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Title: Characteristics and Operative Outcomes for Children Undergoing Repair of Truncus Arteriosus: A Contemporary Multicenter Analysis

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This is the author's manuscript of the article published in final edited form as:
Mastropietro, C. W., Amula, V., Sassalos, P., Buckley, J. R., Smerling, A. J., Iliopoulos, I., … Costello, J. M. (2019). Characteristics and Operative Outcomes for Children Undergoing Repair of Truncus Arteriosus: A Contemporary Multicenter Analysis. The Journal of Thoracic and Cardiovascular Surgery. https://doi.org/10.1016/j.jtcvs.2018.12.115

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Funding: Funding from the Department of Pediatrics at Indiana University School of Medicine was provided for this study through a Riley Children's Foundation Grant (Intramural) for administrative support for the study. No honorarium or other form of payment was provided to anyone to produce the manuscript.

Conflicts of Interest: None of the authors have conflicts of interest to disclose.

Keywords: Truncus Arteriosus, Cardiopulmonary Bypass, Risk Factors, Cardiopulmonary Resuscitation, Extracorporeal Membrane Oxygenation, Body Surface Area, Postoperative Care, Early Diagnosis

Manuscript word count: 3500

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Glossary of Abbreviations

CI: confidence intervals

CPB: cardiopulmonary bypass

CPR**:** cardiopulmonary resuscitation

ECMO: extracorporeal membrane oxygenation

IAA: interrupted aortic arch

MACE: major adverse cardiac events

OR: odds ratio

ROC: receiver operative characteristic

RV-PA: right ventricle-to-pulmonary artery

STS-CHSD: Society of Thoracic Surgeons Congenital Heart Surgery Database

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Abstract

Objective: We sought to describe characteristics and operative outcomes of children who underwent repair of truncus arteriosus and identify risk factors for the occurrence of major adverse cardiac events (MACE) in the immediate postoperative period in a contemporary multicenter cohort.

Methods: We conducted a retrospective review of children who underwent repair of truncus arteriosus between 2009 and 2016 at 15 centers within the United States. Patients with associated interrupted or obstructed aortic arch were excluded. MACE was defined as the need for postoperative extracorporeal membrane oxygenation (ECMO), cardiopulmonary resuscitation (CPR), or operative mortality. Risk factors for MACE were identified using multivariable logistic regression analysis and reported as odds ratios (OR) with 95% confidence intervals (CI).

Results: We reviewed 216 patients. MACE occurred in 44 patients (20%) and did not vary significantly over time. Twenty-two patients (10%) received postoperative ECMO, 26 (12%) received CPR, and 15 (7%) suffered operative mortality. With multivariable logistic regression analysis (which included adjustment for center effect), factors independently associated with MACE were failure to diagnose truncus arteriosus prior to discharge from the nursery (OR:3.1; 95%CI:1.3,7.4), cardiopulmonary bypass duration greater than 150 minutes (OR:3.5; 95%CI:1.5,8.5), and right ventricle-to-pulmonary artery conduit diameter greater than 50mm/m^2 (OR:4.7; 95%CI:2.0,11.1).

Conclusions: In a contemporary multicenter analysis, 20% of children undergoing repair of truncus arteriosus experienced MACE. Early diagnosis, shorter duration of cardiopulmonary bypass, and use of smaller diameter right ventricle-to-pulmonary artery conduits represent potentially modifiable factors that could decrease morbidity and mortality in this fragile patient population.

Abstract Word Count: 246

Central Picture

Modifiable risk factors for major adverse cardiac events after truncus arteriosus repair

Central Message

One-fifth of children who underwent repair of truncus arteriosus suffered major adverse cardiac events. We identified potentially modifiable risk factors for the occurrence of these events.

Perspective Statement

In a multicenter cohort, 20% of children suffered major adverse cardiac events (MACE) following repair of truncus arteriosus. Diagnosis after nursery discharge, cardiopulmonary bypass duration more than 150 minutes, and right ventricle-to-pulmonary artery conduit diameter greater than 50mm/m^2 were identified as independent and potentially modifiable risk factors for MACE in these children.

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Introduction

Over the past 15 years, survival following surgery for congenital heart disease has steadily improved.[1] For certain lesions however, surgical mortality and the rate of postoperative complications remains relatively high.[2-5] For children born with a common arterial trunk, or truncus arteriosus, surgical mortality between 2005 and 2009 reported from the Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD) was 9.2%.[2] More recently, operative mortality in neonates who underwent repair of truncus arteriosus between 2013 and 2016 was 10.8%.[3] Another study from the STS-CHSD reported the need for extracorporeal membrane oxygenation (ECMO) after repair of truncus arteriosus to be 9.4%, which was high relative to other operations, and mortality in this subset was 71%.[4] The occurrence of other complications following repair of truncus arteriosus are also notably frequent relative to other lesions.[5]

Prior studies have identified moderate-to-severe truncal valve regurgitation or interrupted aortic arch to be risk factors for mortality and complications following repair of truncus arteriosus.[6-8] These co-existent lesions however represent a relatively small proportion of patients. Between 2000-2009, 572 patients were entered into the STS-CHSD as having surgical repair of truncus arteriosus, yet only 22 underwent concomitant repair of their truncal valve, 34 underwent concomitant repair of interrupted aortic arch (IAA), and 5 underwent concomitant repair of both additional lesions.[6] Of the remaining 511 patients, 45 (9%) died. Thus, a considerable portion of children with truncus arteriosus suffer early mortality despite the absence of IAA or concomitant truncal valve surgery.

To date, most data on operative outcomes following repair of truncus arteriosus are from single-center studies.[7-15] These data, while useful, are often difficult to interpret and generalize due to variations in preoperative, surgical, and postoperative management that exist between centers. We aim to describe characteristics and operative outcomes of children who

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underwent repair of truncus arteriosus using a contemporary multicenter dataset. From these data, we aim to identify risk factors for poor outcome after repair of truncus arteriosus, as defined as the occurrence of major adverse cardiac events (MACE) in the postoperative period. We hypothesized that analysis of data compiled from multiple centers that includes variables not recorded in the STS-CHSD would allow us to identify previously unrecognized risk factors for poor outcome after repair of truncus arteriosus.

Methods

Study Population

We performed a retrospective review of all patients who underwent primary surgical repair of truncus arteriosus at fifteen tertiary care pediatric referral centers between 2009 and 2016. A list of participating institutions is provided in Table 1 (online). The study was approved by the institutional review boards at all centers and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Due to the retrospective nature of the data collected, the need for informed consent was waived.

The following patients were excluded from the analysis:

- Children who underwent pulmonary artery banding but died prior to repair
- Children with hemitruncus (i.e., right pulmonary artery coming off the aorta) or pseudotruncus (i.e., pulmonary atresia with major aortopulmonary collaterals)
- Children who underwent concomitant repair of truncus arteriosus with IAA or aortic arch obstruction (Van Praagh Type A4), which is designated as a STAT mortality category 5 procedure, in contrast to repair of truncus arteriosus (Van Praagh Type A1-A3), which is a STAT mortality category 4 procedure [1] (Data for children with this lesion will be reported by our research group elsewhere.)

Data Collection and Definitions

A comprehensive list of variables and definitions is included in Table 2 (online). Right ventricle-to-pulmonary artery (RV-PA) conduit diameter was indexed to body surface area (BSA) to adjust the absolute values for differences in body size across subjects. The primary outcome of interest was the occurrence of MACE defined as intraoperative or postoperative cardiopulmonary resuscitation (CPR), extracorporeal membrane oxygenation (ECMO), or operative mortality. This composite outcome measure has been utilized elsewhere in the cardiac surgical literature.[18,19]

Statistical Analysis

Data are represented as medians with 25th and 75th percentiles for continuous variables and absolute counts with percentages for categorical variables unless otherwise noted. To determine risk factors associated with MACE after repair of truncus arteriosus, we performed a bivariate analysis using Wilcoxon rank sum test, χ-square test and Fisher's exact test as appropriate for individual variables. All variables with *P*-values < 0.2 on bivariate analyses were considered for inclusion in our multivariate logistic regression model. The multivariable model was also analyzed as a mixed model with center as a random effect. We treated the effect of center on the model as a random (as opposed to fixed) variable because the centers involved in the study represent a random sample of the population of all congenital cardiac centers, with considerable variation in center volume, preoperative and postoperative care models, and geographic location. Linearity in the logit was examined for continuous variables prior to model-building; variables with evidence of non-linearity were converted to categorical variables using receiver operative characteristics (ROC) analysis to identify optimal cut-points. This approach (as opposed to transformation of the continuous data) was chosen to facilitate clinical interpretation of the data analysis. Variables with *P*-values < 0.05 after multivariable analysis were identified as independent risk factors for MACE after surgical repair of truncus arteriosus. All statistical analyses were performed using STATA version 14 and SAS version 9.4.

