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Perioperative Factors Influence the Long Term Outcomes of Children and Adolescents with Repaired Tetralogy of Fallot

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Abstract

Introduction—Tetralogy of Fallot (TOF) often carries long-term seqüelae following surgical intervention. We hypothesized that early perioperative factors are associated with long-term adverse right ventricular (RV) remodeling, diminished exercise capacity and increased morbidity.

Methods—We conducted a retrospective cohort study of patients operated for TOF that underwent cardiac magnetic resonance imaging study (CMR), exercise stress test (EST), and detailed review of past medical history. Outcome variables included measures of RV size, and function, maximal work rate and oxygen consumption, and interim hospitalizations, surgeries and catheterizations.

Results—Thirty-nine subjects were included. Age at surgical repair was 0.3 ± 0.3 years and age at testing was 9.7 ± 1.4 years. On CMR, there was borderline RV dilation with moderate pulmonary insufficiency (PI) [RF 32% (8; 43)] and normal RV ejection fraction [60% (55; 67)]. On EST, there was low percent-predicted maximal oxygen consumption (77±20%), and percent predicted maximal work rate (84±23%). On multivariable analysis, mechanical ventilation and Blalock-Taussig (BT) shunt prior to complete surgical repair were associated with the number of future hospitalizations. Duration of cardiopulmonary bypass and prior BT shunt were associated with future catheterizations. Prior BT shunt was a predictor of worse RVEF, while duration of mechanical ventilation and use of transannular patch were predictors of worse PI. Longer duration of mechanical ventilation (or LOS) was associated with worse maximal work rate.

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The study protocol was approved by the Institutional Review Board for the Protection of Human Subjects at Children's Hospital of Philadelphia.

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Conclusions—Surgical and perioperative factors may portend long-term RV remodeling and outcome in TOF. Further studies are warranted to explore these associations and potential underlying mechanisms.

INTRODUCTION

Despite the excellent operative survival for TOF in the current era (>95%), affected individuals require substantial medical care and experience lifelong morbidity and early mortality.[1–3] Post-surgical pulmonary insufficiency (PI) with consequential right ventricular (RV) remodeling and dysfunction is thought to contribute significantly to long-term outcomes such as decreased exercise performance, increased incidence of arrhythmias and risk of sudden death.[4–6] However, the RV appears to have variable adaptation to volume overload such that pulmonary valve replacement (PVR) is required earlier for some patients, and much later or not at all for others with the same degree of PI.[7,8] Factors associated with RV remodeling, i.e., changes in RV size (dilation), geometry (mass), and function beyond PI are poorly understood.[1,9–12,13] Finally, even less is known about the potential influence or predictive value of perioperative events on long-term outcomes in this patient population. This study sought to investigate whether early events in the initial peri-operative period are associated with interim events and cardiovascular status in children and adolescents operated for TOF.

METHODS

Study population and data collection

The cohort for this analysis stems from two prior studies that examined the influence of 22q11.2 deletion syndrome on outcome after surgical intervention for TOF.[14,15] The first study (perioperative TOF) consisted of a retrospective longitudinal cohort study of the impact of 22q11.2 deletion syndrome on peri-operative outcomes; this study performed detailed review of the medical records of patients operated at our institution with extraction of daily information from the medical records. Variables of interest and potential predictors included genetic syndrome, prior BT shunt, age at repair, operative technique (transannular patch, right ventricle to pulmonary artery conduit, non-transannular patch), cardiopulmonary and deep hypothermic circulatory arrest times, duration of post-operative mechanical ventilation, length of postoperative hospital stay, and number of in-hospital cardiac catheterizations.

The second study (cross sectional TOF) recruited patients 8–18 years with repaired TOF that underwent cardiac magnetic resonance (CMR), exercise stress test (EST) and review of the medical records and/ or interview with parents for interim medical history. The number of hospitalizations, catheterizations, and cardiac and non-cardiac operations between initial surgical intervention for TOF and the cross sectional study were recorded.

