Long term follow-up of left ventricular performance and size of the great arteries before and after one- and two-stage arterial switch operation of simple transposition

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Abstract

Objective: Long-term angiographic evaluation of left ventricular performance and size of the great arteries after one-stage neonatal versus two-stage arterial switch operation (ASO) of simple transposition. Methods: Analysis of cineangiographic studies obtained during the process of two-stage ASO for 34 patients and after neonatal repair for 52 patients. Results: At early follow-up after two-stage ASO the left ventricular enddiastolic volume (LVEDV) was +1.8 standard deviations (S.D.) larger than LVEDV of control patients, but normalized completely (0.0 S.D.) at late follow-up. In contrast, after neonatal repair the LVEDV was always normal, and the median EF was significantly higher than after two-stage ASO (73 vs. 68%). The diameters of the native pulmonary annulus and sinus increased significantly after pulmonary artery banding to +4.5 and +4.8 S.D., respectively. After ASO, a significant decrease of the respective sizes occurred from early to late follow-up (annulus: +6.0 to +2.1 S.D.; sinus: +7.1 to +4.1 S.D.). After neonatal ASO the neoaortic annulus and sinus were only +1.5 and +2.7 S.D. larger than the comparable normal structures. The differences to the two-stage group were significant. In both groups, the neoaortic anastomosis had no diameters significantly different from normal. After one- and two-stage repair, the size of the neopulmonary annulus and sinus decreased similarly in both groups from early to late follow-up (annulus: +0.9 to −2.4 S.D.; +0.3 to −2.8 S.D.; sinus: −0.7 to −1.6 S.D.; −0.7 to −1.8 S.D.). Conclusions: Neonatal ASO has definite advantages over two-stage repair concerning LV-performance and the degree of dilation of the neoaortic root. The significantly reduced size of the neopulmonary root after both procedures is remarkable, but fortunately mostly without clinical significance.

Keywords: Simple transposition; Arterial switch operation; Left ventricular function; Great arteries

1. Introduction

When the concept of the arterial switch operation (ASO) for transposition of the great arteries was developed 20 years ago, it was expected to avoid disadvantages of atrial level repair like atrial arrhythmias [1,2] and systemic ventricular dysfunction in the long term [3]. Before neonatal ASO became feasible, our institution took an active hand in the evaluation of the two-stage repair with establishing a pulmonary artery band (PAB) and systemic to pulmonary shunt as the first step [4].

The staged treatment may have long term disadvantages for the left ventricular performance because of the sudden increase of afterload at PAB as well as for the dimensions of the great arteries, especially concerning the enlargement of the definitive aortic root after the initial PAB, but similarly the pulmonary root after reconstruction in front of the aorta. Therefore, we compared the angiographic data obtained during long-term follow-up of patients up to 16 years after two-stage repair and 11 years after neonatal repair of simple transposition.
2. Patients and methods

2.1. Patients

The total study group consisted of 86 patients with simple transposition, who had cineangiographic examinations during the process of two-stage ASO between 1978 and 1986 (n = 34, 95% of survivors, group 1) or after one-stage neonatal repair between 1985 and 1995 (n = 52, 91% of survivors; group 2). Six (18%) patients of group 1 and 10 (19%) of group 2 had an additional small ventricular septal defect with no hemodynamic significance, which eventually was closed by suture.

2.1.1. Group 1

The median age at the time of the PAB (with an additional systemic-to-pulmonary artery shunt in 23/34) was 11 (1–59) months, and of ASO 16 (2.5–63) months. The time intervals between PAB and ASO ranged between 0.5 and 16.5 months (median 3.9). Cardiac catheterizations were performed after birth, shortly before PAB and ASO, respectively, and at different time intervals after repair [median 45 (1–193) months]; LV/RV pressure ratio before ASO ranged between 0.47 and 2.00 (median 1.06). Eleven children (18%) underwent more than one angiographic study at follow-up after ASO. Six children had relevant stenoses (systolic gradient >30 mmHg) of the distal pulmonary trunk or at the pulmonary branches, and one had significant aortic regurgitation demonstrated by angiography.

2.1.2. Group 2

The median age of ASO was seven (1–32) days. Cardiac catheterization was performed between 1 and 130 (median 33) months after surgery; 11 children underwent more than one angiographic study at follow-up. Six children (11%) had relevant stenoses (systolic gradient >30 mmHg) of the distal pulmonary trunk or at the pulmonary branches, but no one had aortic regurgitation demonstrated by angiography.