Results

We retrospectively enrolled 216 children who underwent surgical repair of truncus arteriosus (Van Praagh Type A1-A3) between 2009 and 2016 at 15 institutions. Characteristics of the entire cohort are summarized in Tables 3 – 5. Prenatal diagnosis occurred in 63% of patients, whereas 21% were not diagnosed prior to discharge from the nursery, with 14 patients (6%) being diagnosed outside of the neonatal period (>30 days). The distribution of age at diagnosis is depicted in Figure 1 (online). The proportion of patients diagnosed prenatally and after discharge from the nursery did not vary significantly over time (Figure 2, online) and did not vary significantly across centers (p=0.131 and p=0.128, respectively). On the other hand, 17 patients (8%) in the study were discharged to home after their diagnosis was confirmed, with a plan of medical management and elective surgery at a later date. Twelve of these patients (71%) were readmitted prior to their scheduled surgery for acute respiratory failure or congestive heart failure. Moreover, three of the children developed necrotizing enterocolitis (one of whom underwent surgical intervention for perforation) and two suffered cardiac arrests (one of whom received preoperative ECMO support) prior to their surgical repair.

Operatively, 191 patients (88%) received one of three types of RV-PA conduits: pulmonary allograft, aortic allograft, or Contegra® bovine jugular vein conduit. Of the remaining 25 patients, 13 patients received femoral vein allografts, 2 patients received Gortex® conduits, 1 patient received a conduit created from anterior pericardium, 8 patients underwent direct anastomosis of their main pulmonary artery segment to their right ventricle (with or without patch augmentation), and 1 patient with a coexisting unbalanced atrioventricular septal defect had a systemic-to-pulmonary artery shunt placed. For the 209 patients who received RV-PA conduits, the range of the absolute values for the RV-PA conduit diameters utilized was relatively narrow, with all but 3 of these patients receiving a conduit with a diameter between 8mm and 14mm. When indexed to BSA, this range of RV-PA conduit diameters was $29mm/m^2$ to $78mm/m^2$.

For the entire patient population, median postoperative duration of mechanical ventilation was 5 days (range: 1,148), median hospital length-of-stay was 23 days (range: 6,282), and operative mortality was 6.9% (n=15). MACE occurred in 44 patients (20%). The proportions who suffered each type of MACE or other complications are provided in Table 6 (online), and variation in MACE and operative mortality across institutions is provided in Figure 3. Of note, operative mortality in the 22 patients who received ECMO was 36% (n=8). Bivariate analysis of demographic data, underlying comorbidities, and preoperative and operative variables is included in Tables 3 – 5. Preoperatively, patients who experienced MACE were significantly more likely to have been diagnosed after discharge from the nursery and more likely to have developed shock, though patients who were diagnosed after discharge from the nursery were not more likely to develop shock preoperatively – 4 of 45 children (9%) – as compared to 17 of 171 children (10%) diagnosed prenatally or prior to nursery discharge (p=1.00).

We also found that patients with MACE had longer duration of cardiopulmonary bypass and larger diameter RV-PA conduits (indexed to BSA), while aortic cross clamping duration, use of deep hypothermic circulatory arrest, and lowest targeted temperature during surgery were not statistically different between patients with and without MACE. Using ROC analysis, we identified CPB duration greater than 150 minutes and RV-PA conduit diameter greater than $50mm/m^2$ as optimal cut-points for prediction of MACE. The relationships between MACE, RV-PA conduit diameter, and BSA are illustrated in Figure 4, where the significant increase in the MACE in patients with RV-PA conduit diameter greater than $50mm/m^2$ can be visually appreciated. In contrast, the occurrence of MACE was relatively evenly distributed across different body sizes. Moreover, we noted a significantly higher proportion of MACE in patients who received Contegra® conduits, though conduit diameter was significantly larger in the 55 patients who received Contegra® conduits, median 54mm/m^2 (48,57), as compared to the 136 patients who received pulmonary or aortic allografts, median 50mm/m^2 (44,54), p=0.002.

The results of our mixed effects logistic regression analysis are provided in Table 7, including odds ratios (OR) and 95% confidence intervals (CI) for the fixed effects adjusted for center. We identified diagnosis after discharge from the nursery, CPB duration greater than 150 minutes, and RV-PA conduit diameter greater than 50mm/m^2 as factors independently associated with MACE after repair of truncus arteriosus in a model that included preoperative shock. The relationship between the CPB duration and RV-PA conduit diameter with postoperative complications is further explored in Figure 5. Operative mortality, CPR, delayed sternal closure, and postoperative tachyarrhythmias were significantly more common in patients with larger diameter RV-PA conduits (Figure 5A). In contrast, operative mortality, ECMO, and inhaled nitric oxide use were significantly more frequent in patients with prolonged CPB duration (Figure 5B).

We notably did not find an increased occurrence rate of MACE patients who underwent concomitant surgical intervention on their truncal valve (Table 3 and 4). It should be noted that of the six patients who underwent truncal valve replacement at the time of the surgery, MACE occurred in the three patients who first underwent an attempt at truncal valve repair and then underwent a second course of CPB and truncal valve replacement during the same operation (CPB durations: 333, 336, and 356 minutes), while no MACE occurred in the three patients who underwent truncal valve replacement without a prior attempt at truncal valve repair (CPB durations: 217, 291, 323 minutes). Accordingly, to better examine whether the association of MACE and prolonged CPB duration was more related to the duration of CPB itself or the need for concomitant truncal valve intervention that contributed to the prolonged duration of CPB, we performed a sensitivity analysis excluding the 37 patients who underwent truncal valve interventions. In this mixed effects logistic regression analysis, which included adjustments for preoperative shock as a fixed effect and center as a random effect, failure to diagnose truncus arteriosus prior to nursery discharge (OR: 2.8, 95%CI: 1.1,7.4), CPB duration greater than 150 minutes (OR: 3.0; 95%CI: 1.1,7.7), and RV-PA conduit diameter greater than 50mm/m^2 (OR: 3.3, 95%CI: 1.3,8.2) remained independently associated with MACE.

Discussion

In this contemporary multicenter dataset, we found that one in five patients who underwent surgical repair of truncus arteriosus suffered MACE. Furthermore, though operative mortality was lower than prior reports from the STS-CHSD, especially in patients requiring ECMO,[2,4] the occurrence of MACE did not decrease appreciably during the study period and complications were frequent relative to other neonatal operations. For example, 58% of patients in our study underwent delayed sternal closure (planned or unplanned), in contrast to 21% of all neonates reported to the STS-CHSD between 2013 and 2016.[3] Similarly, 6% of children in our study required tracheostomy, in comparison to less than 1% of all patients reported to the STS-CHSD between 2010 and 2015.[20] In other words, though operative mortality for patients undergoing surgery for congenital heart disease may be improving, patients with truncus arteriosus remain at considerable risk for complications and adverse cardiac events including death after surgery.

Fortunately, we identified three independent and potentially modifiable risk factors for MACE after repair of truncus arteriosus: failure to diagnose truncus arteriosus prior to discharge from the nursery, CPB duration greater than 150 minutes, and RV-PA conduit diameter greater than 50mm/m^2. Interestingly, in our multivariable analysis, diagnosis after discharge from the nursery (i.e. late diagnosis) was associated with MACE independent of preoperative shock. Based on this analysis, we speculate that many patients who were diagnosed late presented in an advanced state of compensated congestive heart failure that had not yet progressed to meet the STS-CHSD definition of shock, and neonates need not progress to a late stage of shock before their burden of illness will influence their postoperative course. Early diagnosis prior to the development of shock with lactic acidosis should therefore be the aim of current neonatal screening protocols.

In 2009, the American Academy of Pediatrics and American Heart Association published a joint statement on pulse oximetry screening as a means to detecting undiagnosed congenital heart disease prior to nursery discharge.[21] In 2012, the Department of Health and Human Services endorsed this practice.[22] In 2017, data from the National Center for Health Statistics showed a significant decrease in infant cardiac deaths between 2007 and 2013 in states that had implemented statewide mandatory policies for newborn screening for critical congenital heart disease as compared with states without these policies.[23] As of 2017, all states except Idaho and Kansas mandate newborn screening for critical congenital heart disease.[24]. Data on the adherence to these practices at individual centers, however, are sparse. In one recent report from a center where the practice of routine pulse oximetry screening for congenital heart disease was adopted and then audited, compliance with their protocol was 88%, which is good but not optimal.[25] The association of late diagnosis with MACE after repair of truncus arteriosus in our study and the aforementioned data on the benefits of routine pulse oximetry screening for congenital heart disease support the further expansion of this practice and the establishment of infrastructure at the local level to ensure that these programs are operating appropriately.