For this analysis, we identified the subjects from the perioperative TOF cohort that were enrolled in the cross sectional TOF study. As such, the perioperative, interim history, and long-term data were available for all subjects. Inclusion criteria were confirmed diagnosis of TOF (via review of the medical chart and echocardiograms), and surgical repair for TOF in one surgical procedure that included relief of right ventricular outflow tract obstruction (if necessary), and closure of the ventricular septal defect, whether or not this procedure was preceded by palliation with a Blalock Taussig (BT) shunt. Exclusion criteria were genetic syndromes other than 22q11.2 deletion syndrome, and those with TOF and multiple aorto-pulmonary collateral vessels.

Outcomes included: interim events (cardiac catheterizations and reoperations), hospitalizations; CMR measures of RV remodeling (RV function, dilation, and mass), and pulmonary insufficiency; EST parameters (maximal work rate and percent-predicted maximal VO2).

The EST and CMR protocols used in the cross sectional TOF study were previously described.[14] In short, CMR studies evaluated right ventricular function, mass, volumes and pulmonary regurgitant fraction. EST informed about resting spirometry including the forced vital capacity, which was considered normal if >80% of predicted. At peak exercise, data included maximal oxygen consumption (VO2), maximal physical working capacity as measured by maximal work rate, oxygen pulse (a surrogate of ventricular stroke volume), and the maximal respiratory exchange ratio (RER) to identify subjects who achieved maximal effort. An EST was considered maximal effort if the RER was 1.10. The percent predicted of maximal VO2 (mVO2), the VO2 at the anaerobic threshold and maximal work were calculated for each patient according to normative values and considered normal if > 80% of predicted.[16,17] Aerobic capacity as a measure of exercise performance was defined by percent-predicted mVO2 and VO2 at the anaerobic threshold.

Statistical Analysis

Continuous variables are presented as mean and standard deviation or as median with the first and third quartile values. Categorical variables are described using count and percentages. Linear regression was used to test continuous outcomes. Logistic regression was used for categorical outcomes and Poisson regression adjusting for age at testing was used to assess the independent associations between perioperative factors and the number of hospitalizations, catheterizations, and non-cardiac operations. We tested for potential interactions and the term was left in the model if significant. For EST covariates, analyses were adjusted for the RER to account for maximal tests. Sub-analyses were performed to test the association of interventions in the neonatal period (complete surgical repair or palliation with BT shunt followed by complete repair) with interim events and cardiovascular status in the long term. Multivariable models were built respecting sample size constraints. Variables that had a P value <0.2 on univariable analysis were added to the final model and retained if the P value was <0.05. Statistical significance was reached for p-values < 0.05 (2-sided tests). All analyses were performed using SAS statistical software version 9.2 (Cary, NC, USA).

Results

1. Study cohort

We identified 39 subjects that met eligibility criteria of which 12 (31%) had a 22q11.2 deletion. All subjects underwent complete repair in one surgical procedure, of which five (13%) had palliation with BT shunt prior to complete repair. There was a predominance of males (80%) and whites (85%). More than one-third of the subjects underwent complete repair in the newborn period (Table 1). Most subjects received transannular patches and 24% underwent a cardiac catheterization after the complete repair during the initial hospital stay (Table 2).

2. Interim events and clinical status at the cross sectional study

Most subjects (87%) had two or more subsequent hospital admissions following the initial complete surgical repair and most subjects underwent at least one post-discharge cardiac catheterization (69%). Fourteen subjects (36%) had subsequent cardiac reoperations. One-half of the subjects had subsequent non-cardiac operations. (Table 2)

On CMR, RV function was preserved in the group overall, while residual PI was in the moderate range [32 % (IQR 8; 43)]. There was overall borderline RV dilation with mean RV end-diastolic volume (EDV) Z score of +2 ± 2.7 (Table 2).

On EST, 49% of subjects exercised to a maximal effort. There was overall diminished aerobic capacity, as measured by the percent of predicted maximal oxygen consumption (mVO2). Resting spirometry revealed diminished percent of predicted forced vital capacity (75 ± 17%), suggestive of restrictive lung physiology (Table 2).

