Long-term outcome after the arterial switch operation: 43 years of experience

Roel L.F. van der Palen a,*, Nico A. Blom a,b, Irene M. Kuipers b, Lukas A.J. Rammeloo c, Monique R.M. Jongbloed d, Thelma C. Konings e, Berto J. Bouma a, David R. Koolbergen g,h and Mark G. Hazekamp g,h

a Division of Pediatric Cardiology, Department of Pediatrics, Leiden University Medical Center, Leiden, Netherlands
b Division of Pediatric Cardiology, Department of Pediatrics, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands
c Division of Pediatric Cardiology, Department of Pediatrics, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Netherlands
d Department of Cardiology, Leiden University Medical Center, Leiden, Netherlands
e Department of Cardiology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Netherlands
f Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands
g Department of Cardiothoracic Surgery, Leiden University Medical Center, Leiden, Netherlands
h Department of Cardiothoracic Surgery, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands

* Corresponding author. Division of Pediatric Cardiology, Department of Pediatrics, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, Netherlands. Tel: +31-71-5262835; e-mail: r.vanderpalen@lumc.nl (R.L.F. van der Palen).

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Abstract

OBJECTIVES: The objective of this study was to assess our 43-year experience with arterial switch operation (ASO) for transposition of the great arteries (TGA) by analysing cardiac outcome measures (hospital and late mortality, reoperations and catheter interventions, significant coronary artery obstruction) and to identify risk factors for reoperation and catheter interventions.

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**METHODS:** A total of 490 patients who underwent ASO for TGA from 1977 to 2020 were included in this retrospective, single-centre study. Data on reoperation and catheter intervention of hospital survivors were estimated by the Kaplan–Meier method and compared using a long-rank test. Risk factors for reoperation and/or catheter intervention were assessed by multivariate Cox regression analysis.

**RESULTS:** Hospital mortality occurred in 43 patients (8.8%), late death in 12 patients (2.9%) and 43 patients were lost to follow-up. Median follow-up time of 413 hospital survivors was 15.6 (interquartile range 7.0–22.4) years. Reoperations were performed in 83 patients (117 reoperations). Neoaortic valve regurgitation with root dilatation was the second most common indication for reoperation (15/83 patients, 18.1%) after right ventricular outflow tract obstruction (50/83 patients, 60.2%). Risk factors for any reoperation on multivariable analysis were: TGA morphological subtype [TGA with ventricular septal defect: hazard ratio (HR) = 1.99, 95% confidence interval (CI) 1.18–3.36; \(P = 0.010\) and Taussig-Bing: HR = 2.17, 95% CI 1.02–4.64; \(P = 0.045\)], aortic arch repair associated with ASO (HR = 3.03, 95% CI 1.62–5.69; \(P = 0.001\)) and a non-usual coronary artery anatomy (HR = 2.41, 95% CI 1.45–4.00, \(P = 0.001\)). One hundred and one catheter interventions were performed in 54 patients, usually for relief of supravalvular pulmonary stenosis (44/54 patients, 81.5%) or arch obstruction (10/54 patients, 18.5%). Main risk factor for catheter intervention on multivariable analysis was aortic arch repair associated with ASO (HR = 2.95, 95% CI 1.37–6.36; \(P = 0.006\)). Significant coronary artery stenosis was relatively uncommon (9/413 patients, 2.2%) but may be underrepresented.

**CONCLUSIONS:** Patients after ASO typically have good long-term clinical outcomes but reoperations and interventions remain necessary in some patients. Neoaortic valve regurgitation with root dilatation is the second most common indication for reoperation after right ventricular outflow tract obstruction and an increasing need for neoaortic valve and root redo surgery in future is to be expected.

**Keywords:** Transposition of the great arteries • Arterial switch operation • Reoperation • Intervention

**ABBREVIATIONS**

| Abbreviation | Description |
|--------------|-------------|
| AR           | Aortic regurgitation |
| ASO          | Arterial switch operation |
| CI           | Confidence interval |
| CTA          | Computed tomography angiography |
| HR           | Hazard ratio |
| IQR          | Interquartile range |
| PA           | Pulmonary artery |
| RVOT         | Right ventricular outflow tract |
| RVOTO        | Right ventricular outflow tract obstruction |
| TAVI         | Transcatheter aortic valve implantation |
| TBA          | Taussig-Bing anomaly |
| TGA          | Transposition of the great arteries |
| TGA-IVS      | TGA with intact ventricular septum |
| TGA-VSD      | TGA with ventricular septal defect |

**INTRODUCTION**

For more than 40 years, the arterial switch operation (ASO) is the standard surgical treatment for transposition of the great arteries (TGA). Surgical results with low perioperative mortality over the last decades have now led to focus on the long-term outcomes. Health condition and quality-of-life assessments recently showed that most adult patients perceive normal functional health status, similar to healthy peers [1]. Cardiovascular outcome and survival from mid- and long-term follow-up studies are based on data from 20- up to 30-year post-ASO. In these reports, residual lesions are reported such as supravalvular pulmonary stenosis [2-4], neoaortic root dilatation, neoaortic valve insufficiency [5, 6] and coronary artery problems [7-9]. The purpose of this study was to assess our 43-year experience with ASO and to determine late mortality and morbidity, including coronary artery stenosis, arrhythmias and cardiac device implantations, as well as the need for reoperation and catheter intervention, and finally, to identify risk factors for cardiovascular reoperation and catheter intervention.

