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Excellent survival and low incidence of arrhythmias, stroke and heart failure long-term after surgical ASD closure at young age

A prospective follow-up study of 21–33 years

J.W. Roos-Hesselink[a]*, F.J. Meijboom[a], S.E.C. Spitaels[a], R. van Domburg[a], E.H.M. van Rijen[c], E.M.W.J. Utens[c], A.J.J.C. Bogers[b], M.L. Simoons[a]

[a] *Departments of Cardiology and Cardiothoracic Surgery, Thoraxcenter, Erasmus Medical Center, Rotterdam, The Netherlands*
[b] *Department of Cardiothoracic Surgery, Thoraxcenter, Erasmus Medical Centre, Rotterdam, The Netherlands*
[c] *Department of Child and Adolescent Psychiatry, Sophia Children's Hospital, Rotterdam, The Netherlands*

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KEYWORDS
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Aims Although studies have suggested good long-term results, arrhythmias, pulmonary hypertension and left ventricular dysfunction are mentioned as sequelae long-term after surgical atrial septal defect closure at young age. Most studies were performed only by questionnaire and in a retrospective manner. The long-term outcome is very important with regard to future employment and acceptance on insurance schemes.
Methods and Results One hundred and thirty-five consecutive ASD-patients, operated on in childhood, were studied longitudinally with ECG, echocardiography, exercise testing and Holter-recording 15 (10–22) and 26 (21–33) years after surgery. During follow-up no cardiovascular mortality, stroke, heart failure and no pulmonary hypertension occurred. Symptomatic supraventricular tachyarrhythmias were present in 6% after 15 years, and an additional 2% occurred in the last decade; 5% needed pacemaker implantation. No relation was found between arrhythmias and type of ASD, baseline data, right ventricular dimensions, or age at operation. Left and right ventricular function and dimension remained unchanged. Slightly more patients had right atrial dilatation at last follow-up. Exercise capacity was comparable with the normal Dutch population.
Conclusions The long-term outcome after ASD closure at young age shows excellent survival and low morbidity. The incidence of supraventricular arrhythmias is lower than in natural history studies of ASD patients and also lower than after surgical correction at adult age.

* *Correspondence:* J. W. Roos-Hesselink, Thoraxcenter Ba 308, Erasmus Medical Centre Rotterdam, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands

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Introduction

Secundum type atrial septal defect can cause volume overload of the right heart with late development of right heart failure, elevated pulmonary vascular resistance, atrial arrhythmias, or systemic embolism.[1–4] Closure is recommended to avoid these sequelae. More recently atrial septal defect closure with a device using cardiac catheterization has gained acceptance.[5] Small residual shunts are often found with this technique.[6] For comparison of surgical and device closure it is important to have good insight into the long-term outcome of surgical correction. Results of medium-term follow-up study after surgical correction are good, but prospective studies of long-term follow-up focussing on arrhythmias, cardiac failure, exercise capacity, residual shunts and stroke are rare. It has been postulated that after early repair of atrial septal defect, survival is good, but sinus node dysfunction, atrial fibrillation and flutter, right ventricular dilatation, pulmonary hypertension and left ventricular dysfunction are mentioned as sequelae,[7–13] although the incidence of these sequelae in consecutive series of patients who were operated on at a young age is not known. Murphy *et al*. studied the 27–32 year outcome after surgical repair of ASD in all age groups and the incidence of postoperative atrial arrhythmias appeared related to the age of the patient at the time of repair.[8] However, this study included only 33 patients operated on at a young age (operated <11 years) and was performed retrospectively and by written questionnaires and telephone interviews. Meijboom et al. reported a good outcome 9–20 years after ASD closure at a young age, with a low incidence of symptomatic arrhythmias, however, signs of sinus node disease and ventricular ectopy were found on 24-h Holter recordings in up to 45% of the patients.[14]

The aim of this study is to provide data on mortality and morbidity, which is critically important with regard to employment and acceptance on insurance schemes in long-term survivors of repair of atrial septal defects, and can also be used for comparison with the recently developed device closure techniques.