3. Perioperative predictors of interim events and clinical status assessed by CMR and EST at the time of the cross sectional study

Perioperative factors associated with interim hospitalizations—On univariable analysis, there were multiple factors associated with the number of future hospitalizations, including older age at repair, history of palliation with BT shunt, 22q11.2 deletion syndrome, length of hospital stay, duration of mechanical ventilation, duration of DHCA, use of RV-PA conduits, number of catheterizations, and number of cardiovascular complications during the initial hospitalization for complete surgical repair (Table 3). On multivariable analysis, length of mechanical ventilation and previous palliation with BT shunt were independently associated with future hospitalizations. After adjusting for surgical intervention in the neonatal period (neonatal TOF repair or those who had a BT shunt in the neonatal period followed by complete repair) and for presence of 22q11.2 deletion syndrome, longer length of mechanical ventilation was independently associated with future hospitalizations. (Table 4)

Perioperative factors associated with interim catheterizations—On univariable analysis, age at initial surgical repair, previous palliation with BT shunt, longer CPB time, use of right ventricle-pulmonary artery conduit, and catheterization during the hospitalization for the initial complete repair were associated with subsequent catheterizations.

On multivariable analysis adjusting for intervention in the neonatal period, factors independently associated with subsequent catheterizations were duration of CPB and prior BT shunt. (Table 4)

Perioperative factors associated with interim non-cardiac operations—On univariable analysis, 22q11.2 deletion, age at initial repair, length of hospital stay, DHCA, and duration of mechanical ventilation were associated with future non-cardiac surgeries, while on multivariable analysis, duration of mechanical ventilation (interchangeably with length of hospital stay, as those predictors are collinear) was independently associated with future non-cardiac surgeries, adjusting for presence of 22q11.2 deletion (Table 4).

Perioperative factors associated with cardiac status measured by CMR—Prior palliation with BT shunt was the only perioperative factor associated with RV ejection fraction on univariable analysis. Although the RV ejection fraction was overall preserved, it was nine percentage points lower in those who had a prior BT shunt as compared to those who did not, independently of age at the time of surgical repair.

Duration of post-operative mechanical ventilation and transannular patch (but not right-ventricle to pulmonary artery conduits) were associated with PI. Mechanical ventilation was inversely associated with PI. In the multivariable model, these two predictors explain 45% of the PI (R^2= 0.45) (Table 4). There were no significant perioperative predictors of indexed RV mass.

Perioperative factors associated with exercise performance—On univariable analysis, duration of mechanical ventilation and length of hospital stay were inversely associated with maximal work rate. Because those variables were collinear (Pearson correlation coefficient 0.78, p value< 0.0001), only the length of stay was used in the model (mechanical ventilation has the same impact on maximal work rate). There were no significant perioperative predictors of mVO2.

Discussion

Although survival in TOF is favorable, this population experiences significant disease burden in the years following repair.[14] However, little is known about the effect of the early events surrounding the surgical repair, some of which are potentially modifiable, on long-term outcomes. In this small study of 39 children and adolescents with TOF with complete perioperative, interim and cross sectional data, we identified potential associations of early surgical factors with long-term outcomes. In particular, we found that longer duration of mechanical ventilation, prior BT shunt and longer hospital stay (interchangeably with mechanical ventilation) are associated with future hospitalizations, non-cardiac operations, lower physical working capacity, subsequent catheterizations and lower right ventricular ejection fraction.

Duration of mechanical ventilation was directly associated with several measures of later morbidity, including number of subsequent hospitalizations, non-cardiac surgeries, and physical working capacity on EST. A study by Kim et al found that duration of mechanical ventilation had modest effect on long-term RV dilation in TOF, an observation not confirmed by our study.[18] However, we found find an inverse association of mechanical ventilation with PI, and this association was independent of use of a transannular patch. It is possible that pulmonary vasculature and airway factors play a role in this association; however, we cannot substantiate that possibility in this retrospective study. To our knowledge, there has been no prior investigation of this association.

