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# Risk factor analysis for a complicated postoperative course after neonatal arterial switch operation: The role of troponin T

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## Abstract

**Objective:** To find risk factors for a complicated early postoperative course after arterial switch operation (ASO) in neonates with d-transposition of the great arteries (dTGA). In addition to anatomical and surgical parameters, the predictive value of early postoperative troponin T (TnT) values in correlation to the early postoperative course after ASO is analyzed.

**Methods:** Seventy-nine neonates (57 (72%) male) with simple dTGA treated by ASO between 2009 and 2016 were included in the analysis. A complicated early postoperative course (30 days) was defined by one of the following criteria: (A) moderate to severe cardiac dysfunction without rhythm disturbances, (B) rhythm disturbances causing hemodynamic instability with the need for medical treatment, (C) signs for ischemia in ECG, (D) need for surgical or catheter interventional reinterventions other than diagnostic, or (E) other reasons.

**Results:** Forty of 79 patients (51%) showed a complicated early postoperative course after ASO, with 2 patients dying after 13 and 16 days. Patients with a complicated early postoperative course had a longer PICU stay ($P < .001$), needed longer mechanical ventilator support ($P = .001$) and longer inotropic support ($P = .03$), and more reinterventions (surgical or catheter interventional) were necessary ($P = .001$). Only the presence of a VSD ($P = .001$) and longer surgery duration ($P = .026$) were associated to a complicated postoperative course. TnT values only showed a trend toward higher values in patients with a complicated postoperative course ($P = .06$). A secondary rise in TnT was seen in 10 patients, ranging from 11.6% to 410.2%, of whom 7 could be classified in the complicated postoperative group.

**Conclusions:** The postoperative course after ASO in dTGA neonates is influenced by other cardiac comorbidities like a VSD with the need for surgical treatment, influencing surgery duration. Postoperative higher TnT values reflect a longer and more vulnerable intraoperative course with limited predictive value on the early postoperative course.

KEYWORDS
arterial switch operation, dTGA, early postoperative outcome, troponin T

## 1 | INTRODUCTION

In children with d-transposition of the great arteries (dTGA), the arterial switch operation (ASO) has become the surgical treatment of choice in the last decades, if the coronary anatomy is suitable for this technique.[1] ASO showed good short and long term results with an early mortality rate of 2.8% and a late mortality rate of 0.9% in a 25-year experience (mean follow-up time 10.6 years).[2,3] Even in adults, formerly treated with ASO during their neonatal period, acute coronary complications are uncommon.[4] Nevertheless, higher early postoperative mortality

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rates of up to 12% have been described[3] and factors associated with negative influence on the early postoperative course after ASO are under investigation.

Troponins I and T (TnI and TnT) are highly specific biomarkers for myocardial damage,[5] not only used in coronary heart disease in adult patients but also for risk stratification after surgery for congenital heart disease (CHD).[6–8] It has been shown, that higher TnI values in a mixed group of CHD patients were associated with a worse early postoperative outcome.[6]

Aim of our investigation was to find risk factors for a complicated early postoperative course after ASO in neonates. In addition, we evaluated the predictive value of early postoperative TnT values on the early postoperative course after ASO.