**METHODS**

**Study population**

Patients who underwent ASO for TGA at the Leiden University Medical Center, Leiden, between January 1977 and January 2020 were included in this study. TGA subgroups based on anatomic differences included: TGA with intact ventricular septum (TGA-IVS); TGA with ventricular septal defect (TGA-VSD) and double outlet right ventricle with subpulmonary VSD (i.e. Taussig-Bing anomaly, TBA). Data on demographics, morphologic and surgical details, reoperations, catheter interventions, coronary artery problems, atrial or ventricular arrhythmias, the need for cardiac devices (pacemaker and implantable cardioverter-defibrillator) and mortality were collected from hospital and outpatient records. Hospital mortality was defined as death occurring before hospital discharge; late mortality was defined as death after hospital discharge. Reoperations and catheter interventions were subdivided in early (<30 days post-ASO) and late reoperations/interventions (>30 days post-ASO). Re-explo- rations for perioperative complications (e.g. for bleeding) were not included. Catheter ablations for arrhythmias were not included as catheter intervention but were reported separately. Rhythm disorders after hospital discharge were assessed. Left ventricular outflow tract obstruction was included as a separate variable; patients with TGA-VSD and (sub)pulmonary stenosis were only included when ASO had been performed (n = 4) and were classified into the TGA-VSD group. The local Committee for Medical Ethics of the Amsterdam and Leiden University Medical Centers approved the study and waived the need for informed consent. Data collection was completed in January 2020.

**Surgical procedure**

A description of the ASO procedure in our centre and indications for two-stage correction for TGA have been reported previously [10]: coronary artery translocation was performed by the button technique whenever feasible or by trap-door technique.
otherwise. In case of posterior common ostium (Yacoub types B and C), the technique as described by Yacoub was used [11]. The neopulmonary artery (PA) was reconstructed by using a pantaloon-shaped patch of fresh autologous pericardium. The Lecompte manoeuvre has been applied whenever possible since 1981; before that time, a classical Jatene procedure with implantation of a conduit between the right ventricle and PA was performed. A Lecompte manoeuvre, \( n \) was avoided when a side-to-side relationship of the right ventricle and PA was performed. A Lecompte manoeuvre, \( n \) was used to test for differences between intervention-free (reoperation, catheter intervention or both) survival curves among morphological TGA subtypes. A Cox regression model was used to assess the independent predictive values of different variables on primary outcome measures reoperation and/or catheter intervention, resulting in cause-specific hazard ratios (HRs) for the variables. Risk factors known from literature and potential explanatory variables were entered into the equation at the same time. Included risk factors from literature were: ‘TGA morphological subtype’, ‘arch abnormality’, for which surgical repair was performed; ‘left ventricular outflow tract obstruction’; PA banding prior to ASO, ‘prior PA banding’; ‘coronary artery anatomy’, divided into 2 categories: (i) usual coronary artery anatomy: T1Cx-2R, 1L-2CxR and 1L-2R, no Cx and (ii) non-usual coronary artery anatomy: other than (i); ‘weight at ASO’. Potential explanatory variables included in the models were: ‘sex’; use of ‘Lecompte manoeuvre’; divided into 2 categories: (i) usual coronary artery anatomy: T1Cx-2R, 1L-2CxR and 1L-2R, no Cx and (ii) non-usual coronary artery anatomy: other than (i); ‘weight at ASO’. Potential explanatory variables included in the models were: ‘sex’; use of ‘Lecompte manoeuvre’ with the ASO. A \( P \)-value \(<0.05 \) (2-sided) was considered statistically significant.

### Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 23.0. Clinical characteristics were presented as frequency (%) for categorical variables or as median (interquartile range, IQR or range). The normality of the distribution was tested using the Shapiro–Wilk test. Differences in frequencies of baseline characteristics and outcome parameters between TGA subgroups were assessed by the Fisher–Freeman–Halton exact test. A Kruskal–Wallis test was performed to test for differences in continuous data between the TGA subgroups. Primary outcome parameters were reoperations and catheter interventions. Secondary outcome parameters were hospital and late mortality, arrhythmias and coronary artery problems.