In young adults previously born prematurely (and without congenital heart disease), post-natal duration of mechanical ventilation is associated with greater RV mass in adulthood. Prolonged ventilation may reflect underlying pathologappr\y of the pulmonary vasculature and consequently greater RV mass.[19] Alternatively, prolonged mechanical ventilation could cause lung injury with long term consequences. As compared to premature infants, the duration of mechanical ventilation in the TOF population is unlikely to be as prolonged.[20] Thus whether or not the same mechanisms are operative in the TOF population merits future investigation.

In children with TOF, the duration of mechanical ventilation tends to correlate inversely with endurance times measured on EST five to ten years after surgical repair.[21] Mulla et al reported that aerobic capacity appears to be limited primarily by cardiac function in patients with TOF repaired with a transannular patch.[22] The current study identified new associations between perioperative factors and later physical working capacity. Thus, post-operative mechanical ventilation appears to be associated with long-term morbidity via mechanisms (other than 22q11.2 deletion syndrome) that have yet to be elucidated. It is possible that longer postoperative mechanical ventilation reflects an underlying pathology and/ or contributes to long-term co-morbidities.

We found that a prior BT shunt was associated with more hospitalizations, subsequent catheterizations and lower right ventricular ejection fraction. It is not surprising that those with prior use of a BT shunt could have more subsequent cardiac catheterizations since a percentage of those subjects undergo catheterizations to evaluate the pulmonary arteries prior to and following completion of repair. Given an institutional preference for complete repair over BT shunts even for symptomatic neonates, it is possible that in our study those who underwent BT shunts (minority) were part of a sicker cohort of subjects in whom complete repair was postponed. The early complications associated with BT shunts are well known and in the long term, a prior BT shunt has been associated with increased late mortality.[23,24,25] The association of prior BT shunt with lower ejection fraction was unexpected. Even though the ejection fraction was still preserved in those with a prior BT shunt, it was nine percentage points lower in the group with, as compared to those without a prior BT shunt. This association might reflect a potentially sicker population undergoing BT shunt prior to complete TOF repair, and/ or be a reflection of extended pressure load on the RV with continued cyanosis conferred by a BT shunt. Whether having had a BT shunt will eventually be associated with RV dysfunction can only be defined in a future study examining outcomes in patients at an older age.

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We acknowledge limitations to this study, including a small sample size and retrospective design. Nonetheless, we have carefully reviewed the medical records and confirmed the past history with parents upon enrollment in the cross sectional study. Moreover, we report a higher than usual prevalence of 22q11.2 deletion, likely due to the fact that the study that originated this analysis focused on the influence of 22q11.2 deletion syndrome on outcome, and therefore 221q11.2 status was known for all patients. A slightly higher number of males could be also be secondary to a selected patient population.

In conclusion, our study results suggest that surgical and perioperative factors are associated with RV remodeling and long-term outcomes. Whether these perioperative factors reflect underlying pathology and/or contribute to the risk for long-term morbidities remains to be defined. Either way, these factors may serve as predictors of later complications or medical course that could be modified to improve outcomes and help families and caregivers anticipate clinical complications. Further studies are warranted to define the mechanisms underlying these associations.

