Long-Term Results of Cardiac and General Health Status in Children After Neonatal Arterial Switch Operation

Hedwig H. Hövels-Gürich, MD, Marie-Christine Seghaye, MD, Qing Ma, MD, Maria Miškova, Ralf Minkenberg, Dipl Phys, Bruno J. Messmer, MD, and Götz von Bernuth, MD

Departments of Pediatric Cardiology and Thoracic and Cardiovascular Surgery, University Hospital, Aachen University of Technology, and Institute For Medical Research and Information Processing, Aachen, Germany

Background. **The purpose of this study was to assess cardiac and general health status 8 to 14 years after neonatal arterial switch operation for transposition of the great arteries.**

Methods. **Sixty unselected children with intact ventricular septum (78.3%) or ventricular septal defect (21.7%) without or with aortic isthmic stenosis (5.1%) were examined 10.5 ± 1.6 (mean ± SD) years after neonatal switch and 5.3 ± 1.6 years after mid-term evaluation. Complete clinical examination, standard and 24-hour Holter electrocardiogram, M-mode, 2D-, Doppler, and color Doppler echocardiography were performed. Results were compared with normal values and to mid-term follow-up results.**

Results. **Rates of reoperation after arterial switch operation and operation to correct concomitant coarctation were 3.3% and 5.1%, respectively. No patient needed medication, and 93.3% had no limitation of physical activity. All children had normal height and weight; 31.6% had abnormal thoracic configuration after median sternotomy. Most patients (91.7%) were in sinus rhythm. Incidence of complete right bundle branch block (10.0%) was unchanged, as was prevalence of ectopic activity (occasional atrial ectopy 20.0%, ventricular ectopy: occasional 21.7%; frequent 1.7%). Left ventricular dimensions and shortening fraction did not change over time. Diameters of neo-aortic valve annulus and neo-aortic root did not increase, and z-scores decreased between mid-term and present evaluation. Incidence of neo-aortic insufficiency was 13.3% and remained unchanged in comparison with the pre-examination value. Neo-aortic stenosis was not seen. Compared with mid-term follow-up, incidence (41.6%) and degree of supravalvular pulmonary stenosis increased.**

Conclusions. **Good cardiac results persist 10 years after neonatal arterial switch operation for transposition of the great arteries. Encouraging findings include preservation of left ventricular function, low incidence of rhythm disturbances, lack of further neo-aortic root dilatation, and unchanged incidence of neo-aortic insufficiency compared with mid-term follow-up. Increased incidence and degree of supravalvular pulmonary stenosis are of concern.**

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The neonatal arterial switch operation (ASO) has become the surgical procedure of choice for correction of transposition of the great arteries (TGA) with or without ventricular septal defect (VSD), as demonstrated by encouraging early and mid-term cardiac results [1–4] as well as normal exercise capacity in most patients [5, 6]. Current interest is focused on long-term studies of which there are still few [7–9]. Further information should be obtained as to which extent typical postoperative complications, such as aortic insufficiency or supravalvular pulmonary stenosis, are prevalent in children aged 8 to 14 years after surgery. In addition, the advantages of anatomic correction over the physiologic repair of Mustard and Senning with respect to arrhythmias and function of the systemic ventricle should be investigated as the duration of follow-up increases. The aim of the present longitudinal study was therefore to evaluate by noninvasive methods general health status and long-term cardiac findings of a homogeneous group of children 10 years after ASO by reassessment and to compare the results with those of the same cohort 5 years previously [4].

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Address reprint requests to Dr Hövels-Gürich, Department of Pediatric Cardiology, University Hospital, Aachen University of Technology, Pauwelsstrasse 30, D-52057 Aachen, Germany; e-mail: hhoevels-guerich@ukaachen.de.

Patients and Methods

Demographic Data

Between March 1986 and February 1992, 96 consecutive newborns with TGA underwent ASO in our institution. There were 89 long-term survivors, 77 of whom (86.5%) had undergone mid-term follow-up examination at 3.2 to 9.4 years of age (5.4 ± 1.6 years) [4]. After approval by the

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Human Ethical Committee of the Aachen University of Technology (May 8, 2000) and written consent of the parents, 60 unselected children of this group (67.4% of the survivors, 77.9% of the participants of the mid-term examination) returned for a longitudinal reassessment after a mean period of 10.5 ± 1.6 years after ASO. The study was conducted by 1 examiner (H.H.H.-G.) during a period of 8 months. There was no subsequent death or loss to follow-up. Participation was determined mainly by the distance of the family's residence from our institution. Questionnaires completed by the parents and treating physicians revealed that none of the nonparticipants had died and that their rates of reoperation (1/29; 3.4%) and reintervention (1/29; 3.4%) were not different from those of the study group.

