were in good physical health. The mean values of length, body weight, and systolic and diastolic blood pressure, corrected for age and sex, did not differ from that of the normal Dutch population.

Echocardiography. An enlarged right ventricle was present in 27 patients (26%), of whom 2 (2%) had a residual ASD with considerable left to right shunting. There was no right ventricular hypertrophy in any of the patients. The left ventricular end-diastolic diameter was normal in 101 patients (97%). The shortening fraction of the left ventricle was normal in 84 patients (81%), and was decreased in 20 patients (19%). In all patients with a diminished shortening fraction the motion of the interventricular septum was abnormal: paradoxical in 6 patients (6%) and hypokinetic in 14 patients (13%). None of these patients had residual left to right shunting or substantial pulmonary regurgitation. Hemodynamically insignificant mitral regurgitation was seen in 12 patients, of whom 3 had mitral valve prolapse. In 44 patients (42%) a hemodynamically insignificant tricuspid regurgitation was observed, with a peak velocity of 2.2 ± 0.3 m/sec. Hemodynamically insignificant pulmonary incompetence, present in 46 patients (44%), was < 2.2 m/sec in all. The right ventricular dimensions in the group of patients who were operated upon before the age of 3 years did not differ significantly from that in the group of patients who were operated upon at an older age. Comparison of preoperative shunt size, age at surgery, and duration of follow-up in patients with and without abnormal echo-cardiographic findings (abnormal dimensions of left or right ventricle, shortening fraction

less than 30%, abnormal septal motion, tricuspid regurgitation, mitral regurgitation) demonstrated no significant differences between these 2 groups.

Bicycle Ergometry. The mean exercise capacity was 104 ± 17% (range 76 to 153%) of the expected value. Twelve patients (12%) had a decreased exercise capacity. There were no substantial arrhythmias during or after exercise. The patients with diminished exercise capacity did not differ significantly from those with a normal test result with regard to pre-operative shunt size, echocardiographic findings (right ventricular size, motion of the interventricular septum, shortening fraction of the left ventricle), age at the time of the operation or duration of follow-up.

Standard 12-lead electrocardiogram. Ninety-three patients (90%) were in sinus rhythm, 6 patients (6%) had a low atrial rhythm, and 1 patient had a nodal rhythm. Pacemaker activity was registered in the 4 patients with such a device. Ectopic ventricular activity was registered in 2 patients: both had monoform premature ventricular contractions. First degree A-V block was seen in 12 patients (12%) and complete right bundle branch block in 12 patients (12%). Criteria for right ventricular hypertrophy were met in 12 patients (12%), who all had echocardiographic evidence of right ventricular dilatation without hypertrophy.

24 Hour Ambulatory electrocardiogram. Abnormal findings on 24 hour electrocardiogram were seen in 66 (67%) out of 98 patients. Supraventricular arrhythmias were seen in 44 patients (45%), of whom 38 (39%) showed signs of sinus node dysfunction according to the criteria proposed by Kugler, and 6 patients (6%) had non-sustained supraventricular tachycardias. None of the patients had atrial flutter or fibrillation. Ventricular arrhythmias were seen in 42 patients (43%). Of these, 39 had multiform premature ventricular contractions, ventricular doublets, or both, and 3 patients had a short ventricular tachycardia of maximally 3 consecutive beats. None of the patients had a sustained ventricular tachycardia. A combination of ventricular and supraventricular arrhythmias were seen in 21 patients (21%).

Conduction disturbances were seen in 17 patients (17%): 14 patients had (episodes of) first degree atrioventricular block and 2 patients had a type II second degree atrioventricular block. A 3rd degree atrioventricular block was seen in the patient who had a pacemaker inserted because of already pre-existing complete heart block prior to surgery. The prevalence of arrhythmias or conduction disturbances in the secundum group did not differ from that in the sinus venosus group. The presence or absence of arrhythmia at follow-up was not related to differences in localisation of the ASD (secundum type or sinus venosus type), baseline data (such as pre-operative shunt size, age at the time of the operation or surgical techniques), right ventricular dimensions at follow-up, age at the time of the follow-up study or duration of follow-up.

DISCUSSION

This study demonstrates that many years after surgery a large majority of the patients consider themselves as healthy, have a normal exercise capacity, and have no signs of the major risk factor in the natural history: elevated pulmonary artery pressure. Ninety-six patients (92%) were free from any medical or surgical intervention since the operation. However, a substantial number of patients proved to have anatomical or electrophysiological abnormalities, of which right ventricular dilatation, abnormal septal motion, sinus node dysfunction and ventricular arrhythmias were the most frequent.

The incidence of right ventricular dilatation (26%) was low compared to that in other

reports, in which the duration of follow-up was shorter and the mean age at operation (much) older[7,14]. Within our study population, however, these 2 factors were not associated with differences in right ventricular size. Therefore, on the basis of our data we cannot endorse that older age at operation and shorter duration of follow-up are related to right ventricular dilatation. Furthermore, our data do not support the assumption that surgery before the age of 3 years diminishes the incidence of persisting right ventricular dilatation[7]. The occurrence of abnormal septal motion, causing diminished shortening fraction of the left ventricle, is comparable with data of others[8]. Residual right ventricular dilatation and diminished shortening fraction of the left ventricle were not related to diminished exercise capacity or symptomatic (or asymptomatic) arrhythmias. Therefore these findings have little clinical importance.

The percentage of patients with symptomatic supraventricular arrhythmias (7%) is comparable to that in other series, as is the number of pacemaker implantations (4%)[15,16]. This emphasizes that symptomatic arrhythmia is an important, although infrequent, complication after surgical closure of an ASD.

The percentage of patients with asymptomatic supraventricular arrhythmias was high: 45%. Most of these patients had signs of sinus node dysfunction. Many other studies reported sinus node dysfunction before and after surgical correction of ASD, with a varying incidence (6% to 80%)[5,17-22]. Therefore it is possible that the asymptomatic supraventricular arrhythmias are expressions of compromised sinus node function, which eventually may give rise to clinical problems. However, results from 24 hour electrocardiogram studies in the normal population also often reveal supraventricular arrhythmias[23-27]. If Kugler's criteria were applied to these normal populations, the incidence of sinus node dysfunction would vary between 1% and 50%. This demonstrates that, in the absence of well defined normal values, the interpretation, clinical significance and prognostic value of these asymptomatic supraventricular arrhythmias remain unclear.

An unexpected finding was the high incidence (43%) of ventricular arrhythmias in our study, occurring significantly more frequent than in samples of the normal population. In contrast to supraventricular arrhythmias, ventricular arrhythmias have not been associated with the natural history of ASDs[28-30]. Kaplan and Perloff[31] reported the occurrence after surgical closure to be unusual, others report an incidence of 25% of isolated premature ventricular contractions[6]. The cause of these ventricular arrhythmias is unclear. It seems unlikely that they are surgically induced, and there was no relation to a dilated right ventricle. Until now there were no clinical consequences; all these patients were asymptomatic. Furthermore, there were no patients with sustained ventricular tachycardia. Longer follow-up will be necessary to assess whether these ventricular arrhythmias will become clinically relevant.

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CHAPTER 3

LONG-TERM FOLLOW-UP AFTER SURGICAL CLOSURE OF VENTRICULAR SEPTAL DEFECT IN INFANCY AND CHILDHOOD

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ABSTRACT

Objectives. The purpose of this study was to assess the health related quality of life of patients who underwent surgical closure of a ventricular septal defect at young age between 1968 and 1980.

Background. Since the beginning of open heart surgery for congenital cardiac malformations, the surgical techniques have been improved continuously. Due to these improvements even infants became eligible for surgical repair. Data on health related quality of life of non-selected patients long term after surgical repair at young age are not available. We therefore conducted a follow-up study of 176 infants and children consecutively operated upon in one institution between 1968 and 1980.

Methods. Patients who were alive and could be traced by using local registrars offices received an invitation to participate in the follow-up study, consisting of an interview, physical examination, echocardiography, exercise testing, 12 lead electrocardiography and 24 hour electrocardiography.

Results. One hundred and nine patients (78% of those eligible for follow-up) participated. Mean duration of follow-up (±SD) was 14.5 ± 2.6 years. Eighty-four percent of the patients assessed their health as good or very good. At physical examination all patients were in good health. Echocardiography demonstrated a small residual ventricular septal defect in 7 patients (6%). There were no signs of pulmonary hypertension. The mean exercise capacity in these patients was 100% ± 17% (range 56-141%) of the predicted values. None of the patients had symptomatic arrhythmias.

Conclusion. Long-term results of surgical closure of ventricular septal defect in infancy and childhood are good. Pulmonary hypertension is absent. Personal health assessment is comparable to that of the normal population, as is the exercise capacity, despite the fact that many patients have anatomical, hemodynamical or electrophysiological sequelae.

INTRODUCTION

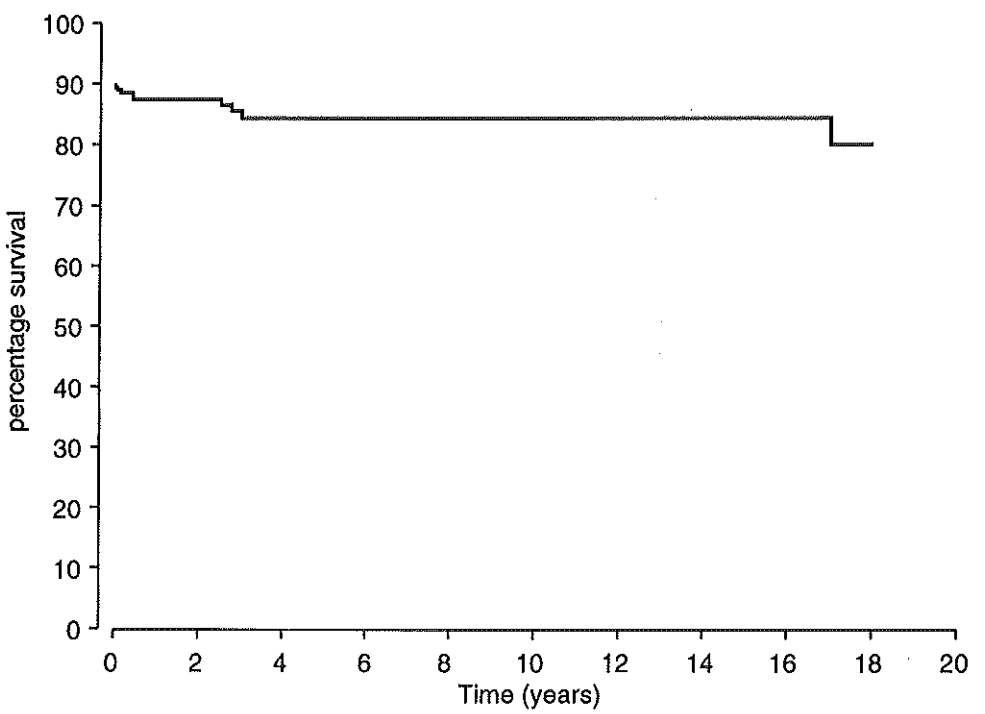
The long-term outcome of surgical closure of ventricular septal defect is known to be good: both morbidity and mortality are considerably reduced from those of patients without intervention[1-6]. Nevertheless, many surgically treated patients have residual abnormalities. Persisting pulmonary hypertension, ventricular arrhythmias, conduction disturbances, left ventricular dysfunction and abnormal response to exercise have been reported[7-11]. However, most long-term follow-up studies examined patients operated

on in the 1950's and 1960's[12]. Since then, significant changes have taken place: prerequisites such as minimal age or minimal weight of surgical candidates disappeared gradually, in parallel with many improvements in operative and perioperative care[13]. As a result, many patients whose condition would have been considered inoperable in the past, have been operated on in infancy or childhood. For these patients there are no long-term follow-up data on functional cardiac status based on consecutive series of patients examined many years after the operation. We therefore conducted a long-term follow-up study of 176 consecutive patients who had undergone surgical closure of ventricular septal defect in infancy or childhood in the period between 1968 and 1980. The aim of the study was to obtain more insight into the health related quality of life of these patients, examine the relations among anatomical, hemodynamical and electrophysiological sequelae, and assess the impact on the long-term outcome of the changes in patient selection and surgical techniques that occurred between 1968 and 1980.

METHODS

Patient selection and follow-up procedure. The study group comprised 176 patients with an isolated ventricular septal defect who operated on before 15 years of age at our institution in the period between 1968 and 1980 .The follow-up study started in April 1989. The patients were traced through the offices of local registrars. Twenty-three patients (13%) had died, four (2%) of these >2 years postoperatively (figure I).

Figure I **Kaplan-Meier survival curve of patients who underwent surgical closure of a ventricular septal defect in infancy or childhood**



The cause of these late deaths has been determined; one patient without documented residual abnormalities died suddenly 2.5 years postoperatively, two patients with pulmonary hypertension despite banding of the pulmonary artery before the surgical repair died, respectively 2.5 and 16.5 years postoperatively and 1 patient died of non-cardiac causes. Nine patients (5%) had moved abroad and six (3%) could not be traced. The remaining 139 patients received a letter explaining the objective of the study and invitation them to participate. A total of 109 patients (78% of those eligible for follow-up) agreed to participate. The mean ± SD interval between operation and follow-up was 14.5 ± 2.6 years (range 9.3 to 22.9 years). The mean age at the time of follow-up was 18.9 ± 5.7 years (range 9.6 to 32.9). Sixty-five (60%) patients were male and 44 (40%) female. All participants underwent a complete cardiological examination, including medical history, physical examination, standard 12-lead and 24 hour ambulatory electrocardiography, echocardiography (M-mode, two-dimensional echo, pulsed wave, continuous wave, and color flow Doppler studies) and exercise testing.
The study was approved by the local Medical Ethical Committee.
Measurements and definitions. The baseline characteristics were collected from the patient files. Part of the medical history consisted of a questionnaire from the Netherlands Central Bureau of Statistics that has been validated in a sample of 1510 Dutch adults <35 years of age[14] and uses standardized (multiple choice) questions to elicit a person's assessment on his or hers own health status.
Electrocardiographic (ECG) indication of right ventricular hypertrophy existed when in the frontal plane the QRS axis was between 90 and 180 degrees, and the R or R' wave in lead V_1 was >5 mm with R or R' wave > the S wave, in the absence of a right bundle branch block. Right bundle branch block was defined as a combination of a QRS axis between 90 and 180 degrees in the frontal plane, an RSR' pattern with R'> R in lead V_1, a deep slurred S in lead V_6 and a duration of the QRS complex of at least 0.12 seconds.
Echocardiography was performed with a Toshiba SSH 160-A echocardiograph. Left ventricular dimensions were measured in a parasternal long axis view and compared with normal values corrected for gender and body weight. Values between the 5th and 95th percentile were considered normal. A shortening fraction of the left ventricle of 30% to 40% was considered normal, a value <30% was considered decreased, and a value >40% was considered increased. Left ventricular hypertrophy was considered present if the enddiastolic diameter of both the interventricular septum and the left ventricular posterior wall was >95th percentile for gender and bodyweight.
Echocardiographic evidence of pulmonary hypertension was considered present if, in absence of right ventricular outflow obstruction, the flow velocity of tricuspid regurgitation >3.5 m/sec or if marked right ventricular hypertrophy was seen. Pulmonary regurgitation with a flow velocity >2.5 m/sec was also considered to be a sign of pulmonary hypertension. Because right ventricular dilatation or hypertrophy cannot be measured reliably, these features were judged independently by two experienced investigators. Trivial tricuspid and pulmonary regurgitation with a low velocity were not considered abnormal.
Exercise capacity was assessed by bicycle ergometry with stepwise increments of workload of 20 W/min. Patients were encouraged to exercise until exhaustion. Exercise capacity was defined as decreased if it was <80% of the predicted value (corrected for age, gender and body length), which is well below 2 SD below the predicted value, the exercise capacity was defined as decreased. Patients were excluded from the exercise

test if they could not be motivated to a maximal effort, or if a concomitant disease could influence the test result.

Arrhythmias were defined as symptomatic if antiarrhythmic treatment (drugs, direct current counter shock or pacemaker implantation) had been necessary. Sinus node dysfunction was assumed to be present if the patient had a bradycardia-tachycardia syndrome or atrial flutter or fibrillation. The following supraventricular arrhythmias were considered minor indicators of sinus node dysfunction: indications of a sinoatrial block, a beat to beat variation in heart rate >200%, sudden change from sinus rhythm to escape rhythm with a frequency > 25% less than that of the sinus rhythm, nighttime bradycardia < 30 beats/min and daytime bradycardia < 40 beats/min[15]. Ectopic ventricular activity, recorded during the 24 hour ECG, was considered abnormal if monoform premature contractions occurred at a rate >3600/24 hour or if premature ventricular contractions were multiform or presented as doublets or ventricular tachycardia. Nonsustained ventricular tachycardia was defined as at least 3 but <10 consecutive beats originating from a ventricle, with a rate >120 beats/min. Ventricular tachycardia of >10 consecutive beats was defined as sustained.

Pulmonary hypertension was assumed to be present if at least two of the following three indicators were present: an abnormal loud second heart sound, ECG indications of right ventricular hypertrophy, and echocardiographic evidence of pulmonary hypertension.

Data analysis. All values are expressed as mean value ± SD unless otherwise indicated. Chi-square analysis and the Fisher's exact test were used for to compare discrete variables and the Student t test was used to compare continuous variables in the presence of a normal distribution. The Mann-Whitney rank-sum test was used in the presence of a non-Gaussian distribution. Two proportions were compared using the difference of the rate of events in two groups calculated according to Greenland and Robins[16]. Analysis of variance by linear regression was performed with the help of the SAS statistical package for personal computers. In all analyses the chosen level of significance was $p < 0.05$.

RESULTS

Baseline characteristics. The baseline characteristics of the total group of 176 patients were compared with those of the 109 patients who participated in the follow-up study (Table 1 to 3). There were no significant differences between these two groups.

History. All 109 participants were asked to describe their health status (Table 4). Ninety-seven patients (89%) had had no medical or surgical intervention since the operation. Twelve patients (11%) had been admitted to the hospital after surgical closure of the ventricular septal defect (Table 5). No patient used antiarrhythmic drugs or other cardiac medication. Seventy-eight patients (72%) had been discharged from routine outpatient follow-up a few years postoperatively. Differences in preoperative hemodynamic findings, surgical techniques, age at the time of operation or duration of follow-up were not correlated with differences in personal health assessment.

Physical Examination. All 109 patients were found to be in good health. The mean values for body length, body weight and blood pressure corrected for age and gender did not differ from those of the normal Dutch population. Central cyanosis or signs of heart failure were not seen in any patient. A loud second heart sound was heard in 19 patients, but none had echocardiographic or ECG evidence of right ventricular hypertrophy.

Table I **Hemodynamic data at preoperative cardiac catheterisation**

	1968-1971		1972-1974		1975-1977		1978-1980	
	total n = 16	in follow-up n = 8	total n = 64	in follow-up n = 37	total n = 65	in follow-up n = 43	total n = 31	in follow-up n = 21
QP/QS	1.5 (0.45)	1.5 (0.52)	2.5 (1.1)	2.2 (1.1)	2.1 (1.1)	2.0 (1.1)	2.5 (1.3)	2.5 (1.1)
range	1.0-3.4	1.0-3.4	1.0-5.0	1.1-5.0	0.8-6.0	0.8-6.0	0.7-5.1	0.7-4.2
Pulmonary resistance in dyne/sec cm^{-5}	–	–	276 (200)	205 (154)	160 (187)	125 (130)	275 (276)	249 (154)
range	–	–	95-800	95-800	50-748	50-404	62-1020	62-825
Peak systolic pressure in MPA (mm Hg)	30 (47)	25 (8)	52 (37)	37 (40)	53 (38)	42 (36)	66 (32)	58 (31)
range	20-92	20-72	15-100	15-90	16-104	16-104	23-98	23-90

QP/QS = pulmonary flow in relation to systemic flow. The values of pulmonary resistance are corrected for body weight and hematocrit. All values are expressed as the median value (interquartile distance) and the range. MPA = main pulmonary artery

Table II **Baseline characteristics of all patients versus those of participants in the follow-up study**

	1968-1971		1972-1974		1975-1977		1978-1980	
	total n = 16	in follow-up n = 8	total n = 64	in follow-up n = 37	total n = 65	in follow-up n = 43	total n = 31	in follow-up n = 21
Age at operation (in years)	7.6 ± 4.0	7.6 ± 3.0	4.7 ± 3.7	5.4 ± 3.7	3.6 ± 4.1	4.5 ± 4.3	1.3 ± 2.0	1.8 ± 2.9
Age <1 year	0	0	10 (16%)	4 (11%)	30 (46%)	15 (35%)	20 (65%)	15 (71%)
VSD closure with patch	14 (88%)	8 (100%)	58 (90%)	31 (84%)	59 (91%)	40 (93%)	29 (94%)	19 (91%)
Cold cardioplegia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	18 (28%)	14 (33%)	23 (74%)	14 (67%)
Transatrial repair	1 (6%)	0	21 (33%)	9 (24%)	47 (72%)	27 (63%)	21 (68%)	13 (62%)
Previous banding	1 (6%)	0	8 (13%)	3 (8%)	4 (6%)	2 (5%)	3 (10%)	1 (5%)
Number of patients that died	2 (13%)		9 (14%)		9 (14%)		3 (10%)	

QP/QS = pulmonary flow in relation to systemic flow. None of the differences between the total group of patients, and the patients who participated in the follow-up study was statistically significant.

Table III **Site and type of Ventricular Septal Defect**

Localisation of VSD	total (n = 176)	follow-up study (n = 109)	died (n = 22)
Perimembranous	136	91	15
Muscular	8	1	4
Outlet	6	2	0
Inlet	2	1	0
Fallot type	5	3	0
Subpulmonary	1	1	0
Doubly committed	5	3	1
Multiple	5	2	1
Gerbode type (LV-RA)	4	3	0
Unknown	6	1	1

LV-RA = left ventricle to right atrium

Table IV **Personal health assessment of 109 patients long term after surgical closure of a ventricular septal defect compared with a sample of 1510 persons of the normal Dutch population younger than 35 years of age**

	study patients	normal Dutch population	p-value
excellent	24 (22%)	611 (40%)	< 0.01
good	68 (62%)	755 (50%)	< 0.05
fair	16 (15%)	127 (9%)	NS
not good	1 (1%)	17 (1%)	NS
bad	0 (0%)	0 (0%)	NS

Data presented indicate number (%) of patients in each group

Echocardiography. Echocardiographic findings were normal in 38 patients (35%); the remaining 71 patients had one or more abnormalities.

Residual defects. A small residual ventricular septal defects was demonstrated by Doppler color flow mapping in eight patients (7%). Mild mitral regurgitation could be demonstrated by Doppler color flow study in 15 patients (14%), of whom 7 had mild mitral valve prolapse. A discrete subaortic ridge, giving rise to an accelerated flow velocity >4.0 m/sec, was detected in three patients (3%). Mild to moderate aortic regurgitation, which had been documented in 2 patients pre-operatively, was seen in 12 patients (11%). Seven of these 12 patients originally had a perimembranous ventricular septal defect, 2 an outlet type defect, 1 a subpulmonary ventricular septal defect and 2 a doubly committed ventricular septal defect; none of the 12 had residual ventricular septal defect or a prolapse of an aortic cusp. The maximal flow velocity in the right ventricular outflow tract was 0.9 ± 0.3 m/sec and across the pulmonary valve 1.2 ± 0.4 m/sec, indicating that no patient had signs of right ventricular outflow tract obstruction or valvular

pulmonary stenosis. The presence of a residual ventricular septal defect was not related to the type of surgical approach (Table 6). Longer duration of follow-up and older age at the time of the operation were not correlated with an increase in incidence of aortic and mitral regurgitation.

Pulmonary hypertension. No patient had echocardiographic evidence of right ventricular hypertrophy. Tricuspid regurgitation could be demonstrated by Doppler color flow study in 70 patients. Its maximal flow velocity, measured with continuous wave Doppler technique in 47 patients, was 2.4 ± 0.4 m/sec (range 1.8 to 3.4). Trivial pulmonary regurgitation was demonstrated by Doppler color flow study in 69 patients (63%). The maximal flow velocity could be measured in 29 patients and was 1.5 ± 0.3 m/sec (range 1.0 to 1.9). In three patients the velocity of the jet of the ventricular septal defect could be measured: it exceeded 4.0 m/sec in all three.

Left atrial dimensions. Left atrial dimensions could be measured in 105 patients and were within normal range in 101 (96%). Four patients had a left atrial end-systolic diameter exceeding the 95th percentile for bodyweight; none of them had a residual ventricular septal defect or a mitral incompetence.

Left ventricular dimensions and function. Left ventricular end-diastolic diameter could be measured in 102 patients and was normal in 88 (86%). The left ventricle was small (<5th percentile) in 4 patients (4%), and enlarged (>95th percentile) in 10 (10%). The fractional shortening of the left ventricle was normal in 62 patients (61%), increased in 17 (17%), and decreased in 23 (22%). The pattern of septal motion was abnormal in 21 of these 23 patients: paradoxic in 6, and hypokinetic in 15. Left ventricular hypertrophy was seen in 3 patients. Fractional shortening did not differ between patients who had a normal-sized or a dilated left ventricle. By multivariate analysis, none of the following parameters were independent predictors for decreased fractional shortening: pulmonary vascular resistance >400 dynes/sec.cm-5, ventriculotomy, absence of cardioplegia, age at operation >1 year, and interval from operation >15 years.

Table V **Reason for hospital admission after surgical closure of ventricular septal defect**

Endocarditis		2
Pacemaker implantation	surgical atrioventricular block	2
Repeat cardiac surgery	residual VSD	2
	persisting ductus arteriosus	1
	discrete subaortic stenosis	1
	RV-outflow tract obstruction	3
	aortic coarctation	1
		12

VSD = ventricular septal defect; RV = right ventricular

Bicycle Ergometry. One hundred and two patients exercised to exhaustion. The mean exercise capacity in these patients was 100% ± 17% (range 56% to 141%) of predicted value. Exercise capacity was decreased in 17 patients (16%). No patients, not even

those with documented ventricular arrhythmias on the 24 h ECG, had arrhythmias during or directly after exercise. The exercise capacity of patients with decreased fractional shortening on echocardiography and of patients with signs of sinus node dysfunction did not differ from that of patients with a normal shortening fraction and patients without sinus node dysfunction. Exercise capacity was significantly better ($p = 0.02$) in patients who had a preoperative pulmonary vascular resistance <400 dynes/sec.cm^{-5} than those with a higher preoperative value. Linear regression showed that this was the only independent predictor for decreased exercise capacity. Other possible influences on exercise capacity (ventriculotomy, no cardioplegia, age >1 year at the time of the operation, interval from operation to follow-up >15 years) did not reach statistical significance.

Electrocardiography. The ECG findings were completely normal in 56 patients (51%). A total of 102 patients (93%) had normal sinus rhythm, 5 (5%) had an atrial rhythm and 2 had a pacemaker rhythm. The mean PR interval was 0.15 ± 0.03 seconds (range 0.08 to 0.22). Criteria for right ventricular hypertrophy were met in one patient, who had a normal second heart sound at physical examination, and proved to have no signs of pulmonary hypertension at echocardiography. Complete right bundle branch block was seen in 35 patients (32%), of whom 18 underwent a transatrial approach to repair and 17 a ventriculotomy (Table VI). No significant differences were found between patients with or without a bundle branch block with regard to localisation of the ventricular septal defect, age at the time of the operation, or type of repair (transatrial or transventricular, direct closure or patch).

Table VI **Differences in incidence of sequelae between patients who underwent transatrial repair and repair through a ventriculotomy**

	With ventriculotomy n = 56	With transatrial repair n = 47
ECHOCARDIOGRAPHY		
residual VSD	5 (9%)	3 (6%)
EXERCISE TEST		
<80% of predicted value	10 (18%)	7 (15%)
ECG		
RBBB	17 (30%)	18 (33%)
24 HOUR ECG		
ventricular arrhythmias	26 (46%)	17 (36%)
supraventricular arrhythmias	11 (20%)	10 (21%)

The surgical approach for ventricular septal defect was unknown in four patients.
VSD = ventricular septal defect; RBBB = right bundle branch block; ECG = electrocardiography

Twenty-four hour ECG. The results of the 24 h ECG of 106 patients are shown in Table 7. There were no significant differences between patients with a transatrial repair

Table VII **Result of 24-hour ECG in 106 patients**

	Number of patients
NO ARRHYTHMIA	51 (48%)
VENTRICULAR ARRHYTHMIA	45 (42%)
monoform PVC >3600/24 hour	0
multiform PVC	34
PVC doublet	12
VT 3-10 beats	6
VT > 10 beats	0
SUPRAVENTRICULAR ARRHYTHMIA	21 (20%)
atrial flutter / fibrillation	0
bradycardia / tachycardia	0
supraventricular tachycardia	0
bradycardia < 30 beats/min	1
escape rhythm > 25% slower than sr	1
beat-to-beat variation > 200%	13
SA exit block	11

PVC = premature ventricular complex; VT = ventricular tachycardia; sr = sinus rhythm; SA = sino-atrial

and patients with repair via a ventriculotomy with regard to incidence and type of arrhythmias (Table VI). The use of cardioplegia was not associated with a lower incidence of arrhythmias, and there were no significant differences concerning age at the time of the surgery, interval from operation to follow-up and age at the time of follow-up between patients with and without arrhythmias.

DISCUSSION

This study shows that the long term outcome after surgical closure of ventricular septal defect in infancy and childhood is good. Late mortality is low (2%) and pulmonary hypertension - the most important risk factor for premature death in both untreated patients and those operated on at an older age - is almost completely prevented. Eighty-four percent of the patients described their health as "excellent" or "good". Nearly 90% had no medical or surgical intervention since the operation, and over 80% of the patients had a normal exercise capacity. Even though their long-term health related quality of life is good, many patients have anatomic, haemodynamic or electrophysiological sequelae.

Anatomical and hemodynamical sequelae. The most important finding is the absence of right ventricular hypertrophy or other signs of pulmonary hypertension, even in patients who had an elevated pulmonary vascular resistance preoperatively. However, the fact that preoperative elevated pulmonary vascular resistance was the only independent predictor for decreased exercise capacity at the follow-up study indicates that the condition of the pulmonary vascular bed at the time of surgical repair, regardless of the age at operation, may be an important determinant for the cardiac long-term postoperative cardiac performance.

In contrast to the natural history of the ventricular septal defect, in which right-sided heart problems play a dominant role, most anatomic and hemodynamic sequelae in our study group were located on the left side of the heart. In 47 patients (43%) these sequelae were seen either solitary or in combination: mitral regurgitation, discrete subaortic stenosis, aortic regurgitation, left ventricular hypertrophy, dilation of the left ventricle and decreased fractional shortening of the left ventricle. These findings seem to have few clinical consequences to date; these patients did not differ from patients with a completely normal echocardiogram in cardiac related complaints, exercise capacity or incidence of arrhythmias.

Virtually all patients with a decreased fractional shortening of the left ventricle had abnormal septal motion. Because all of these patients had a normal exercise capacity it is highly unlikely that a decreased fractional shortening represents a depressed left ventricular function in these patients. This finding emphasizes the point that interpretations of echocardiographic findings which are valid for normal hearts are not necessarily applicable to hearts that are abnormal due to a congenital malformation or cardiac surgery, or both.

Aortic regurgitation is well known to be associated with ventricular septal defects (Laubry-Pezzi syndrome), especially if the defect is of the doubly committed or subaortic type[17]. However, over 50% of our patients with aortic regurgitation had a perimembranous ventricular septal defect, which was not directly adjacent to the aortic valve, and none of the patients had signs of a prolapse of the right anterior aortic cusp. Therefore it is possible that a mechanism other than prolapse of the aortic valve may play a role in the development of the aortic regurgitation, but because of the nature of this study it is impossible to retrieve this information.