We present a longitudinal follow-up of 21–33 years (mean 27 years) after surgical closure of an atrial septal defect in 135 patients who underwent this operation at the Thoraxcentre between 1968 and 1980 and were <15 years of age at the time of surgery. Stroke, heart failure, incidence of arrhythmias, changes in ECG, exercise capacity and echocardiographic parameters were studied. In addition, the predictive value of the asymptomatic arrhythmias seen on the Holter recordings 10 years ago is determined.[14]

Methods

Patients

All patients who underwent surgical repair for secundum type ASD or sinus venosus type ASD at our institution between 1968 and 1980 and who were <15 years of age at the time of the operation were included in the study. The first follow-up study was performed in 1990,[14] the second from September 2000 to December 2001. The cardiac examination included medical history, physical examination, standard 12-lead electrocardiography (ECG), 24-h ambulatory electrocardiography (Holter), echocardiography, and bicycle ergometry. If the patient refused to visit the clinic, a written questionnaire was sent to the patients to obtain information on morbidity. The institutional Medical Ethical Committee approved the study. All patients gave their consent.

Electrocardiography

Standard 12-lead surface electrocardiograms were analysed for the height of the P wave (measured in lead II), duration of the P wave and the PR interval (measured from the initial deflection of the P wave to the initial deflection of the QRS complex). A first-degree atrioventricular block was defined by a PR interval >200 ms. In addition, the widest QRS duration was determined (from the initial deflection of the QRS complex to where the terminal deflection crosses the baseline, taken in any chest lead with the widest complex and where the deflections were acute enough to permit accurate assessment). A QRS duration >120 ms was defined to be a complete bundle branch block. A single observer made all ECG measurements (J.R.-H.).

Holter monitoring

A three-channel recorder was used. Sinus node dysfunction was assessed during 24 h Holter monitoring using the modified Kugler criteria: nodal escape rhythm, sinus arrest >3 s or severe sinus bradycardia (<40 beats . min^{-1} at night or <50 beats . min^{-1} during daytime).[13]

Echocardiography

Two-dimensional echocardiography and echo-Doppler studies were performed using a Hewlett-Packard Sonos 5500 echocardiograph. All

Table 1 Demographic data, data of pre-operative cardiac catheterization and surgical data showing the group in total, the group investigated in 1990 and in 2001 and finally the group who did not participate in the second follow-up study (no second study)

	Total	1990	2001	No second study
Number of patients	135	104	94	41
Male	59 (44%)	44 (42%)	39 (41%)	20 (49%)
Female	76 (56%)	60 (58%)	55 (59%)	21 (51%)
Cardiac catheterization				
QP-QS ratio	2.3:1	2.3:1	2.3:1	2.3:1
Peak systolic PA pressure	26	26	26	26
PAPVD	27%	26%	26%	27%
Surgical data				
Age at operation (years)	7.5±3.5	7.3	7.5	7.5
Complete CPB (% of patients)	96	96	96	96
Direct closure (% of patients)	76	75	75	76
Closure with patch (% of patients)	24	25	25	24
Sinus venosus type ASD (% of patients)	22	22	23	21
Follow-up since surgery		15	26	—
Age at the time of study		22	33	—

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

echocardiographic studies were performed on the same machine. Left atrial dimension and left ventricular end-diastolic and end-systolic dimensions were assessed using M-mode echocardiography in the parasternal view. A left atrium dimension >45 mm and a left ventricular end-diastolic dimension of >58 mm were considered enlarged. A fractional shortening less then 0.30 was defined as decreased. Parasternal, apical four-chamber and subcostal views were used to assess right atrium and right ventricular dimensions. This was done by visual estimation by two experienced cardiologists (F.M. and S.S.). Multiple echocardiographic views were examined using colour flow to identify residual shunts. Doppler-echocardiography was used for the assessment of blood flow velocities. Right ventricular systolic pressure was estimated from tricuspid regurgitation jet velocity; diastolic pulmonary pressure from the pulmonary regurgitation flow velocity. Pulmonary hypertension was defined as a tricuspid regurgitation flow velocity >3.0 or a pulmonary regurgitation flow velocity >2.5 m . s^{-1}.

Bicycle ergometry

Maximal exercise capacity was assessed by 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 height. Exercise capacity <85% of the predicted value was considered to be decreased.