Forty-six (76.7%) of the 60 patients included in the present study were male and 14 (23.3%) were female. Birth weight ranged from 2.1 to 5.4 kg (3.5 ± 0.5 kg). Forty-seven patients (78.3%) had a simple TGA, 11 (18.4%) had an unimportant VSD that was not closed surgically, and 2 (3.3%) had a VSD closed through the right atrium during ASO. Three patients (5.1%) had a coarctation of the aorta corrected at a later date. Most of the neonates (82%) had undergone balloon atrioseptostomy, and all had been treated with prostaglandin E_1 before surgery.

Coronary artery status according to Gittenberger-de Groot and associates [10] was usual (type A I) in 50 (83.3%) of the studied patients. In 3 cases (5.0%), the circumflex coronary artery arose from the right coronary artery (type AB I); in 3 cases (5.0%) right coronary artery and circumflex coronary artery were inverted (type AB II); in 2 (3.3%) a single ostium for the left and right coronary arteries was noted to arise from the right posterior facing sinus (type B I); and in 2 (3.3%) a single ostium for the left and right coronary arteries was noted to arise from the left anterior facing sinus (type A II).

Surgical Management

In the study group, the age at ASO ranged from 2 to 39 days (7.1 ± 5.1 days); 2 patients were older than 12 days. Uniform surgery was performed under deep hypothermic circulatory arrest with an esophageal temperature of 14° to 17°C (15.1 ± 1.0°C) and combined low flow cardiopulmonary bypass, as described previously [4]. The coronary arteries were punched out with a button and transplanted into the neo-aortic root with 7.0 PDS. Reconstruction of the coronary artery excision sites was uniform with insertion of two autologous pericardial patches. Direct anastomosis between the distal pulmonary stump and the neopulmonary trunk was performed with 6.0 PDS.

Follow-Up Study Protocol

The 60 unselected patients were evaluated at an age of 7.9 to 14.3 years (10.5 ± 1.6 years). The protocol included an interview with the child and his or her accompanying persons as well as clinical pediatric and cardiological examination performed by 1 pediatric cardiologist.

A 12-lead standard electrocardiogram (ECG) at rest and a 24-hour Holter ECG were performed and analyzed applying generally accepted criteria [11–13]. M-mode, two-dimensional, Doppler, and color Doppler echocardiography were performed with an ATL-HDI 3000 CV unit (Advanced Technology Laboratories, Solingen, Germany). Standard long-axis and 4-chamber views were used to visualize the aorta and the ventricles. Pulsed and continuous wave Doppler were applied to assess valvular competence and to identify obstructions of the great vessels or their branches. Color Doppler was used to examine neo-aortic and neopulmonary insufficiency or intracardiac shunts.

Left heart dimensions and shortening fraction were compared with those of normal children [14]. Neo-aortic diameters were compared with those of normal children [15] and with those of the previous study. Still frames were taken from the parasternal long-axis view at the end of systole. The internal diameter of the valvular annulus was measured at the hinge point of the valve leaflets, the internal diameter of the neo-aortic root at its maximal width.

Doppler peak instantaneous gradients were calculated using the simplified Bernoulli equation. Supravalvular pulmonary stenosis was classified by Doppler gradients as absent (up to 16 mm Hg), trivial (17 to 24 mm Hg), mild (25 to 39 mm Hg), moderate (40 to 59 mm Hg), and severe (more than 59 mm Hg) [16]. Insufficiency of the neo-aortic and neopulmonary valves was quantified by color Doppler as absent, mild (1 to 3 mm diastolic backflow), moderate (4 to 6 mm diastolic backflow), or severe (more than 6 mm diastolic backflow) [17, 18].