Kaplan–Meier analyses were performed to estimate overall survival and reoperation and catheter intervention-free survival of hospital survivors, and to estimate differences in reoperation rate and type based on era. Patients with late mortality, without having had reoperation (7/12 patients) or catheter intervention (10/12 patients) before death occurred, were censored at the age of death in this analysis (considering late death as competing risk resulted in similar percentages of freedom from reoperation/catheter intervention). The log-rank test was used to test for differences between intervention-free (reoperation, catheter intervention or both) survival curves among morphological TGA subtypes. A Cox regression model was used to assess the independent predictive values of different variables on primary outcome measures reoperation and/or catheter intervention, resulting in cause-specific hazard ratios (HRs) for the variables. Risk factors known from literature and potential explanatory variables were entered into the equation at the same time. Included risk factors from literature were: ‘TGA morphological subtype’, ‘arch abnormality’, for which surgical repair was performed; ‘left ventricular outflow tract obstruction’; PA banding prior to ASO, ‘prior PA banding’; ‘coronary artery anatomy’, divided into 2 categories: (i) usual coronary artery anatomy: T1Cx-2R, 1L-2CxR and 1L-2R, no Cx and (ii) non-usual coronary artery anatomy: other than (i); ‘weight at ASO’. Potential explanatory variables included in the models were: ‘sex’; use of ‘Lecompte manoeuvre’ with the ASO. A \( P \)-value \(<0.05 \) (2-sided) was considered statistically significant.

### Table 1: Demographics and preoperative anatomy

| Study cohort (N = 413) | TGA-IVS (N = 258) | TGA-VSD (N = 117) | TBA (N = 38) | \( P \)-value |
|-----------------------|------------------|------------------|--------------|--------------|
| Male, \( n \) (%)      | 280 (67.8)       | 184 (71.3)       | 72 (61.5)    | 24 (63.2)    | 0.133       |
| Age follow-up (years)* | 15.6 (0.1–41.1)  | 15.7 (0.1–40.1)  | 15.8 (0.2–41.1) | 12.3 (0.1–36.3) | 0.661       |
| Age follow-up (years)* | 15.6 (0.1–45.8)  | 15.7 (0.1–40.6)  | 15.8 (0.2–45.8) | 12.4 (0.1–36.9) | 0.706       |
| Coexisting findings, \( n \) (%) | 35 (8.5) | 3 (1.2) | 14 (12.0) | 18 (47.4) | 5.5*10^{-16} |
| Bicuspid pulmonary valve | 27 (6.5) | 16 (6.2) | 10 (8.5) | 1 (2.6) | 0.337       |
| LVOTO                  | 16 (3.9)         | 1 (0.4)          | 10 (8.5)     | 5 (13.2)     | 3.0*10^{-4} |
| Coronary anatomy, \( n \) (%) | 341 (82.6) | 224 (86.8) | 94 (80.3) | 23 (60.5) | 3.1*10^{-4} |
| Other                  | 67 (16.4)        | 31 (12.0)        | 21 (17.9)    | 15 (3.9)     |             |
| Unknown                | 5 (1.2)          | 3 (1.2)          | 2 (1.7)      | 0 (0)        | 0.812       |
| Intramural course of LAD | 12 (2.9) | 8 (3.1) | 4 (3.4) | 0 (0) |             |
| Preoperative procedures, \( n \) (%) | 216 (52.3) | 151 (58.5) | 57 (48.7) | 8 (21.1) | 4.0*10^{-5} |
| Balloon atrial septostomy | 30 (7.2) | 11 (4.3) | 15 (12.8) | 4 (10.5) | 0.007       |
| Arterial switch operation |                   |                  |              |              |             |
| One stage, \( n \) (%) | 371 (89.8)       | 246 (95.3)       | 94 (80.3)    | 31 (81.6)    | 1.0*10^{-5} |
| Median age             | 37 (8 days)      | 7 days           | 11 days      | 23 days      | 9.2*10^{-13} |
| Two stage, \( n \) (%) | 42 (10.2)        | 12 (4.7)         | 23 (19.7)    | 7 (18.4)     | 1.0*10^{-5} |
| Median age             | 376 (91.0)       | 243 (94.2)       | 108 (92.3)   | 25 (65.8)    | 2.1*10^{-7} |

*Median age (range) post-ASO.

\( ^{\text{a}} \)Median age (range) post-birth.

\( ^{\text{b}} \)Coronary anatomy description according to the Leiden Convention.

\( ^{\text{c}} \)P-values based on Fisher–Freeman–Halton exact test for frequencies and Kruskal–Wallis test for median values of continue data.

ASO: arterial switch operation; IVS: intact ventricular septum; L or LAD: left anterior descending coronary artery; LVOTO: left ventricular outflow tract obstruction; PAB: pulmonary artery banding; R: right coronary artery; TBA: Taussig-Bing anomaly; TGA: transposition of the great arteries; VSD: ventricular septal defect.
CARDIAC FAILURE AFTER PA EMBOLISM FROM A CALCIFIED IN-STENT VEGETATION WAS NOT SIGNIFICANTLY DIFFERENT BETWEEN TGA SUBGROUPS (P = 0.005) (FIG. 1).

Arrhythmias, ablation and cardiac devices

Conduction disorders or late arrhythmias appeared in 26 patients post-ASO (6.3%). Details are presented in Supplementary Material, Table S1. In short, 8 patients had a complete atrioventricular block requiring pacemaker implantation (2 after reoperation). Eight patients presented with ventricular tachyarrhythmias at a median follow-up of 15.4 (IQR 12.3–18.5) years post-ASO. Supraventricular arrhythmias were diagnosed in 12 patients at a median age of 17.8 (IQR 8.1–24.1) years.