The 7% incidence of residual ventricular septal defects in these patients is lower than that of earlier studies[11,18]. It is unlikely that we have missed a substantial number of residual defects, because in addition to auscultation we used color Doppler echocardiography, a particularly sensitive method for detecting residual defects. Probably this low incidence is real and reflects the more frequent achievement of complete closure of the ventricular septal defect in the later than in the early years of cardiac surgery.

Electrophysiologic sequelae. The number of patients with symptomatic electrophysiologic sequelae is low: no patient used antiarrhythmic drugs, and only two (2%) had a surgically induced complete atrioventricular block, a smaller number than reported in earlier series. This observation reflects the increased knowledge and ability of the surgeons to avoid damage to the conduction tissue. Asymptomatic electro-physiologic sequelae were found in a high proportion of the patients. Ventricular arrhythmia in relation to surgery for ventricular septal defect is well known[19], but the large number of patients with supraventricular arrhythmia was an unexpected finding. None of these patients had supraventricular tachycardia or hard evidence for sinus node dysfunction; all had arrhythmia that could be interpreted as minor indicators of sinus node dysfunction, and, as such, a possible predictor for later symptomatic arrhythmias. This interpretation would be in agreement with Moller et al[12], who reported that in their series of 258 patients evaluated 30 to 35 years after surgical closure of ventricular septal defect, 13 out of 20 patients with symptomatic arrhythmias had supraventricular arrhythmias, that in some could be considered as a sign of sinus node dysfunction. A possible cause of such arrhythmia is cannulation of the right atrium for cardiopulmonary bypass, which is known to be associated with sinus node dysfunction[22]. However, in 24 h ECG studies in nor-

mal adolescents and young adults[21-24], such arrhythmia was also frequently present and was not associated with increased morbidity or mortality. Longitudinal follow-up studies will be necessary to determine the clinical relevance of such asymptomatic arrhythmia.

Ventricular fibrillation, which is reported to be rare in patients after surgical closure of a ventricular septal defect[22], was not documented in our study group. The ventricular arrhythmias that were recorded seem to have little clinical significance: all patients were asymptomatic, and none had arrhythmia induced by exertion. In patients with a normal heart,such findings would indicate a good prognosis. However, in patients with a structural heart disease, especially after cardiac surgery, the significance of ventricular arrhythmias might differ from that in the normal heart, and the prognostic value is less clear[25]. The cause of ventricular arrhythmias remains subject to speculation[10,12,26]. The surgical scar in the right ventricular anterior wall is not likely to play a causative role as the incidence of ventricular arrhythmias in patients who underwent a transatrial repair was as high as in patients who had underwent a repair by way of a ventriculotomy. It is also known that the incidence of ventricular arrhythmias in patients who have not been operated is high, varying from 20% in patients with small defects to up to 90% in patients with Eisenmenger's syndrome[11]. This observation suggests that ventricular arrhythmia is an inherent part of the natural history and that surgical intervention possibly plays only a modulating role.

Right bundle branch block is rare (<10%) in patients who have not been operated on;[11] therefore it is probably caused by the surgical intervention. The finding that the incidence of right bundle branch block is as high in the group who had a transatrial repair as in those who had a ventriculotomy probably indicates that the right bundle branch is damaged proximally by the closure of the ventricular septal defect itself and not by the ventriculotomy. Even so, the postoperative right bundle branch block has little clinical significance[27].

Influence on sequelae of longer interval from operation to follow-up study. A longer interval between operation and follow-up was not associated with an increase in incidence of any of the sequelae, a decrease in exercise capacity or a less good personal health assessment. This indication that the sequelae do not appear gradually with time suggests that the outlook is promising for even longer follow-up.

Secular trends in patient selection and surgical technique. The minimal age at which surgical repair could be carried out changed considerably between 1968 and 1980, as did the surgical techniques. Patients operated on in the first half of the study period were generally older at the time of surgery (only a few were <1 year of age), had a smaller left-to-right shunt, did not receive cold cardioplegia, and had a transventricular repair. In the second half of the study period the patients were generally younger (often <1 year of age), had a larger left-to-right shunt, received cold cardioplegia, and had a transatrial repair. None of these differences accounted for differences in the nature and occurrence of sequelae. It is possible that the beneficial effect of the newer surgical techniques in the second half of the period is completely balanced by the selection of patients with less severe defects in the early period. However, this determination cannot be derived from our data. What our data show is that the use of cold cardioplegia and a transatrial approach have not resulted in greater long-term survival and fewer sequelae than were obtained with the older techniques.

Selection bias. Although the proportion of eligible patients who participated in the study was high (78%), it was not 100%. However, it is unlikely that a selection bias is present. All patients were traced uniformly and asked to participate in the follow-up study. In addition, there were no differences in the baseline characteristics between the patients who participated and those who did not. Therefore we conclude that the results of the group of patients we examined is representative of the whole study population.
Conclusion. Long-term results of surgical closure of ventricular septal defect in infants and children are good; late mortality is low and pulmonary hypertension is almost completely prevented. The personal health assessment of this patient group is similar to that of the normal population, as is their exercise capacity. Many patients have anatomic, hemodynamic or electrophysiologic sequelae. However, irrespective of the interval between operation and follow-up, virtually all patients were asymptomatic. Within our study population it could not be demonstrated that newer surgical techniques, in particular transatrial repair and use of cardioplegia, were associated with further improvement of long term results.

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CHAPTER 4

CARDIAC STATUS AND HEALTH RELATED QUALITY OF LIFE LONG-TERM AFTER SURGICAL REPAIR OF TETRALOGY OF FALLOT IN INFANCY AND CHILDHOOD

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ABSTRACT

The long-term results of surgical repair of tetralogy of Fallot was assessed by means of extensive cardiological examination of 77 nonselected patients 14.7± 2.9 years after surgical repair of tetralogy of Fallot in infancy and childhood. Due to the frequent use of a transannular patch (56%) for the relief of right ventricular outflow tract obstruction, the prevalence of elevated right ventricular systolic pressure was low (8%), but the prevalence of substantial right ventricular dilatation with severe pulmonary regurgitation high (58%). The exercise capacity of patients with a substantially dilated right ventricle proved to be significantly lower (83 ±19% of predicted) than that of patients with a near normal sized right ventricle (96 ±13%). Eight out of 10 patients who had needed treatment for symptomatic arrhythmia had supraventricular arrhythmia, which makes supraventricular arrhythmia -in numbers- a more important sequel in the long-term survivors than ventricular arrhythmia. Older age at the time of the operation and longer duration of follow-up were not associated with an increase in prevalence or clinical significance of sequelae.

INTRODUCTION

Reports on the long-term results of surgical repair of tetralogy of Fallot are numerous and emphasize on several complications that may occur. However, most reports deal with either selected patient populations which do not reveal the real prevalence of postoperative sequelae[1-3] or with consecutive series of patients in which only questionnaires were used[4,5]. Because the absence of symptoms does not rule out the presence of (undetected) sequelae[6], questionnaires do not give insight into the prevalence of sequelae either. Therefore we conducted a follow-up study in a consecutive series of patients long-term after surgical repair of tetralogy of Fallot in infancy or childhood by means of extensive cardiological examination. Special emphasis was put on the relation between anatomic, hemodynamic and electrophysiologic sequelae, and on the impact of the differences in age at operation, duration of follow-up and surgical techniques on the long-term results.

METHODS

Patient selection and follow-up procedure. The follow-up study started in April 1989. The clinical records of all 142 patients who underwent surgical repair of tetralogy of Fallot in our institution between 1968 and 1980, and who were younger than 15 years of age at the time of surgery, were reviewed for baseline characteristics. The year 1968

was chosen as starting point because in this year the first open heart operation was performed in our institution, and 1980 was chosen as end point to have at least 10 years of follow-up for all patients. Patients were traced using local registrars offices. Twenty-seven patients (19%) had died, of whom 4 (3%) more than 1 year after surgery. Four patients (3%) had moved abroad and 2 (2%) were untraceable. The remaining 109 patients received a letter in which the objective of the study was explained with an invitation to participate in an extensive cardiological examination. A total of 77 patients (71% of those eligible for follow-up) agreed to participate. Forty-five patients were male (58%) and 32 female (42%). The baseline characteristics of the 77 participants are shown in Table I. Because of the many changes in baseline variables between 1968 and 1980, this period was arbitrarily divided in two to create 2 subgroups: patients operated upon before 1976 and patients operated upon since then. These 2 subgroups were analyzed separately. There were no differences in baseline characteristics between the patients who participated in the follow-up study and the patients who were known to be alive but did not participate in the follow-up study. The cardiac examination included medical history, physical examination, standard 12-lead electrocardiography, echocardiography (M-mode, 2-D echo, pulsed-,continuous wave-, and color flow Doppler), exercise testing by bicycle ergometry and 24 hour electrocardiography.
The study was approved by the local Medical Ethical Committee.

Measurements and definitions. The diagnosis of tetralogy of Fallot was established during preoperative diagnostic cardiac catheterization. Patients with pulmonary atresia were excluded.

The *history* consisted partly of a standardized questionnaire on personal health assessment validated in a sample of 1510 Dutch adults under the age of 35 years[7].

Echocardiography was performed with a Toshiba SSH 160-A. Elevated systolic right ventricular pressure was judged to be present if the velocity of a tricuspid regurgitation jet or pulmonary artery flow exceeded 3.5 m/sec, or if a nonrestrictive ventricular septal defect was found. Since right ventricular dilatation cannot be measured reliably, this feature was judged independently by two experienced investigators. Substantial right ventricular dilatation was defined as the presence of a right ventricle that was equal or larger in diameter than the left ventricle in both the parasternal long-axis view and in the apical 4-chamber view. The degree of pulmonary regurgitation (minimal, mild, moderate, severe) was estimated with color-Doppler by the width and length of the regurgitant jet in the right ventricle, and with pulsed Doppler by the velocity and pattern of the regurgitant flow in the right ventricular outflow tract and pulmonary artery[8].

Maximal exercise capacity was assessed by bicycle ergometry with stepwise increments of the workload of 20 Watts per minute until the patient was exhausted. Patients were not tested if a concomitant factor could affect the test result (severe psychomotor retardation, spastic hemiplegia).

Arrhythmias were defined as symptomatic if patients used anti-arrhythmic drugs, if direct-current counter shock had been necessary in the past or if a pacemaker had been implanted. Sinus node dysfunction was defined as the presence of atrial flutter, atrial fibrillation and a bradycardia-tachycardia syndrome. The following phenomena were interpreted as possible indicators of sinus node dysfunction: a sino-atrial block, a beat-to-beat variation of the heart rate of more than 200%, a sudden change from sinus rhythm to an escape rhythm with a frequency > 25% lower than the sinus rhythm, a nighttime bradycardia < 30 beats per minute and a daytime bradycardia < 40 beats per

Table I **Baseline characteristics**

	year of operation 1968-1975	year of operation 1976-1980	year of operation 1968-1980
number of patients	39	38	77
Palliation			
no palliation	24 (61%)	28 (74%)	52 (68%)
Waterston shunt	5 (13%)	8 (21%)	13 (17%)
Blalock-Taussig shunt	10 (26%)	2 (5%)	12 (15%)
Surgical repair			
age at repair (yrs)	5.9 ± 3.0	2.6 ± 2.0	4.7 ± 3.4
(range)	(0.3-12.7)	(0.1-6.8)	(0.1-13.0)
CPB; moderate hypothermia	29 (74%)	17 (45%)	46 (60%)
deep hypothermia/ circ. standstill	10 (26%)	21 (55%)	31 (40%)
cold cardioplegia	7 (18%)	24 (63%)	31 (40%)
VSD closure with dacron patch	39 (100%)	38 (100%)	77 (100%)
relief RVOT obstruction by:			
- transannular patch	13 (33%)	30 (79%)	43 (56%)
- infundibulectomy	17 (44%)	6 (16%)	23 (30%)
- patch; not transannular	2 (5%)	1 (3%)	3 (4%)
- AO-monocusp RV-PA	7 (18%)	0	7 (9%)
- Hancock prosthesis	0	1 (3%)	1 (1%)
Reoperations			
number of patients	6 (15%)	7 (18%)	13 (17%)
interval surgical repair-reoperation	7.8 ± 8.7 yr (0.1-21.6)	3.0 ± 3.6 yr (0.1-8.3)	5.4 ± 6.8 yr (0.1-21.6)
type of reoperation:			
- closure residual VSD	1 (3%)	5 (13%)	6 (8%)
- relief residual RVOT-obstruction	3 (8%)	1 (3%)	4 (5%)
- Hancock prosthesis because severe PR	0	1 (3%)	1 (1%)
- Pacemaker implantation			
because of AV-block	1 (3%)	0	1 (1%)
because of SND	1 (3%)	1 (3%)	2 (3%)
Antiarrhythmic medication			
because of SVT/AF/AFl	4 (10%)	1 (3%)	5 (6%)
because of sustained VT	1 (2%)	0	1 (1%)
because of sustained VT and SVT	0	1 (2%)	1 (1%)

CPB = cardiopulmonary bypass; VSD = ventricular septal defect; RVOT = right ventricular outflow tract; AO = aorta; RV-PA = right ventricle to pulmonary artery; AV = atrio-ventricular; SND = sinus node dysfunction; SVT = supraventricular tachycardia; AF = atrial fibrillation; AFl = atrial flutter; VT = ventricular tachycardia

minute[9]. Premature ventricular contractions, recorded during the 24 hr electrocardiogram were considered to be abnormal if monoform premature ventricular contractions occurred in a frequency exceeding 3600/24 hour, if premature ventricular contractions were multiform, or if premature ventricular contractions presented as doublets or ventricular tachycardia. Short ventricular tachycardia was defined as at least 3 and not more than 10 consecutive beats originating from a ventricle, with a rate exceeding 120 beats per minute.

Data analysis. All values are expressed with their mean value and standard deviation, unless indicated otherwise. The Chi-square and Fisher's exact test were used for the comparison of discrete variables and Student's t-test was applied to compare continuous variables in the presence of a normal distribution. In the presence of a non-Gaussian distribution the Mann-Whitney rank-sum test was used. In all analyses the level of significance was chosen at $p < 0.05$.

RESULTS

History. Fifty-three patients (69%) had been seen by a cardiologist or pediatric cardiologist regularly at least once every three years, in contrast to 24 patients (31%) who were not regularly seen in the last 10 years. All patients were asked their opinion about their own health. The outcome was compared with that of the normal population (Table II).

Table II **Personal health assessment of 77 patients long term after complete repair of tetralogy of Fallot compared with a sample of 1510 Dutch adults under the age of 35 years**

	Fallot patients	normal population	
Excellent	13 (17%)	611 (40%)	p <0.001
Good	50 (65%)	755 (50%)	p <0.014
Fair	11 (14%)	127 (9%)	n.s.
Not good	3 (4%)	17 (1%)	n.s.
Bad	0 (0%)	0 (0%)	n.s.

The personal health assessment of patients who had not been checked regularly by a (pediatric) cardiologist was significantly better than that of patients who were regularly checked. A less than "good" personal health assessment was not associated with older age at the time of surgical repair, longer duration of follow-up, and medical or surgical interventions after the surgical repair. All 3 patients who assessed their health as "not good" proved to have substantial abnormalities at echocardiographic examination: 2 had a large nonrestrictive ventricular septal defect, and all 3 had elevated systolic right ventricular pressure.

Physical Examination. The mean values of length, body weight, and blood pressure corrected for age and sex, did not differ significantly from that of the normal Dutch population. A systolic murmur was heard in 75 patients (97%) and a diastolic murmur in 63 patients (82%). Nine patients (12%) had moderate to severe chest deformity and scoliosis.

Table III **Summary of the results of the echocardiography, bicycle exercise test and 24-hour ECG**

	year of operation 1968-1975	year of operation 1976-1980	year of operation 1968-1980
number of patients	39	38	77
age at the time of the follow-up study (range)	22.9 ± 4,5 yrs (15.9-34.9)	15.0 ± 3.1 yrs (9.9-20.6)	19.0 ± 5,5 yrs (9.9-34.9)
duration of follow-up (range)	17.0 ± 2.7 yrs (14.5-22.2)	12.4 ± 1.6 yrs (9.5-15.2)	14.7 ± 2.9 yrs (9.5-22.2)
Echocardiography			
RV size			
near normal/moderately dilated RV and mild/moderate PR	19 (49%)	13 (35%)	32 (42%)
severely dilated RV and moderate/severe PR	20 (51%)	25 (65%)	45 (58%)
RV pressure			
normal	36 (92%)	35 (92%)	71 (92%)
elevated	3 (8%)	3 (8%)	6 (8%)
Ventricular septum			
intact	28 (72%)	35 (92%)	63 (82%)
large VSD	2 (5%)	0	2 (3%)
small VSD	9 (23%)	3 (8%)	12 (15%)
Exercise test			
maximal exercise capacity (% of normal, range)	88% ± 16% (46-117%)	89% ± 17% (38-118%)	90% ± 18% (38-118%)
< 50%	1 (3%)	1 (3%)	2 (3%)
50-80%	6 (18%)	7 (19%)	13 (18%)
> 80%	27 (79%)	29 (78%)	56 (79%)
not tested	5	1	6
24-hour ECG			
number of pts without arrhythmia	8 (26%)	11 (31%)	19 (28%)
number of pts with arrhythmia	23 (74%)	25 (69%)	48 (72%)
no registration	8	2	10
number of pts with ventricular arrhythmia	16 (52%)	17 (49%)	33 (49%)
multiform PVC's	13 (42%)	14 (39%)	27 (40%)
PVC doublets	6 (19%)	9 (25%)	15 (22%)
VT 3-10 beats	2 (6%)	3 (8%)	5 (7%)
VT > 10 beats	0	1 (3%)	1 (1%)
number of pts with supraventr. arrhythmia	7 (22%)	12 (33%)	19 (28%)
SVT	1 (3%)	3 (8%)	4 (6%)
possible SND	6 (19%)	8 (22%)	14 (21%)
AF	0	0	0
AFl	0	0	0
brady/tachycardia syndrome	0	1 (3%)	1 (3%)

RV = right ventricle; PR = pulmonary regurgitation; VSD = ventricular septal defect; PVC = premature ventricular contraction; VT = ventricular tachycardia; SND = sinus node dysfunction; AF = atrial flutter; pts = patients

Of these, 3 had a lateral thoracotomy because of a shunt (2x Blalock, 1x Waterston) prior to the surgical repair, and 2 others had a severe psychomotor retardation and a spastic hemiplegia. Four patients (5%) had psychomotor retardation and spastic hemiplegia.

Echocardiography. In Table III the findings concerning right ventricular size, systolic right ventricular pressure and interventricular septum are summarized. The left ventricular outflow tract was unobstructed in all patients. The aortic annulus was dilated (>p95 for body weight) in 3 patients (4%). Twelve patients (16%) had evidence of minimal aortic regurgitation; severe aortic regurgitation was not seen. Moderate to severe tricuspid regurgitation was seen in 17 patients (22%). All had a severely dilated right ventricle. The antegrade flow velocity in the pulmonary artery did not differ significantly between patients with and without a transannular patch (1.7 ± 0.7 m/sec versus 2.0 ± 0.8 m/sec; $p = 0.09$). Severe pulmonary regurgitation and substantial dilatation of the right ventricle were seen more often after surgical repair with the use of a transannular patch ($p < 0.01$) or an aortic monocusp ($p<0.05$) than after other surgical techniques. The following baseline variables were tested, but proved to be not significantly correlated with substantial right ventricular dilatation and pulmonary regurgitation: older age at the time of the operation, longer duration of follow-up, moderate hypothermia and complete cardiopulmonary bypass versus deep hypothermia and circulatory arrest, and absence of cold cardioplegia. The prevalence of substantial right ventricular dilatation and severe pulmonary regurgitation was significantly higher in patients who had been regularly seen by a (pediatric) cardiologist than in patients who had not been seen regularly. Other hemodynamic variables did not differ in the 2 groups.

Bicycle Ergometry. Seventy-one patients exercised to maximum effort. Four patients were not tested because of mental retardation, and 2 patients refused. The results are summarized in Table III. The mean value for maximal exercise capacity (89% ± 16%) is significantly lower than that of the normal population ($p<0.01$). Patients with a near normal/moderately dilated right ventricle had a maximal exercise capacity of 96% ± 13%, versus 83% ± 19% in patients with a substantially dilated right ventricle ($p = 0.002$). The maximal exercise capacity of the 6 patients with an elevated systolic right ventricular pressure was 87 ± 12%, which is neither significantly different from that of patients with a near normal/moderately dilated right ventricle, nor from that of patients with a substantially dilated right ventricle. Fourteen of the 15 patients with an exercise capacity of <80% of predicted had a substantially dilated right ventricle. The maximal exercise capacity of patients who had a transannular patch (86% ± 18%) or an aortic monocusp (81% ± 15%) at the surgical repair was significantly lower ($p < 0.03$) than that of patients who had an other type of relief of the right ventricular outflow tract obstruction (95% ± 14%). There was no significant difference in maximal exercise capacity between patients who were checked regularly by a (pediatric) cardiologist and patients who were not. Palliative surgery prior to the surgical repair, older age at the time of the surgical repair and longer duration of follow-up were not associated with a decreased exercise capacity. Eleven patients had arrhythmia during or directly after the exercise test. One patient, who was not known to have ventricular arrhythmia, developed a short ventricular tachycardia (<10 beats) at exercise. Nine patients, of whom only 3 patients had ventricular arrhythmia at the 24 hour ECG registration, had multiple premature ventricular contractions. One patient who was known to have a supraventricular tachycardia with a 2:1 conduction developed a 1:1 conduction at exercise.

12-lead electrocardiography. A narrow QRS complex was seen in 20 patients (26%), of whom 11 (14%) had a completely normal electrocardiogram, and the remaining 9 patients showed signs of right ventricular hypertrophy. A wide QRS complex was found in 57 patients (74%). Forty-five patients (58%) had a complete right bundle branch block, 9 patients (12%) had both a complete right bundle branch block and a left anterior hemiblock, and 3 patients (4%) had a pacemaker rhythm with a wide QRS complex. The mean P-R interval was 0.15 ± 0.03 seconds (range 0.10 to 0.24 seconds).
No significant differences were found between patients with a bundle branch block, and those without, with regard to the type of surgical relief of the right ventricular outflow tract obstruction, age at the time of the operation, or duration of follow-up.
Twenty-four hour electrocardiography. A complete 24 hour electrocardiogram could be obtained in 67 patients. The results are summarized in Table III. In 39 patients with a dilated right ventricle in whom a 24 hour electrocardiogram was obtained, 23 (59%) had ventricular arrhythmia. Of the 28 patients with a normal or slightly enlarged right ventricle, 10 (36%) had ventricular arrhythmia. This difference is not significant ($p = 0.1$). Five patients with an elevated systolic right ventricular pressure had a complete 24-hour ECG registration; 3 had ventricular arrhythmia, of whom 2 had ventricular tachycardia. This prevalence is significantly higher than that in patients with a normal pressure right ventricle (2 of 5 patients versus 3 of 62 patients; $p=0.04$). Older age at the time of surgery, longer duration of follow-up and older age at the time of the follow-up study were not associated with a higher prevalence of ventricular or supraventricular arrhythmia. There was no significant difference in prevalence of ventricular or supraventricular arrhythmias between patients who received cold cardioplegia at surgical repair and patients who did not, neither between patients in whom deep hypothermia with circulatory arrest was used and patients who had underwent the procedure under moderate hypothermia and cardiopulmonary bypass. In patients who had a palliative procedure prior to surgical repair, or who had been re-operated, the prevalence of arrhythmia was not higher than patients who had been operated once. There was no difference in prevalence or type of arrhythmia on the 24 hour electrocardiogram between patients who were checked regularly by a (pediatric) cardiologist and patients who were not.

DISCUSSION

This study shows that the long-term results of surgical repair of tetralogy of Fallot in infancy and childhood are good in terms of health assessment and exercise capacity: 82% of the long-term survivors describe their health as "excellent" or "good, and 79% had an (almost) normal exercise capacity of >80% of the predicted value. If one considers the patients who assessed their health as "good" and "excellent" as one group, the personal health assessment is even as good as that of the normal Dutch population. A similar good health assessment after surgical repair of tetralogy of Fallot was reported by others[10]. Obviously, a "good" health assessment is an important determinant for the quality of life. However, we did not find a correlation between a "good" or "excellent" health assessment and the absence of symptoms (decreased exercise capacity) or sequelae (substantial right ventricular dilatation, ventricular or supraventricular arrhythmia). This confirms that personal health assessment is not a good indicator for the "objective" clinical condition of the patient[11].
If the long-term results of the surgical repair of tetralogy of Fallot would be judged on

the presence of a normal cardiac anatomy or electrophysiology, the score is not good: 58% of the patients had a substantial dilatation of the right ventricle with severe pulmonary regurgitation and 72% of the patients had (ventricular or supraventricular) arrhythmia at the 24 hour electrocardiogram. The prevalence of the postoperative sequelae in our study population is reliably assessed as a result of the study design, but the clinical significance of many sequelae is still unclear and remains subject to debate.

Anatomic and hemodynamic sequelae. The prevalence of elevated right ventricular systolic pressure due to residual right ventricular outflow obstruction is relatively low (8%)[5,12,27]. This is probably partly due to the absence of patient selection in our follow-up study; patients with elevated right ventricular systolic pressure are likely to have symptoms, and are therefore probably over-represented in other types of follow-up studies. Another explanation is that the frequent use of a transannular patch in our study population is responsible for both the relatively low prevalence of elevated right ventricular systolic pressure, and the high prevalence of substantial right ventricular dilatation and severe pulmonary regurgitation.

The clinical importance of elevated right ventricular systolic pressure is its association with ventricular arrhythmias and late sudden death[13-15]. Also in our study the prevalence of ventricular tachycardia was significantly higher in these patients than in patients with normal systolic right ventricular pressure. Pooled data of 39 studies on postoperative tetralogy of Fallot (comprising 4627 patients) revealed that 80% of the patients who had died suddenly had both abnormal hemodynamics (especially elevated right ventricular systolic pressure) and ventricular arrhythmias on the 24 hour electrocardiogram[16]. Therefore, treatment for these patients must be considered by surgical relief of the residual right ventricular outflow tract obstruction only or in combination with antiarrhythmic medication.

The interpretation of the clinical importance of right ventricular dilatation and pulmonary regurgitation is much more controversial than that of elevated right ventricular pressure. Because there is no standardized method to quantify either pulmonary regurgitation or right ventricular dimensions, these features are assessed by means of many different techniques in the many follow-up studies (clinical evidence[17], angiography[18,19] radionuclide angiography[3], echocardiography)[20], which makes comparison in this respect between studies very hazardous.

In our study we did not find a correlation between substantial right ventricular dilatation and arrhythmia[21]. However, like others[3,4,22,23] we did find that the exercise capacity was substantially decreased in patients with substantial right ventricular dilatation and severe pulmonary regurgitation. Because it has been demonstrated that even very long-standing pulmonary regurgitation and right ventricular dilatation (>30 years) has no negative effect on long-term survival[24], a decreased exercise capacity seems to be the only consequence of substantial right ventricular dilatation. Longer follow-up will be necessary to see whether these assumptions will hold out to be true.

Other anatomic sequelae that were frequently seen were residual ventricular septal defect and aortic regurgitation. Except for 2 patients who had a large, non-restrictive ventricular septal defect who were operated upon as a result of this finding at the follow-up study, these sequelae had no hemodynamic significance.

Electrophysiological sequelae. In our study there were 2 patients (2%) with sustained ventricular tachycardia. About the clinical significance of sustained ventricular tachycardia there is not much discussion: these patients are considered to be at risk for sudden

death and antiarrhythmic medication is indicated. Furthermore, 32 patients (48%) had complex ventricular premature ventricular complexes, including 5 patients with nonsustained ventricular tachycardia. This is within the wide scatter of the reported prevalence of ventricular arrhythmia (range 2-77%)[18] and comparable with the prevalence of ventricular arrhythmias in 2 studies of consecutive patients (respectively 41 and 42%)[25,26]. The clinical significance of asymptomatic complex premature ventricular complexes and non-sustained ventricular arrhythmia is still controversial[15]. Are they possible determinants for the occurrence of sustained arrhythmia (and sudden death) and should they therefore be treated prophylactically, even if the risk for a sustained ventricular tachycardia is very small[17]? Or have these patients such a low risk for development of sustained ventricular tachycardia that prophylactical treatment with potentially dangerous side effects should be omitted?[27] Due to the nature of this study our data do not provide new arguments to support one of the two opposing views.
Supraventricular arrhythmia and sinus node dysfunction have been reported earlier in postoperative tetralogy of Fallot[14,25,28]. In our study population, 7 of the 10 patients who were treated because of rhythm disturbances, had supraventricular arrhythmia. This emphasizes that supraventricular arrhythmia and sinus node dysfunction are clinically important sequelae after surgical repair of tetralogy of Fallot, of which the clinical importance has been underestimated so far. Next to these patients with symptomatic supraventricular arrhythmia, 28% of the patients had asymptomatic supraventricular arrhythmia. It can be questioned whether these arrhythmias are "abnormal", because 24 hour electrocardiogram studies in normal adolescents and young adults have demonstrated that these arrhythmias are also frequently present in the normal population[29-32]. On the other hand, in this group of patients with such a high prevalence of proven sinus node dysfunction, it is possible that these findings are indeed signs of a compromised sinus node function, and as such predictors for clinically relevant arrhythmias later. Possible causative mechanisms could be cannulation of the right atrium for cardiopulmonary bypass[33], or decreased right ventricular function leading to elevated right atrial pressures and dimensions. More specific studies on this subject, and longer duration of follow-up will be necessary to establish the clinical importance of these findings.
Reoperation. Freedom from reoperation is one of the hallmarks of successful surgical repair. In our study population the freedom from reoperation was 88%, which is similar to results published by others[34]. Like in other series, the most important indication for reoperation was closure of a residual ventricular septal defect[35]. Only 1 patient with severe pulmonary regurgitation and right sided heart failure had a pulmonary valve replacement. The benefits of pulmonary valve replacement for this indication has been well documented[36]. Others have advocated pulmonary valve replacement as an essential part of the treatment of symptomatic ventricular arrhythmias in the presence of poor right ventricular hemodynamics and severe pulmonary regurgitation. Only improvement of the right ventricular hemodynamic situation would make successful medical therapy possible. However, our data indicate that there is no correlation between right ventricular dilatation and symptomatic arrhythmia, and therefore we do not support this view. Furthermore no study on the efficacy of this regimen has been published yet.
In contrast to other reports there were no deaths associated with reoperation, and we did not find an increased prevalence of ventricular arrhythmias in patients who were reoperated compared to patients who were not reoperated[37].

Year of operation, age at surgical repair and duration of follow-up. These factors are closely related to each other. They changed significantly and simultaneously in the period between 1968 and 1980[38]. All could possibly affect the eventual outcome of the surgical repair. Except for the use of a transannular patch, which proved to be associated with severe pulmonary regurgitation and right ventricular dilatation, univariate analysis failed to identify a single determinant in these baseline characteristics that was associated with one of the sequelae at follow-up. We did not find a correlation between older age at surgical repair and ventricular arrhythmia; this is in contrast to the findings of many others[39-41]. Unlike others we did neither find that longer duration of follow-up was associated with an increase in prevalence of substantial right ventricular dilatation, nor with a decrease in exercise capacity[42], nor with an increase of the prevalence of arrhythmia. This suggests that the factor time has little impact on the long-term results of surgical repair of tetralogy of Fallot, and therefore that the outlook for the future of these patients is promising. Because at univariate analysis whether differences in baseline characteristics lead to significant differences in sequelae at follow-up, only 1 determinant (transannular patch) proved to be statistically significant and all other determinants (age at surgical repair, palliation prior to the surgical repair, moderate or deep hypothermia, cold cardioplegia, reoperation, duration of follow-up, age at follow-up) had p-values>0.15, we did not perform multivariate analysis.