It should also be noted that 17 patients were discharged to home *after* diagnosis, of whom 71% were readmitted with life-threatening illnesses prior to repair. This observation argues against sending these children home without surgical intervention. Indeed, the feasibility and practicality of performing the surgical repair of truncus arteriosus in the neonatal period have long been established and confirmed by many single center studies.[7, 9-11] Thus, early surgical intervention for repair of truncus arteriosus should be pursued whenever possible to minimize the risk of preoperative morbidity.

Prolonged duration of CPB is a well-described risk factor for worse outcomes after pediatric cardiac surgery.[26,27] Based on the observed association between longer duration of CPB and use of ECMO or inhaled nitric oxide, we presume that longer durations of CPB in our patients could have predisposed them to myocardial depression and pulmonary hypertensive crises that necessitated these adjunctive therapies. Notably, the relationship between prolonged CPB duration and adverse outcomes persisted when operations with concomitant truncal valve procedures were excluded. We are not, however, advocating that the quality of repair be sacrificed in an effort to be more expeditious. Rather, awareness of the association between MACE and prolonged duration of CPB after repair of truncus arteriosus should emphasize the importance of minimizing exposure to CPB whenever possible.

Perhaps the most compelling and easily modifiable identified risk factor for MACE after repair of truncus arteriosus is larger diameter of RV-PA conduit, specifically greater than $50mm/m^2$. (For reference, in Figure 6, absolute RV-PA conduit diameters that fall below the threshold of $50mm/m^2$ for body surface areas between $0.15m^2$ and $0.25\ m^2$ are provided.) In a single-center study of 83 patients, Tlaskal and colleagues also noted a trend toward increase mortality in patients with larger absolute RV-PA conduit diameters.[12] To our knowledge, our study represents the first to examine RV-PA conduit diameter indexed to body surface area as an important variable to consider when planning surgical correction for these children. Based on our data, the pathophysiologic explanation for this finding cannot be clearly discerned. We speculate that larger diameter conduits could be associated with increased ventriculotomy size relative to the size of the neonatal myocardium that could exacerbate restrictive right ventricular physiology or provide an arrhythmogenic substrate during the recovery period. Larger conduits could suffer from distortion or compression during sternal closure leading to conduit insufficiency, pulmonary artery distortion, or prolonged duration of open sternotomy, predisposing patients to infectious or respiratory complications. A combination of these possibilities could be responsible for the worse outcomes in patients with conduit diameters greater than 50mm/m^2. Future studies examining the relationship between conduit size and postoperative outcomes should be designed to more specifically investigate these or other potential pathophysiologic mechanisms.

Nearly all patients who undergo repair of truncus arteriosus will require replacement of their RV-PA conduit later in life and, consequently, many surgeons will err on the side of larger conduit diameters in an attempt to extend the period of time before conduit revision is needed. Indeed, several studies have associated smaller absolute conduit diameter with earlier need for reintervention,[28-31] with some authors advocating “oversizing” of the conduit to prevent early graft failure.[30] In a seminal study from the Congenital Heart Surgery Society of 429 children with various congenital heart lesions who required RV-PA conduits, use of smaller conduits were associated with earlier reinterventions, leading the authors to conclude “insertion of the largest conduit possible (within the constraints of our data and patient size) would be expected to postpone explantation prompted by the somatic growth of the patient.”[31] Based on our data, use of larger conduits to promote long-term durability could come at a cost for some patients. None of the eight patients who underwent direct anastomoses of the pulmonary artery suffered MACE, and studies have reported longer freedom from reoperation in patients who underwent direct anastomoses.[32-34] Additionally, a recent study reported the potential of modified repair of truncus arteriosus in which the branch pulmonary arteries are left in situ and septated from the truncal root may promote conduit longevity.[35] Further research focused on these modifications or other innovations could mitigate the impetus to use larger conduits at the initial repair of truncus arteriosus and, possibly, reduce the risk of MACE. Accordingly, additional research in children with congenital heart disease who receive RV-PA conduits should aim to determine a range of conduit diameters that could optimally balance the risks of short- and long-term morbidity and mortality.

This study has the limitations inherent to its retrospective design. For example, data on RV-PA conduit diameter were obtained retrospectively from operative reports and not confirmed by direct measurement via postoperative echocardiogram. If actual RV-PA conduit diameters differed from what was provided by the tissue record, the accuracy of our RV-PA conduit measurements would be affected. We also acknowledge that the components of our composite primary outcome measure differ in terms of severity (i.e., mortality is a worse than CPR or EMCO alone). On the other hand, etiologies for the need for CPR, need for ECMO, or operative mortality were likely similar in many patients (e.g., myocardial depression, pulmonary hypertensive crises, arrhythmias, multiorgan dysfunction) and most clinicians would agree that any of the three included outcomes are undesirable. Notably, we did not include long-term outcomes in this study but rather maintained the focus on early outcomes. Lastly, patients for this study were identified by institutional surgical databases, which did not allow us to report data on patients who may have been diagnosed with truncus arteriosus but died before surgical intervention. The strength of this study is its collaborative multicenter design, which allowed us to obtain data on variables not entered into current databases such as the STS-CHSD as well as identify risk factors for MACE after repair of truncus arteriosus that are independent of center. Future analyses will focus on post-discharge outcomes including freedom from conduit intervention, truncal valve intervention, or death.

Conclusions

Operative mortality and other adverse cardiac events after repair of truncus arteriosus continue to be relatively common. In our contemporary multicenter study, operative mortality was 6.9% and MACE occurred in one-fifth of patients. We hope that future investigations will reveal that attention to the independent and potentially modifiable risk factors identified in this report – diagnosis after discharge from the nursery, duration of CPB greater than 150 minutes, and RV-PA conduit diameter greater than 50 mm/m^2 – will lead to improvements in the operative and early postoperative outcomes in these fragile children. We also suggest that neonatal repair becomes the preferred option for surgical timing at all centers, as patients who are discharged to home with medical management after diagnosis of truncus arteriosus are at considerable risk of preoperative morbidity.

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Acknowledgements

We like to acknowledge and thank the following individuals who assisted the authors with administrative tasks, data collection, or review of echocardiograms for this study:

- Amy Moravec, BS, Ann & Robert H. Lurie Children's Hospital of Chicago
- Kari Nelson, B.A., MSN, CPNP, University of Wisconsin-American Family Children's Hospital
- Josh Belfer MD, Resident in Pediatrics, Cohen Children's Medical Center of New York
- Eva Cheung MD, Assistant Professor, Department of Pediatrics, Division of Cardiology, Columbia University College of Physicians & Surgeons, Morgan Stanley Children's Hospital of New York, New York, NY
- Linda M. Lambert MSN-cFNP, Administrative Director of Research, Heart Center - Primary Children's Hospital, University of Utah
- Lisa Michelle Hansen, Clinical Research Coordinator, Heart Center - Primary Children's Hospital, University of Utah

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Figures

Figure 1 (online). Histogram demonstrating the variation in age at diagnosis of patients with truncus arteriosus included in the study. Most patients (n=188, 87%) were prenatally diagnosed or diagnosed within the first week of life, while 14 patients (6%) were diagnosed outside the neonatal period (>30 days), which includes an outlier not represented in the histogram - a child who was adopted from outside the United States with a presumed diagnosis of Tetralogy of Fallot but was found have truncus arteriosus upon evaluation on day of life 1275 (3.5 years).

Figure 2 (online). Trends in the diagnosis of truncus arteriosus over time. The percentage of patients diagnosed with truncus arteriosus prenatally (green bars), postnatally but prior to discharge from the nursery (yellow bars), and postnatally after discharge from the nursery (red bars). The variations in the percentage of patients diagnosed prenatally and patients diagnosed after discharge from the nursery over the duration of the study period were not statistically significant − p=0.48 and p=0.98, respectively.

Figure 3. Variation across centers in the number of patients who underwent repair of truncus arteriosus and the occurrence of major adverse cardiovascular events (MACE). Each bar contains the number of patients who suffered operative mortality (black portion), number who suffered cardiac arrest or received extracorporeal membrane oxygenation but survived (red portion), and number who did not suffer MACE (grey portion of bars). Centers are arranged in order of increasing surgical volume of patients who underwent truncus arteriosus repair during the study period.