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References

1. Hickey EJ, Veldtman G, Bradley TJ, et al. Late risk of outcomes for adults with repaired tetralogy of Fallot from an inception cohort spanning four decades. Eur J Cardiothorac Surg. 2009; 35(1):156–164. [PubMed: 18848456]
2. Starr JP. Tetralogy of fallot: yesterday and today. World J Surg. 2010; 34(4):658–668. [PubMed: 20091166]
3. Frigiola A, Hughes M, Turner MS, et al. Physiologic and Phenotypic Characteristics of Late Survivors of Tetralogy of Fallot Repair Who Are Free From Pulmonary Valve Replacement. Circulation. 2013; 128:1861–1868. [PubMed: 24065608]
4. Carvalho JS, Shinebourne EA, Busst C, Rigby ML, Redington AN. Exercise capacity after complete repair of tetralogy of Fallot: deleterious effects of residual pulmonary regurgitation. Br Heart J. 1992; 67(6):470–473. [PubMed: 1622697]
5. Garne E, Nielsen G, Hansen OK, Emmertsen K. Tetralogy of Fallot. A population-based study of epidemiology, associated malformations and survival in western Denmark 1984–1992. Scand Cardiovasc J. 1999; 33(1):45–48. [PubMed: 10093859]
6. Knauth AL, Gauvreau K, Powell AJ, et al. Ventricular size and function assessed by cardiac MRI predict major adverse clinical outcomes late after tetralogy of Fallot repair. Heart. 2008; 94(2):211–216. [PubMed: 17135219]
7. Cheung EW, Wong WH, Cheung YF. Meta-analysis of pulmonary valve replacement after operative repair of tetralogy of fallot. Am J Cardiol. 2010; 106(4):552–557. [PubMed: 20691315]
8. Frigiola A, Hughes M, Turner M, et al. Physiological and phenotypic characteristics of late survivors of tetralogy of fallot repair who are free from pulmonary valve replacement. Circulation. 2013; 128(17):1861–1868. [PubMed: 24065608]
9. Benson DW. The genetics of congenital heart disease: a point in the revolution. Cardiol Clin. 2002; 20(3):385–394. vi. [PubMed: 12371007]
10. Greenway SC, Pereira AC, Lin JC, et al. De novo copy number variants identify new genes and loci in isolated sporadic tetralogy of Fallot. Nat Genet. 2009; 41(8):931–935. [PubMed: 19597493]
11. Rauch R, Hofbeck M, Zweier C, et al. Comprehensive genotype-phenotype analysis in 230 patients with tetralogy of Fallot. J Med Genet. 2010; 47(5):321–331. [PubMed: 19948535]

12. Valente AM, Gauvreau K, Assenza GE, et al. Contemporary predictors of death and sustained ventricular tachycardia in patients with repaired tetralogy of Fallot enrolled in the INDICATOR cohort. Heart. 2014; 100(3):247–253. [PubMed: 24179163]
13. Murphy JG, Gersh BJ, Mair DD, et al. Long-term outcome in patients undergoing surgical repair of tetralogy of Fallot. N Engl J Med. 1993; 329(9):593–599. [PubMed: 7688102]
14. Mercer-Rosa L, Paridon SM, Fogel MA, et al. 22q11.2 deletion status and disease burden in children and adolescents with tetralogy of Fallot. Circ Cardiovasc Genet. 2015; 8(1):74–81. [PubMed: 25561045]
15. Mercer-Rosa L, Pinto N, Yang W, Tanel R, Goldmuntz E. 22q11.2 Deletion syndrome is associated with perioperative outcome in tetralogy of Fallot. J Thorac Cardiovasc Surg. 2013; 146(4):868–873. [PubMed: 23312975]
16. Cooper DM, Weiler-Ravell D, Whipp BJ, Wasserman K. Aerobic parameters of exercise as a function of body size during growth in children. J Appl Physiol. 1984; 56(3):628–634. [PubMed: 6706770]
17. Howley ET, Bassett DR Jr, Welch HG. Criteria for maximal oxygen uptake: review and commentary. Med Sci Sports Exerc. 1995; 27(9):1292–1301. [PubMed: 8531628]
18. Kim H, Sung SC, Kim SH, et al. Early and late outcomes of total repair of tetralogy of Fallot: risk factors for late right ventricular dilatation. Interact Cardiovasc Thorac Surg. 2013; 17(6):956–962. [PubMed: 23956267]
19. Lewandowski AJ, Bradlow WM, Augustine D, et al. Right ventricular systolic dysfunction in young adults born preterm. Circulation. 2013; 128(7):713–720. [PubMed: 23940387]
20. Zhang H, Zhang J, Zhao S. Airway damage of prematurity: The impact of prolonged intubation, ventilation, and chronic lung disease. Semin Fetal Neonatal Med. 2016; 21(4):246–253. [PubMed: 27129915]
21. Hovels-Gurich HH, Konrad K, Skorzenski D, et al. Long-term neurodevelopmental outcome and exercise capacity after corrective surgery for tetralogy of Fallot or ventricular septal defect in infancy. Ann Thorac Surg. 2006; 81(3):958–966. [PubMed: 16488701]
22. Mulla N, Simpson P, Sullivan NM, Paridon SM. Determinants of aerobic capacity during exercise following complete repair of tetralogy of Fallot with a transannular patch. Pediatr Cardiol. 1997; 18(5):350–356. [PubMed: 9270103]
23. Williams JA, Bansal AK, Kim BJ, et al. Two thousand Blalock-Taussig shunts: a six-decade experience. Ann Thorac Surg. 2007; 84(6):2070–2075. [PubMed: 18036938]
24. Al Jubair KA, Al Fagih MR, Al Jarallah AS, et al. Results of 546 Blalock-Taussig shunts performed in 478 patients. Cardiol Young. 1998; 8(4):486–490. [PubMed: 9855103]
25. Cuypers JA, Menting ME, Konings EE, et al. Unnatural history of tetralogy of Fallot: prospective follow-up of 40 years after surgical correction. Circulation. 2014; 130(22):1944–1953. [PubMed: 25341442]