## 2 | METHODS

All patients with simple dTGA treated with ASO in the years 2009–2016 in our institution were identified from our database. Simple TGA was defined by the International Pediatric and Congenital Cardiac Code of the Association for European Pediatric and Congenital Cardiology (IPCCC-AEPC) ICD-10 Code Q20.3 and could be accompanied by a foramen ovale (PFO, $\leq$ 3 mm), atrial septal defect (ASD, $>$ 3 mm), persistent arterial duct (PDA), ventricular septal defect (VSD), and/or vessel diseases like coarctation of the aorta (CoA). Any other cardiac comorbidity [eg, atrioventricular septal defect (AVSD) or double outlet right ventricle (DORV)] classifying TGA as complex TGA was not included in the study. According to the RACHS-1 classification, patients could be categorized in risk categories 3 (ASO only) and 4 (ASO with closure of ventricular septal defect).[9] ASO were performed using moderately hypothermic cardiopulmonary bypass and cardioplegic arrest, using Neckar, Custodiol, or Kirsch-Haes as cardioplegic solutions. If necessary, repetition of cardioplegia by selective cannulation of the coronary buttons was performed. ASO consisted of switching aortic and pulmonary roots, Lecompte-maneuver, coronary button transfer, ligation of PDA, and closure of ASD and/or VSD as appropriate. Medical records including parameters of pediatric intensive care unit (PICU) stay, laboratory analysis and reinterventions were retrospectively reviewed. We defined a complicated postoperative course if at least one of the following situations occurred in the first 30 days after ASO: (A) moderate to severe cardiac dysfunction without rhythm disturbances, (B) rhythm disturbances (supraventricular or ventricular) causing hemodynamic instability with the need for medical treatment, (C) signs for ischemia in ECG like ST changes or other repolarization disturbances, (D) need for surgical or catheter interventional reinterventions other than diagnostic or chest closure (beside others: surgical thoracic revision on PICU, surgical treatment of residual CoA, or VSD, permanent pacemaker implantation), and (E) other reasons (beside others: necrotizing enterocolitis, wound infections, sepsis). Beside baseline characteristics (gestational age, weight, height, and anatomical description of dTGA) intraoperative parameters (duration of surgery, extra corporal circulation (ECC) time, aortic cross clamp time, cardioplegic solution, number of cardioplegia repetition, and lowest body core temperature of the patient) were correlated with the early postoperative course in the first 30 days after ASO and the TnT course. Since 2009 TnT (Elecsys, TnT high sensitive, Roche, Basel, Switzerland) is measured in our institution, before that TnI has been measured. Troponin T values are measured directly postoperatively, 24 and 48 h after surgery on a regular base. Patients were selected for additional controls afterwards during the first week after ASO if the decline of TnT levels before were judged to be inappropriate.

### 2.1 | Statistics

Data are presented as median (IQ-range) or mean $\pm$ standard deviation (*SD*), as appropriate. Categorical data are expressed as counts and percentages. Comparisons of percentages were performed by the use of Pearson's chi-square test or Fisher's exact test when appropriate, those of mean values by students' *t*-test and those of median values by the Mann–Whitney *U*-test. If correlation occurred, the correlation coefficient was calculated and classified according to Cohen,[10] $r = .10$ corresponds to a weak, $r = .30$ to a medium and $r = .50$ to a strong correlation. Significance testing was 2-sided with the significance level set at $P < .05$. Statistical analyses were performed using SPSS version 22.0 (IBM, Armonk, New York).

The local ethical committee approved the study.

## 3 | RESULTS

### 3.1 | Patient characteristics and anatomical findings

In total, 79 neonates (57 (72%) male) with simple dTGA treated by ASO were included in the analysis. In all children, beside Rashkind procedure, no other palliative surgery before ASO was necessary and no other surgical technique beside ASO was performed despite several different coronary patterns. Six infants were born prematurely (<37 week of gestation) (8%) and 5 children (6%) were small for gestational age. Thirty-eight children (48%) had a restrictive atrial septal defect (<3 mm) and a Rashkind procedure was performed in 59 children (75%). Associated cardiac lesions were a VSD in 21 patients (27%), aortic coarctation in 6 patients (8%), and AV valve regurgitation more than moderate in 6 patients (8%), most likely due to hemodynamic load, as anatomical AV valve abnormalities were not found. A usual coronary anatomy [right coronary artery (RCA) from right facing sinus, left coronary artery (LCA) from left facing sinus (1LCx2R)] was found in 52 children (66%), the most common variant with circumflex artery from RCA (1L2RCx) in 9 children (11%), a single coronary ostium in 6 children (8%), and other coronary abnormalities in 12 children (15%). Baseline characteristics of the study population are summarized in Table 1.