Statistical Analysis

Results were expressed by the median value and interquartile ranges, assuming nonnormal distribution of the data, or as percentages. The outcome data included both categorical and continuous variables. Fisher exact tests and χ^2 tests were used to analyze categorical variables. For comparison of variables at different times of assessment within the study group, the paired nonparametric Wilcoxon test was used. For comparison of variables between subgroups, the nonparametric Mann-Whitney *U*-test was administered. Neo-aortic diameters were expressed as z-scores. Statistical analysis was performed using the SPSS for Windows software, version 10.0 (SPSS GmbH Software, Munich, Germany). All statistical tests were performed using a significance level of 0.05.

Results

Reintervention Rate and Health Status

During follow-up, 2 of the 60 patients (3.3%) of the study group had undergone reoperation after neonatal ASO. One of those patients had undergone enlargement of the right ventricular outflow tract with resection of a severe obstruction and reconstruction with a patch at the age of 3 years. Another clinically asymptomatic patient (coronary pattern type B I) with severe ST-T wave depression in a routine exercise testing had needed an internal

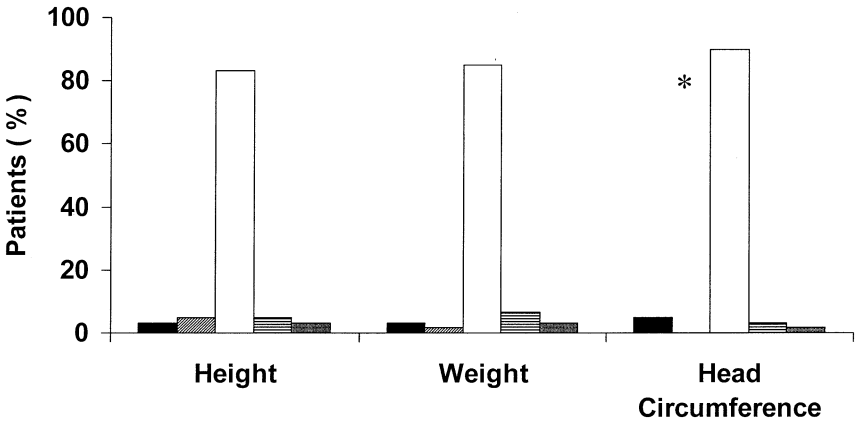

Fig 1. Somatic development in 60 patients 7.9 to 14.3 years (mean 10.5 years) after neonatal arterial switch operation. Normal height and weight and reduced head circumference (*), compared with the normal population (comparison of measurements based on Brandt [20]). Percentiles: ■ = < 3; ▨ = 3 to 10; □ = 10 to 90; ▤ = 90 to 97; ▩ = > 97.

mammary bypass graft to the proximal anterior descending coronary artery at the age of 5 years after complete occlusion of the main left coronary artery with retrograde perfusion of its branches through collaterals from the right coronary system. Follow-up cineangiography revealed a mild stenosis at the site of anastomosis to the left coronary artery. A concomitant aortic isthmic stenosis had become hemodynamically important during follow-up in 3 (5.1%) of the 60 patients, all with an intact ventricular septum, leading to a second operation to correct aortic coarctation by end-to-end anastomosis at ages 1 month, 2 years, and 5 years, respectively. One patient (1.7%) underwent catheter intervention with dilatation of a severe stenosis of the neopulmonary valve and the main pulmonary artery at age 14 years.

Fifty-six (93.3%) of the 60 patients had no limitation of physical activity (class I according to the New York Heart Association); 4 patients (6.7%) could not be staged because of neurologic impairment (3 patients) and methylphenidate treatment [1], respectively. All patients were without cardiac medication. A detailed report on neurodevelopmental status of the cohort is available in a separate publication [19].

Height and weight of the 60 patients were normal compared with the general population [20]. In contrast, fronto-occipital head circumference was reduced compared with the normal: microcephaly (< 3rd percentile in 3 patients) was due to velo-facio-cardiac syndrome in 1, to embryo-fetal alcohol syndrome in another, and to harmonic somatic developmental delay in the remaining patient (Fig 1). Systolic and diastolic arterial blood pressures at rest were normal in all children. None of the children had clinical signs of cardiac insufficiency.

Systolic heart murmurs were noted in 58 (98.7%) patients, usually at the base of the heart. Eleven patients (18.3%) had murmurs grade I, 34 (56.7%) grade II, 10 (16.7%) grade III, and 3 (5.0%) grade IV. Grade III and grade IV murmurs were associated—isolated or combined—with hemodynamically unimportant VSD (n = 4), supravalvular pulmonary stenosis of mild (n = 5), moderate (n = 4), or severe (n = 2) degree, or mild residual aortic isthmic stenosis (n = 1), respectively.