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Figure 4. Major adverse cardiovascular events (MACE) in relation to body surface area (BSA) and the diameter of surgically-placed right ventricle-to-pulmonary artery (RV-PA) conduit in patients who underwent repair of truncus arteriosus. Patients who experienced MACE (n=44, red circles) were significantly more likely to have RV-PA conduits greater than 50 mm/m^2in diameter (dotted reference line) than patients who did not experience MACE. Specifically, 33 of 44 patients (75%) who suffered MACE had RV-PA conduits greater than 50 mm/m^2, as compared to 79 of 172 patients (46%) who did suffer MACE, p=0.001. Importantly, though smaller patients were more likely to have larger diameter RV-PA conduits, no significant relationship between the occurrence of MACE and body size was observed.

Figure 5A. Patients with right ventricle-to-pulmonary artery (RV-PA) conduits greater than 50mm/m^2 in diameter were significantly more likely to suffer operative mortality and receive cardiopulmonary resuscitation (CPR) (i.e. major cardiac adverse events (MACE). Patients with RV-PA conduits greater than 50mm/m^2 were also more likely to experience tachyarrhythmias or undergo delayed sternal closure. In contrast, use of extracorporeal membrane oxygenation (ECMO) or inhaled nitric oxide (iNO) were not significantly more likely to occur in patients with conduit diameters greater than 50mm/m^2. *statistically significant, p<0.05

Figure 5B. Patients with cardiopulmonary bypass duration (CPB) greater than 150 minutes were more likely to suffer operative mortality and receive extracorporeal membrane oxygenation (ECMO) (i.e. major adverse cardiac events (MACE), and more likely to be administered inhaled nitric oxide (iNO). The occurrence of cardiopulmonary resuscitation (CPR), tachyarrhythmias, and delayed sternal closure, however, were not statistically more likely in patients with CPB durations greater than 150 minutes. *statistically significant, p<0.05

Figure 6 (online). Absolute right ventricle-to-pulmonary artery (RV-PA) conduit diameters for patients with body surface areas between 0.15 – 0.25 mm^2 (10th percentile – 90th percentile of study population) that will result in diameters indexed to body surface area up to 50mm/m^2. RV-PA conduit diameters above the green bars at each body surface area may increase the risk of major adverse cardiovascular events (MACE) after repair of truncus arteriosus.

Videos

Video. A PowerPoint slideshow accompanied by audio explanations for each slide featuring the most notable findings of our study.

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Table 3. Comparison of Patients with and without Major Adverse Cardiac Events (MACE) after Repair of Truncus Arteriosus (2009 – 2016) – Demographic information and Baseline Patient Characteristics

Variable[a]	All patients (*N*=216)	No MACE (n=172)	MACE (n=44)	*p*-value
Prenatal diagnosis	135 (63%)	111 (65%)	24 (55%)	0.22
Age at diagnosis (days)	0 (0, 2)	0 (0, 1)	0 (0, 3)	0.13
Not diagnosed before discharge	45 (21%)	31 (18%)	14 (32%)	0.04
Sent home after diagnosis	17 (8%)	15 (9%)	2 (5%)	0.29
Not diagnosed before discharge or sent home after diagnosis	62 (29%)	46 (27%)	16 (36%)	0.21
Truncus Type (Van Praagh)				0.15
A1	112 (52%)	94 (55%)	18 (41%)	
A2	90 (42%)	66 (38%)	24 (55%)	
A3	14 (7%)	12 (7%)	2 (5%)	
Prematurity (<37 weeks)	42 (19%)	30 (17%)	12 (27%)	0.14
Female sex	108 (50%)	87 (51%)	21 (48%)	0.74
Race				0.72
White	147 (68%)	119 (69%)	28 (64%)	
Black	33 (15%)	26 (15%)	7 (16%)	
Other / Unknown	36 (17%)	27 (16%)	9 (20%)	
Latino / Hispanic ethnicity	27 (13%)	21 (12%)	6 (14%)	0.80
Chromosomal anomaly, any	83 (38%)	68 (40%)	15 (34%)	0.51
DiGeorge/22q.11 deletion	61 (28%)	53 (31%)	8 (18%)	0.10
Non-cardiac anatomic anomaly	63 (29%)	48 (28%)	15 (34%)	0.42
Year of surgical repair				0.24
2009	17 (8%)	14 (8%)	3 (7%)	
2010	25 (12%)	21 (12%)	4 (9%)	
2011	31 (14%)	21 (12%)	10 (23%)	
2012	30 (14%)	28 (16%)	2 (5%)	
2013	27 (13%)	22 (13%)	5 (11%)	
2014	28 (13%)	23 (13%)	5 (11%)	
2015	34 (16%)	27 (16%)	7 (16%)	
2016	24 (11%)	16 (9%)	8 (18%)	

[a] Continuous variables represented as median (25th%, 75th%); categorical data represented as absolute counts (%)

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Table 4. Comparison of Patients With and Without Major Adverse Cardiac Events (MACE) after Repair of Truncus Arteriosus (2009 – 2016) – Preoperative Clinical Data

Variable [a]	All patients (*N*=216)	No MACE (n=172)	MACE (n=44)	*p*-value
Echocardiographic Data				
Ventricular Function				
Depressed RV function	31 (14%)	23 (13%)	8 (18%)	0.42
Depressed LV function	22 (10%)	15 (9%)	7 (16%)	0.17
Truncal Valve anatomy				
Bicuspid	27 (13%)	23 (13%)	4 (9%)	0.85
Tricuspid	114 (53%)	89 (52%)	25 (57%)	
Quadricuspid	73 (34%)	58 (34%)	15 (34%)	
Dysplastic	2 (1%)	2 (1%)	0 (0%)	
Truncus Valve Insufficiency				
None / Trivial	99 (46%)	83 (48%)	16 (36%)	0.38
Mild	51 (24%)	41 (24%)	10 (23%)	
Mild-to-Moderate/Moderate	49 (23%)	36 (21%)	13 (30%)	
Moderate-to-Severe/Severe	17 (8%)	12 (7%)	5 (11%)	
Truncal Valve Stenosis				
None	153 (71%)	121 (70%)	32 (73%)	0.15
Mild/Mild-to-Moderate	50 (23%)	38 (22%)	12 (27%)	
Moderate/Severe	13 (6%)	13 (8%)	0 (0%)	
Coronary artery abnormalities	28 (13%)	21 (12%)	7 (16%)	0.52
Preoperative shock	21 (10%)	12 (7%)	9 (20%)	0.02
Preoperative inotropic infusion [b]	35 (16%)	27 (16%)	8 (18%)	0.69
Preoperative ventilation [c]	45 (21%)	34 (20%)	11 (25%)	0.45
Preoperative infection	27 (13%)	25 (15%)	2 (5%)	0.07
Preoperative seizures	6 (3%)	6 (4%)	0 (0%)	0.35
Preoperative stroke	7 (3%)	7 (4%)	0 (0%)	0.17
Pulmonary artery banding	3 (1%)	3 (2%)	0 (0%)	1.00

[a] Continuous variables represented as median (25^{th}%, 75^{th}%); categorical data represented as absolute counts (%)
[b] Dopamine, dobutamine, epinephrine, and milrinone infusion(s) within 24 hours of surgery
[c] Includes only patients who required endotracheal intubation at any point preoperatively and remained on mechanical ventilation until to surgery

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Table 5. Comparison of Patients With and Without Major Adverse Cardiac Events (MACE) after Repair of Truncus Arteriosus (2009 – 2016) – Operative Data

Variable [a]	All patients (*N*=216)	No MACE (n=172)	MACE (n=44)	*p*-value
Age at surgery (days)	10 (7, 24)	9.5 (7, 23)	11 (6.5, 32)	0.38
Time from diagnosis to surgery (days)	8 (5.5, 15)	7.5 (5.5, 15)	9 (5.5, 18)	0.46
Weight at surgery (kg)	3.1 (2.7, 3.5)	3.1 (2.7, 3.5)	3 (2.5, 3.5)	0.39
Body surface area (m^2)	0.21 (0.19,0.23)	0.21 (0.19,0.23)	0.21 (0.18,0.23)	0.60
Cardiopulmonary bypass (min)	150 (124, 186)	144 (122, 182)	165 (141, 235)	0.001
Cardiopulmonary bypass > 150 min	107 (50%)	78 (45%)	29 (66%)	0.015
Aortic cross clamp (min)	86 (73, 111)	87 (70, 110)	85 (78, 116)	0.34
Hypothermic circulatory arrest	31 (14%)	24 (14%)	7 (16%)	0.74
Lowest temperature (℃)	25 (21, 28)	25 (22, 28)	25 (21, 28)	0.95
Modified Ultrafiltration	139 (64%)	113 (66%)	26 (59%)	0.41
Intraoperative steroids	161 (75%)	132 (77%)	29 (67%)	0.14
Intraoperative Factor VIIa	34 (16%)	26 (15%)	8 (18%)	0.62
RV-PA conduit type				0.04
Aortic allograft	53 (25%)	42 (24%)	11 (25%)	
Pulmonary allograft	83 (38%)	72 (42%)	11 (25%)	
Contegra conduit	55 (26%)	37 (22%)	18 (41%)	
Other / None	25 (12%)	21 (12%)	4 (9%)	
RV-PA conduit size (mm) [b]	11 (9, 12)	10 (9, 12)	12 (9. 12)	0.22
RV-PA conduit size (mm/m^2) [b]	51 (45.6, 56.4)	49.9 (44.9, 55.5)	52.9 (49, 57.3)	0.01
RV-PA conduit size > 50 mm/m^2	112 (52%)	79 (46%)	33 (75%)	0.001
Truncal valve repaired	34 (16%)	25 (15%)	9 (21%)	0.34
Truncal valve replaced	6 (3%)	3 (2%)	3 (7%)	0.10