Selection bias. Apart from selecting the patients on grounds of the definition of the study population - patients with a tetralogy of Fallot who underwent surgical repair before the age of 15 years who were operated upon in our institution between 1968 and 1980 - patients were not purposely selected. We examined only 71% of those eligible for follow-up, and not 100%, and we were not informed about the reasons why patients who did not participate in the follow-up study actually refused and therefore we cannot exclude that we saw an, unintentionally, selected patient group. However, all patients were approached uniformly, and there were no significant differences in any of the baseline characteristics as summarized in table I between patients who participated in the follow-up study and those who did not. Therefore we assume that there was no selection bias and consider the patients who participated in the follow-up study as a nonselected population.

Conclusion. Long-term follow-up of a non-selected group of patients, who underwent surgical repair of tetralogy of Fallot reveals a substantial prevalence of sequelae, similar to that in earlier reports on selected patient groups. However, the prevalence and clinical relevance of these sequelae and their correlations with age at surgery, different surgical techniques and duration of follow-up are assessed more reliably. The frequent use of a transannular patch, which is a reflection of the state of the art of the surgical approach in the 1960's and 1970's, but substantially different from current day techniques, has lead to a low prevalence of elevated systolic right ventricular pressures and therefore a low prevalence of potentially life threatening ventricular arrhythmias. The negative aspect of this approach was the high prevalence of (obligatory) severe pulmonary regurgitation and right ventricular dilatation, which was clearly associated with a decreased exercise capacity.

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CHAPTER 5

LONG-TERM FOLLOW-UP (10 TO 17 YEARS) AFTER MUSTARD REPAIR FOR TRANSPOSITION OF THE GREAT ARTERIES

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ABSTRACT

Background. The management strategies of patients who underwent a Mustard repair for transposition of the great arteries have been changed in the 1970's: infants became eligible for direct surgical repair, therefore Blalock-Hanlon atrioseptostomy could be avoided. In addition, cold cardioplegia was introduced for myocardial preservation, but data are lacking whether these changes had a positive effect on the long-term outcome. We therefore conducted a follow-up study of all 91 patients who underwent a Mustard repair for transposition of the great arteries in our institution between 1973 and 1980 in order to assess the incidence and clinical importance of sequelae as well as health related quality of life of these patients.

Methods. Patients who were alive and could be traced by using local registrars offices received an invitation to participate in the follow-up study, which consisted of an interview, physical examination, echocardiography, exercise testing, standard 12 lead and 24-hour electrocardiography.

Results. Patients operated upon in the first 4 years had a significantly higher mortality and higher incidence of sinus node dysfunction than patients operated upon in the subsequent 4 years (respectively 25% versus 2% and 41% versus 3%). In contrast, the incidence of baffle obstruction needing reoperation was significantly higher in the second group. There were no significant differences in echocardiographic findings and exercise capacity between patients operated upon in the first 4 years and in the subsequent 4 years: none of the patients had right ventricular failure, a mild degree of baffle leakage or obstruction was seen in 22% of the patients, and the mean exercise capacity was decreased: 84 ± 16%.

Conclusion. The changes that have been introduced between 1973 and 1980 have resulted in a considerable reduction of mortality and incidence of sinus node dysfunction, but also in a more frequent need for reoperations.

INTRODUCTION.

Since the introduction of the atrial switch procedure, the outlook for patients with transposition of the great arteries has improved considerably[1]. However, the first follow-up results reported in 1972 by El Said[2] made clear that right ventricular failure, sinus node dysfunction and baffle-related problems were serious drawbacks of these surgical techniques. Therefore, after the introduction of the arterial switch, the atrial switch procedure was gradually abandoned as the treatment of choice.

Cardiologists now face a large number of patients who underwent a Mustard or Senning

type procedure presenting with late complications, and this number will probably increase in the future. There is little information about the real incidence of complications, since studies on the long-term follow-up in consecutive series of patients who are actually examined at follow-up are scarce[3,4]. Changes in surgical techniques have been introduced in the 1970's to reduce the incidence of sequelae, but data are lacking whether these had a positive effect on the long-term outcome. Therefore, we conducted a follow-up study to evaluate the anatomic, hemodynamic and electrophysiologic status as well as the health related quality of life of all patients who underwent a Mustard repair in our institution between 1973 and 1980.

METHODS

Patient selection and follow-up procedure. In the period between 1973 and 1980 91 patients younger than 15 years of age underwent a Mustard repair for transposition of the great arteries at our institution. The year 1973 was chosen as starting point because the first Mustard repair was performed in our institution in that year, and 1980 was chosen as end point to have at least 10 years of follow-up. The follow-up study started in April 1989. Patients were traced through the offices of local registrars. Eighteen patients had died, and 5 had moved abroad. The remaining 68 patients received a letter explaining the objective of the study and inviting them to participate. Fifty-eight patients (79% of the survivors; 85% of those eligible for follow-up) responded positively and took part in an extensive cardiological examination in 1990 and 1991. Forty of these patients (69%) were male and 18 (31%) female. The mean (± SD) interval between operation and follow-up was 14.0 ± 2.1 years (range from 10.1 to 17.6 years). The age at follow-up was 15.8 ± 3.9 years (range from 10.4 to 27.8 years). The baseline characteristics were derived from the patient files. The examination at follow-up consisted of medical history, physical examination, standard 12-lead and 24-hour electrocardiography, exercise testing, M-mode and two-dimensional echocardiography, pulsed-, continuous wave and color flow Doppler studies.

The study was approved by the local Medical Ethical Review Board.

Measurements and definitions. Transposition of the great arteries was defined as simple if there were no or minor concomitant abnormalities such as atrial septal defect, ventricular septal defect which did not require surgical closure or a persisting ductus arteriosus. If the concomitant abnormality consisted of a left ventricular outflow tract obstruction or a ventricular septal defect that required surgical closure, the transposition was defined as complex.

The medical history comprised of a questionnaire from the Netherlands Central Bureau of Statistics which has been validated in a sample of 1510 Dutch adults <35 years of age[5]. It uses standardized (multiple choice) questions to elicit a person's assessment of his or her health status.

Echocardiographic examination was performed with a Toshiba SSH 160-A echocardiograph. Baffle obstruction was diagnosed if there was both evidence of obstruction in the two-dimensional image and the Doppler flow pattern in superior or inferior caval vein showed a pattern with a maximal antegrade flow in ventricular systole, instead of a maximal antegrade flow in diastole, which is the normal pattern after a Mustard repair[6,7]. Obstruction to pulmonary venous drainage was diagnosed if the peak velocity of the pulmonary vein flow at the junction with the pulmonary venous atrium exceeded 1.5 m/sec. Right ventricular dimensions and contractility were judged by visual estimate by

an experienced echocardiographist and a pediatric cardiologist. We did not measure these features because it is generally accepted to be unquantifiable. Right ventricular failure was defined to be present if there was a gross dilatation and a poor contractility of the right ventricle in the presence of a substantial tricuspid regurgitation and a flow velocity in the ascending aorta of less than 0.7 m/sec. The degree of tricuspid regurgitation (minimal, moderate, severe) was estimated with color-Doppler by the width and length of the regurgitant. Pulmonary hypertension was assumed to be present if a pulmonary regurgitation was found with a flow velocity exceeding 3.5 m/sec, or if a mitral regurgitation was found with a flow velocity >4.0 m/sec in the absence of left ventricular outflow tract obstruction. Left ventricular pressure was calculated using the simplified Bernouilly equation on the flow velocity of the mitral regurgitation (if present) or the flow velocity in the pulmonary artery. If the velocity of this jet exceeded 3.5 m/sec, and the left ventricle was not flattened but had a round shape, the left ventricular pressure was considered to be elevated.

Maximal exercise capacity was assessed by bicycle ergometry with stepwise increments of the workload of 20 W/min. Patients were encouraged to exercise until exhaustion. Patients were excluded from the exercise test if they could not be motivated to exercise maximally or if a concomitant factor (asthma, psychomotor retardation or spastic hemiplegia) might influence the outcome of the test.

Arrhythmia. Sinus node dysfunction was defined to be present when the patient had a bradycardia-tachycardia syndrome, atrial flutter or fibrillation. The following supraventricular arrhythmias were considered as minor indications of sinus node dysfunction: sino-atrial block, a sinus arrhythmia with a beat-to-beat variation of the heart rate of more than 200%, sudden change from sinus rhythm to an escape rhythm with a frequency >25% lower than the sinus rhythm, nighttime bradycardia < 30 beats per minute and daytime bradycardia < 40 beats per minute[8]. Ectopic ventricular activity, recorded during the 24 hr electrocardiogram was considered abnormal if monoform premature ventricular contractions occurred at a rate >3600/24 hour, or if premature ventricular contractions were multiform or presented as doublets or ventricular tachycardia. Nonsustained ventricular tachycardia was defined as >3 but <10 consecutive beats originating from a ventricle, with a rate >120 beats/min.

Data analysis. Because the study population was inhomogeneous in terms of baseline characteristics, as a result of the changes in age at operation, type of palliation prior to the Mustard repair (Blalock-Hanlon or only balloon atrioseptostomy), and surgical techniques (complete cardiopulmonary bypass or circulatory arrest with deep hypothermia, use of cold cardioplegia) that were gradually introduced between 1973 and 1980, the population was divided into 2 groups. All analyses were performed for the total group of patients, and separately for patients operated upon in the first 4 years (1973-1976) and patients operated upon in the subsequent 4 years (1977-1980). Survival was calculated according to Kaplan-Meier analysis. The Chi-square and Fisher's exact test were used for the comparison of discrete variables and Student's t-test to compare normally distributed continuous variables in 2 groups. In the presence of a non-Gaussian distribution the Mann-Whitney rank-sum test was used. Comparison of continuous variables in more than 2 groups was performed with analysis of variance. All values are expressed with their mean value ± SD unless indicated otherwise. In all analyses the level of significance was chosen at $p < 0.05$.

Table I **Baseline characteristics of 91 consecutive patients who underwent a Mustard repair for transposition of the great arteries between January 1973 and December 1980**

	1973-1976 n = 50	1977-1980 n = 41	1973-1980 n = 91
Number of patients			
simple TGA	31	24	55
complex TGA	19	17	36
Age at operation in years ± SD			
simple TGA	2.2 ± 2.0	0.6 ± 0.3*	1.5 ± 1.7
complex TGA	3.6 ± 3.1	1.0 ± 1.0	2.4 ± 2.7
Palliation			
no palliation	5 (10%)	3 (7%)	8 (9%)
Blalock-Hanlon atrioseptostomy	15 (30%)	0*	15 (16%)
Rashkind balloon atrioseptostomy	29 (58%)	36 (88%)	65 (71%)
unknown	1 (2%)	2 (5%)	3 (3%)
Surgical technique			
complete CPB and hypothermia >20°C	18 (36%)	0*	18 (20%)
circulatory arrest and hypothermia <20°C	28 (56%)	36 (88%)*	64 (70%)
unknown	4 (8%)	5 (12%)	9 (10%)
cold cardioplegia	4 (8%)	34 (83%)*	38 (42%)
Pacemaker implantation			
pacemaker because of SND	7 (14%)	1 (2%)	8 (9%)
pacemaker because complete AV-block	3 (6%)	1 (2%)	4 (4%)
Reoperation because of baffle problems			
VCS-baffle obstruction	0	3 (7%)	3 (3%)
VCI-baffle obstruction	0	1 (2%)	1 (1%)
baffle leakage	0	3 (7%)	3 (3%)
obstruction pulmonary venous return	0	2 (5%)	2 (2%)
Reoperation; other indications			
resection LVOT obstruction	0	1 (2%)	1 (1%)
homograft LV-AP	0	1 (2%)	1 (1%)
arterial switch	1 (2%)	1 (2%)	2 (2%)
resection aortic coarctation	0	1 (2%)	1 (1%)
closure residual VSD	0	2 (5%)	2 (2%)
closure PDA	1 (2%)	0	1 (1%)
Interventional catheterization			
VCS-baffle obstruction	1 (2%)	0	1 (1%)
Mortality	15 (30%)	3 (7%)*	18 (20%)
early <30 days postoperatively	3 (6%)	2 (5%)	5 (5%)
late >30 days postoperatively	12 (24%)	1 (2%)*	13 (14%)

TGA = transposition of the great arteries; CPB = cardiopulmonary bypass; SND = sinus node dysfunction; AV = atrio-ventricular; VCS = vena cava superior; VCI = vena cava inferior; LVOT = left ventricular outflow tract; LV-AP = left ventricle to pulmonary artery; VSD = ventricular septal defect; PDA = persisting ductus arteriosus. * = Significant difference between 1973-1976 and 1977-1980.

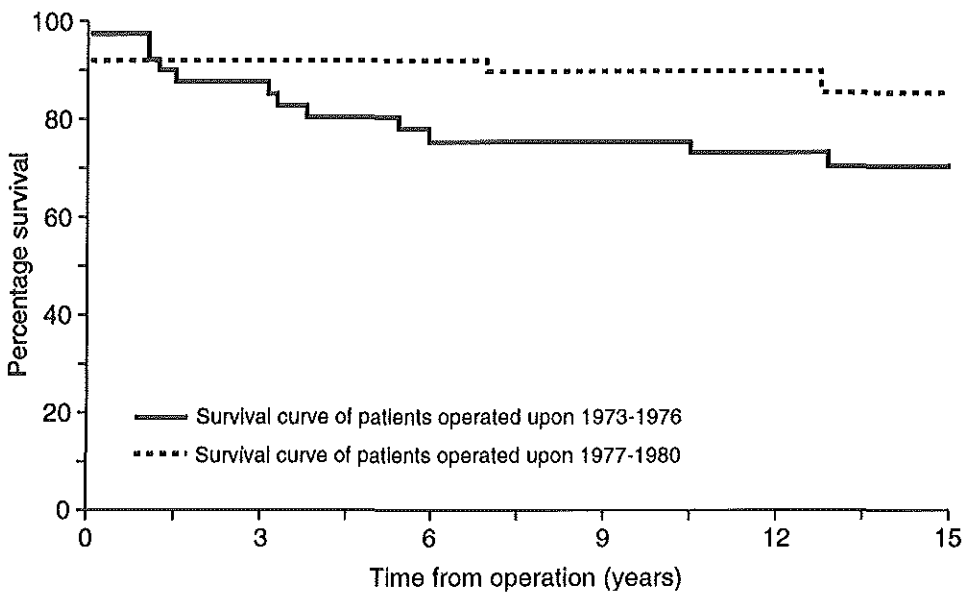
RESULTS

Baseline characteristics. The baseline characteristics of the total group of 91 patients are shown in table I. Significant differences between the first and the second period of 4 years are indicated in this table. Between the 58 patients who participated in the follow-up study and the 15 patients who were known to be alive but did not participate there were no significant differences concerning morphological diagnosis (simple/complex transposition), type of palliation before the Mustard repair, year of operation and age at the time of surgical repair.

Clinical course until follow-up.

Survival. The survival up to 15 years after the Mustard repair is shown in Figure I.

Figure I

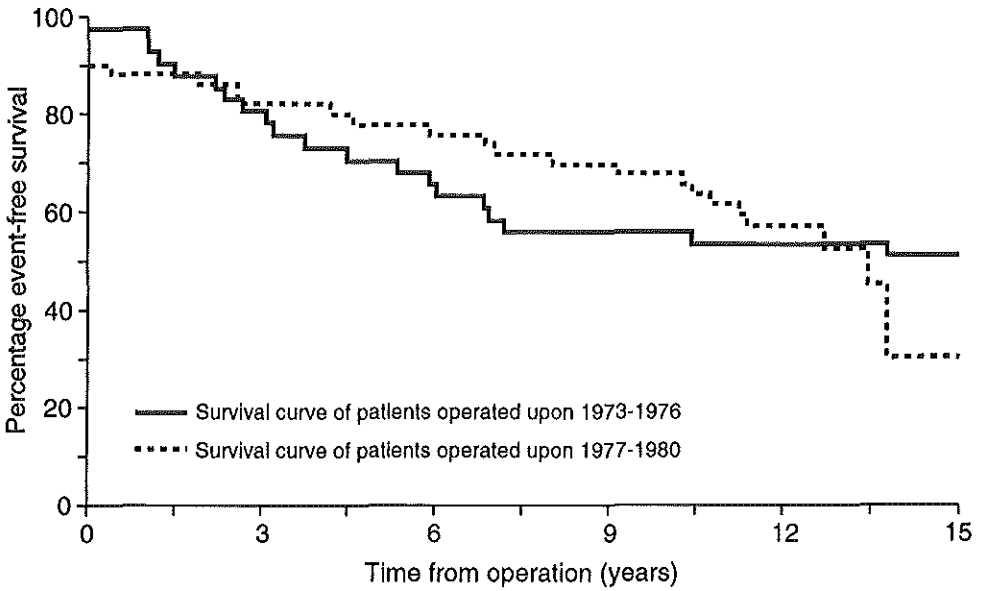


The median interval between operation and follow-up was 13.9 years. The survival of patients operated upon between 1977 and 1980 was significantly better than that of patients operated upon between 1973 and 1976. The survival of patients with a simple transposition was not significantly better than that of patients with a complex transposition ($p=0.8$). The mean interval between the Mustard repair and late death was 5.4 ± 4.4 years (range 1.1 to 12.9 years).

The cause of death of patients who died late postoperatively was known in 6 patients: 3 had right ventricular failure and pulmonary edema diagnosed directly after surgery, and 3 others had atrial flutter/fibrillation. One of these patients had (at least at his last check) a properly functioning pacemaker implanted for sinus node dysfunction. Seven other patients, all operated upon between 1973 and 1976, died suddenly late postoperatively. The cause of death could not be retrieved; none of these patients had previously documented arrhythmia or major anatomical sequelae.

Reoperation. Figure II shows the 15 year survival free from death and reoperation. The type of surgical reintervention is listed in Table 1. The interval between Mustard operation

Figure II



and pacemaker implantation was 7.5 ± 3.6 years (range 2.7 to 13.8 years). The interval between Mustard repair and reoperation was 6.7 ± 4.0 years (range 1.9 to 11.3 years). The indication for an arterial switch after the Mustard repair was pulmonary venous obstruction which had led to elevated left ventricular systolic pressure in one patient, and a large, residual, nonrestrictive ventricular septal defect which also resulted in an elevated left ventricular systolic pressure in another patient. Reoperation was not associated with mortality.

Current health status.

History. All 58 patients who participated in the follow-up study were asked to describe their health status (Table II).

Table II **Personal health assessment of 58 patients long term after Mustard repair for transposition of the great arteries compared with a sample of 1510 persons of the normal Dutch population younger than 35 years of age**

	Mustard patients	normal population
Excellent	12 (21%)	611 (40%)*
Good	39 (67%)	755 (50%)*
Fair	7 (12%)	127 (9%)
Not good	0 (0%)	17 (1%)
Bad	0 (0%)	0 (0%)

* = significant difference between Mustard patients and normal population

Table III **Results echocardiography of 58 patients at follow-up**

	1973-1976 n = 27	1977-1980 n = 31	1973-1980 n = 58
"Normal Mustard"	**12 (44%)**	**17 (55%)**	**29 (50%)**
Right ventricular failure	0	0	0
Baffle related problems	**6 (22%)**	**7 (23%)**	**13 (22%)**
VCS-baffle obstruction	3 (11%)	3 (10%)	6 (10%)
VCI-baffle leakage	1 (4%)	2 (6%)	3 (5%)
VCI-baffle obstruction	-	1 (3%)	1 (2%)
pulmonary venous obstruction	2 (7%)	1 (3%)	3 (5%)
Elevated LV-pressure	**7 (26%)**	**4 (13%)**	**11 (19%)**
pulmonary hypertension	2 (7%)	0	2 (3%)
fixed subpulmonary stenosis	5 (19%)	4 (13%)	9 (16%)
Tricuspid regurgitation	**15 (56%)**	**21 (68%)**	**36 (62%)**
moderate	14 (52%)	21 (68%)	35 (60%)
severe	1 (4%)	0	1 (2%)
Aortic regurgitation	**4 (15%)**	**4 (13%)**	**8 (14%)**
moderate	4 (15%)	4 (13%)	8 (14%)
severe	0	0	0
Miscellaneous	**3 (11%)**	**3 (10%)**	**6 (10%)**
VSD	2 (7%)	0	2 (3%)
PDA	0	2 (6%)	2 (3%)
normal heart after arterial switch	1 (4%)	1 (3%)	2 (3%)

TGA = transposition of the great arteries; VCS = vena cava superior; VCI = vena cava inferior; LV = left ventricle; VSD = ventricular septal defect; PDA = persisting ductus arteriosus.

Forty-four patients (77%) reported that they were fatigued sooner at exercise than others. This proportion is significantly higher than that in the normal population (13%; $p<0.05$). Six patients (11%) were taking antiarrhythmic medication (digoxin 2x, propranolol, verapamil, quinidine, amiodarone). Between patients with an "excellent", "good" and "fair" personal health assessment there were no differences in terms of year of operation (1973-1976 versus 1977-1980), age at the time of surgical repair and the presence of a simple or a complex transposition.

Physical Examination. The mean values of length and body weight were within the normal range (Figures III and IV). Six patients (10%) had moderate to severe chest deformity and scoliosis. Two patients had a spastic hemiplegia and 4 patients had psychomotor retardation.

Echocardiography. The findings are listed in Table III. None of the patients had signs of right ventricular failure. There were no differences between simple and complex transposition concerning type and incidence of sequelae, except for elevated left

ventricular pressure. Two patients with pulmonary hypertension originally had a complex transposition with large ventricular septal defect. Nine patients had a fixed subpulmonary stenosis consisting of a long fibromuscular tunnel. Of these, 7 originally had a complex transposition with subpulmonary stenosis and 2 originally had a simple transposition with a documented normal left ventricular outflow tract pre-operatively and without a ventricular septal defect. Three out of 13 patients who had signs of baffle obstruction or leakage at follow-up had been reoperated in the past because of baffle-related problems.

Bicycle Ergometry. Six patients were excluded from the test because of spastic hemiplegia (n=2) or psychomotor retardation (n=4). One patient refused the test. Fifty-one patients exercised to maximum effort. The maximal exercise capacity in these patients was 84% ± 16% (range 50 to 125%) of the predicted values.

There were no significant differences in exercise capacity between several subgroups that were analyzed separately: patients with a "normal Mustard" versus patients with echocardiographic evidence of anatomical or hemodynamical sequelae, patients with signs of sinus node dysfunction versus patients without, patients with antiarrhythmic medication versus patients without, patients with simple transposition versus patients with a complex transposition, patients operated upon before 1977 versus patients operated upon afterwards, and patients <1 year of age at the time of the operation versus those >1 year of age.

The patients who judged their health as "excellent" had a maximal exercise capacity of 94 ± 15% of predicted, the patients who judged it to be "good" 81 ± 19%, and those who judged their health as "fair" 71 ± 16%. These differences are significant ($p = 0.02$). Patients who complained about early fatigue at exercise had a significantly lower exercise capacity than patients who judged their exercise capacity as normal. None of the patients developed increased ventricular ectopic activity during or directly after the exercise test.

Standard 12-lead electrocardiography. A narrow QRS pattern was seen in 49 patients (86%), of whom 47 had signs of right ventricular dominance. The 2 patients with an arterial switch operation after the Mustard repair had a completely normal electrocardiogram. Eight patients had a wide QRS-pattern: 5 patients had a right bundle branch block, and 3 patients a left bundle branch block. Thirty-five patients (60%) had a regular sinus rhythm, 8 patients (14%) had a stable atrial rhythm, 4 (7%) a stable junctional rhythm, and 3 (5%) a supraventricular rhythm with a wandering pacemaker. Of the remaining 8 patients, 7 (12%) had a pacemaker rhythm and 1 (2%) had an atrial flutter with 3:1 conduction. The mean P-R interval was 0.16 ± 0.03 seconds (range 0.08 to 0.26 seconds). None of the 10 patients with echocardiographic evidence of elevated left ventricular pressure had electrocardiographic signs of increased left ventricular activity.

There were no electrocardiographic differences between the group of patients who originally had a simple transposition of the great arteries and the patients with a complex transposition.

Twenty-four hour electrocardiography. The results of the 24 hour electrocardiogram, which could be obtained of all 58 patients, is shown in Table 4. Eight of these 58 patients had a pacemaker implanted in the past. Seven had a predominant pacemaker rhythm. The remaining patient, who had a pacemaker (and digoxin and propranolol) because of sinus node dysfunction, had no pacemaker activity during the 24-hour electrocardiogram

Figure III

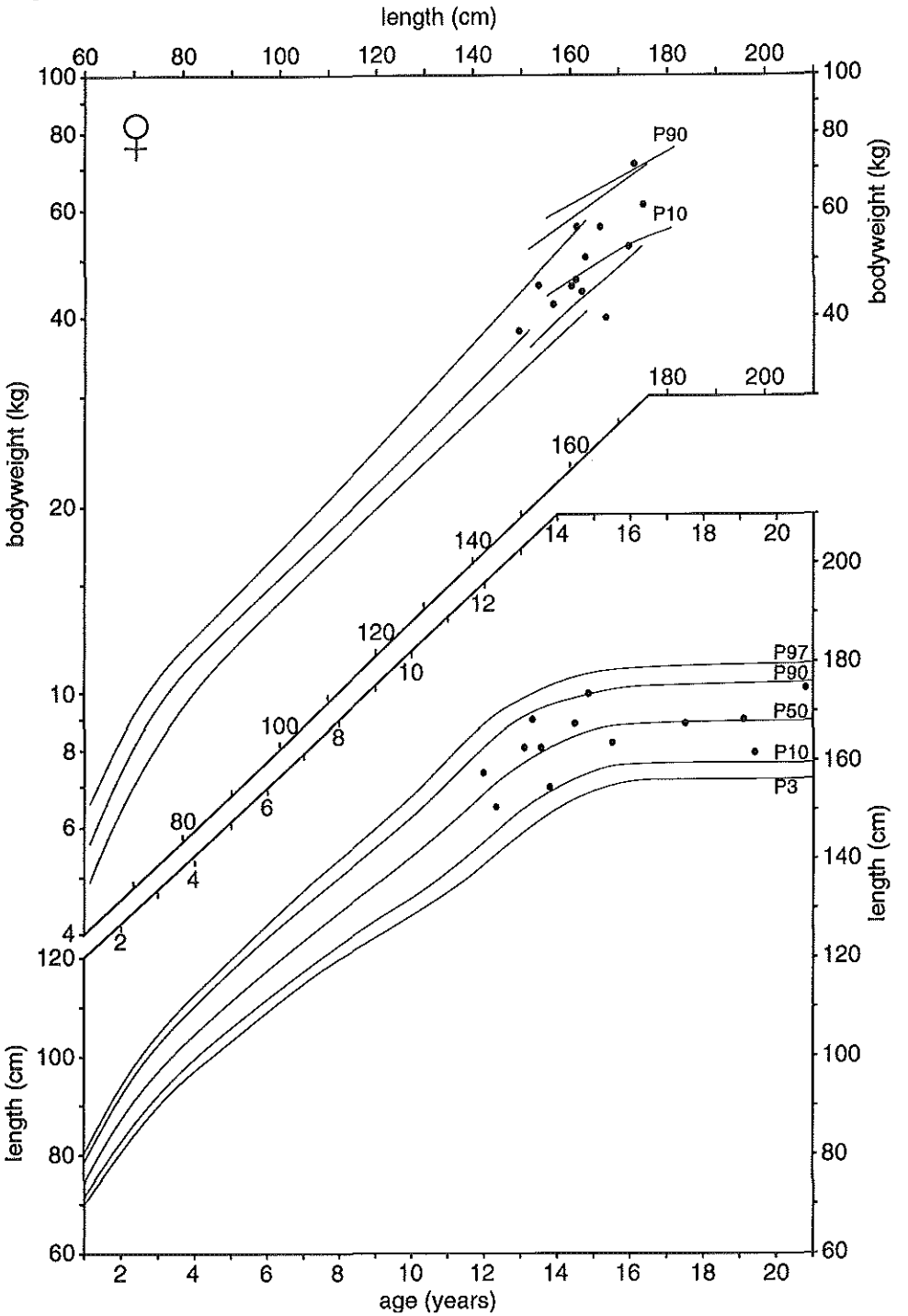

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Figure IV

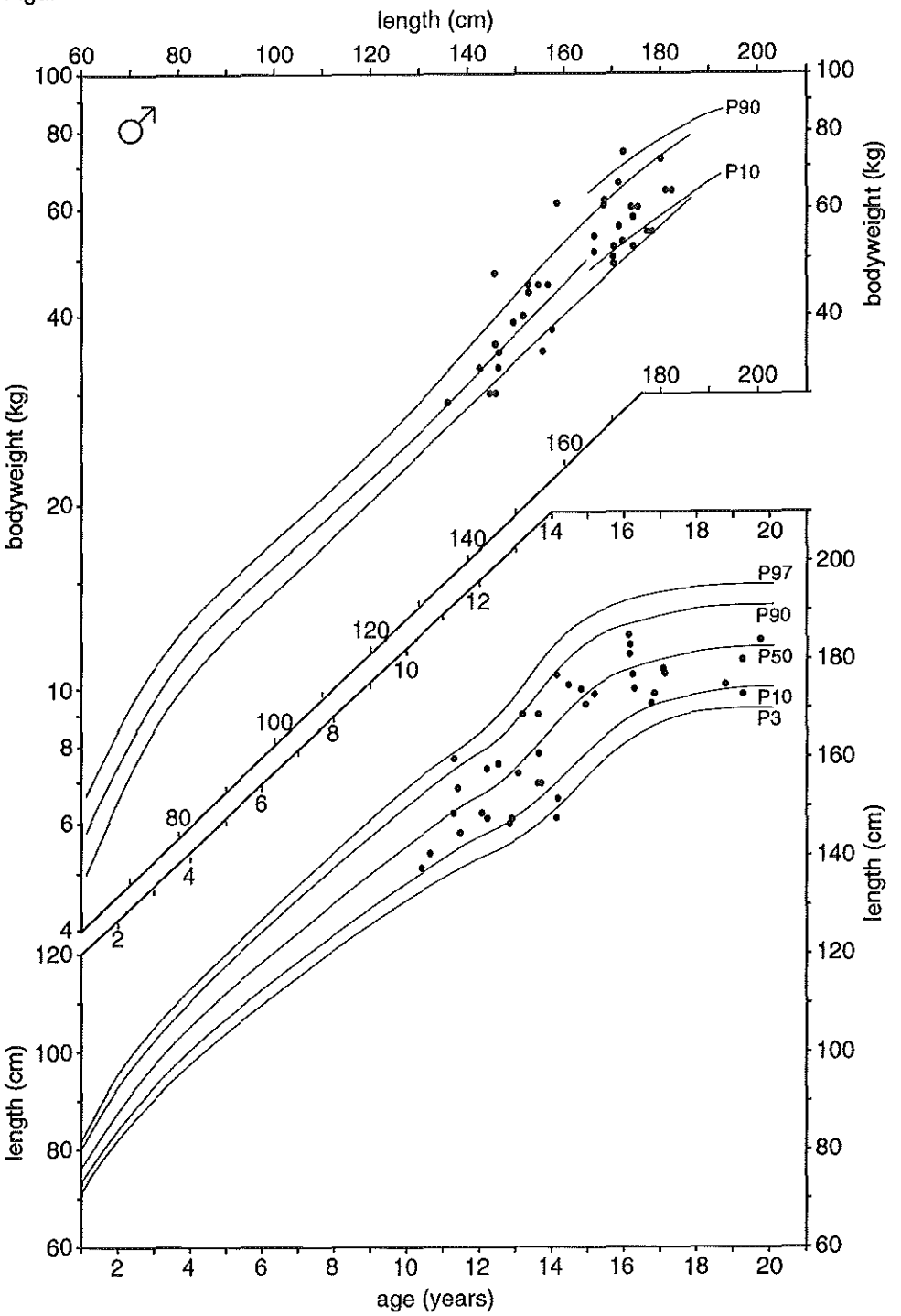
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Table IV **Results of 24-hour ECG-registration of 58 patients at follow-up**

	1973-1976 n = 27	1977-1980 n = 31	1973-1980 n = 58
No arrhythmia	**1 (4%)**	**14 (45%)***	**15 (26%)**
Supraventricular arrhythmia	**17 (65%)**	**6 (19%)***	**23 (40%)**
atrial flutter	2 (7%)	0	2 (4%)
bradycardia-tachycardia syndrome	5 (19%)	0	5 (9%)
other signs of SND	10 (37%)	6 (19%)	16 (28%)
Ventricular arrhythmia	**15 (58%)**	**10 (32%)**	**25 (43%)**
VT > 10 beats	0	0	0
VT 3-10 beats	3 (11%)	1 (3%)	4 (7%)
PVC doublets	2 (7%)	1 (3%)	3 (5%)
multiform PVC's	10 (37%)	8 (26%)	18 (31%)
AV-block	**1 (4%)**	**1 (3%)**	**2 (2%)**
complete	1 (4%)	0	1 (2%)
2nd degree Mobitz type	0	1 (4%)	1 (2%)
Pacemaker rhythm	**5 (19%)**	**2 (6%)**	**7 (12%)**
originally SND	4 (15%)	1 (3%)	5 (9%)
AV-block	1 (4%)	1 (3%)	2 (4%)

SND = sinus node dysfunction; PVC = premature ventricular complex; VT = ventricular tachycardia; AV = atrio-ventricular. * = Significant difference between 1973-1976 and 1977-1980

but continuous atrial flutter. The 24-hour electrocardiogram of the 6 patients who used antiarrhythmic medication (of whom 2 had a pacemaker to support the antiarrhythmic treatment) showed an atrial flutter in 2 patients, a bradycardia\tachycardia in 1 patient, a continuous pacemaker rhythm in 1 patient and no arrhythmia in 2 patients.