Arrhythmias were defined to be symptomatic if antiarrhythmic medication was prescribed, cardioversion was necessary, catheter ablation or surgical arrhythmia treatment had been applied, or pacemaker implantation had been necessary. Major events were defined as cardiac surgery, stroke, symptomatic arrhythmia, or an episode of heart failure.

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 patients as a total, as well as separately for the secundum type ASD and the sinus venosus type group. Results of the total group will be presented, unless significant differences were observed between the two subgroups.

Results

Patients

All 135 patients who had undergone primary surgical ASD (secundum and sinus venosus type) repair in the Thoraxcentre between 1968 and 1980 at age <15 years, were included. A secundum type ASD was present in 105, and a sinus venosus type ASD in 30 patients. Age at operation was 7.5±3.5 years (range 0–14). There was no in-hospital or early mortality. The baseline characteristics off all 135 patients are described in

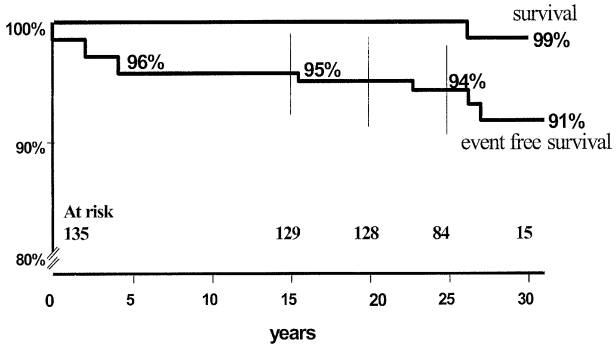

Figure 1 Survival and survival free of major events (death, n = 1; cardiac surgery, n = 1; stroke, n = 0; symptomatic arrhythmia, n = 10; episode of heart failure, n = 0).

Table 1. The details of preoperative clinical findings, including cardiac catheterization, data on surgical technique and postoperative course have been described earlier.[14] Information on survival was obtained in all 135 patients. During follow-up, no cardiovascular mortality occurred, one patient died, due to suicide, 15 years after his operation, 134 survived. Survival and survival free of major events are given in Fig. 1.

After a mean follow-up of 15 years (range 10–22), 104 patients (77%) participated in the first follow-up study.[14] Of these, 94 patients (70% of the original 135 patients and 90% of the 104 patients studied in 1990) fully participated in the second follow-up study after a mean follow-up of 26 years (range 21–33) after surgery with a mean age at the time of study of 33 years. No significant differences were found between the baseline characteristics of the patients who participated and the patients who did not participate in the follow-up studies (Table 1). The four patients who received the written questionnaire returned it, and they are in good clinical health, have not been admitted to hospital and have not experienced tachyarrhythmias.

Major cardiac events

Before 1990 one additional cardiac operation was performed for closure of a patent arterial duct. No cardiac operations were necessary between 1990 and 2001. No stroke and no episodes of heart failure occurred during follow-up. No patient was using diuretics. In 1990 symptomatic supraventricular arrhythmias were present in seven patients (6%): three were treated medically for periods of atrial flutter or fibrillation, and four others needed pacemaker implantation. Of these seven patients, three were readmitted between 1990 and 2001: one patient suffered from pacemaker endocarditis, he was treated with antibiotics for 6 weeks and the pacing system was replaced, while two other patients needed pacemaker battery replacement. Between 1990 and 2001, three additional patients had new symptomatic arrhythmias: one needed pacemaker implantation for sinus node disease, one patient had recurrent atrial flutter treated with several electrical cardioversions and radiofrequency catheter ablation, and one patient received medical therapy for supraventricular arrhythmias. Analyses were performed, investigating the role of localization of the ASD (secundum type or sinus venosus type), baseline data (such as pre-operative shunt size, age at operation, year of operation, and surgical techniques), right ventricular and atrial dimensions at follow-up, age at follow-up and duration of follow-up in relation to the presence or absence of symptomatic arrhythmias. No relation was found.