### 3.2 | Postoperative course

According to the criteria mentioned in the methods section, 40 of 79 patients (51%) showed a complicated early postoperative course after ASO. Cardiac dysfunction (category A) was found in 3 patients (8%), hemodynamic relevant rhythm disturbances (category B) were found in 32 patients (80%), signs for ischemia in ECG (category C) in 2 patients

**TABLE 1** Comparison of patients with complicated and not-complicated postoperative course after ASO

| Variable | Total | Complicated | Not-complicated | *P* value |
|---|---|---|---|---|
| Numbers of patients, *n* (%) | 79 (100) | 40 (51) | 39 (49) | – |
| Male, *n* (%) | 57 (72) | 31 (77) | 26 (67) | .283 |
| GD (d) | 277 (270–285) | 275 (264–284) | 278 (273–285) | .168 |
| Weight (g) | 3460 (2960–3880) | 3340 (2870–3870) | 3580 (3000–3910) | .339 |
| Length (cm) | 50 (48–52) | 50 (48–51) | 51(49–52) | .222 |
| Anatomy of atrial septum: | | | | .057 |
| - No atrial septal defect, *n* (%) | 1 (1) | 0 (0) | 1 (3) | |
| - PFO <3 mm, *n* (%) | 37 (47) | 14 (35) | 23 (59) | |
| - ASD II >3 mm, *n* (%) | 41 (52) | 26 (65) | 15 (38) | |
| VSD, *n* (%) | 21 (27) | 17 (43) | 4 (10) | .001 |
| Coronary anatomy: *n* (%) | | | | .653 |
| - Normal | 52 (66) | 24 (60) | 28 (72) | |
| - LCX ex RCA | 9 (11) | 6 (15) | 3 (8) | |
| - Single-coronary ostium | 6 (8) | 3 (7) | 3 (8) | |
| - Others | 12 (15) | 7 (17) | 5 (13) | |
| Rashkind, *n* (%) | 59 (75) | 27 (68) | 32 (82) | .137 |
| Age at OP (d) | 9 (7–12) | 9 (7–12) | 9 (6–13) | .848 |
| OP time (min) | 268 (214–300) | 285 (246–319) | 258 (198–282) | .026 |
| ECC time (min) | 169 (128–198) | 174 (150–199) | 158 (120–195) | .157 |
| ACC time (min) | 111 (89–134) | 112 (98–133) | 104 (84–136) | .448 |
| Postop hospital LOS (d) | 17 (14–24) | 23 (16–30) | 15 (13–17) | <.001 |
| Ventilation time (d) | 3 (2–4) | 3 (2–5) | 2 (1–3) | .001 |
| Inotropics/vasopressors duration (d) | 4 (2–5) | 4 (3–6) | 3 (2–4) | .025 |
| PICU stay (d) | 6 (4–7) | 7 (5–10) | 5 (3–6) | <.001 |
| Reoperation, *n* (%) | 28 (35) | 21 (53) | 7 (18) | .001 |
| Open thorax, *n* (%) | 34 (43) | 22 (55) | 12 (31) | .030 |
| Duration open thorax (d) | 2 (2–3) | 3 (2–4) | 2 (2–3) | .130 |
| Total hospital stay (d) | 28 (23–37) | 33 (27–40) | 24 (21–29) | <.001 |
| Troponin T before OP (μg/L) | 0.10 (0.07-0.48) | 0.09 (0.08-0.90) | 0.10 (0.07-0.47) | .856 |
| Troponin T directly after OP (μg/L) | 5.90 (4.03–8.40) | 6.60 (4.3–9.64) | 5.13 (3.65-7.6) | .06 |
| Troponin T 24 h after OP (μg/L) | 3.09 (2.13-4.29) | 3.65 (2.29-4.65) | 2.82 (2.07-4.04) | .06 |
| Troponin T 48 h after OP (μg/L) | 2.25 (1.60-3.18) | 2.30 (1.50-3.52) | 1.85 (1.57-2.98) | .288 |
| Troponin T >48 h to 1 week after OP (μg/L) | 0.87 (0.36-1.75) | 0.83 (0.34-1.83) | 0.90 (0.42-1.77) | .954 |
| Creatinine before OP (μmol/L) | 48.0 (37.8–58) | 47.0 (37.3–57.3) | 48.0 (38.5–57.3) | .392 |
| Creatinine 24 h after OP (μmol/L) | 51.0 (40–61) | 55.0 (46.3–63.0) | 47.0 (39.0–56.0) | .032 |
| Creatinine 48 h after OP (μmol/L) | 62.0 (47.8–72.3) | 61.0 (42.0–79.5) | 63.0 (48.0–69.0) | .374 |
| Creatinine >48 h to 1 wk after OP (μmol/L) | 48.0 (32.5–59) | 47.0 (33.0–61.0) | 49.0 (29.0–59.0) | .728 |