The total number of surviving patients with sinus node dysfunction (either asymptomatic or treated with a pacemaker) was 12 (21%), of whom 11 were operated upon between 1973-1976. Four out of 12 patients who had a pacemaker implantation in the past were not evaluated at follow-up; 1 patient had died suddenly (arrhythmia?) despite a good functioning pacemaker, 1 patient had left abroad, and 2 patients refused to participate in the follow-up study.

There was no difference in the incidence of ventricular or supraventricular arrhythmia between patients with simple and complex transposition, or between patients with a "normal Mustard" and patients with anatomical or hemodynamic sequelae. Atrial flutter or bradycardia-tachycardia syndrome was seen in 5 of the 9 patients who had a Blalock-Hanlon atrioseptostomy before the Mustard repair, and in 2 of the 17 patients who had a Rashkind procedure in the same period (p=0.02). At multivariate analysis none of the possible risk factors for sinus node dysfunction (older age at the time of the surgical correction, no cold cardioplegia, Blalock-Hanlon atrioseptostomy) reached statistical significance.

DISCUSSION

There is a striking difference in outcome between patients operated upon before 1977 and those operated on afterwards. In the "early" group both late mortality (25%) and incidence of sinus node dysfunction (41%) were significantly higher than in the "late" group (respectively 2% and 3%). It is unlikely that these differences are the result of the differences in interval after operation, because the mean interval between Mustard repair and "event" (albeit death or pacemaker implantation for sinus node dysfunction) was significantly shorter than even the minimum duration of follow-up for the "late" group. Therefore, in contrast to others[9,10], we conclude that the better outcome in the "second" group is the result of a positive net effect of the changes that were designed to prevent sinus node dysfunction and sudden death. It is likely that older age at the time of the operation (longer duration of severe hypoxemia which could affect the myocardium), scarring of the atrium (Blalock-Hanlon atrioseptostomy), limited myocardial preservation durante operationem (no cold cardioplegia) and less experience of the surgeon all contributed. However, multivariate analysis failed to single out one statistically significant independent determinant. We agree with others[3,11] that the prognosis for patients with a Mustard type correction is not necessarily as dim as expected on the basis of earlier data[12].

Notwithstanding the good survival and the low incidence of sinus node dysfunction in the group of patients operated upon since 1977, there is still ample reason for concern for most patients that cardiologists will see in daily practice, because many patients were operated upon in the earlier years of cardiac surgery.

Arrhythmia. Although not entirely absent in the "late" group, the problem of sinus node dysfunction is almost completely confined to the "early" group of patients. This is probably a reflection of the state of the art of cardiac surgery in the early years before the improvements had been implemented.

It is noteworthy that 1 patient died suddenly despite the presence of a pacemaker. This is in agreement with the finding of others that implantation of a pacemaker does not totally prevent sudden death[10], which is probably due to ventricular fibrillation, whether or not induced by supraventricular arrhythmia. Because of the association between arrhythmia and late death it seems justified to approach these arrhythmia's more aggressively; implantable anti-tachyarrhythmia devices should be considered in selected patients.

Minor indications of sinus node dysfunction were often present in the "early" group (37%), but were also found in the "late" group (19%). The interpretation of these arrhythmias detected on a surface electrocardiogram is hazardous, and one can only speculate on the causative mechanism and clinical relevance. On the one hand they can be considered as normal, because they have been reported to occur also in the normal population[13-19]. On the other hand it is known from electrophysiological studies that sinus node recovery time is abnormal in up to 84% of the patients[16,17]. Therefore it is possible that these subtle signs of sinus node dysfunction represent real damage to the sinus node. An already damaged sinus node might be more vulnerable to the changes as a result of ageing, which is a loss of number of sinus node muscle cells[18,19], and deterioration of sinus node function[20,21] leading to an elevated incidence of arrhythmia even in subjects without sinus node disease. Clearly, longer follow-up is needed.

Anatomic and hemodynamic sequelae. The clinical importance of most of the anatomic and hemodynamic sequelae appears to be limited. They were neither associated with a

decreased exercise capacity (compared with patients without sequelae), nor with complaints, nor with an increased incidence of arrhythmia. None of the sequelae that were detected at follow-up resulted in reoperation. Three patients (5%) had serious sequelae that were not amenable for repair: 2 patients had pulmonary hypertension and 1 patient had severe tricuspid regurgitation.

Reoperations for baffle leakage or obstruction were confined to the "late" group. The technical difficulty to create an adequate sized baffle in small children is probably the cause of these problems[22]. There was no mortality associated with reoperation, but 3 of these patients had echocardiographic evidence of residual baffle problems at follow-up. Therefore we conclude that reoperation for baffle obstruction or leakage can be performed safely, but is not always successful from a functional point of view.

Exercise capacity was equally diminished in both the "early" and the "late" group. Apparently, the changes which led to improved survival and a lower incidence of sinus node dysfunction have not improved exercise capacity. The cause of decreased exercise capacity after Mustard repair remains a subject of controversy. It is even questioned whether decreased exercise capacity is inherent to the Mustard type repair or not[23-26]. We believe that decreased exercise capacity is the result of the Mustard repair and is not the result of a flaw in the exercise study protocol, because we found a completely normal exercise capacity (using the same test protocol and normal values) in patients of the same age group after surgical closure of atrial septal defect or ventricular septal defect[27,28]. This corresponds with the perception of the patients themselves that they fatigue earlier than others. The fact that exercise capacity corresponds well with patient's health assessment underlines that exercise capacity is an important determinant for the health related quality of life.

The ability of the right ventricle to function as the systemic ventricle for a lifetime is the last concern. In contrast to others we did not find right ventricular failure in any of the survivors[29]. Others demonstrated with serial measurements that right ventricular performance did not deteriorate over the years[30]. Nonetheless, the concern about long-term right ventricular function remains, and only longer duration of follow-up of this specific patient group will elucidate this.

Conclusion. The incidence of sinus node dysfunction and late sudden death is high in the total group of patients who underwent a Mustard type repair in our institution between 1973 and 1980. However, the changes in management strategies that have been introduced during this period have resulted in a considerable reduction of the incidence of these late complications. This makes the long-term outlook for patients probably better than previously believed on the basis of earlier data, but the frequent need for reoperation and the reduced exercise capacity show that, even for these patients, the Mustard repair has its restrictions.

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CHAPTER 6

LONG-TERM RESULTS OF SURGERY FOR VALVULAR PULMONARY STENOSIS IN INFANCY AND CHILDHOOD

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ABSTRACT.

Objective. The purpose of this study was to assess the long-term outcome after surgery for isolated pulmonary stenosis in terms of cardiac function, sequelae and health related quality of life in relation to the type of surgical repair.

Patients and Methods. A total of 83 consecutive patients underwent surgery for isolated pulmonary valve stenosis between 1968 and 1980. Patients were excluded in whom the pulmonary stenosis was part of a more complex cardiac defect, in particular critical pulmonary stenosis with tricuspid valve hypoplasia or an abnormally small cavity of the right ventricle. Forty-five patients were operated upon using inflow occlusion; of these 11 (24%) participated in the follow-up study. Thirty-eight patients were operated upon with the use of cardiopulmonary bypass; of these 29 (76%) participated in the follow-up study. Of the 40 participants, 9 patients had a surgical repair with the use of a transannular patch, 1 patient had a homograft between right ventricle and pulmonary artery, and 30 patients had only a valvulotomy. Of these, 12 patients had a transventricular approach and 18 patients had a transpulmonary approach. The mean pressure difference between right ventricle and pulmonary artery was 114 ± 34 mmHg preoperatively, and 54 ± 25 mmHg at the end of the surgical procedure. Mean age at the time of the operation had been 5.6 ± 3.8 years. The mean interval between surgery and follow-up was 15.7 ± 3.3 years. The examination at follow-up consisted of questions on current health status, physical examination, echocardiography, exercise testing, standard 12-lead electro-cardiography and 24 hour electrocardiography.

Results. None of the patients had substantial residual pulmonary stenosis; the blood flow velocity in the pulmonary artery was 1.7 ± 0.6 m/sec (range 0.8 to 3.3 m/sec). However, pulmonary regurgitation was common (85% of the patients). Severe pulmonary regurgitation in combination with a severely dilated right ventricle was seen in 10 patients. Of these, 7 had a transannular patch, 2 had a valvulotomy through the pulmonary artery using inflow occlusion, and 1 had a (failing) homograft. Exercise capacity was normal, also in most patients with severe dilatation of the right ventricle. However, the 4 patients with substantially decreased exercise capacity all had severe pulmonary regurgitation. Many patients had arrhythmia on the 24-hour electrocardiogram: 14 patients (38%) had supraventricular arrhythmia and 17 patients (46%) had ventricular arrhythmia. Symptomatic arrhythmia was rare: only 1 patient had a bradycardia-tachycardia syndrome and used antiarrhythmic medication. Longer follow-up was associated with a higher prevalence of ventricular arrhythmia, but a lower prevalence of supraventricular arrhythmia.

Conclusion. Different surgical management techniques for pulmonary stenosis all lead to a good and lasting relief of elevated right ventricular pressure, but this is achieved at the cost of pulmonary regurgitation in virtually all patients. A large majority of these patients has no complaints, has asymptomatic arrhythmia at the 24-hour electrocardiogram and has a normal exercise capacity. However, the few patients who developed symptoms of decreased exercise capacity all had severe pulmonary regurgitation. This emphasizes that in the treatment of pulmonary stenosis it should be tried to avoid creation of severe pulmonary regurgitation.

INTRODUCTION

The surgical approach of valvular pulmonary stenosis has changed gradually since R.Brock performed the first closed valvulotomy in 1948[1]. Closed valvulotomy was soon replaced by the open valvulotomy with the use of inflow occlusion, which in term was replaced by valvulotomy with the use of cardiopulmonary bypass. With the latter technique the extent of the surgery could be adapted to the needs of the individual patient and could vary from a commissurotomy only to a complete right ventricular outflow tract reconstruction, with a transannular patch or a homograft, if necessary. Since the introduction of balloon valvuloplasty in 1983[2], the surgical option is largely confined to the more complex forms of pulmonary stenosis which are not amenable for balloon valvuloplasty. The few follow-up studies on results after surgical repair report that survival is excellent and most patients are asymptomatic[3-6]. However, data on anatomic and electrophysiologic sequelae are scarce and refer only to 2 studies[7,8]. Therefore, we conducted a follow-up study in order to assess the cardiac status of a selected group of patients long-term after surgery for isolated pulmonary valvular stenosis, with special emphasis on the differences in surgical techniques in relation to late symptoms and sequelae.

METHODS

Patients. Out of 83 patients under the age of 15 years who were operated upon for isolated pulmonary stenosis in our institution between 1968 and 1980, 40 (49%) participated in the follow-up study. Twenty patients were male, and 20 female. Mean age at the time of the operation was 5.0 ± 3.8 years (range 0.03 to 13.8 years), mean interval between surgery and follow-up was 15.7 ± 3.3 years (range 10.5 to 22.0 years), and mean age at follow-up was 20.7 ± 5.5 years (range 10.7 to 33.2 years).

Methods. The data of the preoperative cardiac catheterisation and details of the surgical procedure were derived from patient's hospital records. Cardiac examination at follow-up included medical history, physical examination, standard 12-lead electrocardiography, echocardiography (M-mode, 2-D echo, pulsed-, continuous wave-, and color flow Doppler), exercise testing by bicycle ergometry and 24 hour electrocardiography.

The study was approved by the local Medical Ethical Committee.

Measurements and definitions. The diagnosis of valvular pulmonary stenosis was established during preoperative diagnostic cardiac catheterization, and was confirmed at surgery. The diagnosis hypoplastic annulus and the decision whether to use a transannular patch was made at surgery.

Patients in whom a pulmonary stenosis was part of a more complex congenital cardiac defect, in particular critical pulmonary stenosis with hypoplastic right ventricle and tricuspid valve stenosis, were excluded. Patients with minor intracardiac defects besides

the pulmonary stenosis, such as patent foramen ovale or small ventricular septal defect, were included.

The *medical history* comprised a questionnaire developed by the Netherlands Central Bureau of Statistics, validated in a sample of 1510 Dutch adults <35 years of age, that uses standardized (multiple choice) questions to elicit a person's assessment of his or her health status[9].

M-mode, two-dimensional echocardiography and pulsed wave, continuous wave, and color flow Doppler studies were performed with a Toshiba SSH 160-A echocardiograph. The function of the pulmonary valve was studied with Doppler echocardiography. A blood flow velocity across the pulmonary valve <1 m/sec was considered normal for both children and adults[10]. A substantial residual pulmonary stenosis was defined to be present if the velocity of the pulmonary artery flow exceeded 3.5 m/sec. Since it is generally accepted that right ventricular dilatation and the degree of pulmonary regurgitation cannot be measured reliably, these features were assessed by visual estimate in both the parasternal long-axis view and the apical 4-chamber view. The right ventricle was defined as moderately dilated if the right ventricle was enlarged, but smaller than the left ventricle. The right ventricle was defined as substantially dilated if the right ventricle was as large or larger than the left ventricle. The degree of pulmonary regurgitation (no to minimal, mild to moderate, severe) was estimated by the width and length of the color-Doppler regurgitant jet in the right ventricle, and by the flow pattern of the regurgitant jet in the right ventricular outflow tract and pulmonary artery measured with pulsed Doppler[11]. The right atrium was defined as dilated if the dimensions of the right atrium exceeded that of the left atrium in the apical 4-chamber view in combination with a bulging of the inter-atrial septum to the left.

Maximal exercise capacity was assessed by bicycle ergometry with stepwise increments of the workload of 20 Watts per minute. Patients were encouraged to exercise until exhaustion. Results were disregarded if patients could not be motivated to exercise maximally or if a concomitant factor (asthma, psychomotor retardation or spastic hemiplegia) influenced the outcome of the test.

In the *standard 12-lead electrocardiogram*, the presence of a right bundle branch block was defined as a RSR' pattern of the QRS complex with a duration of at least 0.12 seconds, with R'> R in V_1. Right ventricular hypertrophy was defined as a heart axis between 90 and 180 degrees in the frontal plane, and in V_1 R or R' > 5 mm with R or R'> S in the absence of a right bundle branch block. Right atrial dilatation was defined as a high peaked p-wave >2.5 mm in lead II or aVF with a duration less than 0.12 sec.

Arrhythmias. Sinus node dysfunction was defined as the presence of atrial flutter, atrial fibrillation and a bradycardia-tachycardia syndrome. The following supraventricular arrhythmias were considered as minor signs of sinus node dysfunction: a sino-atrial block, a beat-to-beat variation of the heart rate of more than 200%, a sudden change from sinus rhythm to an escape rhythm with a frequency > 25% lower than the sinus rhythm, a nighttime bradycardia < 30 beats per minute and a daytime bradycardia < 40 beats per minute[12]. The incidence of these supraventricular arrhythmia was compared to that of the normal population[13-15]. Premature ventricular contractions recorded during the 24 hr electrocardiogram were considered to be abnormal if monoform premature ventricular contractions occurred in a frequency exceeding 3600/24 hour, if premature ventricular contractions were multiform, or if premature ventricular contractions presented as doublets or ventricular tachycardia. Ventricular tachycardia was defined as short if at

least 3 and not more than 10 consecutive beats >120 beats/min originating from a ventricle were recorded, and as sustained if this tachycardia consisted of more than 10 consecutive beats .

Data analysis. All values are expressed with their mean value and standard deviation. The Chi-square and Fisher's exact test were used for the comparison of discrete variables in the presence of a normal distribution. In the presence of a non-Gaussian distribution the Mann-Whitney rank-sum test was used. Comparison of continuous variables in 2 groups was performed with the Student-t test. Regression analysis was used to demonstrate a possible correlation between 2 different continuous variables. A correlation factor (r) <0.4 was considered to represent a poor relation, a correlation factor between 0.4 and 0.8 a fair relation, and >0.8 a good relation. Stepwise multivariate analysis was performed to assess the independent contribution of parameters that were statistically significant at univariate analysis. In all analyses the level of significance was chosen at 0.05.

RESULTS

Baseline characteristics. Right ventricular pressures at preoperative cardiac catheterisation and at the end of the surgical procedure are presented in table I.

The surgical technique in relation to the year of operation, total number of patients and participants in the follow-up study is shown in table II.

Table I **Right ventricular pressure at preoperative cardiac catheterisation and at the end of the surgical procedure**

	preoperative cardiac catheterisation	at the end of the surgical procedure
ΔP RV-PA (mm Hg)	95 ± 39 (range 36-200)	-
RV pressure (mm Hg)	114 ± 34 (range 58-210)	54 ± 25 (range 25-110)
RV / LV pressure ratio	1.2 ± 0.4 (range 0.6-2.1)	0.5 ± 0.3 (range 0.2-1.5)

ΔP = pressure difference; RV = right ventricle; PA = pulmonary artery; LV = left ventricle

Table II

Surgical technique	1968-1974	1975-1980	total 1968-1980	age at operation (years)
Inflow occlusion				
- transpulmonary approach	31 (8)	14 (3)	45 (11)	6.6 ± 3.8
Cardiopulmonary bypass				
- transpulmonary approach	3 (2)	8 (5)	11 (7)	6.4 ± 3.9
- transventricular approach	8 (7)	7 (5)	15 (12)	5.2 ± 2.7
- transannular patch	1 (1)	10 (8)	11 (9)	1.2 ± 11
- homograft RV-PA	1 (1)	0 (0)	1 (1)	9.9
	44 (19)	39 (21)	83 (40)	5.6 ± 3.8

( ) = number of patients examined at follow-up; PA = pulmonary artery; RV = right ventricle

Closure of a patent foramen ovale took place in 21 patients (25%) apart from the valvulotomy. Of these, 17 were seen at follow-up. In 1 patient a small ventricular septal defect was closed directly. Cold cardioplegia was used in 6 patients, of whom 4 were seen at follow-up. Pre-treatment right ventricular peak systolic pressure was significantly higher in patients who underwent valvulotomy through a ventriculotomy than that in patients who underwent a valvulotomy through the pulmonary artery (132 ± 34 mmHg versus 105 ± 30 mmHg;p< 0.001). This first group is relatively over-represented in the follow-up study, with the result that patients who participated in the follow-up study had significantly higher right ventricular pressures at preoperative cardiac catheterisation than patients who did not participate (124 ± 35 mmHg versus 103 ± 28 mmHg; p = 0.004). There was no difference in right ventricular pressure at the end of the surgical procedure between these 2 groups (54 ± 26 mmHg versus 55 ± 23 mmHg; p = 0.8).

Clinical course until follow-up. One patient (1%) had died 10 months after surgical repair as the result of severe brain damage due to an aortic dissection at surgery. Three patients (4%) were reoperated. In one patient, who had a right ventricular outflow tract obstruction, a transannular patch was inserted 2.5 years after the initial valvulotomy with the use of inflow occlusion. One patient had a infundibulectomy 3 years after the insertion of a homograft between the right ventricle and the pulmonary artery. In 1 other patient a persisting patent foramen ovale was closed. Two patients, who both had a valvulotomy with the use of inflow occlusion, underwent a balloon valvuloplasty because of a substantial residual pulmonary stenosis, respectively 16 and 18 years after surgery.

Current health status. *Medical History.* The outcome of patient's own health assessment, compared with that of the normal population, is shown in Table III.

Table III **Personal health assessment of 40 patients 10 to 23 years after surgery for pulmonary stenosis and of 1510 persons of the normal Dutch population < 35 years**

	Study patients	normal Dutch population
Excellent	10 (25%)	611 (40%)
Good	26 (65%)	755 (50%)
Fair	4 (10%)	127 (9%)
Not good	-	17 (1%)
Bad	-	0 (0%)

Data presented indicate number (%) of patients in each group; statistical analysis by χ^2 2x4 table: p = 0.14

The differences between these 2 populations do not reach statistical significance. Differences in health assessment were neither correlated with differences in baseline characteristics (age at operation, interval between operation and follow-up, right ventricular pressure preoperatively and at the end of the surgical procedure) nor with differences in the cardiac status at follow-up (degree of pulmonary regurgitation, maximal exercise capacity, arrhythmia). One patient (2.5%) used antiarrhythmic medication (Sotalol, Verapamil) for symptomatic arrhythmia due to a bradycardia-tachycardia syndrome.

Table IV **Results Echocardiography**

	inflow occlusion valvulotomy through PA n = 11	CPB valvulotomy through PA n = 7	CPB valvulotomy through RV n = 12	CPB transannular patch n = 9	CPB homograft n = 1	TOTAL n = 40
Flow velocity PA m/sec (range)	1.9 ± 0.6 (1.0-3.2)	1.4 ± 0.3 (1.1-1.8)	1.9 ± 0.5 (1.4-3.3)	1.4 ± 0.5 (0.8-2.2)	1.5	1.7 ± 0.6 (0.8-3.3)
Pulmonary regurgitation						
no to minimal	2	4	0	0	0	6 (15%)
local to moderate	6	3	7	2	0	18 (45%)
severe	3	0	5	7	1	16 (40%)
Right ventricular dimensions						
normal	5	1	4	0	0	10 (25%)
dilated	4	6	8	2	0	20 (50%)
severely dilated (RV>LV)	2	0	0	7	1	10 (25%)
Right atrial dimensions						
normal	8	5	10	3	0	26 (65%)
dilated	3	2	2	6	1	14 (35%)
Tricuspid regurgitation						
no to minimal	8	6	10	4	1	29 (72%)
local to moderate	3	0	2	4	0	9 (23%)
severe	0	1	0	1	0	2 (5%)

PA = pulmonary artery; CPB = cardiopulmonary bypass; RV = right ventricle

Physical Examination. The mean values of length, body weight, and blood pressure corrected for age and sex, did not differ significantly from that of the normal Dutch population. A systolic murmur was heard in 38 patients (95%); 1 patient had a 4/6 ejection type murmur, 5 patients had a 3/6 ejection type murmur and in 32 patients the loudness of the murmur was 1/6 or 2/6. A diastolic murmur in 30 patients (75%). Two patients (5%) had severe mental retardation. One patient had Noonan's syndrome.
Echocardiography. An overview of the echocardiographic findings in relation to the type of surgery is given in Table IV. The flow velocity across the pulmonary valve at follow-up examination correlated poorly with right ventricular pressure at the end of the surgical procedure (r=0.2). Neither longer duration of follow-up nor older age at the time of the follow-up study was associated with a higher degree of pulmonary regurgitation or right ventricular dilatation. (N.B. The clinical condition of 2 patients with severe right ventricular dilatation and severe pulmonary regurgitation deteriorated substantially within 1 year after the follow-up study. One patient, who initially had a homograft between right ventricle and pulmonary artery needed a homograft replacement. The other patient, who initially had a right ventricular outflow tract reconstruction with the use of a transannular patch, needed insertion of a homograft due to severe pulmonary regurgitation)
Bicycle Ergometry. Thirty-seven patients exercised to maximum effort. Two patients were not tested because of severe mental retardation and 1 patient refused. The mean value for maximal exercise capacity was 106 ± 19% of predicted. Twenty-five patients (68%) had a normal result (between 80% and 120% of the predicted value), 8 patients (22%) had an exercise capacity which was better than average (>120% of predicted), and 4 patients (11%) had a substantially decreased exercise capacity (<80% of the expected value). These 4 all had a substantially dilated right ventricle with severe pulmonary regurgitation. Nonetheless, the difference in exercise capacity between patients with a normal or slightly dilated right ventricle and patients with a severely dilated right ventricle (108 ± 17% versus 96 ± 21%; p = 0.07) and between patients with or without a transannular patch (99 ± 19% versus 108 ± 17%; p = 0.2) lacked statistical significance. There was also no significant difference in maximal exercise capacity between patients with transpulmonary or transventricular repair (104 ± 13% versus 108 ± 21%; p = 0.5). There was a poor correlation between the result of the exercise test and age at the time of the surgical repair (r = 0.1) and duration of follow-up (r = 0.2). None of the patients developed serious arrhythmia during or after exercise.
12-lead electrocardiography. Thirty-six patients (90%) had a sinus rhythm and 4 (10%) had a regular atrial rhythm. The mean P-R interval was 0.14 ± 0.02 seconds (range 0.10 to 0.20 seconds). One patient had signs of right atrial dilatation. The precordial leads showed a normal pattern in 18 patients (45%), right ventricular hypertrophy in 17 patients(42%) and a right bundle branch block in 5 patients (12%). Of these, 4 had a ventriculotomy at surgical repair and 1 had a transpulmonary approach. The 17 patients with electrocardiographic evidence of right ventricular hypertrophy did have a higher blood flow velocity in the pulmonary artery, and therefore a higher right ventricular pressure, than patients with a normal electrocardiogram (1.8 ± 0.9 m/sec versus 1.5 ± 0.4 m/sec; p=0.02).
Twenty-four hour electrocardiography. A complete 24 hour electrocardiogram could be obtained in 37 patients. The results are summarized in Table V. Three patients had both supraventricular and ventricular arrhythmia, 14 patients had only ventricular arrhythmia and 11 others only supraventricular arrhythmia. At univariate analysis the following

Table V **Results of the 24 hour electrocardiogram in 37 patients**

No arrhythmia	**9 (24%)**
Supraventricular arrhythmia	**14 (38%)**
atrial tachycardia	1 (3%)
bradycardia-tachycardia syndrome	1 (3%)
signs of sinus node dysfunction	12 (32%)
Ventricular arrhythmia	**17 (46%)**
sustained VT	1 (3%)
VT 3-10 beats	2 (5%)
doublets + multiform PVC's	3 (8%)
multiform PVC's	11 (30%)

VT = ventricular tachycardia; PVC = premature ventricular complex

determinants for the occurrence of ventricular arrhythmia proved to be statistically significant: blood flow velocity in the pulmonary artery >1.5 m/sec ($p<0.01$), age at follow-up >20 years ($p=0.01$), and interval between operation and follow-up study >15 years ($p<0.01$). In multivariate analysis by stepwise logistic regression only longer duration of follow-up remained statistically significant. A higher degree of pulmonary regurgitation and a larger right ventricular size were not associated with a higher incidence of ventricular arrhythmia. The following determinants were not associated with either ventricular or supraventricular arrhythmia in univariate analysis: type of surgical repair (ventriculotomy versus no ventriculotomy; transannular patch versus no transannular patch; inflow occlusion versus cardiopulmonary bypass), age at the time of the operation, and right ventricular pressure at preoperative cardiac catheterisation or at the end of the surgical procedure. In patients with right atrial dilatation the occurrence of supraventricular arrhythmia did not differ from that in patients with a normal sized right atrium. In the group of patients with a duration of follow-up < 15 years the prevalence of supraventricular arrhythmia was significantly higher than in the group of patients with a duration of follow-up >15 years ($p=0.01$) both in univariate and in multivariate analysis.

DISCUSSION

This study shows that the survival of patients after surgical management for pulmonary stenosis is good and that, irrespective of the type of surgery, there was good relief of pulmonary stenosis. Moreover, both exercise capacity and subjective wellbeing are comparable to that of the normal Dutch population. However, many patients, although asymptomatic, had hemodynamic sequelae and arrhythmia.

Hemodynamic sequelae and cardiac function. Substantial residual pulmonary stenosis was not detected in any of the patients at follow-up, although the right ventricular pressure was still elevated at the end of the surgical procedure in many patients. This suggests that muscular hypertrophy of the right ventricular outflow tract, which was still present in many patients directly postoperatively, regressed spontaneously in time. With the abolishment of elevated right ventricular pressure, the most important risk factor for premature death in pulmonary stenosis, has disappeared[16,17]. However, this was often

achieved at the cost of creation of pulmonary regurgitation: 75% of the patients had a diastolic regurgitation murmur and 85% of the patients proved to have more than minimal pulmonary regurgitation at echocardiographic examination.
The most important difference in terms of outcome between the surgical techniques is not the extent in which the pulmonary stenosis was relieved -this was successful irrespective of the technique that was used, with at most a mild residual pulmonary stenosis - but is the degree of pulmonary regurgitation. Pulmonary regurgitation is obligatory after the use of a transannular patch and was severe in 7 out of 9 patients (78%) operated upon using this technique. Evidently, pulmonary regurgitation was also created in the other patients, but severe regurgitation occurred less often (8 out of 30 patients; 27%) when other techniques were applied. The clinical importance of severe pulmonary regurgitation and long-standing severe right ventricular dilatation is still subject to debate. Some studies have reported that long-standing pulmonary regurgitation is well tolerated for decades[18,19]. Our finding that exercise capacity was normal also in most patients with moderate to severe pulmonary regurgitation and right ventricular dilatation suggests that it did not affect cardiac function, at least for the duration of the follow-up of up to 22 years. It also confirms earlier reports that exercise capacity after surgical repair of pulmonary stenosis is normal[20]. However, the fact that the 4 patients (which is 11% of the tested population) who had a substantially decreased exercise capacity all had severe pulmonary regurgitation and severe right ventricular dilatation and the fact that 2 other patients became symptomatic and had to be reoperated because of severe pulmonary regurgitation soon after the follow-up study ended, demonstrates that these features do affect cardiac function in a substantial proportion of these patients[21]. So, if patients develop symptoms after surgery for pulmonary stenosis these are caused by severe pulmonary regurgitation. This emphasises that it should be tried to minimize pulmonary regurgitation in the treatment of pulmonary stenosis, may be at the cost of some more residual stenosis. As H.P. Gutgesell stated "a little stenosis might be better than a lot of insufficiency"[22].
Arrhythmia. Ventricular arrhythmia was common in our study population (44%), but none of the patients used antiarrhythmic medication for this indication and there had been no late sudden deaths which could have been attributed to arrhythmia. This is in agreement with the findings of Kopecki et al[5] who showed that none of the patients had developed major arrhythmia 20 to 30 years after surgery. The cause of ventricular arrhythmias remains subject to speculation. It has been demonstrated earlier that these are not inherent to the natural history of the disease but due to the surgical repair[23]. Surprisingly, neither differences in surgical technique (transpulmonary versus transventricular approach; inflow occlusion versus cardiopulmonary bypass) nor differences in hemodynamic condition at follow-up (in particular the degree of right ventricular dilation) were associated with differences in prevalence of arrhythmia. The fact that a longer interval between operation and follow-up was associated with a higher incidence of ventricular arrhythmia indicates that either these arrhythmias increase in time, or that patients operated upon in the early years of the study period had a higher incidence of ventricular arrhythmia as a reflection of a less sophisticated cardiac surgery in that era. Longer follow-up will elucidate this.
Unlike previous studies, in which no comment was made on the occurrence of supraventricular arrhythmia, we found a high prevalence of supraventricular arrhythmia due to sinus node dysfunction. The finding that patients with a duration of follow-up <15

years had a higher prevalence of supraventricular arrhythmia than patients with a follow-up >15 years suggests that one (or more) of the baseline characteristics that had changed over the years might be a causative factor. Cannulation for cardiopulmonary bypass, which could damage the sinus node[24], was rare in the early years of the study and was more frequently used in the later years. However, the prevalence of arrhythmia in patients who were operated upon with only inflow occlusion was similar to that of patients who had cannulation for cardiopulmonary bypass. Other factors, like right atrial enlargement due to pulmonary regurgitation with elevated diastolic right ventricular pressures, loss of atrial compliance due to right atrial incision, and stretching of the interatrial septum due to direct closure of a concomitant atrial septal defect or open foramen ovale could play a causative role on theoretical grounds[25], but this could not be ascertained due to the nature of this study.