Medical history and physical examination

When questioned about their current general health, 88.3% considered their health as very good or good, and 11.7% as moderate. None judged it as poor. This is not different from the health assessment of the normal Dutch population.[16] Patient's own appreciation of their physical condition was better in 13%, the same in 51%, slightly worse in 33% and much worse in 3% compared with that of 11 years previously.[14] On the question whether the patients suffered from palpitations, 20% answered 'yes' in 1990 and 28% in 2001. Physical examination revealed that the mean height of the patients remained unchanged (172.4 mm in 1990 and 172.5 mm in 2000), whereas the mean weight rose from 64.1 kg in 1990 to 73.7 kg in 2000 ($P<0.0001$). The mean pulse rate lowered from 72 to 67 beats . min^{-1} ($P = 0.0004$). Signs of heart failure were not found.

Electrocardiography

Twelve-lead electrocardiograms and 24-h ambulatory electrocardiograms data are presented in Table 2. Sinus rhythm was seen in 1990 in 90% of the patients and 89% in 2001. The PR-interval did not change during this 10-year period. P-wave duration and P-wave height did not change significantly over 10 years. The QRS duration increased, but no new bundle branch block occurred.

Holter monitoring

On 24-h Holter, two patients showed paroxysmal atrial flutter in 2001, which was not present in

Table 2 Standard 12-lead electrocardiogram and 24-h Holter electrocardiogram

	1990	2001	*P* value
ECG			
Rhythm			
Sinus	90%	89%	ns
Atrial	6	5	
Nodal	1	2	
Atrial flutter	—	1	
Pacemaker	3	3	
PR interval	153.7	153.2	ns
PR > 200 ms	3%	5%	ns
QRS duration	88.3	96.1	<0.0001
QTc segment	350	388	ns
P-wave duration	84	85	ns
P-wave height in II	0.30	0.29	ns
P-wave morphology normal	87%	81%	ns
P-wave axis	46′	40′	ns
QRS axis	63′	54′	0.0006
No LVH or RVH	95.9%	95.4%	ns
24-hour Holter			
Supraventricular arrhythmias	45	36	0.02
Sinus node disease	39	27	0.03
SVT	6	18	0.3
Paroxysmal A fibrillation	0	0	ns
Paroxysmal A flutter	0	2	ns
Ventricular arrhythmias	43	25	0.02
Multi PVC/doublets	39	23	0.01
VT 3–10 complex	3	4	ns
VT > l0 complex	—	—	
Conduction disturbances	17	8	0.01
First degree AV block	14	8	ns
Second AV block	2	—	ns
Third AV block	—	—	

SVT = supraventricular tachycardia; PVC = premature ventricular complexes; AV = atrioventricular.

1990. These two patients did not differ from other patients with regard to right atrial enlargement, right ventricular dilatation or left atrial enlargement. Signs of sinus node dysfunction were found in 39% in 1990, and 27% in 2001. One of the patients needed pacemaker implantation in the period 1990–2001. Ventricular arrhythmias including multiform premature ventricular complexes, doublets and short ventricular tachycardias (3–10 complexes) were seen on Holter in 1990 in 43% of the patients. During the following 10 years, none of these patients experienced symptomatic ventricular arrhythmias or sudden death and the incidence of ventricular arrhythmias on 24-h Holter diminished to 25% in 2001.

Echocardiography

Echocardiographic findings are summarized in Table 3 and 4. Residual shunts were not found. Dimension of right ventricle, left atrium and left ventricle remained unchanged over time. The percentage of patients with right atrium dilatation increased from 5.8% in 1990 to 18.7% in 2001 ($P = 0.5$). Mitral valve regurgitation did not progress in 10 years and none of the patients developed substantial pulmonary regurgitation. Haemodynamically insignificant pulmonary and tricuspid regurgitation did not progress, but one patient developed severe aortic regurgitation. No pulmonary hypertension was found and estimated pulmonary artery pressure was stable over time. Left and right ventricular function remained unchanged over the last 10 years, and none of the patients experienced a less than 20% left ventricular shortening fraction at last follow-up. Although 20% of the patients had left ventricular shortening fraction of between 20 and 30%, most of these patients had post-operative abnormal septal motions, but were judged otherwise to have normal systolic function, only 4.5% of the total group was judged as having diminished systolic left ventricular function. Only one patient showed paradoxical septal motion.

Bicycle ergometry

The results of exercise testing in 1990 and 2001 are given in Table 5. The exercise capacity, corrected for age, sex and body height, diminished by 9% in 10 years, but remained comparable with the total Dutch population. During exercise testing, no new arrhythmias were revealed. Pre-operative findings, surgical procedures, echocardiographic parameters, age at the time of operation or duration of follow-up were not predictive for diminished exercise capacity.