Diastolic heart murmurs grade II were noted in 3 patients (5.0%) who had neo-aortic valve regurgitation of mild (n = 1) or moderate (n = 1) degree, or moderate pulmonary insufficiency (n = 1), respectively.

Asymmetry of the right and left hemithoraces with visible prominence of the left ventral ribs was found in 8 (13.3%) of the patients. Eleven patients (18.3%), all without hereditary taint, showed a mild funnel chest. In total, 19 (31.6%) of the patients had a striking thoracic configuration after neonatal median sternotomy. Thoracic deformities were not related to cardiomegaly or surgical technique which was uniform in all patients. Compared with the study 5 years ago, this frequency was significantly higher ($p < 0.05$), due to an increased occurrence of mild funnel chest. Thoracic abnormalities were of a mild degree, and no patient needed specific orthopedic treatment or physiotherapy.

Surface Electrocardiography at Rest

RHYTHM. Fifty-five of the study patients (91.7%) were in sinus rhythm, 4 (6.7%) had an ectopic atrial rhythm, and 1 (1.7%) a junctional rhythm. One patient without history of tachycardia showed Wolff-Parkinson-White syndrome. Four patients (6.7%) had first-degree heart block. Statistical analysis showed a significantly increased incidence of first-degree heart block compared with the study 5 years ago (Table 1).

INTRAVENTRICULAR CONDUCTION ABNORMALITIES. Complete right bundle branch block was seen in 6 patients (10.0%). Three of these had a VSD which, in 2 patients, was closed during ASO. The incidence of complete right bundle branch block was 6.7% in TGA without and 100% in TGA with VSD patch closure. Beyond the incidence of complete right bundle branch block, patients with VSD patch closure did not have different ECG and Holter monitoring results, compared with patients without VSD patch closure.

VENTRICULAR HYPERTROPHY. Two patients, 1 with mild aortic insufficiency and 1 with hemodynamically unimportant VSD, both having normal echocardiographic left ventricular dimensions, met ECG criteria for left ventricular hypertrophy. Fourteen patients (23.3%) had signs of right ventricular hypertrophy: 4 patients had mild, 4 had moderate, and 2 had severe supravalvular pulmonary

Table 1. Standard Electrocardiographic Findings After Neonatal Arterial Switch Operation: Longitudinal Course

	Follow-up 5.3 (1.6) years		Follow-up 10.5 (1.6) years		
	n	%	n	%	p^a
Rhythm					
Sinus	57	95.0	55	91.7	NS
Ectopic atrial	1	1.7	4	6.7	
Junctional	2	3.3	1	1.7	
Atrioventricular conduction					
Normal	59	98.3	56	91.7	<0.05
Primary heart block	0	0	4	6.7	
Preexcitation (WPW)	1	1.7	1	1.7	
Intraventricular conduction					
Normal	55	91.7	54	90.0	NS
Complete RBBB	5	8.3	6	10.0	
VSD patch closure	2	3.3	2	3.3	
No VSD patch closure	3	5.0	4	6.7	
Ventricular hypertrophy					
No	52	86.7	44	73.3	<0.05
LVH	2	3.3	2	3.3	
RVH	6	10.0	14	23.3	
ST-T wave changes					
No	60	100.0	60	100.0	NS

[a] Differences between findings at mean age (SD) 5.3 (1.6) and 10.5 (1.6) years.
LVH = left ventricular hypertrophy; NS = not significant; RBBB = right bundle branch block; RVH = right ventricular hypertrophy; VSD = ventricular septal defect; WPW = Wolff-Parkinson-White syndrome.

n = 60 at both follow-up times.

stenosis; 2 additional patients had pulmonary valve insufficiency; in 2 cases, supravalvular pulmonary stenosis was combined with right ventricular outflow tract obstruction. Frequency of right ventricular hypertrophy increased significantly compared with the study 5 years ago and was significantly correlated to the presence of pulmonary stenosis ($p = 0.001$).

ST-T WAVE CHANGES. None of the patients (the 6 with complete right bundle branch block excluded) had evidence of ischemia at rest.