Abbreviations: *n*, numbers of patients; IQR, interquartile range; GD, gestation days; PFO, persistent foramen ovale; ASD, atrial septal defect; VSD, ventricle septum defect; LCX ex RCA, left circumflex ex right coronary artery; ECC, extra corporal circulation; ACC, aortic cross clamp; OP, operation; PICU, pediatric intensive care unit; LOS, length of stay; h, hours; d, days; wk, week.
Data shown are median and interquartile range (IQR) or number and percentages.

(5%), need for reinterventions (category D) in 26 patients (65%), and other reasons (category E) in 18 patients (45%). Some patients could be classified in more than one category of complications. From the 40 patients, 2 children died 13 and 16 days after ASO: the first patient after myocardial ischemia due to LCA stenosis with consecutive severe junctional ectopic tachycardia (JET), requiring ECMO treatment for 10

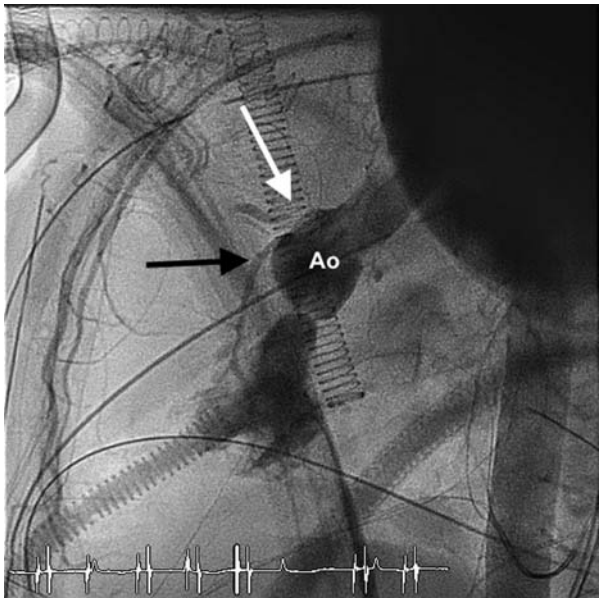


**FIGURE 1** Angiography showing, severe LCA stenosis after arterial switch operation. White arrow: severe stenosis of left coronary artery; black arrow, right coronary artery. Abbreviation: Ao: aorta

days and reoperation without success (Figure 1); the second patient due to severe mitral regurgitation with progressive heart failure with the need for ECMO treatment and reoperation without success. Both had an emergency ASO, one on the first and the other one on the second day of life due to insufficient arterial oxygen saturation despite adequately sized atrial septal defect and PDA.

### 3.3 | Risk factor analysis

Patients with a complicated early postoperative course had a longer PICU stay ($P < .001$), needed longer mechanical ventilator support ($P = .001$) and longer inotropic support ($P = .03$), and more reinterventions (surgical or catheter interventional) were necessary ($P = .001$). Regarding follow-up >30 days after surgery, there was no significant difference in late complications between the two groups ($P = .14$).