Type ASD

Sinus venosus type ASD and secundum type ASD differed with regard to sex: the sinus venosus type ASD patients were predominantly males (66%), whereas in the secundum type ASD group we found predominantly females (63%), (P-value = 0.004). The patients with sinus venosus type ASD had greater shunts (shunt ratio 2.6:1 vs 2.2:1 in the secundum type ASD patients, $P = 0.04$), more often had partially abnormal pulmonary veins, and more often a patch was used during surgery (100% in the sinus venosus group versus 3% in the secundum ASD group). The sinus venosus type and secundum type ASD did not differ significantly with regard to the incidence of arrhythmias, the exercise performance or the outcome on echo-Doppler parameters (dimensions, ventricular function, valve insufficiency, or pulmonary artery pressure).

Table 3 Echocardiograpic parameters comparing 1990 and 2001

	1990	2001	*P*-value
RA dilatation	5.8%	18.7%	0.5
RV dilatation	26.0%	23.5%	0.7
LA dilatation	10.0%	5.9%	0.5
LV dilatation	9.5%	5.7%	0.5
LV systolic function normal	97.1%	95.5%	ns
RV systolic function normal	100%	100%	ns
Valve insufficiency (more than trace)			
AoI	0%	1.1%	ns
MI	11.5%	13.5%	ns
PI	44.2%	45.0%	ns
TI	42.3%	48.3%	ns
Vmax TI	2.1 m . s^{-1}	2.2 m . s^{-1}	ns
Vmax PI	1.6 m . s^{-1}	1.5 m . s^{-1}	ns

RA = right atrium; RV = right ventricle; LA = left atrium; LV = left ventricle; AoI = aortain sufficiency; MI = mural insufficiency; PI = pulmonic insufficiency; TI = tricuspid insufficiency; Vmax = maximal velocity found with Doppler echocardiography.

Table 4 Echocardiographic parameters 2001 in detail

		Enlarged			
Chamber size	Normal		Mild		Moderate
RA	67.0%		14.3%		18.7%
RV	76.9%		11.0%		12.1%
LA	85.5%		5.5%		7.7%
LV	93.3%		4.4%		2.2%
Hypertrophy					
LVH	94.8%		2.6%		2.6%
RVH	94.5%		5.5%		—
Function					
LV function	95.5%		4.5%		—
RV function	100%		—		—
	>30%		20–30%		<20%
Left ventricular fractional shortening	80%		20%		—
Valve regurgitation	No	trace	1+	2+	3/4+
AoI	98.8	1.1	—	—	1.1
MI	52.8	33.7	9.0	3.4	1.1
PI	29.2	25.8	36.0	9.0	—
TI	13.5	38.2	28.1	14.6	5.6
	<2.5 m . s^{-1}		2.5–3.0 m . s^{-1}		>3.0 m . s^{-1}
Vmax TI	88.5%		11.5%		—
	<1.5 m . s^{-1}		1.5–2.0 m . s^{-1}		>2.0 m . s^{-1}
Vmax PI	46.5%		49.3%		4.2%

See legend Table 3. LVH = left ventricular hypertrophy; RVH = right ventricular hypertrophy.

Discussion

The long-term outcome (21–33 years) of children who had undergone surgical closure of haemodynamically significant ASD was investigated in this study. Although the general opinion is that the long-term results will be good, no hard data are available. We present a unique longitudinal study of consecutive patients with long-term (21–33 years) follow-up, studied, not only with written questionnaire or telephone interview, but also with a thorough clinical investigation. We found an excellent survival with no cardiovascular mortality. Complications such as right heart failure, stroke or elevated pulmonary vascular resistance did not

Table 5 Bicycle ergometry

	1990	2001
Number of patients	101	91
Maximum heart rate	92%	92%
Maximum exercise capacity	104%	95%
Significant arrhythmia	—	—

occur. Only one additional cardiac operation was performed (for closure of a patent arterial duct). No residual ASD was found. Pacemaker implantation was performed in four patients before 1990 and in one patient between 1990 and 2001. One pacemaker patient developed endocarditis.