Table 1

Patient Characteristics

Variable	**N=39**
Male, n (%)	31 (80)
White, n (%)	33 (85)
22q11.2 deletion, n (%)	12 (31)
Gestational age (full term> 37 weeks), n (%)	33 (85)
Complete repair in the newborn period, n (%)	13 (33)
Age at complete repair, months (IQR)	2.5 [0.24; 5.5]
Blalock Taussig shunt preceding complete repair, n (%)	5 (13)
Native pulmonary valve	
Stenosis, n (%)	24 (64)
Atresia, n (%)	10 (26)
Absent, n (%)	4 (10)

Table 2

Operative Characteristics and Interim medical history

Characteristics of the Initial complete surgical repair	**N= 39**
Transannular patch, n (%)	29 (74)
Right ventricle to pulmonary artery conduit, n (%)	6 (15)
Non-transannular patch, n (%)	1 (3)
Reconstruction of the RV outflow tract, n (%)	2 (5)
VSD closure only (“pink” TOF), n (%)	1 (3)
Cardiopulmonary bypass time, min (mean ± SD)	76 (± 27)
Deep hypothermic circulatory arrest, min (mean ± SD)*	24 (±22)
Mechanical ventilation, days (mean ± SD)	1.1 (0.5; 4)
Length of hospital stay, days [IQR]	9 [4; 14]
In-hospital cardiac catheterization, n (%)	9 (24)
Interim medical history	
Number of Subsequent Hospitalizations, n (%)	
1	5 (13)
2–6	22 (56)
>=7	12 (31)
Number of Subsequent Cardiac Catheterizations (%)	27 (69)
Number of Cardiac Reoperations (%)	14 (36)
Number of Non-Cardiac Operations (%)	20 (51)

Table 3

Cardiac Magnetic Resonance and EST

Cardiac Magnetic Resonance	**N = 34**
RVEF (%)	61.4 ± 7.3
LVEF (%)	70 ± 6.3
RV EDV (mL)	112 ± 34
RV EDV (mL/m^2)	106 ±32
RV EDV Z score	+2 ± 2.7
RV ESV (mL)	43 ± 17
RV ESV (mL/m^2)	41 ± 15
PV RF (%)	32 (8; 43)
RV mass (grams)	73 ± 21
Indexed RV mass (grams/ m2)	68 ± 29
MPA EDAF (mL)	2 ± 2
Exercise Stress Test	**N= 35**
Maximal test (RER ≥ 1.1), n (%)	17 (49)
Oxygen consumption at peak exercise (mL/Kg/min)	32 ± 8.7
Percent of predicted maximal VO2 (%)	78 ± 20
Oxygen consumption at anaerobic threshold (mL/Kg/min)	22 ± 6
Predicted oxygen consumption at anaerobic threshold (%)	126 ± 33
O2 pulse (mL O2/min)	5.5 ± 1.5
Maximal work rate (watts)	81± 15
Maximal work (watts/kg)	2.5 ± 0.70

Table 4

Univariable Analysis of perioperative predictors of outcome with parameter estimates

