Right ventricular outflow tract reintervention after primary tetralogy of Fallot repair in neonates and young infants

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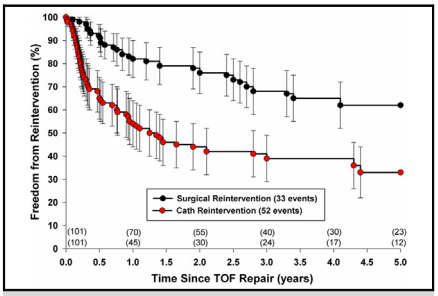
ABSTRACT

Objective: To assess the outcomes following primary tetralogy of Fallot (TOF) repair in neonates and young infants with pulmonary stenosis (PS) and pulmonary atresia and compare differences in reintervention on the right ventricular outflow tract (RVOT) among those undergoing valve sparing repair (VSR), transannular RVOT patch (TAP), and right ventricle–to–pulmonary artery (RV-PA) conduit surgeries.

Methods: Data were collected retrospectively in 101 patients who underwent TOF repair over a 10-year period between January 2005 and September 2015. The primary endpoint was reintervention on the RVOT, defined as a surgical procedure or cardiac catheterization–based RVOT reintervention.

Results: Forty-three patients had TOF/PS, of whom 24 (56%) underwent TAP and 19 (44%) underwent VSR. Fifty-eight patients had TOF/PA, 14 (24%) underwent TAP and 44 (76%) underwent RV-PA conduit repair. Overall patient mortality was 2.9% (3 of 101). Thirty-three patients underwent surgical reintervention, and 52 underwent catheterization-based reintervention. Patients with TOF/PA who underwent RV-PA conduit repair had a higher surgical reintervention rate than those who underwent TAP (45% vs 21%). Patients with TOF/PSs undergoing VSR with a lower median birth weight (2.5 kg vs 3.7 kg) required more surgical reintervention.

Conclusions: Neonatal TOF repair can be performed with low mortality but frequent RVOT reinterventions. Surgical reintervention is earlier and the rate is higher among patients with TOF/PA undergoing RV-PA conduit repair compared with those undergoing TAP. Although there were no overall differences in RVOT reintervention rate between patients with TOF/PS undergoing VSR and those undergoing TAP, a lower birth weight in the patients undergoing VSR is associated with a higher surgical reintervention rate. (J Thorac Cardiovasc Surg 2017;■:1-9)



Kaplan-Meier curves showing freedom from first time reintervention in TOF(PS/PA) patients.

Central Message

Reintervention rates following TOF repair in neonates and young infants vary by weight and RVOT repair type, impacting the surgical RVOT approach and follow-up.

Perspective

Management of hypoxic neonates and young infants with TOF is challenging, with controversy regarding initial surgical strategy. Neonatal TOF repair can be performed with low mortality, but a frequent need for RVOT reintervention. Among patients with TOF/PA, the rate of reintervention is higher after RV-PA conduit repair than after TAP. In patients with TOF/PS, the rate of RVOT reintervention is comparable in patients undergoing VSR and those undergoing TAP; however, in VSR, low birth weight is a risk factor for reintervention.

CONG

The first surgical treatment for Tetralogy of Fallot (TOF) was the palliative Blalock-Taussig (BT) shunt reported in 1945 by Blalock and Taussig,[1] and the first successful complete primary intracardiac repair was reported by Lillehei and colleagues[2] in 1954 using human cross-circulation. In the 1980s, Castaneda and colleagues[3] and Barratt-Boyes and Neutze[4] demonstrated that primary repair could be achieved in infancy with excellent results. With improved outcomes over the past 6 decades, now >95% of children born with TOF are expected to survive into adulthood,[5,6] and over the last 2 decades, early primary repair has been extended to the cyanotic neonate.[7-12] The goals of this single-center series were to assess outcomes following primary neonatal TOF repair in patients with pulmonary

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Abbreviations and Acronyms

BT = Blalock-Taussig
CI = confidence interval
ECMO = extracorporeal membrane oxygenation
HR = hazard ratio
ICU = intensive care unit
IQR = interquartile range
LOS = length of stay
PS = pulmonary stenosis
RVOT = right ventricular outflow tract
RV-PA = right ventricle to pulmonary artery
TAP = transannular patch
TOF = tetralogy of Fallot
VSR = valve-sparing repair

stenosis (PS) and pulmonary atresia, and to compare differences in reintervention on the right ventricular outflow tract (RVOT) among patients undergoing valve-sparing repair (VSR), transannular RVOT patch (TAP) surgery, or right ventricle–to–pulmonary artery (RV-PA) conduit repair.

METHODS

This was an Institutional Review Board–approved retrospective review of all 101 patients with congenital heart disease with PS or pulmonary atresia who underwent TOF repair who underwent TOF repair before 33 days of age between January 2005 and September 2015 at Boston Children's Hospital. The primary endpoint was reintervention on the RVOT, defined as a surgical procedure or a cardiac catheterization–based intervention on the RVOT.