From baseline characteristics only the presence of a VSD was associated to a complicated postoperative course ($P = .001$), in contrast to coronary anomalies ($P = .653$, Table 1). In addition, total duration of surgery had a negative influence on the early postoperative course after ASO (median 285 vs 258 min, $P = .026$), whereas we could not find any influence of ECC time (median 174 vs 158 min, $P = .157$), aortic cross clamp time (median 112 vs 104 min, $P = .448$), type of cardioplegia used ($P = .494$), or number of repetition of cardioplegia ($P = .053$) and lowest body core temperature during surgery ($P = .935$). Surgery duration in dTGA with VSD was significantly longer (median 278 vs 266 min, $P = .049$).

### 3.4 | Troponin T values

TnT values were measured in all children 24 and 48 h after ASO, beyond 48 h till 1 week after ASO in 47 out of the 79 patients. Figure 2A shows the TnT course after ASO in the whole study population. TnT values directly postoperatively (median 5.13 vs 4.39 μg/L, $P = .06$) as well as 24 h after ASO (median 2.82 vs 2.29 μg/L, $P = .06$) showed a trend toward higher values in patients with a complicated postoperative course (Figure 2B).

We found a strong correlation between first postoperative TnT values and duration of surgery ($P < .001$, $r = .573$) and ECC time ($P < .001$, $r = .412$) and a medium strength correlation to aortic cross clamp time ($P = 0.006$, $r = .309$). The type of cardioplegia used had no influence on the height of the TnT values postoperatively ($P = .62$). Concerning early postoperative clinical parameters, there was no correlation between TnT values and duration of PICU stay ($P = .60$, $r = .060$) and mechanical ventilator support ($P = .65$, $r = -0.052$) but a strong correlation to inotropic support ($P < .001$, $r = .391$). A secondary rise in TnT values was observed in 10 patients (12.7%), ranging from 11.6% to 410.2% (median 37.4%) in comparison to the before measured TnT value. Three patients showed a secondary rise at the 24 h control, 4 at the 48 h control and 3 after 48 h up to 1 week after ASO. Seven of the 10 patients (70%) were categorized to the complicated postoperative group, the 2 patients who died belonged to this group, were detected beyond 48 h after ASO and showed the highest TnT rise (1.19 to 4.28 μg/L, 259.7% and 1.86 to 9.48 μg/L, 410.2%). The median rise in TnT in the 3 patients without a complicated postoperative course was 11.6% (range 4.7%-12.1%) in contrast to a median rise in TnT of 76.6% (14.2%-410.2%) in the 7 patients with a complicated postoperative course ($P = .1$).

In those 47 out of 79 patients, in which the treating physicians decided for TnT measurements beyond 48 h after ASO, 26 showed a complicated and 21 an uneventful postoperative course. Specificity (0.54) and sensitivity (0.65) for decision of physician for measuring TnT to identify patients at risk after 48 h is low.

As the renal clearance has an influence on TnT values, renal function was monitored in all patients by measuring blood creatinine values (Jaffe method). Preoperative creatinine values were measured at a median age of 8 days, 1 day before ASO, showing a normal renal function (median blood creatinine 48 μmol/L (IQR 37.8–58.0), normal values for this age group: <60 μmol/L). Creatinine values showed a significant increase up to a median of 62.0 μmol/L (IQR 47.8–72.3) at 48 h after surgery ($P < .0005$), returning to baseline thereafter till 1 week after ASO (compare Table 1). There was a significant difference in creatinine values postoperatively between children with a complicated and a non-complicated course only at 24 h after ASO (median 55 vs 47 μmol/L, $P = .032$). We found a weak to moderate correlation of TnT values and creatinine values ($r = .29$).