Reoperations

In total, 117 reoperations (137 procedures) were performed in 83 patients (20.1%) (Table 2). Twenty-two patients needed 2 or more reoperations (Fig. 2). Seven reoperations were performed within 30 days post-ASO (1.6%, 7/447 patients). Median age at reoperation was 2.0 (IQR 0.3–7.1) years post-ASO. Distribution of TGA morphology among patients who underwent reoperation was: TGA-IVS in 32 (32/258, 12.4%), TGA-VSD in 32 (32/117, 27.4%) and TBA in 19 (19/38, 50.0%) and reoperation-free survival differed significantly between TGA subgroups (P = 6.5*10^-10) (Fig. 3A). Overall freedom from reoperation for the entire TGA population was 85% at 5 years, decreasing to 81%, 79%, 76%, 75%, 71% and 71% at 10, 15, 20, 25, 30 and 35 years after ASO, respectively (Fig. 3A).

The most common indication for reoperation was RVOTO (n = 50, 68 procedures) (Table 2). A hybrid procedure with intraprocedural stent implantation for relief of PA branch stenosis was performed in 7 of 50 patients. Median age at reoperation for RVOTO was 1.3 (IQR 0.3–4.5) years. Twenty-two of these patients had TGA-IVS (8.5%), 15 TGA-VSD (12.8%) and 13 TBA (34.2%) (P = 2.2*10^-4). Neo-aortic valve, root or ascending aorta reoperations for neo-aortic valve insufficiency and/or root dilatation were performed in 15 patients (3.6%) and include 18% of all reoperations (21/117 reoperations). Median age at reoperation for these indications was 15.7 (IQR 11.4–20.0) years post-ASO. Ten patients underwent a Bentall operation, 2 patients had a valve-sparing root replacement, 1 patient had neo-aortic valve repair followed by later valve replacement, 1 patient underwent replacement of the neo-aortic root/ascending aorta by a supracoronary tubular prosthesis and in 1 patient, a switch back Ross operation was performed. Seven of these patients had TGA-IVS (2.7%), 5 TGA-VSD (4.3%) and 3 TBA (7.9%) (P = 0.193).

Neo-aortic arch repair after ASO was necessary in 12 of the 83 reoperated patients (14.5%) and consisted of either reoperations for recoarctation (in 7 patients, after ASO with arch repair) or reoperations for neoacoarctation (in 5 patients; i.e. aortic coarctation following ASO in patients who were not diagnosed with coarctation before or during initial ASO).
Table 2: Reoperation and catheter intervention procedures

| Reoperation (n = 83) | Number of procedures (%) | Number of reoperations |
|---------------------|--------------------------|------------------------|
| RVOTO relief        | 68 (49.6%)               | 50                     |
| Neoaortic valve and root surgery | 21 (15.3%)               | 15                     |
| Neoaortic valve plasty | 1                       | 1                      |
| Neoaortic valve replacement | 3                     | 3                      |
| Bentall operation   | 12                       | 12                     |
| David operation     | 2                        | 2                      |
| Switchback Ross     | 1                        | 1                      |
| Coronary revascularisation | 8 (5.8%)               | 8                      |
| Ostial plasty       | 4                        | 4                      |
| CABG                | 4                        | 4                      |
| Relif arch obstruction | 12 (8.8%)               | 12                     |
| LVOTO relief        | 4 (2.9%)                 | 4                      |
| Miscellaneous*      | 24 (17.5%)               | 22                     |

| Catheter intervention (n = 54) | Number of procedures (%) | Number of patients |
|-------------------------------|--------------------------|-------------------|
| Relief supravalvular PS       | 80 (76.9%)               | 44                |
| Balloon angioplasty           | 27                       |                   |
| MPA                           | 5                        |                   |
| RPA                           | 8                        |                   |
| LPA                           | 5                        |                   |
| Bilateral PA                  | 9                        |                   |
| Stent implantation            | 39                       |                   |
| MPA only                      | 1                        |                   |
| RPA only                      | 13                       |                   |
| LPA only                      | 11                       |                   |
| Bilateral PA                  | 13                       |                   |
| MPA + RPA                     | 10                       |                   |
| Relif arch obstruction        | 15 (14.4%)               | 10                |
| Balloon angioplasty           | 14                       |                   |
| Stent implantation            | 1                        |                   |
| Coronary artery intervention  | 2 (1.9%)                 | 2                  |
| PTCA                          | 1                        |                   |
| Stent implantation            | 1                        |                   |
| Neoaortic valve intervention  | 1 (1.0%)                 | 1                  |
| TAVI                          | 1                        |                   |
| Closure shunts                | 6 (5.8%)                 | 5                  |
| Atrial septal defect          | 5                        |                   |
| Aorta-pulmonary collaterals   | 1                        |                   |

*AV-valve plasty (n = 11), closure residual shunt (ASD/VSD) (n = 5), relief supravalvular aortic stenosis (n = 1), relief MPA aneurysm (n = 3), relief pulmonary vein obstruction (n = 1), pulmonary artery endarterectomy (n = 1).