Apart from the cause, which remains unexplained, the clinical importance is also unknown, except for 1 patient, who had symptomatic arrhythmia due to a bradycardia-tachycardia syndrome. Clearly, longer follow-up is necessary to establish this.

Comparison with results after balloon valvuloplasty. Long-term results of >10 years follow-up are not available yet, but the intermediate-term hemodynamic results of balloon valvuloplasty are reported to be excellent, and at least equal to the results after surgery[26,27]. Furthermore, O'Connor et al[28] reported that ventricular arrhythmia is rare after balloon valvuloplasty and no mention is made of supraventricular arrhythmia. Longer follow-up will be necessary to establish whether balloon valvuloplasty is indeed at least equal in terms of hemodynamic results and superior in terms of prevalence of arrhythmia when compared with surgical repair. Surgical management will continue to be the treatment of choice for patients with a type of pulmonary stenosis which is not amenable to balloon valvuloplasty: a dysplastic pulmonary valve or a hypoplastic annulus.

Selection bias. We only examined 48% of the operated patients. Of these, the proportion of patients who were operated upon with cardiopulmonary bypass was much larger than that of patients operated upon with inflow occlusion. Therefore we saw a selected patient group. Because all but 7 patients operated upon with inflow occlusion were discharged from routine outpatient clinic follow-up within 4 years after surgery, and none of them have reported until date with symptoms or sequelae, we assume that these patients have fared well and that there was a selection bias towards the more complex forms of pulmonary stenosis in this study. This might explain the high prevalence of sequelae in our study population when compared with that of other studies. However, even if one assumes that sequelae were minimal or completely absent in patients who were not seen at follow-up, the overall prevalence of sequelae would be substantial.

In addition it should be emphasized that the results of this study are not representative for the outlook for patients with pulmonary stenosis born today or operated upon in more recent years. The outlook for these patients is probably better, because of the many improvements in surgical and medical management that took place in the last decade.

Conclusion. Different surgical management techniques for pulmonary stenosis all lead to a good and lasting relief of elevated right ventricular pressure, but this is achieved at the cost of pulmonary regurgitation in virtually all patients. This regurgitation is sometimes severe, in particular in patients in whom a transannular patch was used for pulmonary outflow tract reconstruction. The majority of the patients was asymptomatic and both exercise capacity and subjective wellbeing of the group of patients is good and

comparable to that of the normal Dutch population. However, a substantial proportion of the patients developed symptoms, and these were all due to severe pulmonary regurgitation and severe right ventricular dilatation. This emphasizes that in the treatment of pulmonary stenosis it should be tried to avoid creation of severe pulmonary regurgitation.

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CHAPTER 7

HEALTH STATUS LONG-TERM AFTER OPEN HEART SURGERY FOR CONGENITAL HEART DISEASE IN INFANCY OR CHILDHOOD

COMPARISON OF THE RESULTS OF SURGICAL REPAIR OF ATRIAL SEPTAL DEFECT, VENTRICULAR SEPTAL DEFECT, TETRALOGY OF FALLOT, TRANSPOSITION OF THE GREAT ARTERIES AND VALVULAR PULMONARY STENOSIS

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ABSTRACT

Objective. The purpose of this study was to assess the health status of patients long-term after open-heart surgery for congenital heart disease at young age.

Background. Despite many reports on the long-term results of surgical repair for congenital cardiac malformations, there are few data on the prevalence of postoperative sequelae. Therefore we conducted a follow-up study by means of extensive cardiological examination of a representative sample of all patients who underwent surgical repair for one of the 5 most common congenital cardiac malformations in our institution between 1968 and 1980. This facilitates assessment of both prevalence and clinical importance of postoperative sequelae.

Methods. A total of 627 patients <15 years of age underwent surgical repair for one of the 5 following congenital cardiac defects: atrial septal defect (n=135), ventricular septal defect (n=176), tetralogy of Fallot (n=142), transposition of the great arteries (Mustard type repair; n=91) or isolated valvular pulmonary stenosis (n=83). The current status (living or dead) and address were traced through the offices of local registrars. All surviving patients who could be traced received a letter explaining the study and inviting them to participate in the follow-up study which consisted of an extensive cardiological examination, comprising medical history, physical examination, standard 12-lead and 24-hour electrocardiography, exercise testing, M-mode and two-dimensional echocardiography, pulsed-, continuous wave and color flow Doppler studies.

Results. A total of 388 patients (70% of the survivors) participated. The mean interval between surgery and follow-up was 14.6 ± 2.8 years. The way that patients elicited their own health was similar to that of the normal Dutch population, irrespective of their cardiac diagnosis and current health status. A large majority of the patients had no complaints and had a normal exercise capacity. The most common symptoms were decreased exercise capacity and symptomatic arrhythmia necessitating treatment. Of these, the highest prevalence was found in patients after surgery for tetralogy of Fallot and, most prominent, after Mustard repair for transposition of the great arteries. Severe right ventricular dilatation and both ventricular and supraventricular arrhythmia were the most common asymptomatic sequelae present throughout the entire operated population.

Conclusion. A large majority of the patients feels healthy, is asymptomatic and has a normal cardiac function. However, the outlook of these patients on the longer term remains uncertain, because of the very high prevalence of arrhythmia and severe right

ventricular dilatation that was found throughout the whole study population. Longer follow-up will be necessary to elucidate this.

INTRODUCTION

Despite many reports on the long-term results of surgical repair for congenital cardiac malformations that focus on complications that may occur after surgery, there are few data on the prevalence of postoperative sequelae. The reason for this is twofold. Many studies focus on specific sequelae in selected populations[1-6] which per definition will not reflect the prevalence of these sequelae in the total population. Other follow-up studies used questionnaires to assess patient's health status[7-10] and although some of these studies were based on consecutive series of patients and a very high response rate was achieved, this type of study gives no reliable assessment of the prevalence of sequelae either, because the absence of symptoms does not rule out the presence of sequelae. In order to assess both prevalence and clinical importance of postoperative sequelae we conducted a follow-up study by means of extensive cardiological examination of a representative sample of all patients who underwent an surgical repair for one of the 5 most common congenital cardiac malformations in our institution between 1968 and 1980.

Special emphasis was put on the differences in sequelae between the diagnostic subgroups and its impact on patient's health related quality of life.

METHODS

Patient selection and follow-up procedure. A total of 627 patients <15 years of age underwent open heart surgery for atrial septal defect, ventricular septal defect, tetralogy of Fallot, transposition of the great arteries or a valvular pulmonary stenosis. The current status (living or dead) and address of patients were traced through the offices of local registrars. Sixty-nine patients (11%) had died, and 28 (4%) had moved abroad or were otherwise untraceable. Furthermore, 32 patients with a pulmonary stenosis who underwent surgical repair with the use of inflow occlusion were unintentionally disregarded in the initial patient selection and were not approached for the follow-up study. The remaining patients received a letter explaining the objective of the study and inviting them to participate. Three-hundred eighty-eight patients (70% of the survivors) responded positively and took part in an extensive cardiological examination which consisted of medical history, physical examination, standard 12-lead and 24-hour electrocardiography, exercise testing, M-mode and two-dimensional echocardiography, pulsed-, continuous wave and color flow Doppler studies. The mean (± SD) interval between operation and follow-up was 14.6 ± 2.8 years (range from 9.3 to 22.9 years). The study was approved by the local Medical Ethical Review Board.

Measurements and definitions. The *medical history* comprised a questionnaire from the Netherlands Central Bureau of Statistics which has been validated in a sample of 1510 Dutch adults <35 years of age[11]. It uses standardized (multiple choice) questions to elicit a person's assessment of his or her health status.

Echocardiographic examination was performed with a Vingmed CFM 700 or a Toshiba SSH 160-A echocardiograph. Left ventricular dimensions and fractional shortening were measured using M-Mode cardiography and compared with normal values for sex and bodyweight. A fractional shortening <0.30 was defined as decreased. Right ventricular dimensions were judged by visual estimate. Pulmonary hypertension was assumed to

be present if a pulmonary regurgitation was found with a flow velocity exceeding 3.5 m/sec, or if a tricuspid regurgitation was found with a flow velocity >4.0 m/sec in the absence of a right ventricular outflow tract obstruction (in patients with a Mustard repair: mitral regurgitation >4.0 m/sec in the absence of a left ventricular outflow tract obstruction).

Maximal exercise capacity was assessed by bicycle ergometry with stepwise increments of the workload of 20 W/min. Patients were encouraged to exercise until exhaustion. Patients were excluded from the exercise test if they could not be motivated to exercise maximally or if a concomitant factor (asthma, psychomotor retardation or spastic hemiplegia) might influence the outcome of the test.

The *standard 12 lead electrocardiogram* was used for assessment of electrocardiographic evidence of right or left ventricular hypertrophy, and the presence of a right or left bundle branch block.

Heart rhythm analysis was performed by means of a 24 hour electrocardiogram. Sinus node dysfunction was assumed to be present when the patient had a bradycardia-tachycardia syndrome, atrial flutter or fibrillation[12]. The following supraventricular arrhythmias were considered as minor indications of sinus node dysfunction: sino-atrial block, a sinus arrhythmia with a beat-to-beat variation of the heart rate of more than 200%, sudden change from sinus rhythm to an escape rhythm with a frequency > 25% lower than the sinus rhythm, nighttime bradycardia < 30 beats per minute and daytime bradycardia < 40 beats per minute[13].

Ectopic ventricular activity, recorded during the 24 hr electrocardiogram was considered abnormal if monoform premature ventricular contractions occurred at a rate >3600/24 hr, or if premature ventricular contractions were multiform or presented as doublets or ventricular tachycardia. Ventricular tachycardia of >3 but <10 consecutive beats originating from a ventricle with a rate >120 beats/min was defined as nonsustained; a run of more than 10 consecutive beats was defined as sustained.

Data analysis. Survival of the total study population of 627 patients, specified per diagnostic subgroup, was calculated according to Kaplan-Meier analysis[14]. The data on the clinical course after the surgical repair until follow-up and of the cardiological examination at follow-up are presented only of the patients who participated in the follow-up study. All values are expressed with their mean value ± SD unless indicated otherwise. The Chi-square and Fisher's exact test were used for the comparison of discrete variables in the presence of a normal distribution. In the presence of a non-Gaussian distribution the Mann-Whitney rank-sum test was used. Two proportions were compared using the difference of the rate of events in two groups calculated according to the method of Greenland and Robins[15]. Comparison of continuous variables in 2 groups was performed with the Student t-test. Regression analysis was used to demonstrate a possible correlation between different continuous variables. A correlation factor (r) <0.4 was considered to represent a poor relation, a correlation factor between 0.4 and 0.8 a fair relation, and >0.8 a good relation. Stepwise multivariate analysis was performed to assess the independent contribution of parameters that were statistically significant at univariate analysis. In all analyses the level of significance was chosen at 0.05.

RESULTS

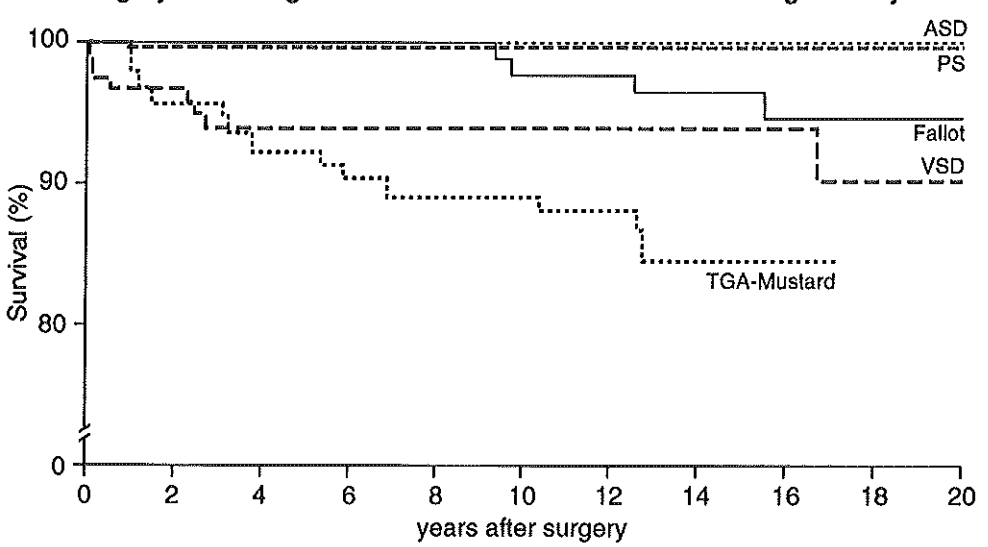
Clinical course until follow-up. The baseline characteristics of the study population are summarized in Table I.

Table I **Baseline characteristics of 627 patients who underwent open heart surgery for a congenital cardiac malformation between 1968 and 1980**

	ASD	VSD	Fallot	TGA-Mustard	PS
number of patients	135	176	142	91	83
deceased	0 (0%)	23 (13%)	27 (19%)	18 (20%)	1 (1%)
participated in follow-up	104 (77%)	109 (71%)	77 (67%)	58 (79%)	40 (48%)
reoperation	1 (1%)*	8 (7%)*	13 (17%)*	12 (21%)*	3 (8%)*
antiarrhythmic medication					
- because SVT	3 (3%)*	0	5 (6%)*	6 (10%)*	1 (3%)*
- because VT	0	0	1 (1%)*	0	0
age at operation (yrs ± SD)	7.5 ± 3.5	4.1 ± 4.0	4.7 ± 3.4	1.8 ± 2.2	5.0 ± 3.8
age at follow-up (yrs ± SD)	21.8 ± 4.8	18.9 ± 5.7	19.0 ± 5.5	15.8 ± 3.9	20.7 ± 5.7

ASD = atrial septal defect; VSD = ventricular septal defect; Fallot = tetralogy of Fallot;TGA-Mustard = transposition of the great arteries after Mustard repair; PS = pulmonary stenosis; SVT = supra-ventricular tachycardia; VT = ventricular tachycardia; * = refers to patients who participated in the follow-up study

Figure I **Kaplan-Meier survival curve of all hospital survivors of open heart surgery for a congenital cardiac malformation before the age of 15 years**



There is a significant difference in mortality between the diagnostic subgroups: low for patients after surgery for atrial septal defect or pulmonary stenosis (respectively 0% and 1%), and substantial for patients after surgery for ventricular septal defect (13%),

tetralogy of Fallot (19%) and transposition of the great arteries (19%). The proportion of total mortality that had been <30 days postoperatively (early mortality) was high for patients with tetralogy of Fallot (15%) and ventricular septal defect (10%), but much lower for patients who underwent a Mustard repair for transposition of the great arteries (5%). The survival of the patients who survived the early postoperative period of 30 days was depicted in the Kaplan-Meier survival table (Figure I). It shows that late mortality (>30 days postoperatively) was high in the Mustard group, and not neglectable in the groups after surgery for tetralogy of Fallot and ventricular septal defect. The primary cause of late death was sudden unexpected death attributed to arrhythmia (1 patient after ventricular septal defect repair, 4 patients after tetralogy of Fallot repair and 7 patients after Mustard repair). Other causes of premature death were documented supraventricular arrhythmia (atrial flutter/fibrillation in 3 patients after a Mustard type repair), right ventricular failure (3 patients after a Mustard type repair), pulmonary hypertension (2 patients after ventricular septal defect closure) and a noncardiac cause (1 patient after ventricular septal defect closure).

Table I also shows a significant difference in number of reoperations between the diagnostic groups: a high proportion of the patients after Mustard repair or after surgical repair of tetralogy of Fallot had needed reoperation (respectively 21% and 17%), in contrast to a much lower proportion in the group of patients after surgery for atrial septal defect (1%), ventricular septal defect (7%) and pulmonary stenosis (8%). Twelve out of 16 patients who had received medical treatment for arrhythmia had either tetralogy of Fallot (6 patients) or transposition of the great arteries (6 patients).

Current health status. *History.* All patients were asked to describe their health status (Table 2). There were no differences in health assessment between the 5 diagnostic subgroups. Comparison of the health assessment of the study population as a whole with that of the normal population, shows that in the study population the proportion "good" is significantly higher, at the cost of the proportion "excellent", which is significantly lower.

Table II **Personal health assessment of 388 study patients and of 1510 persons of the normal Dutch population < 35 years**

	ASD n = 104	VSD n = 109	Fallot n = 77	TGA-Mustard n = 58	PS n = 40	Dutch population n = 1510
excellent	20 (19%)	24 (22%)	13 (17%)	12 (21%)	10 (25%)	611 (40%)
good	70 (67%)	68 (62%)	50 (65%)	39 (67%)	26 (65%)	755 (50%)
fair	14 (13%)	16 (15%)	11 (14%)	7 (12%)	4 (10%)	127 (9%)
not good	0	1 (1%)	3 (4%)	0 (0%)	0 (0%)	17 (1%)
bad	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

ASD = atrial septal defect; VSD = ventricular septal defect; Fallot = tetralogy of Fallot; TGA-Mustard = transposition of the great arteries after Mustard repair; PS = pulmonary stenosis

Physical Examination. The mean values of length and body weight were within the normal range; in this respect there were no differences between the 5 cardiac diagnosis groups.

Table III **Results of echocardiography; substantial abnormalities**

	ASD n = 104	VSD n = 109	Fallot n = 77	TGA-Mustard n = 58	PS n = 40
residual ASD	2 (2%)	1 (1%)	0	3 (5%)	0
residual VSD	0	7 (6%)	14 (18%)	4 (7%)	0
LV FS <0.30	20 (19%)	23 (22%)	24 (31%)	n.m.	10 (25%)
paradox septal motion	6 (6%)	6 (6%)	30 (39%)	n.m.	14 (35%)
RV size ≥ LV size	27 (26%)	0	45 (58%)	56 (97%)	10 (25%)
TI: moderate to severe	0	0	17 (22%)	36 (62%)	2 (5%)
PI: moderate to severe	0	0	45 (58%)	0	16 (40%)
AI: mild	0	12 (11%)	12 (16%)	8 (14%)	0
PS >3 m/sec	0	0	6 (8%)	9 (16%)	2 (5%)

ASD = atrial septal defect; VSD = ventricular septal defect; Fallot = tetralogy of Fallot; TGA-Mustard = transposition of the great arteries after Mustard repair; PS = pulmonary stenosis; n.m. = not measured; LV = left ventricle; RV = right ventricle; TI = tricuspid incompetence; PI = pulmonary incompetence FS = fractional shortening

Echocardiography. The findings are listed in Table 3. The prevalence of echocardiographically detected sequelae was significantly higher in patients after surgical repair of tetralogy of Fallot and a Mustard type repair for transposition of the great arteries than after surgical repair for atrial septal defect, ventricular septal defect, and pulmonary stenosis.

Pulmonary hypertension was absent in the entire population except for 2 patients who underwent a Mustard repair beyond the age of 1.5 years for a transposition of the great arteries with a large ventricular septal defect.

There was no relation between longer duration of follow-up and a higher prevalence of one of the sequelae presented in Table 3 in any of the diagnostic subgroups.

The proportion of patients with a decreased left ventricular shortening was similar in patients after surgical repair for atrial septal defect, ventricular septal defect, tetralogy of Fallot, and pulmonary stenosis. This feature was not measured in patients with a Mustard type repair, in whom the left ventricle is the subpulmonary ventricle. The following determinants for a decreased fractional shortening were analyzed by means of univariate analysis, but proved to be not statistically significant: older age at surgery, earlier year of operation, longer interval between surgery and follow-up study, no cold cardioplegia at surgery and right ventricular diameter exceeding left ventricular diameter at follow-up.

The prevalence of right ventricular dilatation varied considerably between the diagnostic subgroups from 0% in the patients after surgical repair of ventricular septal defect to 98% after a Mustard type repair for transposition of the great arteries. In the group of patients after surgical repair of atrial septal defect, right ventricular dilatation was not associated with other hemodynamic sequelae (in particular pulmonary or tricuspid regurgitation) and was therefore considered a rest of the preoperative right ventricular dilatation. There was no correlation between older age at surgery and right ventricular dilatation. In the group of patients after surgical repair of tetralogy of Fallot and valvular pulmonary stenosis, right ventricular dilatation was associated with moderate to severe

pulmonary regurgitation, which in turn was associated with the use of a transannular patch for relief of the right ventricular outflow tract obstruction at surgery. The right ventricle, which is the systemic ventricle after a Mustard type repair, was dilated in all but 2 patients; they had been reoperated and an arterial switch was performed with take down of the Mustard construction.

Table IV **Maximal exercise capacity assessed by bicycle exercise test**

	ASD n = 100	VSD n = 102	Fallot n = 71	TGA-Mustard n = 49	PS n = 37
Maximal exercise capacity[1]	104 ± 17%	100 ± 17%	90 ± 18%*	84 ± 16%*	106 ± 19%
Number of patients with					
- exercise capacity >120%	18 (18%)	13 (13%)	0 (0%)	1 (2%)	8 (22%)
- exercise capacity 80-120%	70 (70%)	72 (70%)	56 (79%)	29 (59%)	25 (68%)
- exercise capacity 50-80%	12 (12%)	17 (17%)	13 (18%)	18 (37%)	4 (11%)
- exercise capacity < 50%	0 (0%)	0 (0%)	2 (3%)	1 (2%)	0 (0%)

1 = relative to predicted value ± SD; ASD = atrial septal defect; VSD = ventricular septal defect; Fallot = tetralogy of Fallot; TGA-Mustard = transposition of the great arteries after Mustard repair; PS = pulmonary stenosis; * significantly lower than normal

Bicycle Ergometry. The results of the exercise test are summarized in Table 4. The mean exercise capacity of patients after surgical repair of an atrial septal defect, ventricular septal defect, or pulmonary stenosis was normal. In these diagnosis groups a decreased exercise capacity was not associated with hemodynamic or anatomic sequelae at echocardiography. In the group of patients after surgical repair of tetralogy of Fallot a decreased exercise capacity was associated with a poor hemodynamic situation (especially severe pulmonary regurgitation and right ventricular dilatation). In the group of patients after a Mustard repair there was no difference in exercise capacity between patients with a "normal Mustard" and patients with echocardiographically demonstrated abnormalities other than the Mustard repair itself; both groups had a decreased exercise capacity.
Ventricular arrhythmias that were induced or aggravated by exercise were seen only after surgery for tetralogy of Fallot (11 patients).

Table V **Results of the standard 12-lead ECG**

	ASD n = 104	VSD n = 109	Fallot n = 77	TGA-Mustard n = 58	PS n = 40
normal	52 (50%)	48 (43%)	10 (13%)	1 (2%)	18 (45%)
RBBB	12 (12%)	35 (32%)	54 (70%)	5 (9%)	5 (13%)
RVH	12 (13%)*	1 (1%)*	9 (45%)*	47 (96%)*	17 (49%)*

ASD = atrial septal defect; VSD = ventricular septal defect; Fallot = tetralogy of Fallot; TGA-Mustard = transposition of the great arteries after Mustard repair; PS = pulmonary stenosis; RBBB = right bundle branch block; RVH = right ventricular hypertrophy;
* = refers to number of patients with narrow QRS complex

Table VI **Results of the 24 hour ambulatory ECG-registration**

	ASD n = 98	VSD n = 106	Fallot n = 67	TGA-Mustard n = 58	PS n = 37
no arrhythmia	**32 (33%)**	**51 (48%)***	**19 (28%)**	**15 (26%)**	**9 (24%)**
supraventricular arrhythmia	**44 (45%)**	21 (20%)**	**19 (28%)**	**23 (40%)**	**14 (38%)**
- atrial flutter / fibrillation	0 (0%)	0 (0%)	0 (0%)	2 (4%)	0 (0%)
- bradycardia-tachycardia syndrome	1 (1%)	0 (0%)	1 (3%)	5 (9%)	1 (2%)
- possible sinus node dysfunction	37 (38%)	21 (20%)	14 (21%)	16 (28%)	12 (32%)
- supraventricular tachycardia	6 (6%)	0 (0%)	4 (6%)	0 (0%)	1 (2%)
ventricular arrhythmia	**42 (43%)**	**45 (42%)**	**33 (49%)**	**25 (43%)**	**17 (46%)**
- monoform PVC's >3600/24 hour	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
- multiform PVC's	38 (39%)	34 (32%)	27 (40%)	25 (43%)	11 (30%)
- PVC doublet	12 (12%)	12 (11%)	15 (22%)	4 (7%)	3 (8%)
- VT 3-10 beats	3 (3%)	6 (6%)	5 (7%)	4 (7%)	2 (5%)
- VT >10 beats	0 (0%)	0 (0%)	1 (1%)	0 (0%)	1 (3%)
pacemaker	**4 (4%)**	**2 (2%)**	**3 (4%)**	**8 (14%)*****	**0 (0%)**
- for sinus node dysfunction	3 (3%)	0 (0%)	2 (3%)	6 (10%)	0 (0%)
- for complete AV block	1 (1%)	2 (2%)	1 (1%)	2 (3%)	0 (0%)
atrioventricular block					
- first degree (PR interval >0.22 sec)	**14 (14%)**	**0 (0%)**	**5 (7%)**	**14 (24%)**	**0 (0%)**
- second degree Mobitz type	2 (2%)	5 (5%)	3 (4%)	1 (2%)	2 (5%)
- third degree (no pacemaker)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

ASD = atrial septal defect; VSD = ventricular septal defect; Fallot = tetralogy of Fallot; TGA-Mustard = transposition of the great arteries after Mustard repair; PS = pulmonary stenosis; PVC = premature ventricular contraction; VT = ventricular tachycardia; AV = atrioventricular; * = VSD significantly higher than ASD, Fallot, TGA-Mustard and PS; ** = VSD significantly lower than ASD, TGA-Mustard and PS; *** = TGA-Mustard significantly higher than VSD and PS

Results of the electrocardiography. The results of the standard 12-lead electrocardiogram is shown in Table 5, and the results of the 24 hour ambulatory electrocardiogram is shown in table 6. A substantial proportion of the patients of all diagnostic subgroups proved to have arrhythmia, but in the group of patients after surgical repair of ventricular septal defect the prevalence of arrhythmia is significantly lower than in the other groups. This was due to a significantly lower proportion of supraventricular arrhythmia than in the other diagnostic groups; the prevalence of ventricular arrhythmia was comparable to that of other groups. The proportion of patients with a pacemaker in the group of patients after a Mustard repair was significantly higher than that of patients after surgery for pulmonary stenosis or ventricular septal defect. The difference with patients after surgery for atrial septal defect or tetralogy of Fallot lacked significance. There was no relation between hemodynamic sequelae detected with echocardiography (in particular right ventricular dilatation) and arrhythmia except for the group of patients after surgical

repair of tetralogy of Fallot. In this group elevated right ventricular pressure was associated with a higher prevalence of ventricular arrhythmia. In patients after surgical repair of atrial septal defect, ventricular septal defect and tetralogy of Fallot there was no correlation between arrhythmia (either ventricular or supraventricular) and older age at surgery, longer duration of follow-up or older age at follow-up. In patients after surgery for pulmonary stenosis a longer duration of follow-up was associated with a higher prevalence of arrhythmia, and in patients with a Mustard repair for transposition of the great arteries a longer duration of follow-up was associated with a higher incidence of sinus node dysfunction. There was no difference in prevalence of arrhythmia in any of the 5 diagnostic subgroups between patients with or without cold cardioplegia at surgery.

DISCUSSION

This study shows that, if perioperative mortality is disregarded and considered as reflection of the state of the art of perioperative management in cardiac surgery in the 1960's and 1970's, long-term survival after open heart surgery is good for patients with an atrial septal defect, pulmonary stenosis, ventricular septal defect and tetralogy of Fallot, but less good for patients with a Mustard repair for transposition of the great arteries.

Morbidity in the group of survivors is substantial, but varies considerably between the diagnostic subgroups. In the group of patients after surgical repair of tetralogy of Fallot and after Mustard type repair for transposition of the great arteries the proportion of patients who have substantial hemodynamic sequelae is high, which is represented by a high proportion of patients who underwent a reoperation in the period after the initial operation and the follow-up study (respectively 17 and 21%) and by many echocardiographically detected sequelae at follow-up. Also in patients of the other diagnostic subgroups reoperations had been necessary and hemodynamic sequelae were found at follow-up, but in a much lower number. In contrast to general expectations, but in agreement with reports on psychological wellbeing in varying stages of cardiac disease in adults these features do not affect patient's subjective wellbeing[16,17]. There is no difference in personal health assessment between the 5 diagnostic subgroups, despite a considerable difference between these groups in terms of cardiac function (as reflected by maximal exercise capacity), prevalence of symptomatic arrhythmia and prevalence of hemodynamic or anatomic sequelae that necessitated reoperation. This confirms that personal health assessment is not a good indicator for the "objective" clinical condition of the patient[18].

The anatomic and hemodynamic sequelae detected by echocardiography at follow-up largely represent sequelae inherent to the original cardiac malformation or the type of the surgical repair. The fact that there was no relation between longer duration of follow-up and a higher prevalence of sequelae in any of the diagnostic subgroups indicates that these sequelae do not seem to progress in time. However, longer follow-up is necessary to substantiate this.