Patients with TOF/PS underwent either pulmonary VSR or TAP, and patients with TOF/PA underwent either TAP or RV-PA conduit repair. All other primary surgical interventions were excluded from our analysis. Demographic data included date of birth, sex, and intraoperative height, body weight, and body surface area. Patient history data included the primary diagnosis and previous interventions, including catheterizations. Surgical data were obtained from the operative notes. Variables of interest include the date of admission, the date of initial operative repair, indication for operation, date of discharge, morbidity, and any complications before discharge. In addition to the specific RVOT approach, any concomitant procedures were recorded.

The closing date of follow-up for this study was April 1, 2016. Follow-up dates included the dates of most recent follow-up, echocardiography reports, and/or catheterization reports obtained as part of routine examinations. More specifically, data from echocardiography reports included date of echocardiography, estimated right ventricular pressure, maximum RVOT pressure gradient, and degrees of PS, pulmonary regurgitation, tricuspid regurgitation, right ventricular dysfunction, and left ventricular dysfunction.

Statistical Methods

Univariate analyses based on comparing binary proportions regarding reintervention were compared using Fisher's exact test, and categorical data were compared using Pearson's χ^2 test. Patient characteristics; baseline continuous data, such as pulmonary valve z-score and RVOT gradient; and follow-up duration are expressed using median and interquartile range (IQR) because they were found to depart from a normal distribution by the Kolmogorov–Smirnov test, and groups were compared using the Mann–Whitney U-test. Freedom from reintervention was estimated using the Kaplan–Meier product-limit method, and surgical groups (VSR, TAP, and RV-PA conduit) were compared within each diagnosis (TOF/PS or TOF/PA) using the log-rank test.[13] Greenwood's formula was used to construct 95% confidence intervals (CIs) around freedom from catheterization-based and surgical reintervention curves and overall patient survival.[14] Median birth weight at the time of repair for patients with and without reintervention was compared using the Mann–Whitney U test within each of the 3 surgical groups. The candidate variables that were considered in the multivariable analysis included birth weight, age <14 days at surgery, weight <3 kg, era of operation (before or after 2010), RVOT gradient, hospital length of stay (LOS) >21 days, and RVOT repair type. The number of candidate variables was limited to ensure that the regression coefficients remained stable without overfitting the model.[15] Median intensive care unit (ICU) and hospital LOSs were compared among the VSR, TAP, and RV-PA conduit groups using the nonparametric Kruskal–Wallis test.

A Cox proportional hazards regression model was used to identify predictors of reintervention. The multivariable analysis included testing 2-way interactions to assess whether any possible risk factors were dependent on the type of surgical repair.[16] The modulated renewal theory was applied using the nonparametric Nelson–Aalen estimator to derive the cumulative hazard function to compare the risk of catheterization-based reintervention incorporating all repeated episodes of catheterization-based reintervention for the same patient to assess differences between VSR (n = 19) and TAP (n = 24) in patients with TOF/PS and between RV-PA conduit repair (n = 44) and TAP (n = 14) in patients with TOF/PA. This assumes that the hazard for the time intervals between repeated or successive events for the same patient depends on the failure number via a covariate process and is suitable when the process can be expressed in terms of gaps between failure times instead of the total observation time.[16] Thus, each segment has a beginning time and an ending time. Analyses were performed using R with the "survival" package (R version 2.41-3; R Project for Statistical Computing, Vienna, Austria) using the survfit and coxph functions. All reported P values are 2-tailed with a type I error of .05 as the criterion for statistical significance. All statistical analyses were conducted using SPSS version 23.0 (IBM, Armonk, NY).

Definitions

Early surgical reintervention on the RVOT was defined as any surgery performed on the RVOT after the initial surgery for TOF that addressed the RVOT or the RV-PA conduit and included RVOT muscle bundle resection, TAP, RV-PA conduit replacement, or pulmonary artery reintervention. Late surgical reintervention was defined as pulmonary valve replacement. Nonsurgical reintervention was defined as any intervention (1 or more) performed in the cardiac catheterization laboratory on the pulmonary arteries, RVOT, or RV-PA conduit, including balloon dilation or stent placement.

RESULTS

Patient Characteristics

Patient characteristics are summarized by TOF subtype in Table 1 and by initial surgical approach on the RVOT in Table 2. Of the 101 patients undergoing TOF repair between 2005 and 2015, 43 had TOF/PS and 58 had TOF/PA. The median patient age at surgery was 11 days (IQR, 4-20 days), and 61% of the patients were under 14 days of age. The median patient weight at surgery was 2.9 kg (IQR, 2.5-3.7 kg). There was no significant difference in the sex distribution (52% male). Nearly one-half of all patients underwent surgery in 2010 or later, but 85% of the TOF/PS VSR operations were performed in 2010 or later. The median preoperative RVOT gradient in the TOF/PS patients was 50 mmHg (IQR, 42-70 mmHg) and was not