Twenty-Four-Hour Ambulatory Electrocardiographic Monitoring

RHYTHM. Sinus or atrial rhythm was present in 58 of 60 patients (96.7%). Two (3.3%) patients had intermittent periods of atrioventricular dissociation and nodal rhythm at rest. Minimal heart rates in these patients were 30 and 36 beats per minute (bpm), respectively (Table 2).

ATRIOVENTRICULAR CONDUCTION ABNORMALITIES. Two patients (3.3%) showed intermittent short periods of second-degree heart block (Wenckebach type) at low heart rates. The patient with Wolff-Parkinson-White syndrome had sinus rhythm and preexcitation without tachycardia throughout the 24 hours.

RATE. The minimal heart rate ranged from 30 to 66 bpm (median 47, interquartile range 6), the maximal heart rate ranged from 70 to 201 bpm (median 153, interquartile range 40). The mean heart rate at sleep (measured during at least 5 sleeping hours) ranged from 33 to 68 bpm (median 49, interquartile range 7). One patient had short sinus pauses (1.9 to 2.3 seconds) during sinus bradycardia at sleep.

ATRIAL AND VENTRICULAR ECTOPY. The prevalence of atrial and ventricular ectopy was not different from the study 5 years ago. Twelve patients (20.0%) had occasional (fewer than 15 per hour) atrial ectopic beats. Episodes of supraventricular tachycardia were not noticed. Ventricular ectopy was present in 13 patients (21.7%). Occasional ventricular ectopic beats (fewer than 30 per hour) were found in 12 patients (20.0%), whereas 1 (1.7%) had frequent (more than 30 per hour) ventricular ectopic beats during exercise. This patient showed monomorphous premature beats from the right bundle branch block type at heart rates higher than 120 bpm. Cardiac catheterization including coronary angiography at age 9.2 years resulted in mild to moderate insufficiency of the quadricuspid aortic valve with normal left ventricular function and no evidence of stenosis, disruption, or obstruction of the coronary circulation.

Echocardiography

LEFT VENTRICLE. M-mode recordings showed a normal left ventricular end-diastolic diameter in all patients. The shortening fraction ranged from 27% to 47% (median 38%, interquartile range 8%). In 1 patient the shortening fraction was less than 28%. Values did not differ significantly, as compared with the study 5 years ago (Table 3).

Table 2. Holter Monitor Findings After Neonatal Arterial Switch Operation: Longitudinal Course

	Follow-up 5.2 (1.5) years (n = 56)		Follow-up 10.5 (1.6) years (n = 60)	
	n	%	n	%
Rhythm				
Sinus/atrial	53	94.6	58	96.7
Junctional	3	5.4	2	3.3
Atrioventricular conduction				
Normal	55	98.2	57	95.0
Secondary heart block (intermittent)	0	0	2	3.3
Preexcitation (WPW)	1	1.8	1	1.7
Atrial ectopic activity				
No	42	75.0	48	80.0
< 15 beats/h	13	23.2	12	20.0
> 15 beats/h	1	1.8	0	0
Ventricular ectopic activity				
No	47	83.9	47	78.3
< 30 beats/h	9	16.1	12	20.0
> 30 beats/h	0	0	1	1.7

None of the differences between findings at the two ages were significant.

WPW = Wolff-Parkinson-White syndrome.

AORTIC DIMENSIONS AND FUNCTION. The end-systolic neo-aortic valve annulus diameter ranged from 12 to 31 mm (median 20 mm, interquartile range 5 mm) and was not significantly different in comparison to the values 5 years ago (range 16 to 31 mm; median 21 mm, interquartile range 5 mm; $p = 0.09$). Expressed in z-scores, values decreased significantly ($p < 0.001$) between the measurement 5 years ago and the present assessment in which 98% of the patients had values within the 90% confidence interval for control subjects [15] (Fig 2). Six patients with increased z-scores had a simple TGA without VSD and without neo-aortic insufficiency. The end-systolic neo-aortic root diameter ranged from 17 to 36 mm (median 27 mm, interquartile range 6 mm) and decreased in comparison with the values 5 years ago (range 24 to 44 mm; median 32 mm, interquartile range 6 mm; $p < 0.001$). Expressed in z-scores, values also decreased significantly ($p < 0.001$) between the measurement 5 years ago and the present assessment in which 92% of the patients had values within the 90% confidence interval for control subjects [15] (Fig 3). Neo-aortic root dilatation in 5 patients was not correlated to an unusual coronary artery pattern.