Right ventricular dilatation, either associated with severe pulmonary regurgitation (after surgical repair of tetralogy of Fallot or valvular pulmonary stenosis), or not associated with hemodynamic sequelae (after surgical closure of an atrial septal defect) definitely reflects a pathological condition. Although not consistently correlated with decreased exercise capacity, higher prevalence of arrhythmia or a less good subjective wellbeing, right ventricular function seems to be a crucial factor in the long-term performance of

patients after surgical repair of congenital heart disease. The quest for a method to assess right ventricular function and to predict impending right ventricular failure, which would be of major importance for these patients, should be continued ardently.
The left ventricular function seems to be hardly affected in patients after surgery for atrial septal defect, ventricular septal defect, tetralogy of Fallot and pulmonary stenosis, notwithstanding the finding of a decreased left ventricular fractional shortening (in similar proportions) in all these groups. Because patients with a decreased left ventricular fractional shortening did not have a lower exercise capacity than others, this finding seems to be of little clinical significance.
Exercise capacity. A major goal of cardiac surgery is, next to improvement of life expectancy, to preserve or to restore cardiac performance. This study shows that this is achieved in a large majority of patients after surgical repair of atrial septal defect, ventricular septal defect and pulmonary stenosis, and tetralogy of Fallot. However, in this last group only patients with a good hemodynamical result had a normal exercise capacity; a suboptimal surgical result (in particular severe pulmonary regurgitation and right ventricular dilatation) was clearly associated with a substantially decreased exercise capacity. This is in contrast to patients after a Mustard repair, in whom the exercise capacity is substantially decreased even after an optimal surgical result. Therefore we conclude that a decreased exercise capacity is inherent to the Mustard type repair itself. However, even in this subgroup over 60% of the patients had an exercise capacity within the normal range. Assuming that even patients with moderately decreased exercise capacity can, with some adaptations, participate in most normal daily activities, virtually all patients of the total study population will be able to lead a normal professional and social life.
The contribution of the **standard 12-lead electrocardiogram** in the understanding of the cardiac status of patients in this study population is limited; heart rhythm analysis is executed more reliably by a 24 hour electrocardiogram and the feature which can be assessed reliably, the presence of a bundle branch block, is of little clinical importance. Only if the QRS-complex is narrow the standard 12-lead electrocardiogram is useful as complementary evidence for the evaluation of right or left ventricular hypertrophy; information which is primarily based on the echocardiographic examination.
Heart rhythm analysis by 24-hour electrocardiography disclosed a high prevalence of both ventricular and supraventricular arrhythmias in all diagnostic subgroups. Patients after surgical repair of a ventricular septal defect have the least arrhythmias, which is due to a significantly lower prevalence of supraventricular arrhythmias than in other diagnostic subgroups, and it is the only group in which none of the patients used antiarrhythmic medication. The highest prevalence of arrhythmias was surprisingly found in the group of patients after surgery for pulmonary stenosis. However, all but one of these patients were asymptomatic. The highest prevalence of symptomatic arrhythmias in our study, like in many other studies, was in the group of patients with a Mustard repair for transposition of the great arteries. The high incidence of late sudden death in this group emphasizes the clinical importance of arrhythmias in this group. It is remarkable that apart from the patients after atrial septal defect and Mustard repair for transposition of the great arteries, in which extensive atrial surgery is known to cause sinus node dysfunction necessitating treatment (pacemaker implantation, antiarrhythmic medication), supraventricular arrhythmias is frequent in patients after repair of tetralogy of Fallot and pulmonary stenosis. The cause of these arrhythmias in these groups remains

unknown. They might be inherent to the natural history, or be induced by elevated right atrial pressure and right atrial dilatation as a result of right ventricular dilatation and severe pulmonary regurgitation after surgery. However, this cannot be substantiated on the basis of our data.

It is striking that there is no difference in prevalence of ventricular arrhythmias between the 5 diagnostic subgroups. It is also remarkable that only 2 patients (0.5% of the study population) had sustained ventricular tachycardia during the 24-hour electrocardiogram, and that only 1 patient (0.25%) had antiarrhythmic medication for symptomatic ventricular tachycardia versus 15 patients who needed antiarrhythmic medication for supraventricular arrhythmias. From this point of view it would seem as if ventricular arrhythmias are a less important clinical problem than supraventricular arrhythmia. However, 12 patients (3% of the study population) had died suddenly and unexpectedly years after surgery, probably as a result of ventricular tachycardia, versus 3 patients who had died after a documented supraventricular arrhythmia. Therefore we agree with others that ventricular arrhythmias are the most important sequelae in this population, especially after surgical repair of tetralogy of Fallot and Mustard type repair for transposition of the great arteries. It is unknown whether asymptomatic ventricular arrhythmia that is detected by the 24-hour electrocardiogram at follow-up is a predictor of symptomatic, possibly life-threatening ventricular arrhythmia later. Only longer duration of follow-up will elucidate this.

Conduction disturbances are less prevalent in our study population than in older studies; only 6 patients (1.5%) had a complete atrioventricular block postoperatively. This demonstrates the improved surgical knowledge and skills.

Selection bias. Apart from selecting the patients on grounds of the definition of the study population, patients were not purposely selected. We examined 77% of those eligible for follow-up, and not 100%, and we were not informed about the reasons why patients who did not participate in the follow-up study actually refused. Therefore we cannot exclude that there was an unintentional patient selection. However, all patients were approached uniformly, and there were no significant differences in any of the baseline characteristics between patients who participated in the follow-up study and those who did not. Therefore we assume that there was no selection bias and consider the patients who participated in the follow-up study as a nonselected population, in which prevalence of sequelae can be assessed reliably. However, one should refrain from generalization of the results of this study, realizing that it is a one-center (for the Mustard patients even a one-surgeon) experience.

It should be emphasized that this study concerns the long-term results of patients operated upon 10 to 20 years ago, and that these results represent the state of the art of cardiac surgery in these years. Due to many technological improvements in the past decades the outlook for patients operated upon nowadays will probably be much better, but this will have to be substantiated by future follow-up studies.

Conclusion. This study shows that the prevalence of sequelae long-term after open heart surgery for congenital heart disease is high. As could be expected on the basis of the severeness of the initial cardiac malformation and the extent of the surgical procedure, sequelae (both symptomatic and asymptomatic) are much more prevalent in patients after surgery for tetralogy of Fallot and transposition of the great arteries than after surgery for atrial septal defect, ventricular septal defect or pulmonary stenosis. A decreased exercise capacity, presumably indicating impaired cardiac function, was the

most common postoperative problem. However, over 80% of the patients had a normal exercise capacity, which implies that a large majority of the patients will physically be able to lead a normal professional and social life, including (heavy) physical work and (competitive) sports. Symptomatic arrhythmia was less common than decreased exercise capacity, but the clinical relevance is evident. Ventricular arrhythmia was associated with premature death and supraventricular arrhythmia, also potentially life-threatening, was frequently symptomatic in particular after surgery for atrial septal defect, tetralogy of Fallot and Mustard type repair. Longer follow-up will elucidate whether the many asymptomatic arrhythmia now found at follow-up will remain asymptomatic, or will develop into symptomatic arrhythmia that will necessitate treatment and affect patient's life expectancy.
The right ventricle, often severely dilated, probably plays a crucial role in the outlook in terms of cardiac function and possible causative factor for arrhythmia on the longer term. A diagnostic tool to assess right ventricular function, and ideally predict impending right ventricular failure, would be of enormous value.

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CHAPTER 8

BEHAVIOURAL AND EMOTIONAL PROBLEMS IN CHILDREN AND ADOLESCENTS WITH CONGENITAL HEART DISEASE

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ABSTRACT

Behavourial/emotional problems were assessed at least nine years after surgical correction for congenital heart disease (ConHD) in childhood. Parents of 144 10-15-year-old ConHD-children completed the Child Behavior Checklist (CBCL) and 179, 11-17-year-old, ConHD-adolescents completed the Youth Self-Report (YSR). On the CBCL and YSR ConHD-children and adolescents obtained significantly higher problem scores than same-aged peers from normative reference groups. No significant differences were found between problem scores for different cardiac diagnostic groups. A negative correlation was found between CBCL total problem scores and IQ-scores of ConHD-children; for YSR total problem scores no such relationship was found.

INTRODUCTION

Over the last 25 years advances in cardiovascular diagnostic and surgical techniques have reduced mortality rates of children with congenital heart disease (ConHD) substantially. Many children and adolescents with corrected or palliated ConHD experienced repeated hospitalizations and operations.

Follow-up studies into the psychosocial outcome of children and adolescents with ConHD have yielded contradictory results. Several investigators reported negative psychosocial outcomes, such as diminished self-esteem, anxiety, depression and poor emotional or social adjustment (Kitchen, 1978; Linde, 1982; Donovan, 1983; Kramer et al., 1989; Garson and Baer, 1990). Other studies, however, showed favorable outcomes (O'Dougherty et al., 1983; Bleuer et al., 1985; Wright et al., 1985; Jedlicka-Köhler and Wimmer, 1987; DeMaso et al.,1990). Several factors make it difficult to draw firm conclusions from existing studies, including small sample size, heterogeneous sample composition with respect to the type of ConHD, non-standardized assessment procedures and variation in methods across studies.

The present study is part of a follow-up study concerning the long-term medical and psychological outcome in children, adolescents and young adults with operated ConHD. Behavioural/emotional problems were assessed with standardized procedures nine years or longer after surgical correction in early childhood. The frequency of parent and self-reported behavioral/emotional problems in children and adolescents with operated ConHD was compared with that in reference groups from the general population.

The main questions of this study were: (1) to what extent are children and adolescents

with operated ConHD at risk for developing problem behavior compared with normal peers; (2) to what extent are sex and age related to these problems; (3) are children and adolescents with operated ConHD at risk for developing specific problems; (4) to what extent is cardiac diagnosis related to problem behaviors?

METHODS

Instruments. The Child Behavior Checklist (CBCL; Achenbach, 1991) was used to obtain standardized parents' reports of behavioral/emotional problems in children aged 10-15 years. It consists of 20 competence items and 120 problem items. In the present study only the problem section was used. Parents were requested to circle a 0 if the problem item was not true for the child, a 1 if it was somewhat or sometimes true and a 2 if it was very true or often true. The good reliability and discriminative validity of the CBCL problem section established by Achenbach and Edelbrock (1983) were confirmed using the Dutch translation (Verhulst et al., 1985). Social competence items were excluded due to their lower reliability and lesser discriminative validity between children referred or not referred for mental health services (Verhulst et al., 1985).

For 11 to 17 year-olds the Youth Self-Report (YSR; Achenbach, 1991) was used to obtain adolescents' self-reports. The YSR has roughly the same format as the CBCL, except that items are worded in the first person. The YSR contains 17 competence items, 103 problem items that are similar to those of the CBCL, and 16 socially desirable items that replace CBCL items which were inappropriate to ask adolescents. The good reliability for the American YSR problem section (Achenbach & Edelbrock, 1987) was replicated for the Dutch translation (Verhulst et al., 1989). Total problem scores on the CBCL and YSR were computed by summing all 0-1-2 scores, except on items 2, 4 and on the 16 socially desirable items of the YSR (Achenbach, 1991). Both for the CBCL and YSR Achenbach (1991) constructed eight empirical syndromes and two broad-band groups of syndromes: 'internalizing' and 'externalizing'. The names of the syndromes summarize the items comprising each scale. Internalizing problems reflect internal distress, whereas externalizing problems reflect conflicts with other people and their expectations of the child. For both instruments the internalizing group consists of the Anxious/Depressed, Somatic Complaints, and Withdrawn syndromes. The externalizing group consists of the Aggressive and Delinquent Behavior syndromes. The syndromes Social Problems, Thought Problems and Attention Problems belong neither to the internalizing nor the externalizing group.

To assess intelligence of patients aged 10-16 years, the WISC-R short form (Vocabulary and Block Design) was used (Silverstein, 1972). For patients aged 16-17 years the short form of the Groninger Intelligence Test (Kooreman & Luteijn, 1987), a standardized Dutch intelligence test, was used.

Description of the samples. *Patient sample.* The target patient population consisted of 712 consecutive patients who underwent their first open heart surgery for ConHD between January 1, 1968 and January 1, 1980 in the University Hospital of Rotterdam, and who were younger than 15 years at the time of surgery. Patients with Down's syndrome were not included since it was the policy of the cardiac unit not to operate on such patients in those years. At follow-up 102 patients had died and 41 were lost to follow-up because they had moved abroad or because they were untraceable. Of the remaining 569 patients, 70 did not participate for various reasons. Of these 70, 16 patients were aged 10-15 and 21 patients 11-17 years. The remaining non-participants

were 18-35 years. The final study population consisted of 499 participants. For patients under 16 years, parents were also requested to participate. The response rate, corrected for deceased patients and persons lost to follow-up, was 87.7%.
At follow-up, 24 patients were aged 10; 125 patients 11-15; 61 patients 16-17 and 289 patients 18-35 years. For the present study the upper age limit was 18. The subsamples of the present study partly overlapped since the CBCL and YSR partly covered the same age-ranges.
1. CBCL patient sample. Parents of 85 male and 59 female patients (N=144) aged 10-15 years provided usable CBCLs. The respondents were 91% mothers and 9% fathers. The response rate of this subsample, corrected for deceased patients and persons lost to follow-up, was 87.3%.
2. YSR patient sample. A total of 105 boys and 74 girls aged 11-17 years (N=179) provided usable YSRs. The corrected response rate of this subsample was 86.5%.
Reference groups. To compare with CBCL and YSR data obtained from the patient sample, we used data derived from Dutch normative samples assessed with the same instruments. The CBCL reference group consisted of 446 boys and 472 girls, aged 10-15 years, and the YSR reference group of 364 boys and 399 girls between 11-17 years. For details see Verhulst et al. (1985, 1989).
Socio-economic status (SES) was scored on a six-step scale of parental occupation: SES-1: unskilled employees, SES-2: skilled manual employees, SES-3: clericals, technicians, minor professionals, SES-4: owners of small businesses, SES-5: supervisory, lesser professionals and SES-6: executives, major professionals, owners of large business (van Westerlaak et al., 1975). The percentages on each occupational level for the CBCL respectively YSR patient sample were as follows: SES-1: 9.7% and 11.2%; SES-2: 27.8% and 22.3%; SES-3: 18.1% and 22.9%: SES-4: 11.1% and 10.6%; SES-5: 16.0% and 16.2%; SES-6: 17.4% and 16.8%. The results of the CBCL and YSR patient samples were different because the samples consisted of persons with different ages. The differences may further be due to chance fluctuations in sample characteristics and are not due to any systematic bias, as far as is known to the authors. The percentages for the CBCL and YSR reference groups were respectively: SES-1: 6.4% and 1.3%: SES-2: 27.7% and 24.7%; SES-3: 20.2% and 36.7%; SES-4: 13.0% and 8.5%; SES-5: 17.4% and 13.1% and SES-6: 15.4% and 15.7%. There were no significant differences in the SES distribution between the CBCL patient sample and reference group ($X^2 = 3.05$; df = 5; NS). The SES distribution in the YSR patient sample differed significantly ($X^2 = 54.18$, df = 5, $p < 0.001$) from that in the YSR reference group which could be attributed mainly to the smaller proportion of minor professionals and greater proportion of unskilled employees in the patient sample. The reasons for these differences are unknown; they may also be due to chance fluctuations.
Assessment procedure. The definite cardiac diagnosis was checked by a pediatric cardiologist (F.M.). During the psychological investigation, patients aged 11-17 years, completed the YSR in the presence of a clinical psychologist (E.U.), who was blind as to the cardiac diagnosis of the patients. Fourteen patients needed help in completing the YSR because of reading difficulties. Parents of patients, aged 10-15 years, completed the CBCL independently from their child in a separate room. 9 CBCLs and 13 YSRs with instructions were mailed in a prepaid return envelope, because patients and/or parents preferred to complete questionnaires at home. In these cases intelligence tests could not be performed.

RESULTS

CBCL results. *Proportions of problem children.* The proportions of children in the CBCL patient sample and reference group who scored in the deviant range of the CBCL were compared. The 90th percentile of the cumulative frequency distribution of the CBCL total problem scores obtained for the reference group was chosen as the cutoff to distinguish problem from non-problem children. To assess age effects, two categories (10-12 and 13-15 years) were formed based on the median split of the patient sample.

Table I **Mean CBCL total problem scores and percentages of ConHD and 'reference' children exceeding cutoff scores**

	Mean total problem scores		% > cutoff		
	ConHD (n)	Reference (n)	ConHD	Reference	Binomial test
boys 10-12 yr	26.6 (40)	21.2 (228)	17.5	10.5	ns
boys 13-15 yr	33.4 (45)	18.7 (218)	33.3	10.1	p <0.001
girls 10-12 yr	31.2 (26)	19.1 (243)	30.8	9.9	p <0.002
girls 13-15 yr	27.3 (33)	16.9 (229)	27.3	9.6	p <0.002
total sample	29.7 (144)	19.0 (918)	27.1	10.3	p <0.001

Table II **Differences in mean problem scores for CBCL syndromes and total problem scores of ConHD and reference children in ANCOVAs**

Syndromes	Mean total problem scores		
	ConHD (n = 144)	Reference group* (n = 91)	%
withdrawn	3.1	2.0	2.6
somatic complaints	2.0	0.9	4.9
anxious / depressed	3.9	2.5	2.3
social problems	3.1	1.4	6.6
thought problems	0.7	0.3	4.7
attention problems	5.7	3.3	5.5
delinquent behavior	1.5	1.1	0.6
agressive behavior	7.2	5.4	1.0
internalizing	9.0	5.4	4.4
externalizing	8.7	6.4	1.0
total problem score	29.7	19.0	4.6

* = % of variance accounted for by significant *group effect
(p <0.005, applying Bonferroni correction for 10 comparisons)

Table I shows the proportions of problem children in both samples and the significance of differences between the independent proportions. Due to gaps between rank ordered scores, the percentages of children from the reference group scoring above the 90th percentile were not exactly 10%. The percentage of problem children in the total patient sample (27.1) was significantly (p<0.001) greater than that in the total reference group

(10.3). All the differences, reported in table I, remained significant after applying a Bonferroni correction for five comparisons.

Mean problem scores. Table I also shows the mean total problem scores by each sex and both age categories for the patient and the reference group. To test differences in mean total problem scores and mean scores for syndromes, ANCOVAs were computed in a group (patient sample versus comparison group) x sex (boys versus girls) x age (10-12 versus 13-15 years) factorial design. SES was partialled out as covariate since in a separate ANOVA computed on the mean total problem score, SES was found to have a significant main effect ($p<0.01$), accounting for 1.6% of variance, with higher problem scores for lower SES.

Table II shows the mean scores for the patient and reference group for total problems, the eight syndromes, internalizing and externalizing, as well as the ANCOVA results. The numbers in table II indicate the magnitude of significant ($p<0.05$) effects in terms of the percentage of variance accounted for. According to Cohen's (1977) criteria for analyses of covariance, effects accounting for 1-5.9% of variance are judged small; 5.9-13.8% are considered medium and >13.8% are considered large. The difference in mean total problem scores between the patient and reference group accounted for 4.6% of variance, which was small according to Cohen's (1977) criteria. On all scales, parents of ConHD-children reported significantly more problems than parents of children in the reference group. According to Cohen's criteria (1977) the group effect for Social Problems was considered medium. All other group effects were small. For Delinquent Behavior, the group effect did not remain significant after applying a Bonferroni correction for 10 comparisons. All other group effects remained significant. No significant two or three way interactions were found after applying a Bonferroni correction.

Diagnostic groups. Within the patient sample a differentiation was made between five diagnostic groups: atrial septal II defect (ASD; N=8, mean age: 12.9 yrs.), ventricular septal defect (VSD; N=43, mean age: 12.5 yrs.), tetralogy of Fallot (F4; N=26, mean age: 12.5 yrs.), transposition of the great arteries (TGA; N=38, mean age: 12.7 yrs.) and pulmonary stenosis (N=9, mean age: 13.2 years).

Table III **Differences in mean problem scores for CBCL syndromes and total problem scores across cardiac diagnostic groups in ANCOVAs**

Syndromes	cardiac diagnosis					main effects
	ASD (n = 8)	VSD (n = 43)	F4 (n = 26)	TGA (n = 38)	PS (n = 9)	
withdrawn	2.4	2.8	2.7	3.9	2.8	ns
somatic complaints	3.1	1.4	1.8	2.5	1.8	ns
anxious / depressed	3.9	3.7	3.7	4.4	3.1	ns
social problems	2.4	3.2	3.2	3.6	2.0	ns
thought problems	1.4	0.7	0.5	1.1	0.6	ns
attention problems	5.9	5.5	5.6	6.9	4.3	ns
delinquent behavior	1.3	1.7	1.4	1.7	1.0	ns
agressive behavior	7.6	7.1	7.4	8.3	6.7	ns
internalizing	9.4	8.0	8.2	10.8	7.7	ns
externalizing	8.9	8.8	8.7	10.1	7.7	ns
total problem score	31.0	29.0	29.1	34.2	26.0	ns

CBCL results of 20 patients (mean age: 12.5 years) were not included in statistical analyses because these patients belonged to a miscellaneous diagnostic group, consisting of small numbers of patients with a variety of congenital heart defects.
To test differences in mean problem scores (see Table III) across the diagnostic groups, ANCOVAs were computed with cardiac diagnosis, sex and age as independent variables (5 x 2 x 2) and SES partialled out as covariate. Cardiac diagnosis did not have a main effect on any of the syndromes, nor on the total problem score. No significant interactions were found.
YSR results. *Proportions of problem children.* The proportions of problem children in the YSR patient sample and reference group were compared, using the 90th percentile of the cumulative frequency distribution of the YSR total problem scores obtained for the reference group as the cutoff. (The cutoffs of the CBCL and YSR differ, since they are determined within each informant's reference group). The median split of the YSR patient sample was used to form two age-groups (11-14 versus 15-17 years).
As can be read from table IV, the percentage of problem children in the total patient sample (20.7) was significantly greater ($p<0.001$) than that in the total reference group (9.8). The differences in percentages of problem children found for the total samples and 11-14-year-olds remained significant after applying a Bonferroni correction for 5 comparisons. The difference found for 15-17-year-old girls could not be regarded significant after correction for chance findings.

Table IV **Mean YSR total problem scores and percentages of ConHD and 'reference' children exceeding cutoff scores**

	Mean total problem scores		% > cutoff		
	ConHD (n)	Reference (n)	ConHD	Reference	Binomial test
boys 11-14 yr	32.4 (57)	23.1 (228)	26.3	10.5	p <0.001
boys 15-17 yr	30.3 (48)	23.9 (136)	14.6	11.0	ns
girls 11-14 yr	39.1 (37)	22.8 (224)	32.4	10.3	p <0.001
girls 15-17 yr	36.4 (37)	26.6 (175)	21.6	9.1	p <0.02
total sample	34.0 (179)	24.0 (763)	20.7	9.8	p <0.001

Mean problem scores. ANOVAs with a 2 (2 groups) x 2 (sex) x 2 (2 age-groups) factorial design were executed to test differences in mean total problem scores and mean scores on syndromes. SES was not partialled out as covariate, since in a separate ANOVA computed on the mean total problem score with SES, group and sex as independent variables, SES did not have a significant main effect.
Table V lists the mean scores of both samples on the total problem score and syndromes as well as the ANOVA results. The difference in mean total problem scores between the patient sample and reference group accounted for 5.5% of variance. On all scales ConHD-children and adolescents reported significantly more problems than same-aged peers from the reference group. All group effects remained significant after applying a Bonferroni correction for ten comparisons.
For somatic complaints, a significant interaction between group x age ($p<0.001$),

Table V **Differences in mean problem scores for YSR syndromes and total problem scores of ConHD and reference adolescents in ANOVAs**

Syndromes	Mean problem scores			group[b] x age %
	ConHD (n = 179)	Reference group[a] (n = 763)	%	
withdrawn	3.2	2.2	3.9	ns
somatic complaints	2.6	1.4	5.9	1.8
anxious / depressed	4.5	3.3	1.6	ns
social problems	2.4	1.5	3.8	ns
thought problems	1.7	0.9	5.2	0.8
attention problems	4.7	3.3	4.7	ns
delinquent behavior	2.9	2.1	1.7	ns
agressive behavior	7.5	5.6	2.5	ns
internalizing	10.3	7.0	4.3	ns
externalizing	10.4	7.7	2.6	ns
total problem score	34.0	24.0	5.5	ns

[a,b] = % of variance accounted for by significant [a]group effect and [b]group x age interaction (p <0.005, applying Bonferroni correction for 10 comparisons)

accounting for 1.8% of variance was found. In the patient sample 11 to 14 year-olds obtained a higher mean score (x=3.1) than 15 to 17 year-olds (x=2.1), whereas in the reference group 11 to 14 year-olds obtained lower scores on Somatic Complaints (x=1.2) than 15 to 17 year-olds (x=1.7). A second interaction between group x age was found for Thought Problems (p<0.01, <1% of variance); 11 to 14 year-olds from the patient sample obtained a higher mean score (x=2.0) than 15 to 17 year-olds (x=1.3), whereas in the reference group the mean scores of both age-groups were only slightly different (11 to 14 years: x=0.9, 15 to 17 years: x=0.8). These interaction effects remained significant after applying a Bonferroni correction for ten comparisons. No further two- or three-way interactions were found.

Table VI **Differences in mean problem scores for YSR syndromes and total problem scores across cardiac diagnostic groups in ANOVAs**

Syndromes	cardiac diagnosis					main effects
	ASD (n = 18)	VSD (n = 43)	F4 (n = 31)	TGA (n = 44)	PS (n = 18)	
withdrawn	2.9	2.7	3.5	3.6	3.7	ns
somatic complaints	2.3	2.4	2.5	3.6	1.7	ns
anxious / depressed	4.3	4.1	4.9	5.0	5.0	ns
social problems	2.1	1.9	2.9	2.8	2.3	ns
thought problems	0.5	1.6	1.9	2.0	2.0	ns
attention problems	4.2	4.2	5.1	5.3	4.8	ns
delinquent behavior	2.8	2.8	2.5	3.2	3.0	ns
agressive behavior	6.6	7.1	7.0	9.0	6.5	ns
internalizing	9.5	9.1	10.9	12.2	10.4	ns
externalizing	9.4	9.9	9.5	12.2	9.5	ns
total problem score	29.8	31.1	35.0	38.8	35.0	ns

Diagnostic groups. The diagnostic groups in the YSR patient sample were as follows: ASD: N=18, mean age: 15.5 yrs.; VSD: N=43, mean age: 14.2 yrs.; F4: N=31, mean age: 14.0 yrs.; TGA: N=44, mean age: 13.6 yrs. and PS: N=18, mean age: 15.3 years. YSR results of 25 patients were excluded from the statistical analyses, since they belonged to the miscellaneous diagnostic group.

Table VI shows that no main effects for cardiac diagnosis were found in ANOVAs computed on mean problem scores, with cardiac diagnosis, sex and age as independent variables. No significant two- or three-way interactions were found.

Somatic complaints. To examine to what extent differences between problem scores for ConHD and reference groups could be attributed to problems concerning somatic functioning, AN(C)OVAs with group (patient versus reference group), sex and age as independent variables (and SES partialled out as covariate) were computed on scores based on items without somatic content. Items excluded from this analyses were: allergy (2), asthma (4), pains, headaches, nausea, problems with eyes, skin problems, stomach problems, vomiting, other physical problems without known medical cause (56a: aches or pains, 56b: headaches, 56c: nausea, feels sick, 56d: problems with eyes, 56e: rashes or other skin problems, 56f: stomaches or cramps, 56g: vomiting, throwing up, 56h: other (describe):..), dizziness (51), overtired (54), underactive (102). Constipation (item 49) was excluded only for the CBCL. Significant ($p<0.001$) differences between ConHd and reference subjects on both CBCL and YSR total problem scores were found, accounting for 3.9% and 4.7% of variance respectively. The differences between both groups were slightly smaller than differences found for scores including items on somatic functioning (decrease of 0.7% for CBCL and 0.8% for YSR scores).

Intellectual functioning. To investigate to what extent problem behaviors were related to intelligence levels, Pearson product moment correlations were computed between the CBCL and YSR total problem scores and the corresponding IQ-scores for the patient samples. IQ-scores were not available for 17 and 19 youngsters from the CBCL and YSR patient sample respectively; 7 and 5 patients from the CBCL and YSR patient sample respectively could not be tested during the psychological investigation due to mental retardation. The other patients did not complete the IQ-tests for other reasons; of these patients 4 and 5 youngsters from the CBL respectively YSR patient sample appeared to show borderline intellectual functioning since they (had) attended schools for special education. The mean IQ-scores were: CBCL patient sample (N= 127): x= 104.0, SD = 16.2; YSR patient sample (N= 160): x= 103.6, sd= 14.7. For the CBCL and YSR reference groups no mean IQ-scores were available. However, the reference groups consisted of general population samples, drawn with a random sampling procedure, and therefore it may be presumed that their distributions of IQ-scores were normally divided with mean IQ-scores of 100. For the CBCL patient sample a significant correlation between total problem scores and IQ-scores was found ($r= -.28$, $p<0.001$), indicating that high problem scores according to parents' reports were related to low IQ-scores. For the YSR patient sample no significant correlation between YSR total problem scores and IQ-scores was found.

Next, the difference was tested between mean CBCL total problem scores for the patient and reference group if patients whose IQ-scores were lower than 85 were excluded from the CBCL patient sample. An ANCOVA was computed, using the problem scores of 114 CBCLs of patients with IQ-scores of 85 and higher. This analysis showed a significant ($p<0.001$) difference in mean total problem scores for patients versus reference

children. The size of this difference (3.7% of variance) was slightly smaller than that of the earlier reported difference (4.6% of variance) found between the mean total problem scores for the reference group and the CBCL patient sample including patients with IQ-scores lower than 85.
To investigate whether the different types of ConHD were accompanied by lowered intellectual capacity, the mean IQ-scores for the different cardiac diagnostic groups from the CBCL patient sample were computed. The results were as follows (numbers of missing observations are presented between parentheses for each group): ASD: mean IQ= 97.6, SD=14.1, (1); VSD: mean IQ=106.0, SD=15.7, (4); F4: mean IQ=109.3, SD=18.0, (3); TGA: mean IQ=98.3, SD=11.8, (6); and PS: mean IQ=99.6, SD=26.3, (2). The percentages of CBCL patients with mental retardation or showing borderline intellectual functioning for each diagnostic group were: ASD: 25.0 (2 of 8); VSD: 9.3 (4 of 43); F4: 15.4 (4 of 26); TGA: 23.7 (9 of 38); and PS: 44.4 (4 of 9). It should be remembered that patients with Down's syndrome were not included in this study. An ANCOVA computed on the mean IQ-scores, with SES partialled out as covariate, showed no main effect for cardiac diagnosis.

DISCUSSION

The present study's results showed that both parents' reports and self-reports of problem behaviors indicated unfavorable outcomes for children and adolescents with ConHd: 27.1% of the CBCL total patient sample, and 20.7% of the YSR total patient sample scored in the deviant range. Scores in the deviant range reflect levels of problem behaviors similar to those of children and adolescents typically referred for mental health services. The proportion of 10-12 year old boys from the CBCL patient sample scoring in the deviant range, was not significantly different from the proportion of same-aged reference boys, scoring in the deviant range. The proportions of 15-17-year-olds of both sexes from the YSR patient sample, scoring in the deviant range, were not significantly different from those in the reference sample. In the present study a broad range of clinically relevant problem behaviors were assessed in a standardized way. Total problem scores and scores on the syndromes for both the CBCL and YSR showed small though significant group effects, indicating significantly more problems for ConHD-children and adolescents than for same sex peers in the reference groups. For CBCL Social Problems the group effect was medium. Only for CBCL Delinquent Behavior the difference found did not remain significant after correction for chance findings. Our results supported those found by Brandhagen et al. (1991) in their 25-year follow-up. They found that adult patients with various types of ConHD experienced more psychologic distress than subjects of a normative group, despite "success" as to educational achievement and occupational level. However, the results of their study are limited because of the low response rate (36.3%= 168 participants).
As can be read from tables II and V, the sizes of the differences between the mean scores on internalizing for the patient sample and the reference group on the CBCL and YSR (respectively 4.4% and 4.3% of variance accounted for) were somewhat larger than those on externalizing (respectively 1.0% and 2.6% accounted for). These findings that ConHD-patients showed more internalizing than externalizing problems can be attributed to the relatively small group effects on Delinquent and Aggressive Behavior. In a follow-up study with young ConHD-adults, Wright et al. (1985) reported low antisocial scores. However, their results are weakened by the fact that a non-standardized

questionnaire was used and the participation rate was low (44%). Some authors (Donovan, 1983; Garson & Baer, 1990) reported social isolation in ConHD-children and adolescents. Social isolation can occur as a result of physical incapacities, restricted leisure-time activities and parental overprotectiveness. The results of the present study showed a medium difference for Social Problems on the CBCL and a small difference on the YSR, indicating that ConHD-children and adolescents experience more problems in their relations with others than healthy peers.