## 4 | DISCUSSION

Risk factors associated with early morbidity and mortality in neonates with dTGA after ASO have been investigated in a variety of studies in the last years.[2,11–13] Especially low birth weight, later ASO (after day 5), longer ECC time, the presence of aortic arch abnormalities, left ventricular outflow tract obstruction (LVOTO) or a VSD are associated

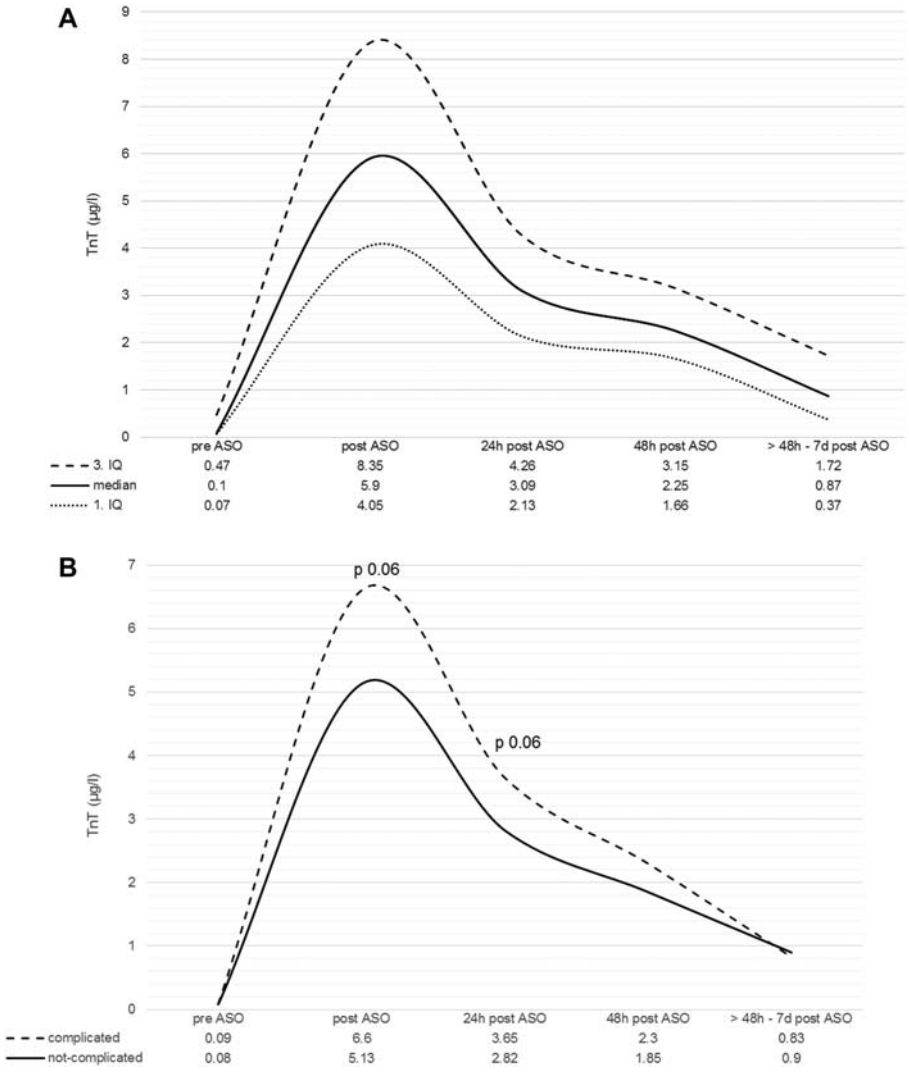


**FIGURE 2** (A) Troponin T course after arterial switch operation in neonates with dTGA. (B) Troponin T course divided in neonates with complicated and not-complicated postoperative courses after arterial switch operation Abbreviations: TnT, Troponin T; dTGA, d-transposition of the great arteries; ASO, arterial switch operation; h, hours; d: days. TnT beyond 48 h measured in 47 of 79 patients

with early mortality, morbidity and higher costs.[1–4,13,14] These knowledge has been respected in the RACHS-1 classification, where simple dTGA with intact ventricular septum is classified in category 3, and dTGA with ventricular septal defect in category 4.[9] The role of TnT levels postoperatively has been poorly investigated as a potential marker for risk stratification, even though it is measured on a regular basis in most pediatric heart centers after ASO.