Era-specific impact on reoperation rate and common reoperation types could not be detected, except for aortic arch repair due to recoarctation (Supplementary Material, Figs S1–S3). Patients who have been operated on for TGA with arch obstruction in the era ‘1977–1989’ were more likely to require an aortic arch reoperation for recoarctation compared to patients with ASO and aortic arch repair performed in later eras (P = 0.005; Supplementary Material, Fig S3).

Univariable Cox regression analysis showed following factors associated with reoperation for any indication: TGA morphological subtype (TGA-VSD and TBA), weight at ASO, aortic arch repair associated with ASO, not having had a Lecompte manoeuvre and a non-usual coronary artery anatomy. On multivariate analysis, TGA morphological subtype (TGA-VSD: HR = 1.99, 95% confidence interval (CI) 1.18–3.36; P = 0.010 and TBA: HR = 2.17, 95% CI 1.02–4.64; P = 0.045), aortic arch repair associated with ASO (HR = 3.03, 95% CI 1.62–5.69; P = 0.001) and a non-usual coronary artery anatomy (HR = 2.41, 95% CI 1.45–4.00; P = 0.001) were identified as independent risk factors for reoperation (Supplementary Material, Table S3).

Catheter interventions

In total, 101 interventions were performed in 54 patients (13.1%) (Table 2). Twenty-eight patients needed 2 or more interventions (Fig 2). Median age at first catheter intervention was 3.7 (IQR 1.3–12.8) years. Distribution of TGA morphology among patients who underwent catheter interventions was: TGA-IVS in 25 (25/258, 9.7%) patients, TGA-VSD in 17 (17/117, 14.5%) patients, TBA in 12 (12/38, 31.6%) patients and reoperation-free survival differed significantly between TGA subgroups (P = 1.2×10−6) (Fig 3B). Overall freedom from catheter intervention for the entire TGA population was 92% at 5 years, decreasing to 91%, 88%, 84%, 83%, 81% and 78% at 10, 15, 20, 25, 30 and 35 years after ASO, respectively (Fig 3B).

The major indication for catheter intervention was relief of RVOTO (n = 44, 80 procedures). In 39 patients (9.4%), 1 or more stent implantation(s) in the PA system were performed to treat supravalvular pulmonary stenosis (including aforementioned intraoperative stent implantations in 7 patients). Distribution of TGA morphology among patients with stent implantations was: TGA-IVS in 21 (21/258, 8.1%) patients, TGA-VSD in 13 (13/117, 11.1%) patients and TBA in 5 (5/38, 13.2%) patients (P = 0.413). One patient received a transcatheter pulmonary valve implantation (Melody®) in neopulmonary valve position.

Reoperations for coronary artery problems were needed in 8 patients (1.9%) at median age of 11.5 (IQR 1.0–24.1) years. Patient-specific and surgical characteristics are summarized in Supplementary Material, Table S2. Number of coronary artery reoperations differed significantly between TGA subgroups: 2 patients had TGA-IVS (0.8%), 2 TGA-VSD (1.7%) and 4 TBA (10.5%) (P = 0.004). Usual coronary artery anatomy (1LCx-2R) was present in 4 patients (50%).
Balloon angioplasty for aortic recoarctation was performed in 10 patients. Catheter interventions for significant coronary artery stenosis were done in 3 patients. As summarized in Supplementary Material, Table S2, percutaneous transluminal coronary angioplasty was performed in 2 patients (prior to or after coronary revascularization); in 1 patient, a drug-eluding stent was implanted for left anterior descending coronary artery ostial stenosis. A transcatheter aortic valve implantation (TAVI) was performed in a single TBA patient (with monocoronary ostium) for recurrent severe neoaortic valve regurgitation, 1.5 year after a valve-sparing root replacement. Although originally developed for the treatment of aortic stenosis, TAVI has emerged as a viable alternative to surgical aortic valve replacement for patients with pure aortic regurgitation (AR) with a high-risk profile for surgery. Furthermore, this technique has proven to be technically feasible and successful for severe AR after David valve-sparing root replacement. With the large experience of TAVI for pure AR in our centre and the patient’s explicit wish to be treated via transcatheter procedure, TAVI was chosen over redo surgery.

Univariable Cox regression analysis showed following factors associated with catheter intervention: TGA morphological subtype (TBA), aortic arch repair associated with ASO and a non-usual coronary artery anatomy. On multivariable analysis, aortic arch repair associated with ASO (HR = 2.95, 95% CI 1.37–6.36; P = 0.006) was identified as independent risk factor for catheter intervention (Supplementary Material, Table S4).