[a] Continuous variables represented as median (25^{th}%, 75^{th}%); categorical data represented as absolute counts (%)
[b] n=207 patients; excludes eight patients who underwent direct anastomoses of main pulmonary artery segment and one patient who underwent placement of systemic-to-pulmonary artery shunt

Table 7. Multivariable Logistic Regression Analysis for Predictors of Operative Mortality after Repair of Truncus Arteriosus (Analyzed as a Mixed Model with a Random Effect of Center)

Fixed Effects	odds ratio	95% confidence interval	p-value
Preoperative shock	3.0	0.97, 9.5	0.056
Undiagnosed at discharge from nursery	3.1	1.3, 7.4	0.012
Cardiopulmonary bypass > 150 min	3.5	1.5, 8.5	0.005
RV-PA conduit size > 50 mm/m^2	4.7	2.0, 11.1	<0.001

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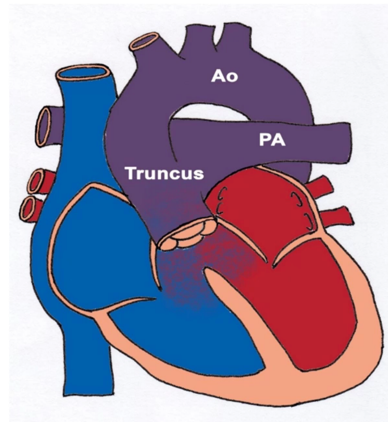
Background

- **Truncus arteriosus**
  - Complex defect most commonly diagnosed in the neonatal period or early infancy
  - Operative morbidity and mortality continues to be significant
  - Risk factors for poor outcomes following surgical repair have been reported in single-center studies



Mastropietro et al. *Pediatric Emergency Medicine Practice*, May 2008.

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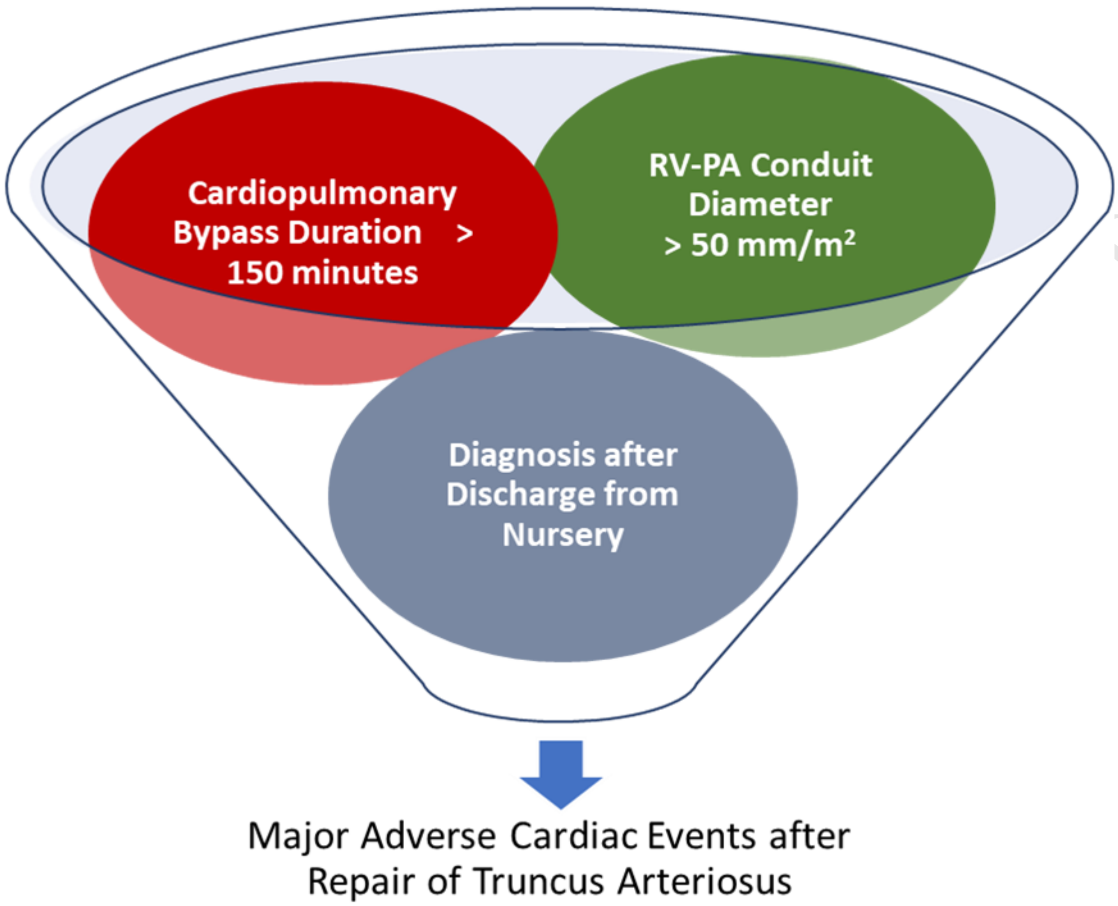

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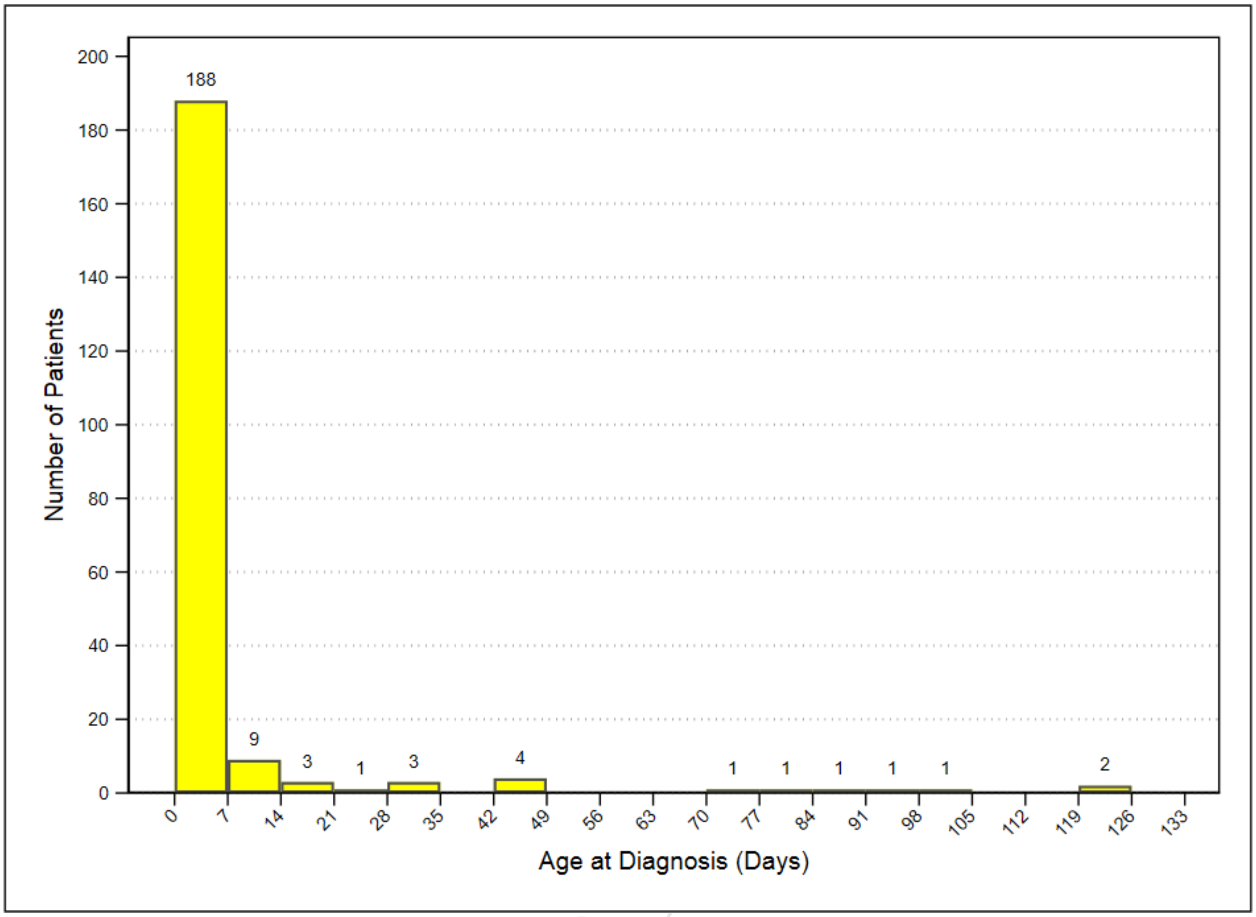