There is no uniform definition of a complicated early postoperative course after ASO. Anderson et al.[12] defined major morbidity as cardiac arrest, extracorporeal membrane oxygenation (ECMO), delayed sternal closure, systemic infection, necrotizing enterocolitis, seizure, stroke on MRI with clinical sequelae, diaphragmatic paralysis/paresis, reoperation before discharge, or readmission at less than 30 days. With this definition they had a rate of 20% of major morbidity. With our definition, focusing on the first days on PICU and adding arrhythmias requiring treatment as well as cardiac dysfunction without arrest, our early postoperative complication rate is higher (51%) but less severe, with an overall mortality rate of 2.5%. Nevertheless, when using our definition, the group of patients with a complicated early postoperative course showed prolonged parameters of PICU stay such as longer mechanical ventilator support, longer inotropic support and a higher reintervention rate, therefore, we assume our classification to be suitable in daily care business on PICU wards.

Our results show the presence of a VSD and longer surgery duration as parameters associated with a complicated postoperative course. All other baseline or surgical parameters showed no association (Table 1). These findings go along with other studies[2,11,13] and the RACHS-1 classification.[9] The results of our and other investigations underline that longer duration of ASO is associated with more complications postoperatively. Hence, additional cardiac findings like a VSD or aortic arch abnormalities with the need for surgical treatment during ASO prolonging the surgical procedure and ECC time, are associated with higher early mortality and morbidity.[1,9,13,15] In contrast, our results showed no influence of coronary

artery variants on the postoperative course, which goes along with the findings from other studies.[1,11]

Duration of cardiac surgery, ECC and aortic cross clamp time correlate well with higher TnT values postoperatively. In accordance, postoperatively longer inotropic support correlates with the level of TnT. As TnT levels have no implication on a complicated or not-complicated postoperative course after ASO in our study but correlate well with surgical parameters like duration of surgery, they seem to describe only the myocardial vulnerability during surgery (especially during longer surgery) and have limited predictive value for the early postoperative course.

A secondary rise in TnT during the first days after ASO was not able to predict adverse events on a reliable basis, as only 70% of children (7 out of 10) with a secondary rise showed a complicated postoperative course. Kozar et al.[16] measured TnT values on regular basis after cardiac surgery and showed maximal values 3–6 h after aortic clamp removal in a heterogeneous group of CHD patients. In accordance to our investigation, they found a correlation of aortic cross clamp time to peak TnT concentrations. Due to the small amount of patients with a secondary rise, we did not find a significant difference in TnT rise between the complicated and non-complicated patient groups, even though the difference was obvious in our cohort (median 76.6% vs 11.6%, $P = 0.1$). Specificity (0.54) and sensitivity (0.65) for measuring TnT as outcome predictor beyond 48 h after ASO in our population was low. Minor increases of TnT shortly after ASO can be found in patients even without a new myocardial injury, for example, in patients with reduced renal clearance, as TnT can be elevated during impaired renal function,[17] or in patients with pressure overload or circulating troponin antibodies.[8,18] In our investigation, circulating troponin antibodies have not been analyzed. Concerning renal function, renal clearance assessed by blood creatinine, was normal in the majority of neonates before ASO at a median age of 8 days (1 day before ASO) and showed a significant increase till 48 h after ASO (Table 1). This increase is most likely due to the inflammatory and ischemic insult imposed by the cardiopulmonary bypass. We observed a normalization of renal function till 1 week after ASO. Children with a complicated postoperative course had significantly higher creatinine values 24 h after ASO only ($P = .032$), nevertheless the values were still in the normal range (median 55 μmol/L). When evaluating renal function in neonates by creatinine values, different creatinine assessments (Jaffe method vs enzymatic method) are possible. In contrast to the enzymatic method, the Jaffe method might underestimate the degree of acute kidney injury according to creatinine values. It has been shown that the GFR has to fall 25%–50% in neonates for enzymatically measured creatinine levels to increase,[19] with the Jaffe method this number might even be higher. In addition, creatinine values reflect maternal renal clearance for at least 72 h after birth and should only be used thereafter for assessment of renal function in newborns.[19] Nevertheless, definition of stage I acute kidney injury (AKI) is referred to as serum creatinine increase of 26.5 μmol/L over 48 h or an increase in serum creatinine ≥150%–200%,[20,21] arguing against an even stage I AKI in our cohort (Table 1). Recently it has been showed that even an increase up to 26 μmol/L in serum creatinine seems to be quite physiological when Jaffe quantification is used in the first week of postnatal life, while a 150% increase of creatinine is likely in this period of neonatal life for any assay applied.[22] We found a weak to moderate correlation of TnT and creatinine values ($r = .29$), assuming that the non-significant elevation of TnT values in children with a complicated course might partially be influenced by the slightly impaired renal function.