Risk factors for any intervention—reoperations or catheter interventions

Of the 413 survivors with follow-up, 302 patients did not receive any reoperation or catheter intervention (73.1%) during follow-up (Fig. 4). One hundred and eleven patients (26.9%) underwent at least 1 reoperation or catheter intervention; 26 patients (6.3%) underwent at least both a reoperation and catheter intervention. Distribution of the 111 patients over the TGA subgroups was: TGA-IVS in 46 (17.8%), TGA-VSD in 41 (35.0%), TBA in 24 (63.2%) patients and the combined reoperation/catheter intervention-free survival differed significantly between TGA subgroups (P = 2.5*10^-12) (Fig. 3C). Overall freedom from reoperation or catheter intervention for the entire TGA population was 81% at 5 years, decreasing to 76%, 73%, 65%, 63%, 61% and 61% at 10, 15, 20, 25, 30 and 35 years after ASO, respectively (Fig. 3C).

Risk analysis for the need of any reoperation(s) or catheter intervention(s) is presented in Table 3. TGA morphological subtype (TGA-VSD and TBA), aortic arch repair associated with ASO, weight at ASO, not having had a Lecompte manoeuvre, prior PA banding and a non-usual coronary artery anatomy were univariable risk factors for the risk of reoperation or catheter intervention. Independent risk factors for either reoperation or catheter intervention for all indications were TGA morphological subtype (TGA-VSD: HR = 1.84, 95% CI 1.18–2.89; P = 0.008), aortic arch repair associated with ASO (HR = 3.72, 95% CI 2.13–6.50; P = 4.0*10^-6) and a non-usual coronary artery anatomy (HR = 1.92, 95% CI 1.20–3.07; P = 0.007).

DISCUSSION

This study evaluated the long-term cardiac outcome in an ASO cohort with one of the longest reported follow-up and focused on late mortality, reoperations and catheter interventions, coronary problems and late arrhythmias. During 43-year experience of ASO, overall survival significantly improved over time, with a late mortality of 2.9% and a decline in hospital mortality to 3.3% for the past 2 decades. The need for 1 or more reoperations and 1 or more catheter interventions was 20% and 13%, respectively, and most reoperations and interventions were performed for RVOT problems. A more complex TGA morphology (TGA-VSD), aortic arch repair associated with ASO, and the presence of a non-usual coronary artery anatomy were found to be independent risk factors for the need for reoperation or intervention for any indication.

In 4 decades of ASO, a significant decrease in perioperative mortality to rates below 5% in high-volume cardiothoracic surgical centres has been achieved [2, 12, 13]. Although survival has greatly improved, recurrent and new lesions remain and require reoperations or catheter interventions. The reoperation rate in this study was 20% which is relatively high compared to other...
Table 3: Univariable and multivariable Cox proportional hazard analysis for reoperation or catheter interventions

| Risk factors                      | Events/total | Univariable | Multivariable* |
|-----------------------------------|--------------|-------------|----------------|
|                                   |              | Hazard ratio| P-value        | Hazard ratio| 95% CI | P-value |
| Morphological subtype             |              |             |                |
| TGA-IVS*                          | 46/258       | 1           | 1.35*10^-10    | 1           |        |
| TGA-VSD                           | 41/117       | 2.30        | 1.51–3.51      | 1.06*10^-4 | 1.84   | 1.18–2.89 | 0.008 |
| TBA                               | 24/38        | 5.33        | 3.25–8.76      | 3.91*10^-11 | 1.92   | 0.95–3.91 | 0.071 |
| Gender                            |              |             |                |
| Male                              | 72/280       | 1           | 1              | 1           |        |
| Female                            | 39/133       | 1.19        | 0.80–1.75      | 0.39        | 1.18   | 0.79–1.77 | 0.41  |
| Weight at ASO (per 1 kg)          |              | 1.10        | 1.04–1.17      | 4.49*10^-4 | 1.03   | 0.95–1.12 | 0.41  |
| LVOTO                             |              |             |                |
| No                                | 106/397      | 1           | 1              | 1           |        |
| Yes                               | 5/16         | 1.13        | 0.54–3.23      | 0.55        | 1.01   | 0.39–2.62 | 0.99  |
| Aortic arch repair                |              |             |                |
| No                                | 84/378       | 1           | 1              | 1           |        |
| Yes                               | 27/35        | 5.75        | 3.69–8.95      | 9.02*10^-15 | 3.72   | 2.13–6.50 | 4.0*10^-6 |
| Lecompte                          |              |             |                |
| No                                | 17/29        | 1           | 1              | 1           |        |
| Yes                               | 93/384       | 0.29        | 0.17–0.48      | 3.00*10^-6 | 0.74   | 0.38–1.43 | 0.37  |
| Prior PAB                         |              |             |                |
| No                                | 99/383       | 1           | 1              | 1           |        |
| Yes                               | 12/30        | 2.00        | 1.10–3.65      | 0.023       | 1.24   | 0.59–2.61 | 0.57  |
| Coronary artery anatomy           |              |             |                |
| Usual (1LCx-2R, 1L-2CxR, 1L-2R, noCx) | 79/341      | 1           | 1              | 1           |        |
| Other (non-usual)                 | 31/67        | 2.65        | 1.74–4.02      | 5.00*10^-6 | 1.92   | 1.20–3.07 | 0.007 |