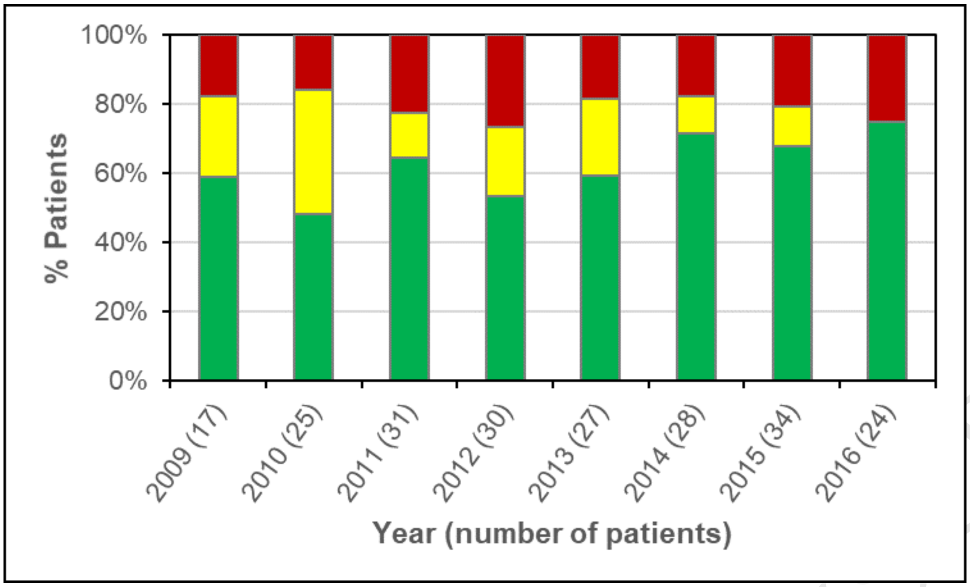

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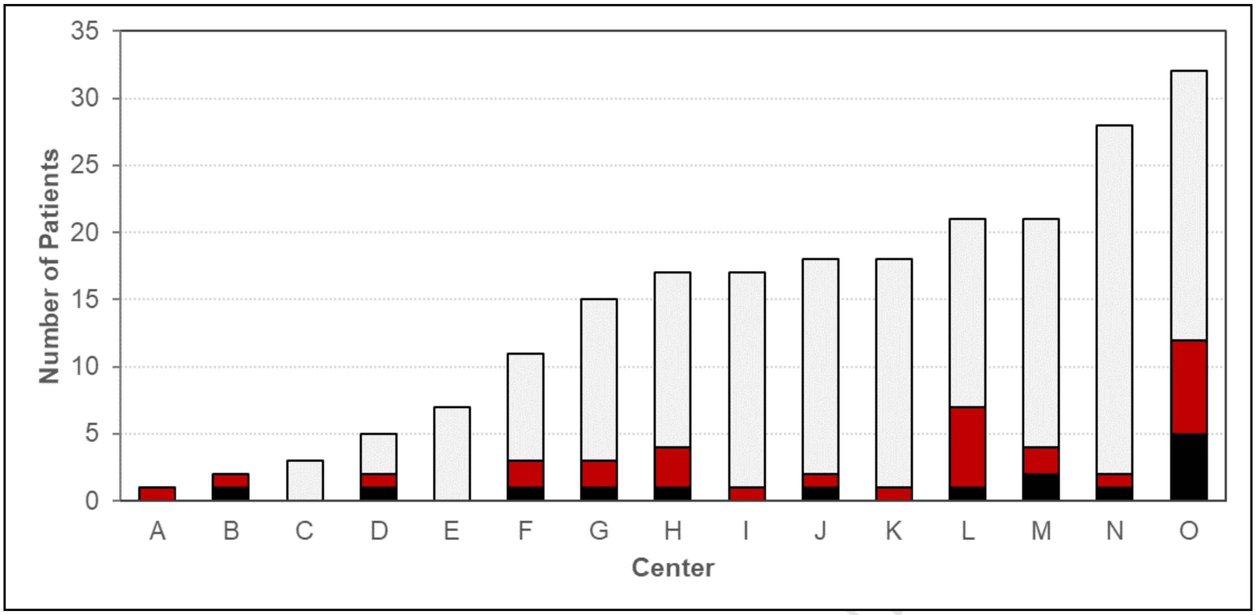

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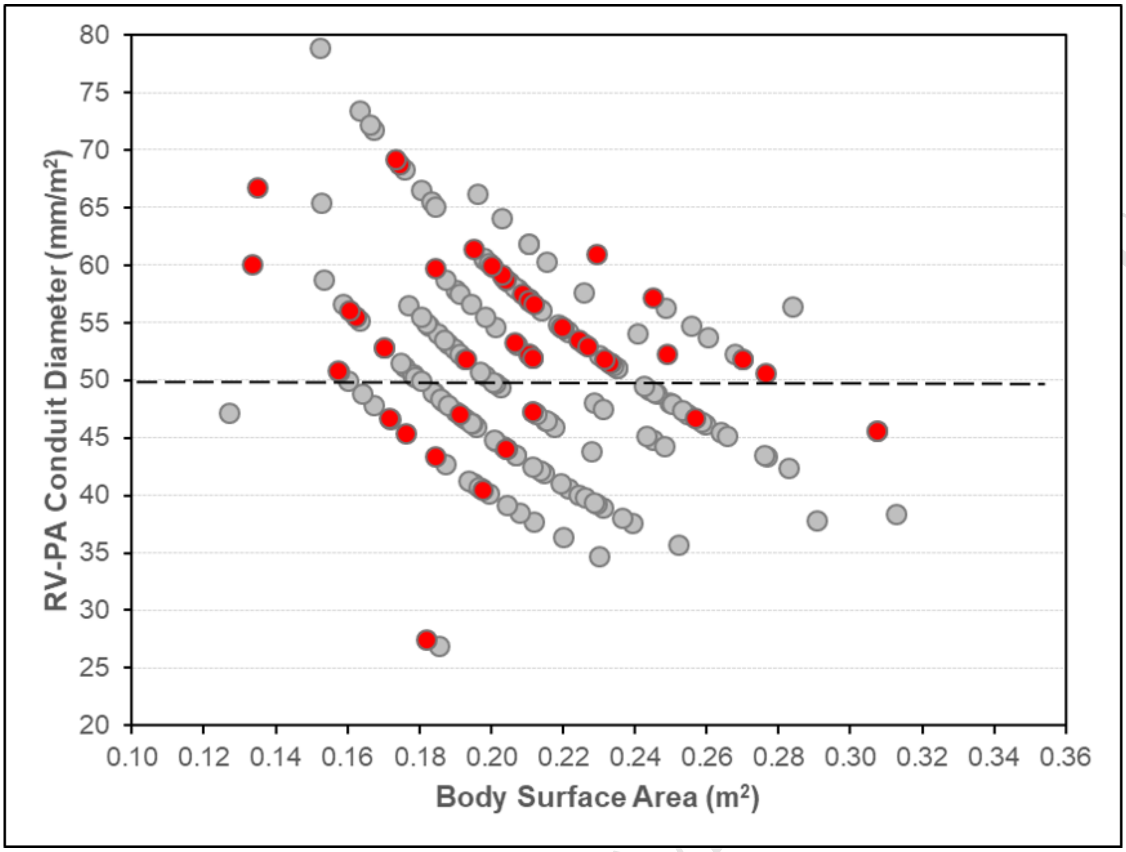
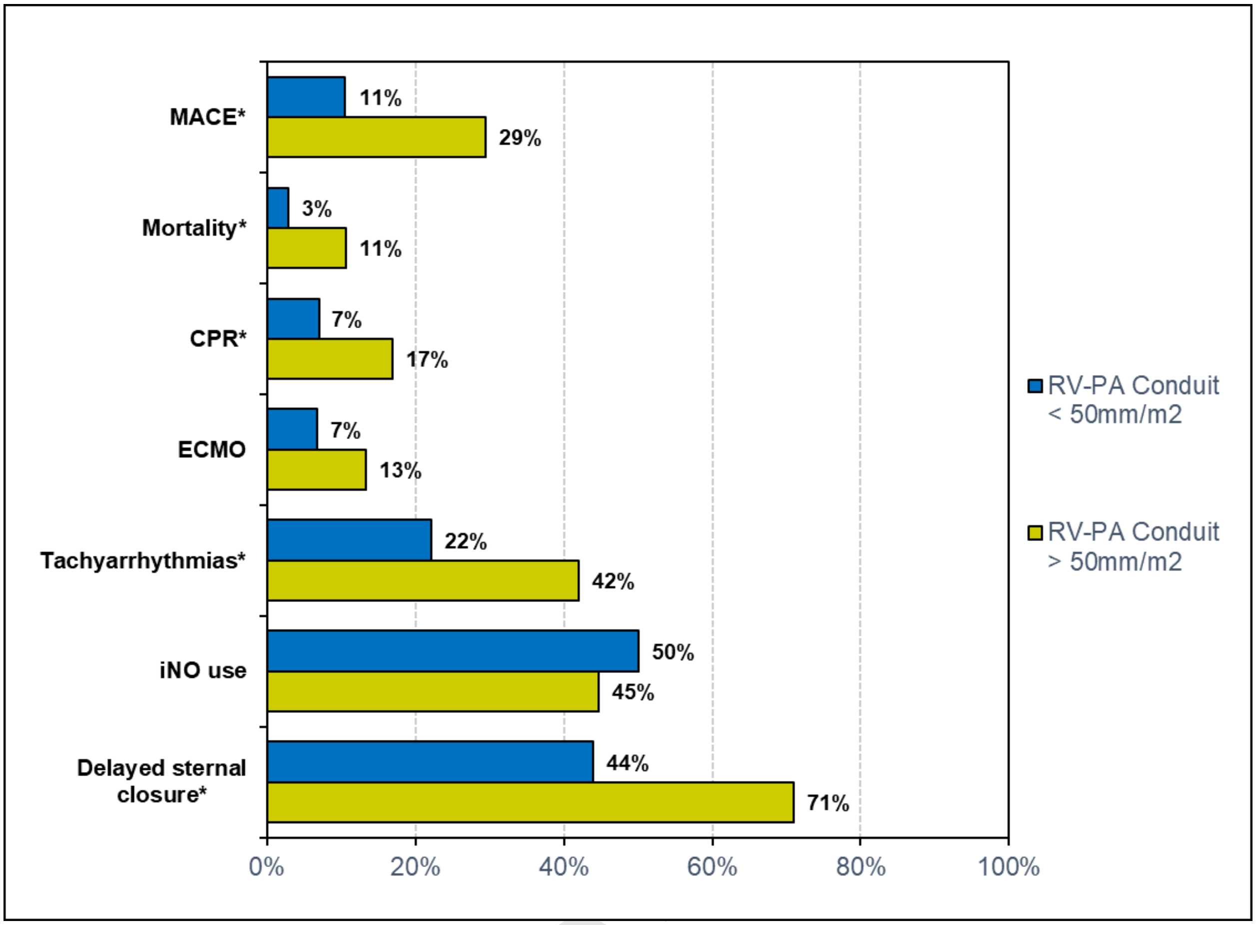