In all neonates the reconstruction of the pulmonary root was performed with a direct anastomosis, mostly using the Lecompte-technique, while in the two-stage group a tube made from different materials (pericard, homologous dura, dacron) was used in 26 (76%) patients to bridge the gap between the native aortic root and the pulmonary bifurcation. The holes of the native aortic sinus where the coronary arteries were explanted were filled with separate pericardial patches, but in the two-stage group also different materials (esp. dura) were used.

2.2. Data collection

At cardiac catheterization biplane angiograms were carried out in the postero-anterior and lateral projection in both ventricles, the aortic root and after correction in the main pulmonary artery. Left ventricular enddiastolic and endsystolic borders were drawn by hand to determine the respective volumes and ejection fraction. The diameters of the native pulmonary/neoaortic root were measured in the lateral projection at the following sites: (1) the annulus at the hinge points of the valve leaflets; (2) the maximal diameter of the aortic root; and (3) the sinutubular junction. Additionally, the native aortic/neopulmonary annulus, measured at the hinge points of the valve leaflets, and sinus were determined in the frontal (frequently 30° cranially angulated) and lateral projection, as these structures may not be circular after the ASO.

2.3. Data analysis

Left ventricular enddiastolic and end systolic volumes (LVEDV and LVESV) were determined by the area-length method. All values were corrected with factors appropriate for spatial orientation and cardiac phase [5], and the results were compared with normal values of our service. The predicted normal LVEDV-value was based on equation 59.2 (BSA)^1.19, with the 95% confidence limits (67–133% of the predicted normal value). The respective equation for the LVESV-value was 14.4 (BSA)^1.20. Ejection fraction (EF) of the left ventricle was calculated as EF = (LVEDV – LVESV)/LVEDV (normal 75 ± 4%).

All diameter measurements of the great arteries were compared to previously obtained normal values for children of our service [6,7]. Before ASO, the native pulmonary annulus and sinus were compared with the aortic annulus and sinus of normal children. After ASO, the neoaoortic annulus and sinus as well as the aortic diameter at the sinutubular junction were compared with the respective normal aortic values, and the neopulmonary annulus and sinus were compared with the respective normal pulmonary values. As the neopulmonary diameters were determined much smaller in the lateral (d1) than in the frontal (d2) projection, we assumed that the shapes were oval, and calculated the area A according to $A = \frac{1}{2} \cdot \pi \cdot d1 \cdot d2$.

For analysis, the pulmonary and aortic diameters at the different levels as well as the left ventricular enddiastolic volumes were calculated as their degree of normality (Z), the number of standard deviations by which the actual value deviated from the mean normal value, where the mean and standard deviation are BSA dependent. Thus, a measurement at the expected normal mean for BSA has a z-score of 0, and a measurement at the upper and lower 95% confidence limits have z-scores of 1.96 and −1.96, respectively. The z-scores of values obtained before and after the median of the postoperative period after one- and two stage repair (approx. 3 and 4 years, respectively) were compared in order to recognize changes of size from early to late follow-up. The mean age at early follow-up was 13 (10) and 39 (15) months for group II and I, respectively, but 81 (30) and 161 (43) months at late follow-up.

The mean z-score for each structure measured before and after surgery was compared with zero using a single-sample
-test. One-way ANOVA was used to determine the relation between the z-scores. For all statistical analyses, a value of $P < 0.05$ was considered significant.

3. Results

3.1. Left ventricular size and function

3.1.1. Group 1

In the two-stage group, before PAB the LVEDV was determined slightly above normal [$z$-score $= +0.7$ (2.2 S.D.)] and the median EF was 71 (51–84)%. The increase of afterload by PAB resulted in a reduced left ventricular systolic function with a median EF of 66 (48–80)%, while LVEDVs were still within normal limits [$z$-score $= +0.2$ (2.0) S.D.]. However, at cardiac catheterization early after ASO the LVEDV showed a significant increase to a $z$-score of $+1.8$ (2.1) S.D.; nine of 23 patients had a LVEDV above $+2$ S.D. At late follow-up (more than 4 years = median; see ‘data analysis’) all patients showed a complete normalization of their LV-size [$z = 0.0$ (1.0) S.D.] (Fig. 1a). However, the median EF did not improve significantly after ASO either at early [69 (58–77)]% or late [68 (64–75)]% follow-up.

3.1.2. Group 2

In the one-stage group (i.e. after neonatal ASO) early as well versus late cardiac catheterization showed a normal LVEDV with $z$-scores of $-0.5$ (1.7) S.D. and $-0.6$ (1.2) S.D., respectively. All values were within normal limits except for six cases, having volumes slightly below 2 S.D. (Fig. 1b). The EF was determined significantly higher [73 (63–86)]% than in the two-stage group.