Reference categories of covariate:
*morphological subtype ‘TGA-IVS’,
*male sex,
*no left ventricular outflow tract obstruction’,
*no aortic arch repair associated with ASO’,
*no Lecompte manoeuvre’,
*no pulmonary artery banding prior to ASO’,
*usual coronary artery anatomy’.
*Variables included for MV analysis: morphological subtype, sex, weight, aortic arch repair, pulmonary artery banding prior to ASO and coronary artery anatomy.
ASO: arterial switch operation; CI: confidence interval; L: left coronary artery; LVOTO: left ventricular outflow tract obstruction; PAB: pulmonary artery banding; R: right coronary artery; TBA: Taussig-Bing anomaly; TGA: transposition of the great arteries; TGA-IVS: TGA with intact ventricular septum; TGA-VSD: TGA with ventricular septal defect.
studies. These studies reported reoperation rates between 5% and 20%, but with shorter duration of follow-up [12–17]. Reoperation rates between studies may vary depending on the complexity of the included TGA patients (TGA-VSD and TBA included or not). Moreover, our early adoption of ASO (1977) has probably influenced the number of reinterventions. With longer follow-up, it is expected that more patients will need a reoperation or catheter intervention, confirmed by the 11% reoperation rate beyond childhood in a study of adult TGA patients post-ASO [17].

**Right ventricular outflow tract procedures**

RVOT problems are the most common indication for reoperations or catheter interventions and often occur in the first years after ASO, as already known from short- and intermediate-term follow-up studies [2–4]. Our data are in line with these reports, with a median age of 1.3 (IQR 0.3–4.5) years at the time of first RVOT reoperation. The overall surgical and percutaneous intervention rates for RVOTO varied from 5% to 28% between the different studies with at least 20-year follow-up [2–4, 14–16], which is also similar to the results of this study.

Approximately 75% of the reoperations and all catheter interventions for RVOTO were performed for supravalvular obstruction in this study. Anatomical and surgical components may play a role in the development of PA stenosis. Patients with concomitant aortic arch obstruction (often TBA patients) are at increased risk for RVOTO [18, 19]. Moreover, the surgical technique and the material used for PA reconstruction, application of Lecompte manoeuvre, extent of mobilization of the PAs, and the age at operation impact the risk of RVOTO [2–4].

Balloon angioplasty for supravalvular pulmonary stenosis is the least invasive option but usually has limited effect and stent implantation is eventually required in most cases, preferably performed at an older age. Although we have not seen complications of branch PA stenting after ASO (first procedures 1994), these procedures should be performed with restraint because severe complications such as coronary artery compression and especially aortic erosion and aorto-pulmonary fistulas have been reported [20].

**Neoaortic reoperations**

Twenty-one surgical procedures and 1 catheter intervention for neoaortic valve regurgitation and/or root dilatation were performed in 15 patients (3.6%), approximately 20% of all reoperations. It is the second most common indication for reoperation, as has been reported in other studies with long follow-up duration [12, 16]. The main indication for neoaortic root reoperation in this study was root dilatation with or without significant neoaortic regurgitation [6, 21]. In two-thirds of cases, surgery was performed in the last decade (2009–2020). Although the total amount of reoperations on the neoaortic valve/root is still low and comparable to other surgical centres [15, 16, 22], we expect that with longer follow-up this may increase. Longitudinal follow-up studies on the neoaortic valve function confirm this concern as root dilatation progresses over time and proved to be an independent risk factor for neoaortic valve impairment [5, 6]. Recently, we showed in a subset of this cohort that 14% of patients had developed root diameters >40mm, with moderate AR in about 25% of them and one-quarter of these patients being below 18 years of age [6].

Thresholds for root replacement in TGA patients after ASO are adapted from international guidelines on bicuspid aortic valve and connective-tissue disease-related aortopathy and are based on absolute diameters. No aortic dissections or ruptures have been reported after ASO to date. In our centre root replacement is indicated if the neoaortic root diameter reaches 55mm according to the guidelines [23], and at smaller sizes if significant neoaortic valve regurgitation is present or if root diameter has rapidly progressed over time. A Bentall operation has been performed in most patients [6, 21], but valve-sparing operation should be considered whenever possible.

**Coronary artery lesions**

In our series, coronary artery reoperations or interventions for partial or total occlusion were required in only 9 patients (2.2%), suggesting that coronary problems do not frequently occur during follow-up so far. Moreover, late mortality was not related to acute coronary artery problems in the patients with identified causes of death. One patient had a near-fatal ventricular fibrillation due to ischaemia based on coronary ostial stenosis. These findings are in line with the results of a systematic review on sudden cardiac death due to coronary complications late after ASO [24]. From that review, sudden cardiac death was extremely rare with only a few possible cases and no proven cases of coronary artery-related sudden death. In our centre, we do not systematically perform coronary imaging during childhood which might have influenced numbers of coronary artery problems. In general, children with complex coronary morphology or those with intraoperative difficulties of coronary artery transfer receive coronary computed tomography angiography (CTA) in the first year after ASO. Furthermore, patients undergo exercise tests in childhood and all asymptomatic patients underwent a coronary CTA at least once in early adolescence [25].