RV-PA Conduit Diameter (mm/m²)
80
75
70
65
60
55
50
45
40
35
30
25
20
0.10
0.12
0.14
0.16
0.18
0.20
0.22
0.24
0.26
0.28
0.30
0.32
0.34
0.36
Body Surface Area (m²)


MACE*
11%
29%
Mortality*
3%
11%
CPR*
7%
17%
ECMO
7%
13%
Tachyarrhythmias*
22%
42%
iNO use
50%
45%
Delayed sternal closure*
44%
71%
0%
20%
40%
60%
80%
100%
RV-PA Conduit < 50mm/m2
RV-PA Conduit > 50mm/m2

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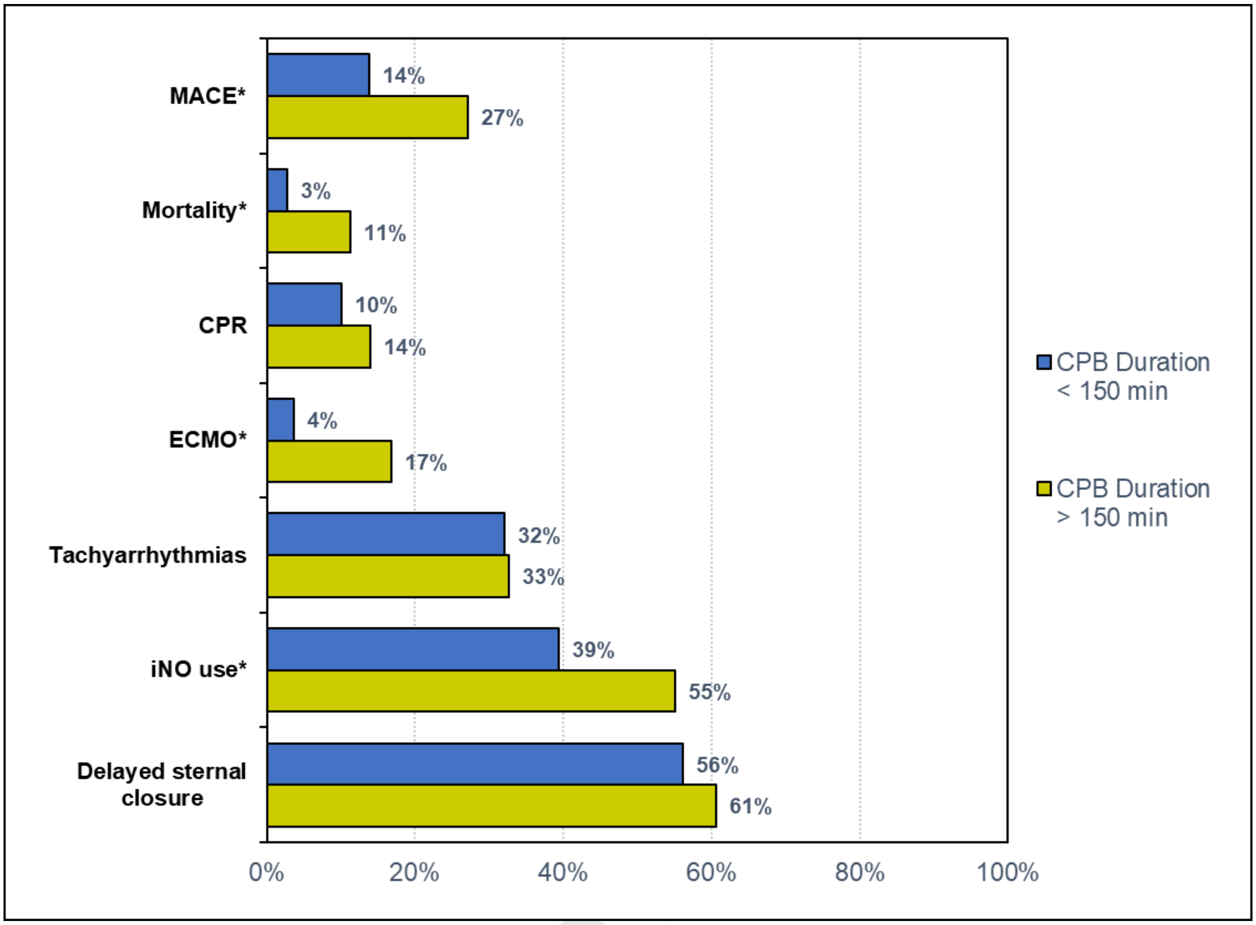

MACE*
14%
27%
Mortality*
3%
11%
CPR
10%
14%
ECMO*
4%
17%
Tachyarrhythmias
32%
33%
iNO use*
39%
55%
Delayed sternal closure
56%
61%
0%
20%
40%
60%
80%
100%
CPB Duration < 150 min
CPB Duration > 150 min

