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Long-term outcomes of staged repair of tetralogy of Fallot

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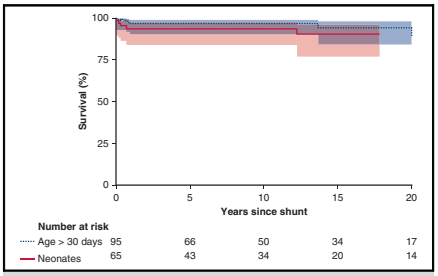
ABSTRACT

Background: The optimal management strategy for symptomatic young infants with tetralogy of Fallot (TOF) is yet to be determined. We aimed to evaluate the long-term outcomes of a staged approach with initial shunt palliation followed by complete repair.

Methods: Between January 1993 and July 2021, 160 children with TOF underwent a systemic-to-pulmonary shunt at our institution, including 65 neonates (41%). The mean duration of follow-up was 12.3 ± 8.1 years.

Results: Hospital mortality was 3% (4 of 160), all occurring in patients with a shunt size-to-weight ratio ≥1.2 mm/kg. Composite morbidity—defined as cardiac arrest, postoperative mechanical circulatory support, or unplanned reoperation—occurred in 21% (33 of 160). On multivariable analysis, a shunt size-to-weight ratio ≥1.2 mm/kg and prematurity were independent predictors of composite morbidity. Interstage mortality was 3% (4 of 156). A limited transannular patch was used in 75% (113 of 150) of TOF repairs. Actuarial survival at 20 years after shunt was 90% (95% confidence interval [CI], 79%-95%). Actuarial freedom from reinterventions at 20 years after TOF repair was 40% (95% CI, 28%-52%). Neonates had comparable composite morbidity, mortality, and late risk of reinterventions to older children.

Conclusions: Staged repair of TOF in symptomatic young infants results in low mortality but high rates of reinterventions at long-term follow-up. A shunt size-to-weight ratio ≥1.2 mm/kg is a significant risk factor for mortality and morbidity prior to complete repair. Neonates undergoing shunt insertion have comparable outcomes to older children. (J Thorac Cardiovasc Surg 2023;165:2169-80)



Survival from shunt, comparing neonates and infants age >30 days at the time of shunt palliation for tetralogy of Fallot. Shaded area defines 95% confidence interval.

CENTRAL MESSAGE

A strategy of staged repair of tetralogy of Fallot in symptomatic young infants is associated with relatively low mortality but high rates of reinterventions.

PERSPECTIVE

The optimal strategy for symptomatic patients with tetralogy of Fallot under 4 months of age is unclear, with some centers opting for early complete repair, while others prefer staged repair. Our findings suggest a staged approach results in relatively low mortality but high rates of reinterventions. Shunt diameter-to-weight ratio ≥1.2 mm/kg was associated with mortality and morbidity.

Tetralogy of Fallot (TOF) accounts for 4% to 5% of all congenital heart defects. After the first report of complete TOF repair in 1955, staged palliation with a systemic-to-pulmonary artery shunt followed by complete repair later in childhood was the mainstay of surgical treatment for TOF over the subsequent 2 decades. Since the 1970s, early single-stage complete repair has been made possible by advances in surgical techniques. Currently, most centers perform elective complete repair for asymptomatic infants between 3 and 12 months of age.[1] The optimal management strategy for symptomatic infants

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Abbreviations and Acronyms

BTS = Blalock–Taussig shunt
CI = confidence interval
CPB = cardiopulmonary bypass
IQR = interquartile range
MBTS = modified Blalock–Taussig shunt
PA = pulmonary artery
PAPR = pulmonary annulus-preserving repair
PR = pulmonary regurgitation
PTFE = polytetrafluoroethylene
PVA = pulmonary valve annulus
RV = right ventricle
RVOT = right ventricular outflow tract
RVOTO = right ventricular outflow tract obstruction
TAP = transannular patch
TOF = tetralogy of Fallot

under 3 months of age remains controversial, however. In particular, the merit of early repair versus shunt palliation in symptomatic neonates has been a subject of considerable debate in the recent literature.