Predictor*	**Outcome**	**Odds ratio**	**CI**	**P value**
22q11.2 deletion syndrome	Hospitalizations (n)	1.78	1.35; 2.34	<0.0001
Previous shunt	Hospitalizations (n)	2.7	1.99; 3.62	<0.0001
Age at initial repair (months)	Hospitalizations (n)	1.06	1.02; 1.10	0.0009
Length of hospital stay (days)	Hospitalizations (n)	1.04	1.03; 1.06	<0.0001
Mechanical ventilation (hours)	Hospitalizations (n)	1.04	1.02; 1.06	<0.0001
DHCA duration (min)	Hospitalizations (n)	1.11	1.04; 1.18	0.0015
Catheterization	Hospitalizations (n)	1.76	1.34; 2.33	<0.0001
RV-PA conduit	Hospitalizations (n)	1.42	1.02; 1.98	0.0404
Cardiovascular complications	Hospitalizations (n)			
1 vs. 0		1.64	1.23; 2.18	0.0007
2 vs. 0		0.84	0.47; 1.49	0.55
5 vs. 0		1.54	0.75; 3.16	0.24
Previous BT shunt	Catheterizations (n)	3.62	2.21; 5.93	<0.0001
Age at initial repair (months)	Catheterizations (n)	1.10	1.03; 1.16	0.0021
CPB time	Catheterizations (n)	1.15	1.06; 1.24	0.001
RV-PA conduit	Catheterizations (n)	1.96	1.15; 3.36	0.01
Catheterization	Catheterizations (n)	2.46	1.53; 3.95	0.0002
Length of stay	Non-cardiac surgery	1.01	(1.01,1.01)	<0.0001
DHCA	Non-cardiac surgery	1.19	(1.04,1.36)	0.0097
Mechanical ventilation	Non-cardiac surgery	0.07	(0.05,0.10)	1.08
	CMR	**Beta**	**R^2**	**P value**
Mechanical ventilation (min)**	PI RF	−0.101	0.14	0.036
DHCA (minutes)	RV mass	0.41	0.19	0.012
DHCA (minutes)	RV mass/m^2	0.26	0.09	0.10
Transannular patch	PI RF	21.8	0.34	0.0005
Transannular patch	RV CO* (log)	0.30	0.23	0.0041
RV-PA conduit	MPA EDAF	0.26	0.25	0.017
	EST	**Beta**	**R^2**	**P value**
Mechanical ventilation (min)	Max work*	−0.001	0.18	0.002
Length of Hospital Stay	O2 pulse	0.078	0.17	0.015
Length of Hospital Stay	Max work	−0.01	0.14	0.043

Table 5

Multivariable models of perioperative predictors of long-term outcome

Predictors	Outcome	OR	CI	P value
	Number of hospitalizations *			
Age at initial repair (months)		1.03	0.99; 1.07	0.175
Mechanical ventilation (hours)		1.05	1.03; 1.07	<0.0001
Previous Shunt		2.57	1.77; 3.72	<0.0001
	Number of catheterizations			
Age at initial repair (months)		1.00	0.92; 1.08	0.93
Duration of CPB (min)/10		1.15	1.05; 1.25	0.0021
Previous Shunt		3.69	2.02; 6.75	<0.0001
	Number of Cardiac Surgeries **			
Previous Shunt		2.07	1.14; 3.75	0.017
	Number of Non- Cardiac Surgeries			
DHCA time/ 10		1.04	0.89; 1.22	0.587
Mechanical ventilation		1.07	10.4; 1.11	<0.0001
	CMR	**Beta**	**R^2**	**P value**
	PI RF			
Mechanical ventilation		−0.092	0.45	0.0203
Transannular patch		−21.02	0.45	0.0003

* Interpretation: If age of complete repair increases by 1 month, the estimated mean number of hospitalizations will increase 9%. If intubation increases by 10 hours, the estimated mean number of hospitalizations will increase 5%.

** Interpretation: the estimated mean number of surgeries for patients with prior shunt is 2.07 times the estimated mean number of surgeries for patients without shunt.

* Mechanical ventilation and LOHS are highly correlated, so those predictors were not added together to the multivariable model.

* LOHS and ventilation were highly correlated (0.78), so only LOHS is included in the model.