3.2. Neo-aortic root

3.2.1. Group 1

In the two-stage group, the native pulmonary annulus and sinus were not significantly larger than the aortic annulus and sinus of control patients (13 and 4% above normal mean, respectively). The mean differences expressed as $z$-values are listed in Table 1. At reexamination after PAB (shortly before ASO), their dimensions had significantly increased to 23% and 40% above normal mean, respectively. A significant correlation of the degree of enlargement to the LV/RV pressure ratio or to the time interval to ASO did not exist. After ASO, the size of the neoaortic annulus remained nearly unchanged, but the neoaortic sinus was measured 52% above normal. An angiographic example for the effect of the enlargement of the neoaortic root on the pulmonary root is given in Fig. 2. When the respective $z$-scores were compared at early versus late follow-up, a significant decrease of size was determined (Fig. 3a,b). The diameters at the sinutubular junction (i.e. aortic anastomosis) were not significantly different from normal $[+1.1$ (1.7) S.D.].

3.2.2. Group 2

After neonatal ASO the neoaortic annulus and sinus were 8% and 23% larger (n.s.) than the comparable normal structures (Table 2). The differences to the two-stage group were significant. When the respective $z$-scores were compared at early versus late follow-up, no differences were determined (Fig. 4a,b). The diameters of the aortic anastomosis at the sinutubular junction were determined slightly below, but not significantly different from normal $[-0.7$ (1.4) S.D.].

3.3. Neo-pulmonary root

3.3.1. Group 1

After two-stage ASO the diameters of the neopulmonary annulus and sinus were determined much smaller in
the lateral than in the frontal view (ratio lateral to frontal diameter: 0.82 and 0.79, respectively). Assuming an oval shape their areas were determined 8% and 18% smaller (n.s.) than those of the comparable normal structures (Table 2). When the respective \( z \)-scores were compared at early versus late follow-up, the decrease of the annulus size (from \(-3\%\) to \(-32\%\) below normal mean) was significant, but not of the sinus (from \(-11\%\) to \(-29\%\)).

3.3.2. Group 2

After neonatal ASO we determined a less pronounced flattening of the pulmonary annulus and sinus (ratio lateral to frontal diameter 0.85 and 0.90) and their areas were not

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<th>Neopulmonary annulus</th>
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<td>2 Stage ASO</td>
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<tr>
<td>Before PAB</td>
<td>4.8 ± 2.2</td>
<td>2.8 ± 1.4</td>
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<td>Before ASO</td>
<td>4.6 ± 3.1</td>
<td>3.3 ± 1.6</td>
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<td>After ASO</td>
<td>-0.7 ± 2.3</td>
<td>-1.1 ± 2.3</td>
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<td>Up to 4 years after ASO</td>
<td>0.3 ± 1.9</td>
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<td>More than 4 years after ASO</td>
<td>-2.8 ± 1.4</td>
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<td>1 Stage ASO</td>
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<td>After ASO</td>
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<td>Up to 3 years after ASO</td>
<td>0.9 ± 3.4</td>
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<td>More than 3 years after ASO</td>
<td>-2.4 ± 2.7</td>
<td>-1.6 ± 2.6</td>
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The data are expressed as \( z \)-values and their standard deviations. PAB, pulmonary artery banding; ASO, arterial switch operation. The values ‘after ASO’ are divided into two subgroups before and after the median of the postoperative follow-up.

3.3.2. Group 2

After neonatal ASO we determined a less pronounced flattening of the pulmonary annulus and sinus (ratio lateral to frontal diameter 0.85 and 0.90) and their areas were not

significantly smaller than the comparable normal structures [annulus – 6\%, sinus – 25\%]. In comparison to the two-stage group a significant difference did not exist. When the respective \( z \)-scores were compared at early versus late follow-up, we determined a decreasing size of the pulmonary root. While the difference was significant for the annulus size (+10\% vs. –28\%), it was not for the sinus size (–11\% vs. –26\%) (Fig. 5a,b).

4. Discussion

4.1. Left ventricular size and function

The most important advantage of arterial level repair of transposition is the preservation of the left ventricle as the systemic one. However, ventricular performance may become compromised by the burden of retraining the low pressure left ventricle by PAB in the two-stage procedure.
and also by the specific risks of the coronary transfer to warrant a normal myocardial perfusion [8]. In addition, especially neonatal cardiac surgery may imply an increased risk for myocardial damage [9].