It has been reported previously that in neonates with various congenital heart defects higher TnT and TnI values were predictors for early in-hospital mortality after cardiac surgery.[6,23,24] Mildh et al. defined a TnT cutoff level of 5.9 μg/L on the first postoperative day as an independent predictor of death at 30 days.[23] As only two patients in our cohort died, statistical analysis is not reasonable due to the small sample size, even though both patients showed a strong secondary increase of TnT values before deterioration beyond 48 h after ASO. Immer et al.[24] found a prolonged postoperative course after open heart surgery in children, presenting with higher TnI levels at ICU admission after surgery. Nevertheless, patients with higher TnI levels also showed a reduced renal function in comparison to those patients with lower TnI values, which needs to be discussed as a confounding parameter, even though TnI clearance is less dependent on renal function than TnT.[25] In all these analysis, dTGA patients are only a subgroup of CHD and not analyzed separately. Imura et al.[26] focused on TnI values up to 48 h after ASO in 31 neonates with simple and complex TGA. In contrast to our investigation, they found a correlation of TnI levels with the duration of ventilator support and PICU stay, whereas inotropic support was similar to our results. In their analysis intraoperative factors had no influence on the TnI levels. In a heterogenous group of CHD without coronary involvement (VSD, Tetralogy of Fallot, DORV, AVSD) serial TnI values during the first 24 h after corrective heart surgery correlated well with a more complicated postoperative course.[24] We believe it is mandatory to analyze either TnI or TnT in a more homogenous group of congenital heart defects, as the complexity of the heart defect affects duration of surgery and as cardioplegia is performed differently in ASO: if more than one administration of cardioplegia is necessary, coronary orifices, which are surgically prepared with coronary buttons during ASO, are probed and cardioplegic solution is flushed directly into the vessel with the risk of local intima violation and stenosis in follow-up. This may well increase the probability for TnI or TnT rises postoperatively.

## 5 | LIMITATIONS

As in all retrospective analysis, the treating physicians were not blinded to the TnT values, which might have guided their treatment strategy and might have potentially both mitigated and exaggerated outcomes and complications. TnT values are influenced by several other factors besides ischemic myocardial insults, and these biasing facts have to be known in detail when interpreting TnT values after ASO. Our classification for an early complicated postoperative course has not been validated yet and is not specific for myocardial ischemia, nevertheless we assume it to represent real life situations on PICU wards and therefore suggest the further prospective evaluation in similar patient groups.

## 6 | CONCLUSION

Taken together, our results suggest that early postoperative TnT values reflect a longer and more vulnerable intraoperative course and should only be used as an additional tool for outcome prediction in neonates after ASO, in combination with other well-known clinical parameters. Height of early TnT after ASO does not correlate with the postoperative course and outcome. Even though a secondary rise of TnT values may represent a secondary myocardial hit, especially beyond 48 h after ASO, the values should be interpreted with caution and only together with other clinical findings and examinations. Several potentially confounding factors have to be taken into account when interpreting TnT levels.[27] In future studies, analysis should be expanded to newer biomarkers.

## CONFLICT OF INTEREST

None.

## AUTHOR CONTRIBUTIONS

*Concept/Design of the study, Data collection, Data analysis, drafting article*: Martin Christmann

*Data collection, Data analysis, Statistics, Critical revision of article*: Alexandra Wipf

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