Neo-aortic valve regurgitation was detected in 8 (13.3%) of 60 patients. In 7 cases, regurgitation was of a mild degree, whereas it was of a moderate degree in the 1 patient with quadricuspid aortic valve. Prevalence of neo-aortic insufficiency was not different compared with the earlier study. No correlation was found between the occurrence of neo-aortic insufficiency and the diameter of neo-aortic valve annulus, whereas neo-aortic insufficiency was significantly correlated to the presence of neo-aortic root dilatation ($p = 0.02$).

No patient had neo-aortic valve or root stenosis, whereas 3 patients had mild residual aortic isthmic stenosis after surgical correction.

PULMONARY STENOSIS. Supravalvular pulmonary stenosis was found in 25 (41.6%) of the patients evaluated: 12 (20.0%) trivial, 6 (10.0%) mild, 5 (8.3%) moderate, and 2 (3.3%) severe. In comparison with the study 5 years ago, incidence of supravalvular pulmonary stenosis increased from 30.0% to 41.6% ($p = 0.001$). Progressive supravalvular pulmonary stenosis during the follow-up period was found in 7 patients (11.7%), 2 of whom (29%) had combined subvalvular or valvular pulmonary stenosis; 5 patients changed from mild to moderate, and 2 patients changed from moderate to severe supravalvular pulmonary stenosis. Incidence and degree of supravalvular pulmonary stenosis were not statistically different if the 2 patients with VSD patch closure were excluded.

PULMONARY INSUFFICIENCY. Pulmonary valve insufficiency was present in 7 patients (11.7%). It was mild in 6 and of moderate degree in 1 asymptomatic patient. Compared with the study 5 years ago, the rate of pulmonary valve insufficiency increased significantly ($p = 0.01$).

Comment

Reinterventions

Compared with other series [7, 8, 21] and even considering the fact that our study did not comprise complex forms of TGA, freedom from reoperation was high 10 years after ASO (97%). A high rate of freedom from any reintervention—95% after 10 years—was comparable to recent results in a large group of patients after ASO for simple TGA [9].

Table 3. Echocardiographic Findings After Neonatal Arterial Switch Operation: Longitudinal Course

	Follow-up 5.3 (1.6) years		Follow-up 10.5 (1.6) years		
	n	%	n	%	p^a
Left ventricular end-diastolic diameter					
Normal	55	91.7	60	100.0	NS
< 3rd percentile	1	1.7	0	0	
> 97th percentile	4	6.7	0	0	
Shortening fraction					
Normal (28% to 2%)	56	93.3	53	88.3	NS
Reduced (< 28%)	1	1.7	1	1.7	
Not measurable	3	5.0	6	10.0	
Aortic insufficiency					
None	53	88.3	52	86.7	NS
Mild	7	11.7	7	11.6	
Moderate	0	0	1	1.7	
Aortic valve stenosis					
None	60	100.0	60	100.0	NS
Aortic isthmic stenosis					
None	57	95.0	57	95.0	NS
Mild	2	3.3	3	5.0	
Moderate	1	1.7	0	0	
Pulmonary stenosis					
None	42	70.0	34	56.7	0.001
Trivial SPS	11	18.3	12	20.0	
Mild SPS	5	8.3	6	10.0	
Moderate SPS	2	3.3	5	8.3	
Severe SPS	0	0	2	3.3	
Valvular/subv. (combined)	1		2		
Not measurable	0	0	1	1.7	
Pulmonary insufficiency					
None	59	98.3	52	86.7	0.01
Mild	1	1.7	6	10.0	
Moderate	0	0	1	1.7	
Not measurable	0	0	1	1.7	

[a] Differences between findings at mean age (SD) 5.3 (1.6) and 10.5 (1.6) years.

NS = not significant; SPS = supravalvular pulmonary stenosis; subv. = subvalvular.

General Health Status

General pediatric health status was good and not different compared with normal children, with the exception of the 4 handicapped patients mentioned above, whereas neurodevelopmental outcome was recently found to be reduced in the same study group [19]. Thoracic abnormalities were frequent with an increased incidence of funnel chest compared with the study 5 years ago [4]. These abnormalities were, however, mild and did not require orthopedic treatment and physiotherapy.