In our two-stage group, LVEDVs were only slightly elevated at examination before PAB and ASO, respectively. Before PAB, this probably reflects the high pulmonary blood flow, which increases to the twofold of normal during the first months of life. After PAB (i.e. before ASO), higher LVEDVs were reported in patients with an arterial $pO_2 > 45$ mmHg, indicating a large systemic-pulmonary artery shunt, but not in patients with lower arterial $pO_2$, who were the majority in our series [10,11]. The fact that LVEDV was found significantly elevated [$z = + 1.8$ (2.1) S.D.] early after two-stage ASO without any evidence of increased volume load due to aortic regurgitation or aorto-pulmonary collaterals make more subtle functional changes required by the ASO likely. This

<table>
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<th>Table 2</th>
<th>Diameters of the neoaortic annulus and sinus</th>
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<td>2 Stage ASO</td>
<td>Before PAB</td>
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The data are expressed as $z$-values and their standard deviations. PAB, pulmonary artery banding; ASO, arterial switch operation. The values 'after ASO' are divided into two subgroups before and after the median of the postoperative follow-up.

Fig. 4. Diameter of the neoartic annulus (a) and sinus (b) after one-stage arterial switch operation.

Fig. 5. Area of the neo-pulmonary annulus (a) and sinus (b) after one-stage arterial switch operation.
view may be supported by the observation of an impaired systolic function, which did not only occur in patients with an increased LVEDV, but also in those with a normal size. Even after later complete normalization of LVEDV the EF remained low. While Ilbawi et al. [11] and Backer et al. [12] reported a normal angiographic EF after two-stage repair, Martin et al. [3] showed borderline or definitely subnormal radionuclid LVEF in five out of eight patients. Further evidence of a depressed LV-contractility after two-stage ASO was found by Takahashi et al. [13] reporting significantly lower stress-shortening- and stress-velocity-indices than after one-stage repair and by Sievers et al. [14] who documented abnormally low values of afterload-adjusted ejection fraction in four of 11 patients. Even after rapid two-stage ASO one-quarter of the patients showed significantly reduced echocardiographic indices of left ventricular function (fractional shortening and velocity of fiber shortening) and contractility (stress-shortening- and stress-velocity relation) [15]. All these studies indicate that the staged treatment disturb the functional integrity of the left ventricle.

In contrast, all these disadvantages can be avoided by neonatal repair, as the left ventricular enddiastolic volumes and ejection fractions remain normal up to 11 years of follow-up. While normal results of size, systolic function and contractility of the left ventricle were obtained in previous early follow-up studies [16,17,13], Colan et al. recently reported a significant trend toward increasing LV-dimension z-scores over a 10-year period [15]. However, the absolute values were still within normal limits. The authors found no explanation for this trend, although they discussed the eventual contribution of enlarged bronchial arteries and relatively high incidence of aortic regurgitation, even if graded as mild. This trend was not observed by our angiographic data, which, however, are relatively scarce at late follow-up.

4.2. Neo-aortic root

Echocardiographic studies of Hourihan et al. [18] on the aortic growth after ASO in infancy showed that the preoperative size of the native annulus was increased by +1.4 S.D. (21%) and of the pulmonary sinus by +1.59 S.D. (25%). As angiographic normal values are not available for the neonate, we did not study this age group. Our measurements before PAB at a median age of 11 months show a similarly increased size of the pulmonary root. From a hemodynamic point of view, this again reflects the high pulmonary blood flow, which increases to the twofold of normal during the first months of life. The significant enlargement of these structures after PAB is most likely a result from increased wall tension and shear forces acting on the thin anatomic pulmonary arterial wall. In the period from birth to PAB the pulmonary artery as well as the pulmonary valve are exposed to low pressure allowing regression or insufficient development of collagen and elastic tissue similarly to the situation when suited to the normal circulation. The abnormally high pressure load after PAB may be the likely cause for the structural abnormalities, for example, fragmentation and shortening of elastic fibers, which have been reported in four of five histologic examinations performed at the time at ASO after previous PAB [19]. However, we were not able to show any correlation between the degree of enlargement and either the LV/RV pressure ratio or the time interval to ASO. The significantly increased aortic annulus size is likely responsible for the regurgitation developing during long-term follow-up after two-stage ASO [17]. While the annulus size remained essentially unchanged after ASO, the further postoperative dilatation of the neo-aortic sinus may also result from surgical manipulations at this site. Hourihan et al. assumed the need of reimplantation of the coronary arteries [18], but detailed comparisons with their PAB-group are limited due to their very small sample size (n = 6) and heterogeneity of simple and complex transposition. Other studies are not available for comparison except the previous report of Sievers et al. [19] presenting early data of only seven patients. The present study includes these patients and increases the number to 28, who underwent a total of 44 angiographic studies during the follow-up period up to 16 years after ASO. The extreme enlargement of the neo-aortic annulus and sinus does concern, although we could demonstrate a significant decrease in the long term; even then they remain much larger than after neonatal repair, which underlines the negative impact of PAB and older age at repair.