Proponents of early primary repair have cited theoretical benefits of early establishment of normal biventricular circulation in optimizing pulmonary vasculature growth and brain development, arguing that early repair can be performed safely and effectively with comparable resource use as staged palliation.[2,3] Advocates of staged repair have argued that the proposed benefits of early repair are largely unproven, that early repair carries significant mortality and morbidity, and that staged palliation may facilitate growth of the right ventricular outflow tract (RVOT) and reduce the need for a transannular patch (TAP).[4,5] The currently reported risk of early mortality in neonates after either approach is approximately 4% to 8% in large multicenter databases.[1,3] Importantly, a recent analysis of the Pediatric Health Information System database reported a significantly higher risk of postoperative cardiac complications and early and 2-year mortality in neonates undergoing complete repair compared with those treated with the staged approach.[6]

Since the early 1980s, our institution has maintained a policy of early shunting of infants under 4 months of age if they were symptomatic from hypoxemia or cyanotic spells or if their branch pulmonary arteries were too small to permit repair.[7] Asymptomatic infants undergo elective primary repair at age 6 months or earlier at 4 months if cyanotic. In this study, we aimed to evaluate the long-term outcome of this strategy of staged repair of symptomatic young infants over a 28-year period, with particular focus on the outcomes of neonatal palliation.

METHODS

We performed this single-center retrospective study at the Royal Children's Hospital Melbourne, Australia, which included 160 consecutive patients with TOF who underwent palliative systemic-to-pulmonary artery shunting between January 1993 and July 2021. During this period, we exclusively performed systemic-to-pulmonary shunts in symptomatic patients under 4 months of age. We excluded patients with associated pulmonary atresia, absent pulmonary valve, or atrioventricular septal defect. Patients referred from overseas were also excluded owing to a lack of follow-up data. Medical records were reviewed for preoperative, intraoperative, and postoperative data. Follow-up of recent clinical status was obtained from correspondence with the patients' current cardiologists or general practitioners. The study design was approved by our institution's Human Research Ethics Committee (38341; 5 April 2019). The need for individual patient consent was waived owing to the study's retrospective nature.

Primary endpoints were hospital mortality and composite morbidity, defined as any of cardiac arrest, need for mechanical circulatory support, or unplanned reoperations. For patients who were receiving prostaglandin support preoperatively, the duration of prostaglandin infusion was defined as the time from admission to shunt palliation. Shunt thrombosis or stenosis was defined as confirmed findings of such at the time of reoperation, angiography, or noninvasive imaging. Low cardiac output was defined as hemodynamic instability requiring 2 or more inotropes on postoperative day 1 or mechanical circulatory support. Pulmonary overcirculation was a clinical diagnosis based on oxygen saturation and requirement for diuretics or afterload reduction to maintain hemodynamic stability. Neonates were infants age $\leq$30 days. Urgent operations were defined as those performed within 2 days, emergent operations were performed without delay, and all other operations were deemed elective. Pulmonary valve annulus (PVA), pulmonary artery (PA), and shunt indices were calculated by dividing PVA size, PA size, and shunt diameter, respectively, by the body surface area. The study period was divided into 4 equal epochsiods (1993-1999, 2000-2006, 2007-2013, 2014-2021) for analysis of change in surgical practice over time.

Surgical Management

We have previously described our surgical management of systemic-to-pulmonary shunts and indications for reoperations after TOF repair at our institution.[7,8] Several techniques of systemic-to-pulmonary shunting were used during the study period, including a right modified Blalock–Taussig shunt (MBTS) and a central shunt, with access via sternotomy or thoracotomy and with or without bypass. Our current preferred technique is a right MBTS with inflow from the innominate artery, performed via sternotomy without bypass. Shunts were constructed using Gore-Tex polytetrafluoroethylene (PTFE) vascular grafts (W.L. Gore & Associates) without heparin coating. For the purpose of this study, an MBTS was defined as a shunt connecting the innominate or subclavian artery to the ipsilateral PA, and a central shunt was defined as a shunt connecting the ascending aorta to the PA using the techniques described by Laks.[9,10] A central shunt was used in cases where anatomy precluded the use of an MBTS, most commonly for an aberrant right subclavian artery but also in cases of diffusely hypoplastic pulmonary arteries. Cardiopulmonary bypass (CPB) was used if the patient demonstrated severe desaturation or instability, for central shunt creation, or if a concomitant procedure was required.

Shunt size was selected based on surgeon preference and according to patient weight and expected time to complete repair. To avoid damaging the PTFE graft, we used fine rubber-shod clamps. A patent ductus arteriosus was routinely ligated. In patients who exhibited pulmonary overcirculation intraoperatively, the shunt was wrapped with another piece of Gore-Tex vascular graft of the same size, which was cut longitudinally and wrapped around the inserted shunt. Occasionally, a second procedure was required to adjust the degree of constriction. Heparin was reversed in cases when shunts were performed on bypass but not reversed for off-bypass shunts.