Standard Electrocardiographic and Holter Monitoring

The advantages of anatomic over atrial repair of TGA with respect to preservation of sinus node function have been well documented [9, 22–26]. Our study presents detailed information concerning long-term longitudinal incidence of significant atrial or ventricular rhythm and conduction disturbances after neonatal ASO, based on systematically evaluated standard ECG and Holter monitoring. Sinus rhythm prevailed in the vast majority of patients without change compared with the mid-term follow-up study [4].

Incidence and severity of ventricular ectopy were not significantly increased compared with our results 5 years ago and were less frequent than in children assessed at mean age 2 years after neonatal ASO [2]. Severe ventricular ectopy such as bigeminy, couplets, or runs of ventricular tachycardia may be an indicator for ventricular dysfunction or coronary insufficiency [27].

The persistent low incidence and innocence of atrial arrhythmia in our study underlines the advantages of arterial versus atrial repair in this respect [22–25].

Echocardiography

Left ventricular abnormalities are rare after anatomic correction of TGA. Follow-up periods up to 15 years

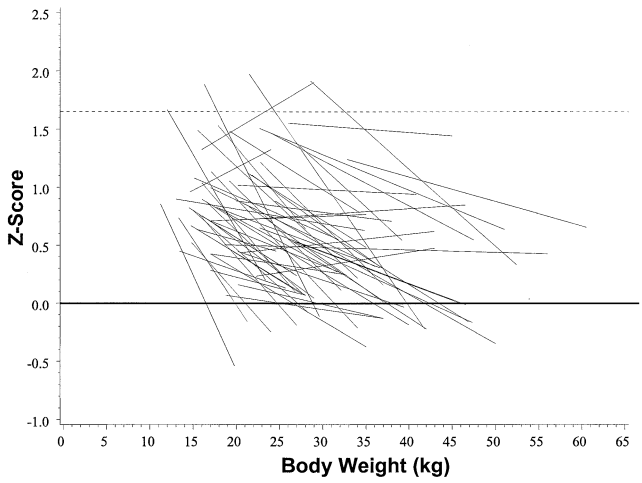

*Fig 2. Echocardiographic end-systolic measurements of the neo-aortic annulus (z-scores) plotted versus body weight in 60 children (*solid lines*) after neonatal arterial switch operation at mean age 5.3 ± 1.6 years and mean age 10.5 ± 1.6 years, respectively. Z-scores show a significant decrease (*$p < 0.001$*) between the two time points of measurement. The* solid horizontal line *represents the regression line and the* dashed horizontal line *represents the 90% confidence interval for age-matched normal children (comparison of measurements based on work by Hofstetter and colleagues [15]).*

reveal no evidence of time-related deterioration of left ventricular function [3, 9]. In our series, echocardiographic assessment of left ventricular dimensions and global function confirmed this observation.

Concern has been raised about neo-aortic root dilatation and concomitant aortic regurgitation in children after neonatal ASO [17, 28], as well as about loss of distensibility of the aortic base [29]. A major finding of our present longitudinal study was the observation that neo-aortic valve annulus as well as root diameters did not increase and that their z-scores decreased, compared with the values at mean age 5.3 years. A recent study by Hutter and colleagues [30] provided information about rapid dilatation of the neo-aorta in the first year of life after neonatal ASO, followed by growth toward normalization of the valve and sinus size during childhood, but was not based on repeated echocardiographic measurements in the same patient group. Our results add important information and extend current knowledge with respect to age-dependent development of the neo-aortic root.