The results of Kramer et al. (1989) showed increased feelings of anxiety in ConHD-children with limited physical capacity. In the present study significant, though small, group effects for Anxious/Depressed were found for both the CBCL and YSR, supporting the findings by Kramer et al. (1989). However, it is clear from our results that ConHD-patients' problem behaviors were not confined to only anxiety but covered a much wider range of problems.

AN(C)OVAs on the CBCL and YSR total problem scores showed no significant three-way interactions, indicating that the changes in problem scores with increase of age for ConHD-boys and girls were not significantly different from those for boys and girls from the reference group.

No significant differences were found in the level of parent reported or self-reported problem behaviors across the different diagnostic groups. Our results are in line with those of DeMaso et al. (1990)) and Brandhagen et al. (1991), who did not find a relationship between the type or severity of the cardiac defect, by itself, and poorer emotional adaptation in children and adults with ConHD. Further, our results showed that the higher CBCL and YSR total problem scores of ConHD-children and adolescents could only partly be explained by somatic complaints.

DeMaso et al. (1990) concluded that poorer overall psychological functioning of children with cyanotic ConHD was strongly associated with central nervous system and IQ impairments. However, in absence of these impairments positive emotional outcomes for most youngsters were found. Our results showed no significant differences in mean IQ-scores of the different cardiac diagnostic groups from the CBCL patient sample. Further, our results showed a negative correlation between problem behaviors reported by parents and intelligence levels of ConHD-children. A slight decrease (1.1%) in variance accounted for was found when CBCL problem scores of patients with IQ-scores lower than 85 were excluded from the CBCL patient sample. This decrease indicated that the higher mean CBCL total problem score of ConHD-children could be partly explained by the problem reporting of parents of children with IQ-scores < 85. However, when the CBCL patient sample was limited to children with IQ-scores above 85, there were still significantly more problems reported by parents of ConHD-children than by parents of the reference group.

From the CBCL and YSR total problem scores, internalizing and externalizing scores (see tables II and V), a trend could be inferred that ConHD-children and adolescents themselves reported more problems than their parents did about them. However, the CBCL and YSR patient samples consisted of subjects with different ages and therefore it was hazardous to compare their results. In order to test effects of different informants (parents versus children), MANOVAs with informant as the within factor were performed on the problem scores of 11-15-year-old patients (69 boys and 48 girls) with both a CBCL and YSR completed. Significant informant effects were found for total problem scores ($p<0.001$), internalizing ($p<0.05$) and externalizing problems ($p<0.001$), indicating

that on these measures more problems were reported by youths themselves than by their parents. A possible explanation for these results is that ConHD-adolescents tend to struggle with their problems for themselves, so that their problems become less visible to their parents. Our results are in line with those of Verhulst and van der Ende (1992), who found that 11-19-year-old adolescents from the general population reported many more problems on the YSR than their parents did about them on the CBCL.
In the present study ConHD-children and adolescents obtained higher total problem and syndrome scores than their healthy peers (except for CBCL Delinquent Behavior). The overall conclusions based on parents' reports were confirmed by those based on children's and adolescents' self-reports. The strengths of the present study were: the high response rate, the differentiation according to diagnostic groups, the use of normative reference groups and of psychometrically sound and valid assessment procedures.
Several authors (O'Dougherty et al., 1983; DeMaso et al., 1990) suggest that a number of factors may put ConHD-children at increased risk for developing later adjustment problems such as age of surgical repair, number of surgeries and hospitalizations, extracardiac anomalies and the quality of the parent-child interaction. Other important factors are: age at which the cardiac diagnosis was made, the duration and nature of hospitalizations, the presence or absence of growth retardation, interference with schooling and the emotional state of the parents, prior to and following surgery. To what extent factors such as these contributed to the problem behaviors described above could not be investigated since the necessary data were not yet systematically available. Another factor to be considered is the fact that during the years of follow-up the surgical techniques and medical treatment of cardiac conditions have been improved and they still continue to be improved. These improvements have been introduced gradually and not in a systematic or controlled way and no definite conclusions could be drawn as to their influence. Therefore, it is questionable whether it is possible to generalize the findings and conclusions of this study to children and adolescents with ConHD operated upon nowadays or in the future. Future research should take the factors mentioned above into consideration so that children who are at highest risk for later maladjustment can be identified and ameliorative strategies can be developed.

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CHAPTER 9

PSYCHOSOCIAL FUNCTIONING OF YOUNG ADULTS AFTER SURGICAL CORRECTION FOR CONGENITAL HEART DISEASE IN CHILDHOOD; A FOLLOW-UP STUDY

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ABSTRACT

To investigate long-term psychosocial outcome of congenital heart disease, the emotional, intellectual and social functioning of 288 (young) adult patients was assessed with standardized assessment procedures 9 to 23 years (mean follow-up interval: 16 years) after surgical correction for congenital heart disease in childhood, and compared with that of reference groups. With respect to emotional functioning: the patients reported significantly fewer feelings of hostility, fewer neurotic complaints and a better self-esteem than reference subjects. Overall, the results concerning social functioning showed favourable outcomes on daily activities (school, employment) and leisure-time activities for (young) adults with congenital heart disease. No significant differences were found between scores of different cardiac diagnostic groups on hostility, neuroticism, self-esteem and leisure-time activities.

The possibility whether the "denial"-mechanism might have contributed to the positive outcomes is discussed.

INTRODUCTION

Congenital heart disease may have an adverse impact on the psychosocial development of afflicted children[1,2]. The physical symptoms may include: growth retardation, delayed pubescence and physical incapacity. The emotional development may be hampered by parental attitudes, such as pampering and overprotection, and maternal anxiety. Physical incapacity may lead to diminished self-esteem and social isolation[3]. Although it has often been hypothesized that congenital heart disease may harm intellectual functioning due to hypoxemia, no consistent relationship between congenital heart disease and intellectual functioning has been found. Little is known about the long-term psychosocial effects of congenital heart disease in adulthood. The few follow-up studies conducted in this field have yielded contradictory results. Several investigators reported maladaptive psychosocial outcomes, such as neurotic symptoms, psychological stress, apprehensiveness, timidity, low venturesomeness, and atypical chest pain[4-7]. However, favourable outcomes such as successful social adaptation and good educational achievement have also been reported[5,7-9]. Several factors make it difficult to draw firm conclusions from existing studies, including small sample size, heterogeneous sample composition with respect to the type of congenital heart disease, low response rate, non-standardized assessment procedures and variation in methods across studies.

The present study is part of a follow-up concerning the long-term medical and psychological outcome in children, adolescents and young adults with operated congenital heart disease[10]. Psychosocial data of young adult patients, who underwent surgical repair of their cardiac defect during childhood, were compared with those of reference groups of the same age from the general population. For both patients and reference subjects the same standardized assessment instruments were used.
The aims of the study were: (1) to compare the emotional, intellectual and social functioning of young adults with operated congenital heart disease with that of reference groups (2) to determine the relationship between cardiac diagnosis and the emotional, intellectual and social functioning of the patients and (3) to determine the effects of sex and age on the level of emotional and intellectual functioning of the patients.

METHODS

Instruments. Emotional functioning. From the Dutch Personality Questionnaire (DPQ)[11], derived from the California Psychological Inventory[12], the scales Hostility (19 items), Self-Esteem (19 items) and Neuroticism (21 items) were used. Hostility measures criticism at and distrust of other persons. It was expected that young adult patients might become hostile to others because of experiences of failure in social contacts and anger about having a cardiac defect. Self-esteem measures a positive attitude towards work, flexibility and being energetic and self-controlled. This scale was chosen since diminished self-esteem in children with congenital heart disease has been reported[13]. Neuroticism measures vague somatic complaints and anxieties, depression and feelings of inadequacy. It was hypothesized that childhood psychosocial stresses might result in neurotic symptoms in adulthood. Besides, neurotic symptoms have been reported in young adults with congenital heart disease[7]. No specific anxiety or depression questionnaires were used in order to reduce the total amount of questions to be answered by the patient sample. The response possibilities of the DPQ are: yes = 2, do not know = 1, and no = 0. A high score on Self-Esteem indicates a high self-esteem. On the other scales, the higher the scores, the poorer the emotional adjustment.
The DPQ-Reference group consisted of 223 healthy males and 113 females, mean age 22.2 years[11]. No I.Q.-scores were available of this reference group, but it is assumed that persons with low intellectual functioning (I.Q.-scores < 86) were not included, since the average educational level was slightly above average.
Reliability and validity. Luteijn et al.[11] found the following alpha-coefficients in the reference group: Hostility (0.78), Self-Esteem (0.74), and Neuroticism (0.88). The one-week test-retest reliabilities in a sample of 85 healthy subjects were respectively: 0.84, 0.88 and 0.86. Hostility correlated positively (r = 0.62) with the scale "criticism of others" of the Minnesota Multiphasic Personality Inventory (MMPI)[14] in a sample of healthy subjects (N = 93), and negatively (r = -.40) with the Personal Relationships-scale of the Gordon Personal Inventory (GPI)[15,11]. Self-esteem correlated positively (r = 0.54) with the Barron Ego-Strength scale16 in a sample of 68 subjects, and also with a Dutch self-esteem scale (r = 0.70)[11]. The correlation between Neuroticism and a similar Dutch neuroticism scale[17] was r = 0.84 in a group of healthy subjects (N = 282) and r = 0.86 in a group of psychiatric patients (N = 101). Neuroticism correlated (r = 0.78) with the ZUNG depression scale in a group of psychiatric patients (N=84)[11,18].
Intellectual functioning. I.Q. was measured with the short form of the Groninger Intelligence Test (GIT)[19], a standardized Dutch Intelligence test. The GIT short form

consists of three subtests: Visualisation, Verbal Induction and Deduction, and Numbers.
Reference group. The GIT short-form was standardized on 440 males and 99 females. Ages were: 16-20 years, 4.5%; 21-30 years, 39.5%; 31-40 years, 49.5%; 41-49 years, 5.6%; and unknown, 1.0%[20]. In accordance with assumption of the normal distribution of intelligence, 16.5% of the reference group had I.Q.-scores of 85 or lower.
Reliability and validity. The alpha coefficients for the three subtests were respectively 0.75, 0.79, 0.85, and for the total IQ-score 0.87. The split-half reliabilties for the tree subtests were respectively 0.78, 0.79 and 0.96[19]. A high correlation was found between the total IQ-scores of the short form and the unabbreviated version (r=0.94, N= 1853 subjects)[20]. In a sample of 66 psychiatric and neurologic patients, a correlation of r=0.91 was found between the IQ-scores of the GIT and the Wechsler-Bellevue[21].
Social functioning: *biographical variables.* A structured interview was designed to assess biographical variables such as living conditions, daily activities, occupational and marital status.
Reference groups. Only for "living conditions" and "daily activities" normative data were available of respectively 269, 386, 1069, and 268, 386, 1068 reference subjects, aged respectively 18-20, 21-34 and 25-35 years[22].
Social functioning: leisure-time activities. These were assessed with 25 standardized, "yes/no"-items (see Table 3), derived from the Netherlands Central Bureau of Statistics[22].
Reference groups. For leisure-time activities normative data were derived from 344 and 441 males, aged respectively 18-24 and 25-34 years, and 331 and 429 females of respectively the same age categories[22]. Since the reference groups for biographical variables and leisure-time activities consisted of representative samples from the general population, probably persons with low intellectual functioning were included. Systematic data about the number of low I.Q.-persons in these reference groups are lacking.
Patient sample. A detailed description of the target population and follow-up sample is published elsewhere[10]. All consecutive patients who underwent their first open heart surgery for congenital heart disease between January 1, 1968 and January 1, 1980 in the University Hospital of Rotterdam, and who were younger than 15 years at the time of surgery, were eligible for follow-up. For the present study the lower age limit was 18. The present study sample consisted of 288 18-35-year-old patients (147 males and 141 females, mean age: 22.7 years). The tertiles as to the age-distribution of the patients were as follows: 37.8% (N= 109) was 18-20, 29.2% (N= 84) was 21-24 and 33.0% (N= 95) was 25-35 years old. The response rate, corrected for deceased patients and persons lost to follow-up, was 85.7%; 48 patients had refused to participate. The medical status: of the 288 participants, 1 patient had Down's syndrome, 1 Turner's syndrome, 1 Marfan's syndrome, and 1 had Reifenstein's syndrome, 1 suffered from the VACTER-association, 3 had a hemiparesis, 3 suffered from renal insufficiency, 1 had unspecified neurological abnormalities, 22 had other extracardiac anomalies, 1 had both a hemiparesis and another extracardiac anomaly, and 2 had renal insufficiency in combination with another extracardiac anomaly. The study sample includes only one patient with Down's syndrome since it was the general policy of the cardiac unit not to operate on such patients before 1980.
Assessment procedure. Patients were interviewed and tested by a clinical psychologist (E.U.), who was blind to their cardiac diagnosis. Patients with low intellectual functioning were verbally questioned, if possible.
Thirty patients preferred to complete a questionnaire-booklet at home. In these cases

intelligence tests could not be performed and structured interviews were done by telephone. In the tables the total numbers answering each question(naire) are indicated.
Statistical analyses. 95% Confidence intervals (C.I.). For the DPQ and GIT 95% confidence intervals around group means were calculated. If the 95% confidence interval around a mean scale score of the patient sample did not overlap that of the reference group, the difference between the group means were considered statistically significant[23]. As to biographical variables, for each tertile of the patient sample and for each one of the corresponding reference groups, the percentages of subjects scoring on any one item concerning living conditions and daily activities were computed. If the 95% confidence interval around a proportion on an item of the patient sample did not overlap that of a corresponding reference group, the difference between the proportions was considered statistically significant[23]. As to leisure-time activities, for each item 95% confidence intervals were computed for each sex and both age groups on the proportion of "yes"-respondents.
Cohen's D. For the DPQ and GIT, Cohen's D's[24] were computed to assess the magnitude of differences in mean scores between the patient sample and the reference groups. According to Cohen's[24] criteria a standardized difference of 0.20 is considered small, 0.50 medium, and 0.80 high.

RESULTS
Emotional functioning: DPQ-results. The patient sample obtained significantly more favourable results than the reference group on Hostility, Self-Esteem and Neuroticism (see table 1)[23]. The differences in mean scores were considered medium[24].
Of the 278 patients who completed the DPQ, 29 patients had I.Q.-scores below 86 and 25 patients completed it at home. Since it was assumed that the DPQ-reference group did not contain any low I.Q.-persons, we computed DPQ-scores for the patient sample after excluding low I.Q-patients (I.Q.< 86) and patients who completed the DPQ at home (DPQ-EX.). The results of the DPQ-EX. group were only slightly different from those of the original 278 patient-respondents (see table I). The DPQ-EX. group also obtained significantly more favourable results than the reference group on Hostility, Self-Esteem and Neuroticism[23].
Intellectual functioning: GIT-results. As is shown in table I, the patient-sample obtained a significantly higher GIT I.Q.-score than its reference group[23] 242 Patients completed the GIT; 29 of them obtained I.Q.-scores below 86. For 46 patients I.Q.-scores are missing: the test could not be completed by 15 mentally retarded patients and one person of the Turkish nationality due to language problems. Of the remaining 30 patients (see assessment procedure), 5 showed borderline mental functioning (I.Q.-scores between 70-85), which was deduced from the type of school of special education they had attended. Of the total patient sample (N = 288), 49 (17%) showed borderline mental functioning or mental retardation (i.e. I.Q.-scores below 86).
Social functioning: biographical variables. The majority (84%) of the patient sample attended school or had a job; 1.7% received a disability pension due to their congenital heart disease, and 3.8% worked in a special labour institution (see table II). The "other" category contains two patients who were severely handicapped both physically and mentally, and one patient who was in the process of emigrating. The occupational status of persons with a job was scored on a 6-step scale[25]. Of the persons with a part-time job, 81.3% indicated that this was unrelated to their heart defect. 92.8% Of 166

Table I **Mean scores, standard deviations, Cohen's D and 95% confidence intervals on the DPQ[a] and GIT[b] for the patient sample and reference groups and the DPQ-EX.[c] group**

DPQ[a]	Patients (n = 278) x	SD	Refer. (n = 336) x	SD	Cohen's D	Confid. interv. (95%) Patients	
Reference							
Hostility	14.4	6.7	18.5	7.1	0.6	13.6; 15.2	17.7; 19.3
Self-esteem	30.3	5.2	26.4	6.2	0.6	29.7; 30.9	25.7; 27.1
Neuroticism	8.2	7.2	14.4	9.7	0.6	7.3; 9.1	13.1; 15.1
DPQ-EX.[c]	Patients (n = 224) x	SD			Cohen's D	Confid. interv. (95%) DPQ-EX.[c]	
Reference							
Hostility	14.2	6.7			0.6	13.4; 15.1	
Self-esteem	30.4	5.4			0.6	29.7; 31.1	
Neuroticism	8.1	7.3			0.6	7.1; 9.1	
GIT[b]	Patients (n = 242) x	SD	Refer. (n = 539) x	SD	Cohen's D	Confid. interv. (95%) Patients	
IQ-score	105.5	15.3	100	15	0.4	104; 107	98.7; 101

[a]Dutch Personality Questionnaires (Luteijn et al., 1975)
[b]Groninger Intelligence Test (Kooreman & Luteijn, 1987)
[c]DPQ-EX.: DPQ-results of patients after exclusion of mailed questionnaire data and data of mentally retarded patients

respondents considered their career prospects to be normal. 21-24-Year-old patients more often received a disability pension than their reference peers (patients: 3.6%, C.I.:0.01-0.10; Reference: 0%, C.I.: 0.0-0.01).; no further significant differences on daily activities were found. Results on living conditions (see table III) show that 18-20-year-old patients less often lived on their own than their reference peers. Twenty-five to 35-year-old patients more often lived with their parents and less often lived on their own than their peers from the general population.

In table IV results on leisure-time activities are shown for both sexes from the patient sample and reference group, according to two age groups (18-24 and 25-34 years). Only significant differences between results of the patient sample and reference group are presented. As for males, the younger patients (18-24 years) appeared to make handicrafts more often, and to visit sports and watch T.V. less often than did their reference peers. The older male patients (25-34 years) reported to visit clubs and to go shopping more often than did their reference peers, whereas the last persons reported to listen to the radio more frequently. With regard to females, the younger patients appeared to do brain-teasers, to play games and to visit clubs more often than their female reference peers. The older female patients reported to visit clubs, to visit discos and to go shopping more often than female reference peers. No further significant differences on leisure-time activities were found between the patient sample and reference group.

Diagnostic groups. As is shown in table V, the patient sample was divided in five cardiac diagnostic groups. Results of a miscellaneous diagnostic group, consisting of

Table II **Results as to biographical variables for the patient sample**

Total patient sample: n = 288	n	%
Marital status	**288**	**(100.0)**
no relationship	128	(44.4)
stable relationship	72	(25.0)
cohabitant	34	(11.8)
married	53	(18.4)
divorced	1	(0.4)
Offspring of adult patients	**288**	**(100.0)**
0 children	255	(88.5)
1 child	19	(6.6)
2 children	12	(4.2)
3 children	1	(0.4)
4 children	1	(0.4)
Daily activities	**288**	**(100.0)**
attending school	80	(27.7)
job	162	(56.3)
unemployed	8	(2.8)
disablement pension	5	(1.7)
volunteer, unpaid work	2	(0.7)
household	17	(5.9)
labour institution for mentally handicapped	11	(3.8)
other	3	(1.0)
Occupational status of persons with paid work (persons in labour institutions included)	**173**	**(100.0)**
1. unskilled employees	22	(12.7)
2. skilled manual employees	39	(22.5)
3. clericals, minor professionals, technicians	84	(48.6)
4. owners of small businesses	3	(1.7)
5. supervisory, lesser professionals	20	(11.6)
6. executives, major professionals	5	(2.9)
Part-time workers	**32**	**(100.0)**
Reason part-time function		
- unrelated to heart disease	26	(81.3)
- heart disease one of several reasons	4	(12.5)
- heart disease the only reason	2	(6.3)
Sick-leave from work previous year	**172**	**(100.0)**
mean number of days	11.2	
Sick-leave according to patients	**170**	**(100.0)**
less than colleagues	91	(53.5)
equal to colleagues	59	(34.7)
more than colleagues	20	(11.8)
Reaseon sick-leave	**129**	**(100.0)**
unrelated to heart disease	117	(90.7)
heart disease one of several reasons	7	(5.5)
heart disease the only reason	5	(3.9)
Perception of carreer possibilities	**166**	**(100.0)**
normal	154	(92.8)
less compared to others	12	(7.2)

Table III **Living conditions for the patient sample and reference groups, with age-categories according to the tertiles of the patient sample**

Patient sample	Age 18-20 years (n = 109)	Age 21-24 years (n = 84)	Age 25-35 years (n = 95)
Living conditions	% (C.I.)	% (C.I.)	% (C.I.)
with parents	90.8 (0.84/0.96)	48.8 (0.38/0.60)	17.9 (0.11/0.27)
on one's own	7.3 (0.03/0.14)	51.2 (0.40/0.62)	82.1 (0.73/0.89)
in institution for mentally handicapped	1.8 (0.00/0.07)	0.0 (0.00/0.04)	0.0 (0.00/0.04)
Reference group	(n = 269)	(n = 386)	(n = 1069)
Living conditions	% (C.I.)	% (C.I.)	% (C.I.)
with parents	79.9 (0.75/0.85)	35.0 (0.30/0.40)	5.9 (0.05/0.08)
on one's own	18.2 (0.14/0.23)	63.5 (0.59/0.68)	93.0 (0.91/0.94)
in institution for mentally handicapped[1]	- (-/-)	- (-/-)	- (-/-)
other	1.9 (0.01/0.04)	1.6 (0.01/0.03)	1.1 (0.01/0.02)

[1]No normative data available on this item
C.I. = 95% Confidence Interval

small numbers of patients with varying congential heart defects were excluded from statistical analyses according to cardiac diagnoses. The 95% confidence intervals showed no significant differences between the diagnostic groups on emotional and social functioning (i.c. the DPQ-scales and leisure-time activities). However, on intellectual functioning the patients with pulmonary stenosis (PS) scored significantly better than patients with Tetralogy of Fallot (F4) (PS: mean I.Q.= 110.0, C.I.: 105-116; F4: mean I.Q.= 98.8, C.I.: 93.6-104). No further significant differences were found between diagnostic groups as to intellectual functioning.

Sex and age effects. Sex and age effects on the emotional and intellectual functioning of the patients were computed on the DPQ-scales and the GIT I.Q.-score. As for sex effects, females reported significantly more complaints on DPQ-Neuroticism (DPQ-N) than males (females: mean DPQ-N= 9.7, C.I.: 8.4-11.0; males: mean DPQ-N= 6.8, C.I.: 5.6-7.9). No further significant sex effects were found. To assess age effects, two categories (18-22 and 23-35 years) were formed based on the median split of the patient sample. The only significant age effect was found on the GIT I.Q.-score: the older persons obtained a significantly better score than the younger ones (respectively: mean I.Q.= 108.4, C.I.: 106-111 and mean I.Q.= 102.8, C.I.: 100-106). Next, on all DPQ-scales and on the GIT I.Q.-score sex and age effects were tested when adjusted to diagnostic category, since the numbers of male versus female and younger versus older patients differed across diagnostic categories. For each diagnostic category, 95%

Table IV **Significant differences between the percentages of the patient sample and reference groups performing leisure-time activities, presented for both sexes and both age-categories**

	18-24 years				25-34 years			
	males		females		males		females	
	patients (n = 93)	references (n = 344)	patients (n = 93)	references (n = 331)	patients (n = 49)	references (n = 441)	patients (n = 44)	references (n = 429)
Item	% (C.I.)	% (C.I.)	% (C.I.)	% (C.I.)	% (C.I.)	% (C.I.)	% (C.I.)	% (C.I.)
Visiting sports	40[1] (0.30/0.51)	63 (0.58/0.68)						
Brain-teasers			41 (0.31/0.52)	20 (0.16/0.24)				
Handicrafts	48 (0.38/0.59)	33 (0.28/0.38)						
Playing games			89 (0.81/0.95)	75 (0.70/0.80)				
Visiting clubs			53 (0.42/0.63)	36 (0.31/0.41)	57 (0.42/0.71)	32 (0.28/0.36)	55 (0.39/0.70)	26 (0.22/0.30)
Visiting discos							46 (0.30/0.61)	25 (0.21/0.29)
Listening radio					82 (0.68/0.91)	94 (0.92/0.96)		
Watching TV	91 (0.84/0.96)	99 (0.98/1.00)						
Shopping					80 (0.66/0.90)	54 (0.49/0.59)	100 (0.92/1.00)	83 (0.79/0.87)

[1]= 1 missing observation; C.I. = 95% confidence interval. No siginificant differences were found on the following 16 items nor reported in the table: swimming, another water sport, practising a sport, theatre, movies, making music/acting, odd jobs, collecting things, walking/cycling, watching video films, personal computer, listening music, reading, visiting a community center, visiting (snack)bars, going to the beach.

Table V **Distribution of the patient sample according to cardiac diagnosis**

Diagnosis	n	mean age (years)
Atrial septal II defect (ASD)	91	22.9
Ventricular septal defect (VSD)	67	22.5
Tetralogy of Fallot (F4)	52	22.4
Transposition of the great arteries (TGA)	15	21.1
Pulmonary stenosis (PS)	29	23.5
Miscellaneous group(Misc.)	34	22.7

confidence intervals around the mean scores on the DPQ-scales and GIT I.Q.-score of male versus female and younger versus older patients were compared. Then, no significant sex or age effects were found.

DISCUSSION

In the present study young adults operated upon for congenital heart disease obtained better scores on emotional functioning (hostility, neurotic symptoms and self-esteem) than their reference peers. The findings on intellectual functioning were difficult to interpret due to missing data, which will be discussed below. Overall, the results on social functioning showed favourable outcomes for the patients. No significant differences were found between the patient sample and reference groups in the proportions of subjects who attended school, had a job, or were unemployed. The only difference found on daily activities was that more 21-to-24-year-old patients received a disability pension than same-aged subjects in the reference group. The 18-to-20 and 25-to-35-year-old patients lived on their own less frequently than the same-aged reference subjects. Leisure-time activities indicated that the patients were well adjusted.

Emotional functioning. Our favourable results on emotional functioning contrast with those of Otterstad et al.[6] and Brandhagen et al.[7], who reported neurotic symptoms in adults with congenital heart disease. A limitation in the study of Otterstad et al.[6] was the use of an unstandardized questionnaire. The assessment instruments used by Brandhagen et al.[7] were adequate, but measured different psychological dimensions than the ones used in our study such as dependency, somatization, anxiety, depression and interpersonal sensitivity. Brandhagen et al.[7] also measured hostility, but found that the scores of their patients deviated significantly from the normative data. However, the hostility scale used in their study was different from ours. Further, the response rate in Brandhagen et al.'s[7] study was only 36.3%.

In an earlier study we found that the 10-18-year-old children and adolescents of our follow-up showed more behavourial and emotional problems than healthy peers from normative reference groups, according to parents' reports and self-reports[10]. These results are not in line with the positive results on emotional functioning in the present study. The contrasting findings may indicate that childhood emotional problems do not persist into adulthood. However, it is difficult to compare the emotional functioning of the children to that of the young adults of our follow-up, since different instruments, the Child Behavior Checklist and Youth Self-Report (CBCL and YSR)[26] were used for the children to assess emotional problems. A possible explanation for the contrasting results

may be that the CBCL and YSR contain items reflecting concrete behavourial and emotional problems such as: I act too young for my age, argue a lot, or destroy my things, whereas the DPQ focusses on a person's own perceptions and experiences. An explanation for the positive outcomes on emotional functioning might be that once the cardiac surgery and hospitalizations are in the past, the adult patients strive hard to obtain a normal life and do not worry about minor difficulties of life, after having survived life threatening surgery. Such an attitude may result in a good social adjustment.
The patients of the present study reported a better self-esteem than subjects from the reference group. Kellerman et al.[27] found no difference in self-esteem between adolescents with chronic diseases and their healthy peers. They speculated that the overall pattern of psychological normalcy they found for adolescents with various chronic diseases could be attributed, partially, to high levels of denial of their disease. Denial is a mechanism also well-known to occur in patients with coronary heart disease[28,29]. Patients can manifest the denial of illness in a variety of ways, from the most extreme form of denying the illness outrightly to a variety of less extreme disavowing behaviors, such as minimizing their emotional distress[29]. We assume that the positive outcomes on emotional functioning found in the present study could also be explained by denial. Furthermore, it can be speculated that the better emotional functioning points into the direction of the assumption of denial, considering the fact that the 18 to 20- and 25 to 35-year-old patients lived on their own less frequently than their same-aged reference subjects. Finally, this assumption is supported by the clinical impression that many patients in our sample reported that they were very achievement-oriented to prove that they were "no less than anybody else". More than half of the patients reported (proudly) that they worked harder and were less absent from work through illness than colleagues. These clinical impressions are in line with the reasoning of Brandhagen et al[7], who explained their finding that adults with congenital heart disease reported neurotic symptoms despite occupational success, by the possibility that the patients were "high achievers".
Intellectual functioning. In their follow-up of adults with ventricular septal defects Otterstad et al.[6] found a generally (high) normal intellectual function, as reflected by a high educational level compared with normal ones. However, in their study no I.Q.-tests were performed. In the present study the adult patients obtained a significantly better mean I.Q.-score than the reference group. Of our total patient sample 17% showed a borderline mental functioning or was mentally retarded, whereas in the reference group 16.5% had I.Q.-scores of 85 or lower. However, our favourable results should be interpreted with great caution since the I.Q.-scores of 46 persons were missing. Furthermore, apart from one exception, patients with Down's syndrome were not included in this study. (Down's syndrome is well known to be associated with congenital heart disease). Probably this has caused a bias in the results as to intellectual functioning in the positive direction.
Social functioning: biographical variables. The present study's results confirm those of Wright et al.,[9] who found that young adults with congenital heart disease were socially well adjusted and capable of productive lives. However, in their study the response rate was low (44%= 188 participants) and a non-standardized questionnaire was used. Our results also correspond with those of Brandhagen et al.,[7] who found "successful" levels of educational and occupational achievement in a 25-year follow-up with adult congenital heart disease patients. Ghisla et al.[8] found in a follow-up that 8% of their patients with

tetralogy of Fallot were not active in the work force. Seventy-two percent of the patients considered their educational and occupational prospects to be normal. Our results indicated a more favourable functioning since 92.8% of our sample considered carreer prospects as normal. However, the study methods of Ghisla et al.[8] differed from ours, since they used a very small sample of Fallot patients and unstandardized telephone interviews. Besides, due to differences between the social systems and labour markets in Switzerland and the Netherlands, opportunities to get a job in these countries may be different for adults with congenital heart disease.

Our results on living conditions showed that the 18 to 20- and 25 to 35-year-old patients lived on their own less frequently than their same-aged reference subjects. Our results correspond with those of Kokkonen and Paavilainen,[30] who reported that more young adults with congenital heart disease were single and lived with their parents compared with randomly selected age-mates. Their follow-up contained methodological flaws such as the use of unstandardized assessment procedures and a heterogeneous patient sample, containing both operated and unoperated patients. According to Kokkonen and Paavilainen[30], the home-based life style was not correlated to the degree of disability, but could be attributed to parental overprotection. The relatively large proportion of patients in our sample living with their parents and having no sexual relationship may also be attributed to parental attitudes, such as pampering and overprotection.

Social functioning: leisure-time activities. Regarding leisure-time activities, most differences found between the patient sample and the reference groups showed positive outcomes for the patient sample. According to Garson and Baer[2] adolescents with congenital heart disease reported limitations in leisure-time activities. On the whole, our results showed no evidence for such limitations.