The development of atrial arrhythmias is described after ASD closure, and has been studied thoroughly in adults.[8,17,18] Studies of long term follow-up in adults demonstrate that the incidence of new atrial arrhythmias is unchanged following surgical closure of ASD compared to those treated conservatively. Some studies suggest that older age at operation is a risk factor for persistent atrial arrhythmias and development of new atrial arrhythmias after surgery,[17–19] while the incidence of atrial arrhythmias appears lower in patients operated at younger age. Nevertheless, Meijboom *et al*. report that up to 45% of the patients had some form of asymptomatic atrial arrhythmias on Holter recording, 15 years after surgery.[8,14] In this same cohort of patients we observed a low incidence (2%) of symptomatic arrhythmias in the subsequent decade and in 36% asymptomatic atrial arrhythmias. No patient had chronic atrial fibrillation, one patient developed persistent atrial flutter, one needed pacemaker implantation, and one patient received antiarrhythmic medication for supraventricular tachycardias. Thus, the predictive value of the asymptomatic arrhythmias seen on Holter recording seems limited. The prevalence of atrial fibrillation in the general population is studied mainly in older age groups and is estimated to be 3/1000 in those aged 45–49 years.[20] The reported incidence of atrial fibrillation and flutter in natural history studies of ASD patients is 15–40% in 30–35-year-olds and comparable with the incidence of arrhythmias after surgical ASD closure at adult age. This is substantially higher then the 3% found in our study,[1,17,18,20] suggesting that early closure is beneficial indeed. The aetiology of late atrial arrhythmias following surgical closure of ASD is not well explained. Long-standing volume overload, varying degrees of pulmonary hypertension, ventricular dysfunction, congenital defects in the atrial conduction tissue, and surgical scars have all been implicated.[22,23] Our data imply that it is unlikely that the congenital defect in the conduction tissue is an important factor in the aetiology of the arrhythmias, since few symptomatic arrhythmias occurred. It is possible that the atria of young patients have greater remodelling potential and that this patient population may therefore be at lower risk for the development of late atrial arrhythmias.[6] Transcatheter device closure may have an extra advantage over surgical closure on the incidence of arrhythmias, but improvement of right heart morphology after device closure and the effect of avoidance of an atriotomy scar remain to be determined.[24] Electrocardiographic parameters such as P wave height and PR interval, which may predict the occurrence of atrial arrhythmias, remained stable for 10 years. This, together with the low incidence of new symptomatic arrhythmias in the last 10 years, leads to the prediction that only few additional arrhythmias will develop in these patients. Continuing follow-up is warranted to verify this assumption.

The clinical condition of the patients appeared excellent at follow-up: the exercise capacity was comparable with normal individuals corrected for age, sex and body height. The incidence of right ventricular dilatation and valve regurgitation on echocardiographic images was low, and not different from 10 years ago. The percentage of patients with a dilated right atrium increased from 5.8 in 1990 to 18.7% in 2001. This was not a significant increase ($P = 0.5$), but also others reported a remaining dilatation of the right atrium after ASD closure compared to controls.[24]

Whether transcatheter device closure will have the same excellent results remains to be determined, especially while up to 50% of the patients have residual shunts after device closure after 1 year of follow-up.[6]

In our study we found no differences in outcome between the patients with sinus venosus type ASD and secundum type ASD with regard to the incidence of arrhythmias, exercise capacity and haemodynamic status.

Study limitations

In this study the follow-up is incomplete. After 15 years 104 (77%) and after 26 years, 94 (70%) from the originally 135 operated patients participated in the study. Since 1990, one patient has died, five were lost and four were unwilling to attend hospital. Nevertheless, the latter four patients did return the questionnaire, and reported to be in good clinical health.

Furthermore, we found no difference in characteristics between the patients who did and who did not participate in the follow-up study, so we expect that the incomplete follow-up will have no impact on the outcome of the study.

Conclusion

The long-term outcome after ASD closure at young age shows an excellent survival with no cardiovascular mortality and low morbidity. The development of supraventricular arrhythmias is lower then in natural history studies of ASD patients and also lower then after surgical correction at adult age. The clinical condition of the patients is very good and stable.

These excellent long-term results are critically important for the employability and insurability, and ASD patients should encounter no obstacles in finding jobs and have life insurance policies consistent with standard rates.

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