The detection of coronary artery abnormalities in the patients who underwent intervention was based on symptoms, abnormal findings from echocardiography or an accidental finding by a surveillance CTA or catheter coronary angiography (all representing one-third of the causes of detection). Treatment for partial or total coronary occlusion was performed by either ostial plasty or by coronary artery bypass graft. Tausig-Bing anomaly patients had the highest prevalence of coronary artery reoperations in this study (4/38 patients, 10.5%). Remarkably, all coronary reoperations in this subgroup were performed during childhood, unlike most coronary procedures in the patients with other TGA subtypes. Given the small number of coronary reoperations, it is unclear whether TBA patients are at increased risk or whether this is related to the prevalent non-usual coronary artery pattern in TBA. Although abnormal coronary artery patterns have been reported as risk factor for early coronary artery obstruction [8, 9, 26], it is suggested that the acquired coronary anatomy after ASO may be more important as a risk factor for late coronary artery obstruction [27]. Correspondingly, half of the patients necessitating coronary reoperation from this study had a usual coronary artery pattern without problems during coronary artery transfer. Acquired abnormal coronary anatomy may result from the surgically created pattern after reimplantation and changes by growth, arterial distortion or root dilatation [25, 27].
Risk factors for reoperation, intervention or combined

Independent risk factors for reoperation in this study were: TGA morphological subtype (TGA-VSD), aortic arch repair associated with ASO and a non-usual coronary artery anatomy. More complex TGA anatomy have been reported to be a risk factor for reoperation in previous studies [12–14]. Not surprisingly, aortic arch repair associated with ASO was reported as independent risk factor for surgical or catheter reintervention. A higher rate of reinterventions was previously described in TGA patients with arch obstruction by our group [18] and in other large series as well [12, 19, 22], particularly indicated for right-sided obstructions next to residual arch obstruction. A non-usual coronary artery anatomy showed to be an independent risk factor for both reoperation and any reoperation or intervention for any indication in this study. Vargo et al. [28] hypothesized that this could be related to the fact that an abnormal coronary artery anatomy sometimes requires an unusual reconstructive technique to avoid compression of the coronary artery button. However, we were not able to prove this in our series. Differences in reoperation rate or type based on era of ASO could not be detected in this series, except for aortic arch repair due to recoarctation. Although these are relatively small numbers, patients operated on for TGA with arch obstruction in the early years after start of the ASO program (era ’1977–1989’) were more likely to require an aortic arch repair for recoarctation compared to patients operated on in later eras.

Rhythm disorders

Arrhythmias requiring ablative therapy or device implantation are fairly uncommon after ASO in this study, which is in concordance with other studies [12, 14]. Most sustained ventricular arrhythmias are related to coronary ischaemia or post myocardial infarction necessitating preventive ventricular tachycardia ablation or implantable cardioverter-defibrillator implantation and, if present, relief of coronary artery obstruction. Supraventricular tachycardia episodes are usually more prevalent in the newborn period and directly after ASO and only very rarely occur later, as was also shown in this study. Pacemaker need for atrioventricular block was low and related to VSD closure (in TGA-VSD and TBA) from early surgical eras (before 2000).

Limitations

Limitations of this study are related to the retrospective design from a single centre. The prevalence of coronary artery stenosis or occlusion identified in this study may be underestimated because coronary surveillance imaging by CTA or coronary angiogram was not performed routinely in all cases.

CONCLUSION

Patients after ASO typically have good clinical outcomes in the long term but reoperations and interventions remain necessary in some patients. RVOT problems are the main indication for surgical and percutaneous interventions with neoaoortic valve or root reoperations as second most common reoperation indication. More complex TGA anatomy (TGA-VSD and TBA), aortic arch re-pair associated with ASO and non-usual coronary artery anatomy were independent risk factors for any reoperations or interventions of any indication. Reoperations for neoaoortic valve insufficiency and/or root dilatation are relatively low but revealed an increased incidence over the last decade. With the reported ongoing neoaoortic root dilatation in adulthood, this observation is of major concern for the future, as this implicates an expected increased need for neoaoortic valve or root redo surgery.

SUPPLEMENTARY MATERIAL

Supplementary material is available at EJCTS online.

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Author contributions

Roel L.F. van der Palen: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Software; Supervision; Validation; Writing—original draft; Writing—review & editing. Nico A. Blom: Conceptualization; Investigation; Methodology; Resources; Supervision; Validation; Writing—review & editing. Irene M. Kuipers: Investigation; Supervision; Validation; Writing—review & editing. Lukas A.J. Rammeloo: Investigation; Resources; Supervision; Validation; Writing—review & editing. Monique R.M. Jongbloed: Investigation; Resources; Supervision; Validation; Writing—review & editing. Thelma C. Konings: Investigation; Supervision; Validation; Writing—review & editing. Berto J. Bouma: Investigation; Resources; Supervision; Validation; Writing—review & editing. David R. Koolbergen: Investigation; Supervision; Validation; Writing—review & editing. Mark G. Hazekamp: Conceptualization; Investigation; Resources; Supervision; Validation; Writing—review & editing.

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