Diagnostic groups. In the present study, no significant differences were found between the results of separate diagnostic groups on emotional and social functioning (i.c. leisure-time activities). Our results are in line with those of DeMaso et al.[31] and Brandhagen et al.,[7] who did not find a relationship between the type or severity of the cardiac defect and the emotional adaptation in children and adults with congenital heart disease. Our follow-up of 10-18-year-old children with congenital heart disease showed neither significant differences between different diagnostic groups in the level of parent reported nor self-reported problem behaviours[10]. It is stressed that, although the results of these studies concerning the emotional outcome were contradictory and study methods differed across studies, in none of these studies a consistent relationship between emotional functioning and cardiac diagnosis was found.

The results on intellectual functioning of the different diagnostic groups may be biased due to missing observations.

Sex and age effects. The female patients of this study reported significantly more neurotic complaints than the male patients. Zeltzer et al.[32] found that females with chronic diseases (females with congenital heart disease included) reported more impact on their physical appearance than males. However, when adjusted for diagnostic category the significant sex effect in the present study for neurotic complaints disappeared.

The strengths of our follow-up were: the large sample size, the use of standardized assessment instruments for which data of reference groups were available, and the differentiation in statistical analyses between cardiac diagnostic groups.

In our opinion, the favourable outcomes as to emotional and social functioning cannot be attributed to sample bias (i.e. that patients with a higher social status or a better

psychological functioning were selected for surgery). Except for the exclusion of Down patients, no selection took place. Our patient sample consisted of a consecutive, unselected series of patients who had consistently been subjected to surgery on the basis of medical criteria. Besides, the social system of health insurances in the Netherlands makes open heart surgery available to patients of all socio-economic classes.
In the present study mentally retarded patients were included and some questionnaire data were gathered by mail. Therefore, we investigated the possible influence of these factors on the results regarding emotional functioning. When the DPQ-data were reanalyzed after the exclusion of patients with I.Q.-scores lower than 86 and patients who completed the DPQ at home, the results of the patient sample were still significantly more favourable than those of the reference groups, which can be considered very positive.
In literature[31,33] it has been reported that a number of factors may put children with congenital heart disease at an increased risk of developing later adjustment problems such as: age at surgical repair, time since surgery, and number of surgeries and hospitalizations. In this follow-up the influence of these factors and of the present health status on the psychosocial functioning of the patient sample could not be investigated since the necessary information was lacking. To what extent the patient sample differed from the reference-groups in terms of physical health could neither be investigated, due to lacking data. Future research should take these factors into consideration to identify adult patients who will show better or worse psychosocial outcomes. Finally, future research should include measures to investigate to what extent denial contributes to positive psychosocial outcomes for adults with congenital heart disease.
Conclusion. In this study, young adults with congenital heart disease reported a better emotional functioning than subjects from the reference group. Results regarding intellectual functioning were difficult to interpret due to missing data. Favourable outcomes were found for the young adult patients regarding social functioning (school, employment and leisure-time activities).

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CHAPTER 10

GENERAL DISCUSSION

One of the pioneers in the field of long-term care for patients who underwent cardiac surgery for congenital heart disease, Joseph K.Perloff, stated in 1973 in his article "Pediatric congenital becomes a postoperative adult; the changing population of congenital heart disease"[1] :"whether we are dealing with correction of congenital cardiac defects or developing rockets to the moon, we must not let the brilliant glare of technologic success obscure our long-term objective to promote the quality of life". He stressed the fact that in the important field of follow-up after cardiac surgery "more is unknown than known". Barry J.Maron remarked in 1977 that "limited attention has been focused on the ultimate fate of patients many years after their apparently successful operations." In 1987, in the chapter "The fate of survivors of surgery for congenital heart disease" in the first edition of the textbook on Pediatric Cardiology edited by Anderson, Macartney and Tynan, is stated: "Cardiac surgery was born of hope and thrived on the tide of enthusiasm which flooded from the recognition that all but the most severe defects were amenable to surgical repair. The last thirty years have been like a breathless tour of the Himalaya's, with one 'last great problem' after another succumbing to the surgeon's knife. Now we must address the irritating question of what has been achieved. What kind of life can be offered to these blue and breathless mites, snatched from the jaws of death." It was emphasized that, even after 30 years, there were very few long-term follow-up studies which could provide data on this subject. In 1988 J.Stark mentioned in his famous lecture "Do we really correct congenital heart defects?" that only 4 follow-up studies had been published with a duration of follow-up of more than 8 years in the leading journal in the field of cardiac surgery in the preceding two years. What is the reason that, although the necessity to acquire more information about the fate of survivors of surgery for congenital heart disease was so obvious, there have been so few comprehensive follow-up studies.

There are a few circumstances that explain this. Prospective follow-up studies, the best (although very slow) way for systematic evaluation of the results of any kind of treatment, were not conducted. This might be explained by lack of manpower: the number of staff members in departments of Pediatric Cardiology and Cardiac Surgery until the 1970's was in general very small according to modern standards. Most physicians were simply too busy doing their actual (short-term) job to be able to do meticulous long-term follow-up of all operated patients. Another probable explanation is that there was a tremendous optimism about the outlook for these patients. Compared with what the outlook should have been without surgery, something that most physicians remembered only too well, the outlook for patients, once operated, was incomparably much better. It must have felt as a kind of blasphemy to question whether the achieved result was actually good enough. Accordingly, many patients were discharged from routine outpatient check-up when there were no symptoms or obvious sequelae.

When the years went by, the euphoria of the early years gradually wore out when more and more patients who had undergone supposedly "corrective" surgery developed symptoms. This created a new problem. As long patients were still children, a pediatric cardiologist would take care, but who would take over the responsibility for these patients when they outgrew the pediatric age group? Adult cardiologists are generally trained in

acquired, not in congenital heart disease and pediatric cardiologists are in general not trained to deal with adult patients, and coping with problems specific for adults. Some recognized this dilemma early and became the pioneers of a new subspeciality: congenital heart disease in adults, or grown-ups with congenital heart disease (GUCH). The example was set in Toronto, where the first specialized medical facility for the care of adults with congenital heart disease was started in the 1960's. Dr. Jane Somerville, who would become one of the most ardent advocates of specialized care for this patients group, developed a similar facility in the National Heart Hospital in London in 1975. Joseph K.Perloff and John S.Child started the Adult Congenital Heart Center in Los Angeles in 1978. A few more centers followed, but not many. A recent survey among members of the Association of European Pediatric Cardiologists (AEPC) confirmed that there were fewer than 10 centers in Europe in which there was a well organized adult congenital heart disease unit with all hospital and outpatient facilities. One of these centers is the Sophia Children's Hospital/Dijkzigt Hospital in Rotterdam. Patient care would benefit by more of these centers, but not too many. Although a growing population, the GUCH-group still comprises relatively few patients, and dilution of facilities by too many centers would lead to dissipation of experience, which is not in the patient's interest[3].

Concentration of care for all patients with congenital heart disease, explicitly including GUCH, was a matter of debate in The Netherlands in the past few years. Both the Dutch Health Council and the professional groups (cardiac surgeons, pediatric cardiologists and adult cardiologists) recognized the need for concentration. Because, as dr.Somerville stated in the lecture "The problem-an overview" during the First International Symposium on Congenital Heart Disease in Adolescents and Adults in Rotterdam in May 1990: "the welfare and the needs of the patient (not status and wishes of individuals, physicians or organizations) must be first consideration", this centralization will hopefully take place in the coming years.

One of the major problems in the GUCH group - late symptoms and sequelae that will have to be detected and treated - will be managed optimally by good quality, centralized care. Other important problems of this patient group, which cannot be solved by the medical profession (alone), are the uncertain employment prospects and poor insurability of patients after cardiac surgery for congenital heart disease. This might be understandable for patients with evident symptoms, such as decreased exercise capacity or symptomatic arrhythmia, but is hard to accept for patients who feel healthy. Because there is an understandable lag between medical developments and acceptance of their impact on late survival, follow-up studies are needed which can provide data on the prevalence and clinical relevance of sequelae. These data would be of value not only for patients and physicians, but also for occupational health advisors and medical advisors of insurance companies. However, apart from the earlier mentioned lack of prospective follow-up studies, there are also amazingly few retrospective follow-up studies of nonselected series of patients who were actually examined at follow-up. There are several studies in which follow-up data were acquired by means of telephonic interviews or written interviews with the patients or their relatives[4-7], but since patients were not examined, many sequelae will have remained undetected. A positive exception in this respect was the large American multi-center study, the Joint Study on the Natural History Study of Congenital Heart Defects, of which the first report was published in 1977[8] and the second in 1993[9]. Apart from these data, confined to the long-term health

status of patients with ventricular septal defect, aortic stenosis and pulmonary stenosis, it is difficult to find information on the health status of patients operated upon for any type of congenital cardiac malformation. It was the lack of this kind of information that prompted the initiation of the follow-up study of which the results are presented in this thesis. This follow-up study focused both on the medical and the psychological aspects long-term after surgery.

The most important conclusions from the medical part of the study were that survival was good in all diagnosis groups except in the Mustard group, that personal health assessment was similar to that of the normal population, that exercise capacity was normal in a large majority of the patients, and that the proportion of symptomatic patients - with substantially decreased exercise capacity or symptomatic arrhythmia - was small. However, the high prevalence of arrhythmia and severe right ventricular dilatation, present throughout the entire study population, was reason for concern for the future.

What is the clinical significance of the arrhythmias? This is clear for the small minority of symptomatic arrhythmias: these represent a definite pathological condition and even with treatment these arrhythmia remain potentially life-threatening. The key question is: what is the significance of asymptomatic arrhythmias? Does ventricular arrhythmia represent damage of the myocardium, such as scarring and loss of electrophysiologic integrity? Do the supraventricular arrhythmia, which we defined as signs of sinus node dysfunction on the basis of the criteria as proposed by Kugler[10], indeed represent damage to the sinus node, or are these criteria too unspecific and did we overestimate the prevalence of sinus node dysfunction? Longer follow-up will reveal whether or not these asymptomatic arrhythmia are predictors of symptomatic arrhythmia later.

Right ventricular dilatation definitely reflects a pathological situation. Although it seemed to be tolerated fairly well for the duration of follow-up of this study, there was an association with decreased exercise capacity, in particular in the group of patients after surgical repair of tetralogy of Fallot. Therefore, concern remains whether longer duration of severe dilatation will not unavoidably lead to right ventricular failure. Longer follow-up of these patients will be mandatory to assess right ventricular function. For this, a diagnostic tool to assess right ventricular size reliably and, ideally, predict impending right ventricular failure would be of enormous value.

The most important outcome of the psychological part of the study was that, irrespective of the cardiac diagnosis, many children and adolescents had social problems, attention problems at school and complaints of anxiety and depressions. In contrast, adult patients compared favourably with a reference group in terms of daily activities, in leisure-time activities and emotional functioning. An effective denial mechanism is the probable explanation for this positive outcome, possibly in combination with the fact that most patients were very achievement-oriented to prove that they were "no less than anybody else". Another important outcome was that, in contrast to American and British reports on employability[11,12] the participation in the professional life of these patients was normal. The ability to participate fully in both professional and social life will be of great value for patient's quality of life.

In conclusion, this study definitely contributed new information on the health status of patients after surgical repair of congenital heart disease. These data could provide a basis for protocols and guidelines for insurance doctors and occupational physicians in the difficult process of judging employability and insurability of this group of patients.

In addition, this study confirms that the interpretation and treatment of the problems

encountered in this patient group requires specific knowledge. The care for these patients should be concentrated in specialized centers for grown-ups with congenital heart disease, with doctors specially trained in this difficult field. Only then can good patient care be achieved.
Many questions remain unanswered or are raised by this study. This emphasises the need for further research on the long-term outlook of these patients.

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CHAPTER 11

SUMMARY & SAMENVATTING

SUMMARY

Cardiac surgery has improved the outlook for patients with congenital heart disease tremendously. Instead of a mortality of 85% before the adult age was reached, survival has now become 85%. However, little is known about the morbidity in the entire group of long-term survivors. This was the reason to start this follow-up study.

Chapter 1 gives an overview of the history of cardiac surgery and how it changed the natural history of congenital heart disease. The aim of this follow-up study is explained: to evaluate both health status and subjective wellbeing of the total group of patients who underwent open heart surgery in our institution between 1968 and 1980 for one of the 5 most common congenital cardiac malformations, and who were younger than 15 years of age at the time of the operation. These cardiac malformations are atrial septal defect, ventricular septal defect, tetralogy of Fallot, transposition of the great arteries and pulmonary stenosis. The study population, methods and follow-up procedure are described. This study differs from almost all other follow-up studies, because in this study a very high percentage of all patients eligible for follow-up were thoroughly examined at follow-up, which enabled assessment of the health status of the entire group.

Chapter 2 contains the long-term results of surgical repair of atrial septal defect in 135 consecutively operated patients. Mean age at the time of the operation was 7.5 ± 3.5 years. None had died and 104 participated in the follow-up study. Age at follow-up was 21.8 ± 4.8 years. The current health status was assessed by means of extensive examination, which consisted of an interview, physical examination, echocardiography, exercise test and both a standard 12-lead and a 24 hour electrocardiogram. Pulmonary hypertension, which is the main risk factor for premature death in these patients, was not present in any of the patients at follow-up. Both exercise capacity and personal health assessment were as good as that of the normal Dutch population. Common sequelae were persisting right ventricular dilatation (26% of the patients) and arrhythmia (67% of the patients). Of these, 6 patients (6%) had symptomatic arrhythmia and needed antiarrhythmic medication.

Chapter 3 deals with the long-term results of surgical closure of ventricular septal defect in 176 consecutively operated patients. Age at the time of the operation was 4.1 ± 4.0 years. Before the start of the follow-up study 23 patients (13%) had died. Pulmonary hypertension, which is the main risk factor for untimely death in these patients, was completely absent in the group of 109 patients who participated in the follow-up study. Mean age at the time of the follow-up study was 18.9 ± 5.7 years. Personal health assessment and exercise capacity were similar to that of the normal Dutch population. Hemodynamically insignificant sequelae at the left side of the heart were common (43%), as were asymptomatic arrhythmia (50%). None of the patients had symptomatic arrhythmia.

Chapter 4 gives an overview of the health status long-term after surgical repair of tetralogy of Fallot in infancy or childhood. Mean age at the time of the operation was 4.7 ± 3.4 years. Of 142 consecutively operated patients, 27 (19%) had died before the start of the follow-up study and 77 (69%) participated in the follow-up study. Age at the

time of the follow-up study was 19.0 ± 5.5 years. Due to the frequent use of a transannular patch for the relief of right ventricular outflow tract obstruction (in 56% of the patients), the prevalence of elevated right ventricular systolic pressure was low (8%), but the prevalence of substantial right ventricular dilatation with severe pulmonary regurgitation high (58%). The exercise capacity of patients with a substantially dilated right ventricle proved to be significantly lower (83 ± 19% of predicted) than that of patients with a near normal sized right ventricle (96 ± 13%). Forty-eight patients had arrhythmia on the 24-hour electrocardiogram. Of these, 10 were treated medically, of whom 8 had supraventricular arrhythmia. This study shows that, next to the notorious ventricular arrhythmia, supraventricular arrhythmia is an important sequel in patients long-term after surgical repair of tetralogy of Fallot. Older age at the time of the operation and longer duration of follow-up were not associated with an increase in prevalence or clinical significance of sequelae.

Chapter 5 contains the long-term results of the Mustard repair for transposition of the great arteries. Of all 91 patients who underwent a Mustard repair for transposition of the great arteries in our institution between 1973 and 1980, 18 had died (20%) and 58 (79% of the survivors) were examined at follow-up. Age at the time of the follow-up study was 15.8 ± 3.9 years. The management strategies changed substantially in the 1970's (e.g. infants became eligible for Mustard repair, cold cardioplegia was introduced). Therefore the patient group was divided in half - those operated upon in the first 4 years (age at surgery 3.0 ± 2.8 years) and those operated upon in the subsequent four years (age at surgery 0.6 ± 0.6 years) - and the results of these 2 groups were compared. Mortality and prevalence of sinus node dysfunction were much higher in the group of patients operated upon in the first 4 years than patients operated upon in the subsequent 4 years (respectively 25% versus 2% and 41% versus 3%). In contrast, the incidence of baffle obstruction needing reoperation was significantly higher in the second group. The 2 groups were similar in terms of personal health assessment (comparable to that of the normal Dutch population), echocardiographic findings (no right ventricular failure) and exercise capacity (decreased in both groups with a mean of 84 ± 16% of predicted).

Chapter 6 comprises the long-term results of 40 out of 83 operated patients who underwent surgery for pulmonary stenosis. Age at the time of the operation was 5.0 ± 3.8 years and age at follow-up was 20.7 ± 5.7 years. There was a definite selection bias in the pulmonary stenosis groups (only 11 out of 45 patients operated upon using inflow occlusion were seen at follow-up versus 29 out of 38 patients operated upon using cardiopulmonary bypass), and therefore the prevalence of sequelae and the health status of the entire patient group could not be determined. Emphasis was put on the differences in outcome in relation to the different surgical approaches. All surgical techniques that were used had resulted in a good reduction of right ventricular pressure; none of the participants proved to have substantial residual pulmonary stenosis. However, many had severe pulmonary regurgitation and right ventricular dilatation. This was tolerated well by a large majority of these patients; both personal health assessment and exercise capacity were as good as that of the normal Dutch population. However, the clinical relevance of severe pulmonary regurgitation (and severe right ventricular dilatation) is underscored by the finding that the few patients who developed symptoms of decreased exercise capacity all had severe pulmonary regurgitation and right ventricular dilatation. Irrespective of the surgical technique that was used, both ventricular and supraventricular arrhythmia were frequently seen (72% of the patients had

arrhythmia), but symptomatic arrhythmia was rare (only one patient needed anti-arrhythmic treatment).
Chapter 7 summarizes the results of the five diagnostic groups that were discussed separately in chapters 2 to 6. The most common sequelae throughout all diagnostic subgroups were arrhythmia and severe right ventricular dilatation. Although a large majority of the patients with these sequelae were asymptomatic at the time of the follow-up study, the outlook for these patients on the longer term remains uncertain. Therefore, longer follow-up is necessary.
Chapter 8 is about behavioral and emotional problems in children and adolescents with congenital heart disease. Irrespective of their cardiac diagnosis, these patients have significantly more problems than their peers in terms of anxiety, depressions, social problems, attention problems and tendency towards internalization of problems. One-fifth to one-quarter of all patients had "problem scores" similar to those of children referred to mental health centers. So, in childhood age until adolescence, the outcome of cardiac surgery for congenital heart disease in terms of psychosocial functioning seems to be unfavorable.
Chapter 9 addresses the psychosocial functioning of young adults after surgical correction for congenital heart disease. In contrast to the findings in the younger age group, the tests in these patients showed favorable outcomes both in daily activities, such as attending school or work, and in leisure-time activities when compared with a reference group. Also in terms of emotional functioning these patients seemed to do better than the reference group; there were significantly less feelings of hostility, fewer neurotic complaints and a better self esteem. Again there were no differences between the cardiac diagnosis groups. This positive outcome is largely attributed to a denial mechanism of these patients, possibly in combination with the fact that most patients were very achievement-oriented to prove that they were "no less than anybody else".
Chapter 10 contains a general discussion. The overall conclusion of this study is that a large majority of the patients feels healthy, is asymptomatic and has a normal cardiac function. However, the outlook of these patients on the longer term remains uncertain, because of the very high prevalence of arrhythmia and severe right ventricular dilatation that was found throughout the whole study population. Longer follow-up will be necessary to elucidate this.

SAMENVATTING.
Door de ontwikkelingen in de hartchirurgie zijn de vooruitzichten van patiënten met een aangeboren hartafwijking enorm verbeterd. In plaats van een sterfte van 85% voordat de volwassen leeftijd bereikt was, werd met hartchirurgie de overleving tot aan de volwassen leeftijd 85%. Er is echter weinig bekend over het voorkomen van restafwijkingen in deze groep patiënten. Dit was de aanleiding om deze follow-up studie te starten.
Hoofdstuk 1 geeft een overzicht over de ontwikkeling van de hartchirurgie en hoe het natuurlijk beloop van verschillende aangeboren hartafwijkingen hierdoor veranderde. Het doel van de studie wordt uitgelegd: het vastleggen van zowel de lichamelijke gezondheidstoestand als van het subjectief welbevinden van alle patiënten die tussen 1968 en 1980 voor hun 15e levensjaar in het Sophia kinderziekenhuis/Dijkzigtziekenhuis Rotterdam een open-hartoperatie ondergingen voor een van de vijf meest voorkomende hartafwijkingen. Deze hartafwijkingen zijn atrium-septumdefect, ventrikel-septumdefect, tetralogie van Fallot, transpositie van de grote vaten en pulmonaalklepstenose. Alle

patiënten die in leven waren en van wie het adres kon worden achterhaald via de burgerlijke stand ontvingen een brief waarin het doel van de studie werd uitgelegd, en waarin zij werden uitgenodigd mee te doen aan het follow-up onderzoek. Wat deze follow-up studie onderscheidt van vrijwel alle andere follow-up studies is het feit dat in deze studie een aanzienlijk percentage van de oorspronkelijk geopereerde patiënten daadwerkelijk uitgebreid zowel medisch als psychologisch werden onderzocht. Dit is de enige manier waarop men een betrouwbare indruk kan krijgen van de gezondheidstoestand van de hele groep patiënten.

Hoofdstuk 2 gaat over de lange-termijnresultaten van chirurgische sluiting van een atrium-septumdefect. Van de in totaal 135 geopereerde patiënten bleek niemand te zijn overleden. Honderdvier patienten deden mee aan het follow-up onderzoek. De gemiddelde leeftijd ten tijde van de operatie was 7.5 ± 3.5 jaar en ten tijde van de follow-up studie 21.8 ± 4.8 jaar. De gezondheidstoestand van de patiënten werd vastgesteld door middel van een uitgebreid onderzoek, bestaande uit een anamnese, lichamelijk onderzoek, echocardiografisch onderzoek, een inspanningstest, een 12-afleidingen elektrocardiogram en een 24-uurs elektrocardiogram. Geen van de geopereerde patiënten bleek pulmonale hypertensie te hebben, terwijl dit in niet-geopereerde patiënten de belangrijkste risicofactor is voor vroegtijdig overlijden is. Het inspanningsvermogen van deze patiënten was normaal. Het oordeel wat deze patiënten hadden over hun eigen gezondheid was even goed als dat wat gezonde Nederlanders hebben over hun eigen gezondheid. De meeste patiënten hadden asymptomatische restafwijkingen, waarvan een persisterende verwijding van de rechter ventrikel (26% van de patiënten) en ritmestoornissen (67% van de patiënten) het meest frequent waren. Zes van de in totaal 67 patiënten met ritmestoornissen hadden klachten ten gevolge van deze ritmestoornissen en werden medicamenteus behandeld.

Hoofdstuk 3 gaat over de lange-termijnresultaten van chirurgische sluiting van een ventrikel septum defect. Van de in totaal 176 geopereerde patiënten bleken 23 te zijn overleden (13%) en deden 109 mee aan het follow-up onderzoek. De gemiddelde leeftijd ten tijde van de operatie bedroeg 4.1 ± 4.0 jaar en ten tijde van het follow-up onderzoek 18.9 ± 5.7 jaar. Bij geen van de participanten werd pulmonale hypertensie, de belangrijkste doodsoorzaak in deze patientengroep voor het tijdperk van de chirurgie, gevonden. Zowel de mening over hun eigen gezondheid als het inspanningsvermogen waren gelijk aan die van de doorsneebevolking. Veel patiënten (43%) bleken bij onderzoek haemodynamisch onbelangrijke restafwijkingen en/of asymptomatische ritmestoornissen (50%) te hebben, maar geen van de patiënten had hiervan klachten.

Hoofdstuk 4 geeft een overzicht over de gezondheidstoestand van patiënten lang na chirurgische correctie van een tetralogie van Fallot. Van de in totaal 142 geopereerde patiënten bleken 27 (19%) te zijn overleden, waarvan het merendeel direct postoperatief. Zevenenzeventig patiënten (69%) deden mee aan het follow-up onderzoek. De gemiddelde leeftijd ten tijde van de operatie was 4.7 ± 3.4 jaar en ten tijde van het follow-up onderzoek 19.0 ± 5.5 jaar. Als direct gevolg van het veelvuldig gebruik van een transannulaire patch bij de operatie (bij 56% van de patiënten) was het aantal patiënten met een aanzienlijke rest-stenose klein (8%), maar meer dan de helft van de patiënten had een ernstige pulmonalisinsufficientie. Het inspanningsvermogen van patiënten met een ernstige pulmonalisinsufficientie (83 ± 19% t.o.v. de norm) bleek significant lager dan die van patiënten zonder ernstige pulmonalisinsufficientie (96 ± 13% t.o.v. de norm). Achtenveertig patiënten (72%) had ritmestoornissen op het 24-uurs electrocardiogram.

Tien van hen werden medicamenteus behandeld, waarvan 8 voor supraventriculaire ritmestoornissen. Dit geeft aan dat, naast de ventriculaire ritmestoornissen waarvan bekend is dat deze soms levensbedreigend zijn, supraventriculaire ritmestoornissen ook een belangrijk probleem vormen in deze patiëntengroep. Hogere leeftijd ten tijde van de operatie (maar wel onder de 15 jaar) en langere duur van follow-up waren niet geassocieerd met een toename in aantal of ernst van de restafwijkingen.

Hoofdstuk 5 bevat de lange-termijnresultaten van de operatie volgens Mustard voor transpositie van de grote vaten. In totaal ondergingen 91 patiënten deze operatie tussen 1973 en 1980. Van hen bleken 18 (20%) te zijn overleden voor de aanvang van het follow-up onderzoek, veelal plotseling meerdere jaren na de operatie. Achtenvijftig patiënten (79% van de in leven zijnde patiënten) deed mee aan het follow-up onderzoek. De gemiddelde leeftijd ten tijde van de operatie bedroeg 1.8 ± 2.2 jaar en ten tijde van het follow-up onderzoek 15.8 ± 3.9 jaar. Daar de behandelingsmethoden aanzienlijk veranderden in de jaren '70 (myocardpreserveringstechnieken werden geïntroduceerd, en steeds kleinere kinderen konden worden geopereerd) werd deze patiënten groep in tweeën verdeeld. Deze 2 groepen - zij die voor 1976 waren geopereerd (gemiddelde leeftijd 3.0 ± 2.8 jaar) en zij geopereerd na die tijd (gemiddelde leeftijd 0.6 ± 0.6 jaar) - werden apart geanalyseerd en de uitkomsten werden vergeleken. In de eerste groep waren zowel mortaliteit als prevalentie van sinusknoopdysfunctie veel hoger dan in de tweede groep (respectievelijk 25% versus 2% en 41% versus 3%). Daarentegen was in de tweede groep, waarin patiënten in het algemeen veel kleiner waren bij de operatie, het aantal reoperaties voor Mustard-baffle gerelateerde problemen veel hoger. De 2 groepen waren vergelijkbaar wat betreft oordeel over hun eigen gezondheid (even goed als dat van de doorsneebevolking), de echocardiografische bevindingen (met name geen rechter- ventrikelfalen) en inspanningsvermogen (in beide groepen verlaagd met een gemiddelde van 84 ± 16% van de norm).

Hoofdstuk 6 gaat over de lange-termijnresultaten van chirurgie voor pulmonaalklepstenose. Daar slechts 40 van de in totaal 83 geopereerde patiënten werden onderzocht bij het follow-up onderzoek, kon geen betrouwbare uitspraak worden gedaan over hoe het met de gehele patiëntengroep was. De gemiddelde leeftijd ten tijde van de operatie was 5.0 ± 3.8 jaar en ten tijde van het follow-up onderzoek 20.7 ± 5.7 jaar. Nadruk werd gelegd op het verband tussen de gebruikte operatie-techniek en de uitkomsten op lange termijn. Ongeacht de toegepaste chirurgische techniek bleek de operatie - het opheffen van de pulmonaalklepstenose - bij alle patiënten goed geslaagd. Geen van de patiënten had een substantiële reststenose. Een pulmonalisinsufficientie was echter veelal het gevolg hiervan. Het meest uitgesproken was dit bij patiënten die een transannulaire patch hadden gekregen bij de operatie (7 van de 9 patiënten hadden ernstige pulmonalisinsufficientie en rechter ventrikeldilatatie), maar ook bij andere operatietechnieken kwam dit voor. Veelal werd dit goed verdragen: zowel inspanningsvermogen als oordeel over de eigen gezondheid waren even goed als die van de Nederlandse doorsneebevolking. Echter, de vier patiënten die klachten hadden van een duidelijk afgenomen inspanningsvermogen hadden alle 4 een ernstige pulmonalisinsufficientie en rechter ventrikeldilatatie. Dit onderstreept het klinisch belang van ernstige pulmonalisinsufficientie. Zowel ventriculaire als supraventriculaire ritmestoornissen kwamen veel voor in deze populatie (bij 72% van de patiënten), maar slechts 1 patiënt gebruikte hiervoor anti-aritmica.

Hoofdstuk 7 geeft een overzicht van de resultaten van de 5 diagnostische groepen die separaat besproken waren in hoofdstuk 2 tot 6. De meest voorkomende problemen na hartchirurgie, ongeacht de oorspronkelijke hartafwijking en de toegepaste chirurgische techniek, zijn ritmestoornissen en ernstige rechter ventrikeldilatatie. Alhoewel de meerderheid van de patiënten met deze restafwijkingen geen klachten hadden ten tijde van het follow-up onderzoek, blijven de vooruitzichten voor de langere termijn voor deze patiënten onzeker. De belangrijkste vraag is of deze restafwijkingen levenslang asymptomatisch zullen blijven, of dat de bevindingen nu voorbodes zijn van rechter ventrikel falen of symptomatische ritmestoornissen later. Langere follow-up zal dit uitwijzen.
Hoofdstuk 8 gaat over de uitkomsten van het psychologisch deel van het onderzoek. Uit dit onderzoek bleek dat, ongeacht de oorspronkelijke hartafwijking, deze patiënten op de kinderleeftijd tot en met de puberteit significant meer problemen hebben dan leeftijdsgenoten. Zij hebben aanzienlijk meer angstige en depressieve gevoelens, hebben meer concentratieproblemen en hebben vaker de neiging problemen te internaliseren. Twintig tot 25% van de patiënten heeft op de gebruikte vragenlijsten scores die vergelijkbaar zijn met die van kinderen verwezen naar centra voor geestelijke gezondheidszorg (RIAGG).
Hoofdstuk 9 bespreekt het psychosociaal functioneren van jong-volwassenen die als kind een open-hartoperatie hebben ondergaan. In tegenstelling tot de bevindingen bij kinderen blijkt dat de volwassenen het in veel opzichten juist beter doen dan de normgroepen: minder emotionele problemen (betere zelfwaardering, minder neurotische klachten) en een actievere vrije-tijdsbesteding. Zowel niveau van scholing als participatie in het arbeidsproces is niet minder dan de doorsneebevolking. Wat dit betreft zijn er geen verschillen tussen de verschillende diagnosegroepen. Deze positieve uitkomsten worden vooral verklaard vanuit het psychologisch mechanisme "ontkenning", waarschijnlijk in combinatie met het feit dat de meeste patiënten erg prestatie-gericht zijn om te laten zien dat zij niet onder doen voor iemand anders.
Hoofdstuk 10 is de algemene discussie. De belangrijkste conclusie van dit onderzoek is dat, alhoewel de overleving na hartchirurgie uitstekend is (uitgezonderd de groep patiënten met een Mustard operatie voor transpositie van de grote vaten), de meeste patiënten restafwijkingen hebben. Het merendeel van deze patiënten heeft geen klachten, voelt zich gezond en heeft een normaal inspanningsvermogen. Veel patiënten hebben echter restafwijkingen, met name rechter ventrikeldilatatie en ritmestoornissen, die ten tijde van het follow-up onderzoek klinisch van weinig betekenis leken, daar zij niet waren geassocieerd met klachten of symptomen, maar waarvan de langere termijn vooruitzichten onzeker zijn. Langere follow-up is noodzakelijk om hierover zekerheid te krijgen.

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