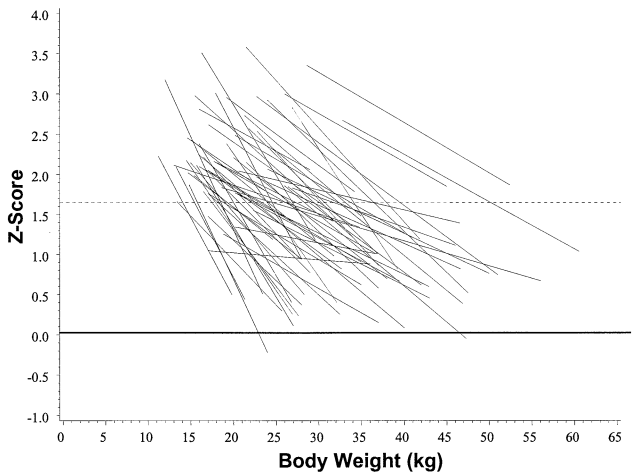

*Fig 3. Echocardiographic end-systolic measurements of the neo-aortic root plotted versus body weight in 60 children (*solid lines*) after neonatal arterial switch operation at mean age 5.3 ± 1.6 years and mean age 10.5 ± 1.6 years, respectively. Z-scores show a significant decrease (*$p < 0.001$*) between the two time points of measurement. The* solid horizontal line *represents the regression line and the* dashed horizontal line *represents the 90% confidence interval for age-matched normal children (comparison of measurements based on work by Hofstetter and colleagues [15]).*

In our study group, incidence of neo-aortic valve regurgitation (13.3%) as assessed by color Doppler was similar to that in reports with a mean mid-term follow-up of 5 to 6 years [7, 9]. Compared with the previous mid-term results of the present patient group, rate and degree of neo-aortic valve regurgitation have not significantly increased with age. Mild neo-aortic insufficiency was not found related to the diameter of the neo-aortic valve annulus, but, in contrast to the findings of Hutter and colleagues [30], to the presence of neo-aortic root dilatation. One can speculate that, with further normalization of neo-aortic root diameter with age, incidence of neo-aortic insufficiency might perhaps not increase significantly in the future.

In our study, neo-aortic valve or outflow tract stenoses were not observed, confirming earlier investigations [7, 9, 30]. Until now, reintervention was unnecessary for left ventricular outflow tract stenosis, predicted to occur with a base incidence of 0.1% per year after neonatal ASO [31].

In our study group as in other mid- and long-term reports [1, 9, 31], supravalvular pulmonary stenosis, especially branch pulmonary stenosis, was the most common postoperative complication after ASO. Reintervention rate for right ventricular outflow obstruction (2.6% after 10 years), including stenoses at subvalvular, valvular, and supravalvular sites, however, was less in our patients, compared with other series [7, 20], and comprised half the predicted base incidence of 0.5% reinterventions per year [31]. Supravalvular pulmonary stenosis in our patients is correlated to the prevalence of right ventricular hypertrophy in ECG. As the incidence of supravalvular pulmonary stenosis is dependent on the time of follow-up, on the method of assessment, and also on the definition of "significant" changes, percentages differ considerably in the various studies and range from about 15% to 50%. Although mild systolic gradients in the right ventricular outflow tract are common, the diagnosis of a "severe" supravalvular pulmonary stenosis is rare and ranges from about 2% to 11% [1, 9, 32]. Supravalvular pulmonary stenosis is not uncommonly found associated with growth failure of the valve annulus and pulmonary valve stenosis [32], especially in patients with concomitant aortic isthmic stenosis [33].

Various mechanisms have been implicated in the development of supravalvular pulmonary stenosis. As re-

ported by Williams and coworkers [31] and Wernovsky [33], proximal supravalvular pulmonary stenosis appears to occur early after surgery, related to hypoplasia of the native aortic annulus, and may be reduced by careful sinus reconstruction. However, distal obstruction may occur early and late after surgery, potentially accompanied by growth retardation of the concerned branches, and has been found to be related to certain unusual coronary artery patterns and the technique of surgical coronary sinus reconstruction [33]. In addition, the Lecompte procedure may induce a flattening of the main pulmonary artery with concomitant reduction of its cross-sectional area [34]. In summary, as demonstrated in our study and others, both incidence and severity of supravalvular pulmonary stenosis increase with age; careful further observation is mandatory, especially in the period of rapid somatic growth during adolescence.

In conclusion, the present study highlights persistent encouraging cardiological results 10 years after neonatal ASO for TGA. General health status is excellent in most children. Incidence of surgical or catheter reinterventions and rhythm abnormalities continues to be rare. Late morbidity mainly consists of pulmonary stenosis or neo-aortic insufficiency. Neo-aortic valve and root diameters do not increase and their z-scores decrease in school-aged children, whereas prevalence and degree of neo-aortic valve insufficiency remain stable in our experience. Rate and severity of supravalvular pulmonary stenosis, however, show persistent increase with age and remain a matter of concern.

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