After one-stage ASO, Hourihan et al. determined increased z-scores of +1.6 S.D. and +2.9 S.D. for the neo-aortic annulus and sinus, respectively, which are similar to our results after neonatal ASO [18]. They showed a significant progression of the dilatation of the neo-aortic sinus up to 6.5 years after ASO. When we statistically compared the differences of the respective z-scores at early and late studies up to 11 years after neonatal repair, we did not observe this trend. The angiographic measurements of the neo-aortic annulus and sinus, which Massin et al. obtained 13.5 (±2.9) months after neonatal ASO, are comparable with our early follow-up data [20]. They confirm a similar distribution of the annular values above the normal mean, while the respective measurements of the aortic sinus seem to lie slightly lower. However, as they used echocardiographic normal values, exact comparisons between both studies are not possible. As all previous authors we compared the aortic measurements with the values of a normal aortic but not a pulmonary root which, however, is the anatomic structure of the neo-aortic root. Indeed, when we compared the size of the neo-aortic root with normal values of the pulmonary root, the z-values differed only by approximately 0.5 (especially for the aortic sinus).
4.3. Neo-aortic anastomosis

In the early times of working with the ASO, concerns had been voiced about a limited growth potential of the aortic anastomosis [23]. After neonatal ASO in our series, the diameter at the anastomosis was only slightly reduced (r = −0.6 (1.4) S.D.) at a mean of 19 months. This is in accordance with the echocardiographic data of Hourihan et al., who found the size of the anastomosis −0.45 S.D. smaller than the ascending aorta of control subjects at a mean follow-up of 22 months after primary ASO in infancy [18]. A similar increase [+1.3 S.D.] of the aortic anastomosis after two-stage repair was already reported by Arensman et al. [22]. It is easily explained by the previous PAB and the older age at corrective surgery.

4.4. Neo-pulmonary root

After one- and also two-stage ASO, we observed a postero-anterior flattening of the pulmonary annulus and sinus. Nakanishi reported exactly the same ratio as our study for the two-stage group (0.82), but a circular shape of the annulus after neonatal repair, indicating absence of flattening [24]. In contrast, Massin et al. determined a more severe flattening of the pulmonary root after neonatal repair compared with our results (0.72 vs. 0.85)[25]. In accordance to these publications we assumed an oval vascular shape and used the respective mathematical model for area calculations. No studies (for example by MRI) of the exact shape of the neo-pulmonary root after ASO are available, which may show plain indentations of the ellipsis at the anterior and posterior aspect. This, however, would change our calculations only to up to 10%. In agreement with our data at a median of 13 months after neonatal ASO, Massin et al. determined a normal cross-sectional area of the pulmonary root at 13.9 months after surgery. In contrast, Nogi et al. reported a decrease of the neopulmonary annulus size by approximately 2 S.D. of normal already at a median follow-up of 18 months after surgery, but they did not mention the origin of their normal values [21]. However, Nakanishi et al. found a reduction of the valve area to 83 ± 14% and 85 ± 26% of normal at a mean age of 2.9 and 5.8 years after one- and two-stage ASO, respectively [24]. Our study does confirm this negative ‘growth-trend’ of the pulmonary root with an approximately 30% reduction of area size at a mean age of 6.7 and 13.4 years after one- and two-stage repair. These late follow-up data up to an age of 11 and 18 years, respectively, are remarkable, but make the development of pressure gradients across the level of the pulmonary annulus and sinus during growth unlikely except for single cases, where the valve area is <50% of normal. The surgical procedure itself seems to be the most likely reason for the narrowing of the pulmonary root. This may occur due to the need of patch closure of the defects where the coronary artery buttons were excised or due to the postero-anterior flattening with the use of the Lecompte maneuver for relocation of the pulmonary artery. Especially the combination of the Lecompte maneuver and an extremely enlarged neoaortic root, e.g. after two-stage ASO may result in a deficient size of the proximal pulmonary root, as illustrated in Fig. 2.

In conclusion, neonatal ASO has significant advantages over two-stage repair concerning LV-performance and the degree of dilation of the neoaortic root, but the significantly reduced size of the neopulmonary root after both procedures is a cause for concern.

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References