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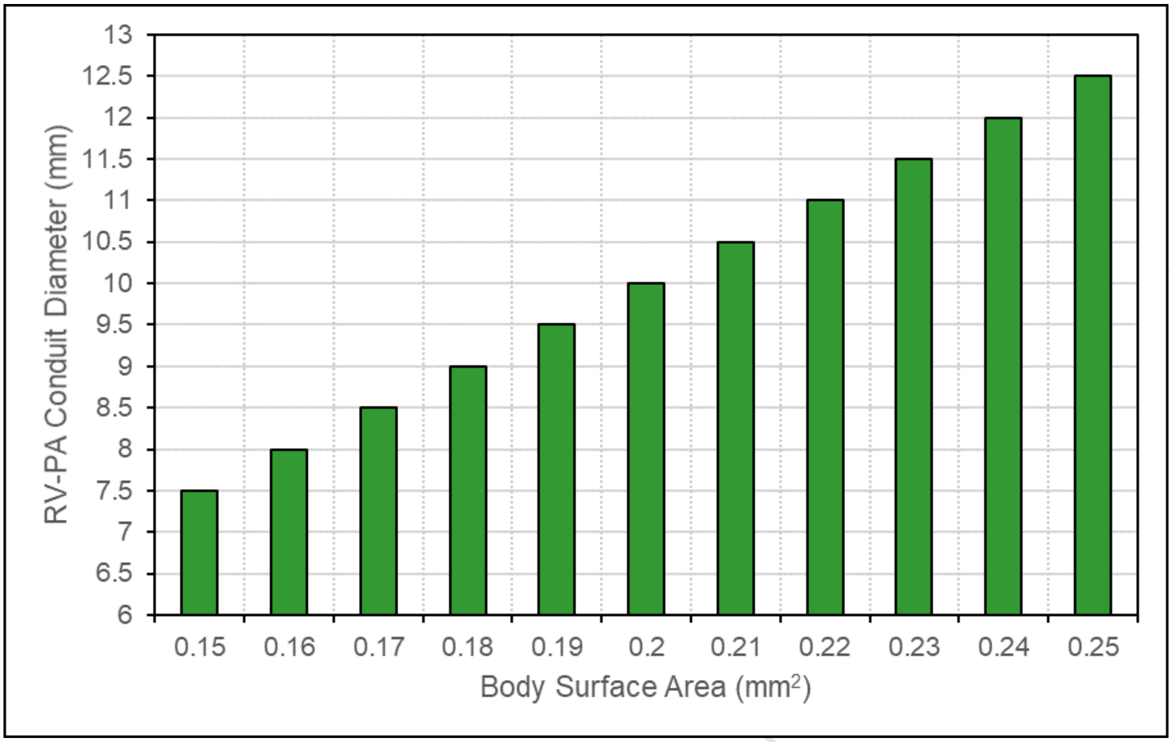

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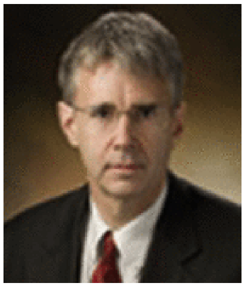

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CoRe PCIC
Collaborative Research
In Pediatric Cardiac
Intensive Care

INDIANA UNIVERSITY
SCHOOL OF MEDICINE

Riley Children's Health
Indiana University Health

Characteristics and Operative Outcomes for Children Undergoing Repair of Truncus Arteriosus: A Contemporary Multicenter Analysis

Christopher W. Mastropietro; Venu Amula; Peter Sassalos; Jason R. Buckley; Arthur J. Smerling; Ilias Iliopoulos; Aimee Jennings; Christine M. Riley; Katherine Cashen; Sukumar Suguna Narasimhulu; Keshava Murty Narayana Gowda; Adnan Bakar; Michael Wilhelm; Aditya Badheka; Elizabeth A.S. Moser; John M. Costello

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Table 1 (online only). Collaborative Research in Pediatric Cardiac Intensive Care (CoRe-PCIC) Participating Institutions

- Riley Hospital for Children, Indianapolis, IN
- Cleveland Clinic, Cleveland, OH
- Children's Hospital of Michigan, Detroit, MI
- Morgan Stanley Children's Hospital of New York, New York, NY
- Cohen Children's Medical Center, New Hyde Park, NY
- Medical University of South Carolina Children's Hospital, Charleston, SC
- Children's National Health System, Washington, DC
- Arnold Palmer Hospital for Children, Orlando, FL
- Seattle Children's Hospital, Seattle, WA
- Ann & Robert H. Lurie Children's Hospital of Chicago, IL
- University of Iowa Stead Family Children's Hospital, Iowa City, IA
- Cincinnati Children's Hospital Medical Center, Cincinnati
- Primary Children's Hospital, Salt Lake City, UT
- University of Michigan C.S. Mott Children's Hospital, Ann Arbor, MI
- American Family Hospital, Madison, WI

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Table 2 (online). Data Collection and Definitions

Preoperative Data

- Age, sex, race, ethnicity, and anthropometric data
- Estimated gestational age at birth
- Prematurity – less than 37 weeks gestation
- Presence of genetic anomalies or non-cardiac anatomic anomalies
- Age and setting of diagnosis, i.e. prenatal diagnosis, diagnosis after birth but prior to discharge from the nursery, or diagnosis after discharge from the nursery
- Type of truncus arteriosus (Van Praagh) [16]
    - Type A1: Identifiable main pulmonary artery segment
    - Type A2: Branch pulmonary arteries come off separately from posterior aorta
    - Type A3: Pulmonary blood flow to one lung is supplied by ductal or collateral blood flow
- Preoperative echocardiography data – ventricular function, truncal valve anatomy, degree of stenosis or regurgitation
- Need for preoperative mechanical ventilation or inotropic infusion(s)
- Preoperative shock – pH less than 7.2 or lactate greater than 4 mg/dL, as defined by the Society of Thoracic Surgeons-Congenital Heart Surgery Database [17]
- Preoperative infection or necrotizing enterocolitis
- Stroke or seizure – patients with clinical or sub-clinical seizure activity were recorded as having seizures
- Pulmonary artery banding prior to surgical repair

Operative Data

- Age, weight, height, and body surface area at surgery
- Duration of cardiopulmonary bypass and aortic cross clamping
- Use of deep hypothermic circulatory arrest

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Table 2 (online). Data Collection and Definitions (*continued*)

Operative Data (continued)

- Lowest intraoperative temperature
- Use of intraoperative systemic corticosteroids, modified ultrafiltration, or factor VIIa
- Right ventricle-to-pulmonary artery conduit size and type
- Truncal valve intervention, e.g. repair or replacement

Postoperative Data

- Use of delayed sternal closure
- Use of extracorporeal membrane oxygenation
- Use of cardiopulmonary resuscitation
- Use of inhaled nitric oxide therapy
- Occurrence of postoperative arrhythmia
- Occurrence of uplanned cardiac catheterization or operation
- Postoperative infection (includes necrotizing enterocolitis)
- Postoperative stroke or seizure
- Occurrence of postoperative respiratory complications - extubation failure, chylothorax, paralyzed diaphragm, vocal cord paralysis, or tracheostomy

Outcome Data

- Initial and total duration of postoperative mechanical ventilation
- Duration of intensive care unit and hospital length-of-stay
- Operative mortality [17]
  - Mortality occurring before discharge from the hospital where the index cardiac operation took place or any secondary acute care facility
  - Any out-of-hospital deaths occurring within 30 days of the index cardiac operation,
  - Any deaths occurring in a secondary chronic care facility (or rehabilitation facility) within 180 days following the index cardiac operation.

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Table 6 (online). Postoperative Complications after Repair of Truncus Arteriosus

Variable	All patients (*N*=216)
Delayed Sternal Closure – Planned	119 (55%)
Delayed Sternal Closure – Unplanned	7 (3%)
CPR	26 (12%)
ECMO	22 (10%)
Initiated in OR	13
Initiated in ICU	9
Inhaled nitric oxide use	102 (47%)
Initiated in OR	69
Initiated in ICU	33
Tachyarrhythmia	63 (29%)
Treated with medication	45
Treated with temporary pacing wires	18
Bradyarrhythmia	7 (3%)
Treated with medication	1
Treated with temporary pacing wires	6
Unplanned cardiac catheterization	25 (12%)
Unplanned reoperation for bleeding	37 (17%)
Unplanned reoperation not for bleeding [a]	17 (8%)
Truncal valve repair / replacement	6
Residual VSD closure	5
Coronary artery revision	3
Pulmonary arterioplasty	3
RV-PA conduit revision	3
Aortopexy	2
Other	9
Infection [b]	42 (19%)
Sepsis/Bacteremia	9
Endocarditis	2
Pneumonia / Tracheitis	16
Urinary tract infection	5
Wound infection / dehiscence	12
Mediastinitis	3
Other	4
Necrotizing enterocolitis	10 (5%)
Extubation failure	22 (10%)
Chylothorax	22 (10%)
Paralyzed diaphragm	6 (3%)
Vocal cord paresis	2 (1%)
Tracheostomy	11 (5%)
Seizures	17 (8%)
Stroke	12 (6%)
Operative mortality	15 (7%)

[a]17 patients required 33 cardiothoracic reoperations for an indication other than bleeding / hemorrhage
[b] 42 patients were diagnosed with 51 postoperative infections

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