Administration of platelets and clotting factors was avoided unless troublesome needle-hole bleeding from the PTFE graft could not be controlled.

Postoperative anticoagulation was initiated on admission to the intensive care unit with 15 units/kg/hour of heparin infusion, which was continued until the patient could tolerate enteral feeding. Aspirin was then started and continued until shunt takedown. Clopidogrel was added to aspirin for patients with 3-mm shunts. Platelet function analysis was not routinely performed before starting antiplatelet therapy. In the event of suspected shunt thrombosis, the chest was reopened, and the shunt was milked from the proximal end to the distal end; failing that, institution of extracorporeal membrane oxygenation support and/or shunt revision was performed. To be considered suitable for discharge, patients needed to have stable saturation without requiring supplemental oxygen and to be on low-dose frusemide. Interstage monitoring with early outpatient cardiologist review was organized in all cases.

For TOF repairs, all ventricular septal defects were closed via right atriotomy and through the tricuspid valve orifice. The presence of anomalous coronary arteries did not influence the surgical approach. The RVOT obstruction (RVOTO) was resected through right atriotomy and a longitudinal incision of the PA. The pulmonary annulus was preserved if it was of predicted size based on body surface area.[11] Otherwise, a limited transannular incision was made, which involved an incision extending through the hinge points of the pulmonary leaflets and up to a few millimeters on the pulmonary infundibulum. This incision was then patched with a mini-TAP,[12] which was either treated with glutaraldehyde or untreated depending on surgeon preference.[7]

Statistical Analysis

Categorical variables were reported as number (percentage) and compared between groups using Fisher's exact test. Continuous variables were reported as mean ± standard deviation or median (interquartile range [IQR]) and compared between groups using the Wilcoxon rank-sum test. Receiver operating characteristic (ROC) curve analysis was performed to identify the optimal threshold of shunt size-to-weight ratio in predicting composite morbidity and hospital mortality. Risk factors for composite morbidity were evaluated with univariable logistic regression, and then noncollinear variables with $P < .10$ were entered into a multivariable model to determine independent predictors. Survival function and freedom from reinterventions were estimated using the Kaplan–Meier method. Predictors of time-related outcomes were tested using Cox regression analysis. Statistical analysis was performed using Stata version 14 (StataCorp). Statistical significance was set at $P < .05$.

RESULTS

Shunt Palliation

Baseline demographics at time of shunt palliation are summarized in Table 1. Of the 160 patients in the study, 65 (41%) were neonates. The median age was 45 days (IQR, 18-84 days), and the median weight was 3.5 kg (IQR, 2.7-4.4 kg).

Characteristics were compared between neonates and older children. Neonates had smaller PVA and PA sizes but comparable indices as the older children. Neonates were more likely to be duct-dependent on prostaglandin and to undergo nonelective surgery. Neonates also were significantly more likely to undergo sternotomy (82% [53 of 65] vs 56% [53 of 95]; $P = .001$) and had a longer time on CPB (mean, 71 ± 40 minutes vs 58 ± 29 minutes; $P = .04$). Older children had a higher RVOT gradient (median, 75 [IQR, 61-88] mm Hg vs 52 [IQR, 41-64] mm Hg, $P < .001$) and a higher incidence of prematurity (23% [22 of 95] vs 9% [6 of 65]; $P = .03$). Of those who received prostaglandin infusion preoperatively, older children received it for a longer duration than neonates before undergoing shunt palliation (median, 9 [IQR, 2-22] days vs 2 [IQR, 1-8] days; $P = .04$). Otherwise, the 2 groups were comparable in terms of associated cardiac and extracardiac anomalies. Of note, premature infants were more likely to be on prostaglandin preoperatively (50% [14 of 28] vs 28% [37 of 132]; $P = .04$) and had a lower operative weight (mean, 2.9 ± 0.9 kg vs 3.8 ± 1.3 kg; $P < .001$).

Operative details of palliative shunt are summarized in Table 2. A right MBTS was the most common type of shunt performed (62%; 99 of 160), followed by central shunt (26%; 41 of 160). There was no difference between neonates and older children in the type of shunts performed. The proximal anastomosis was most frequently performed on the innominate artery in neonates (52%; 33 of 65) and on the subclavian artery in older children (44%; 39 of 95). The median shunt size-to-weight ratio was 1.0 mm/kg (IQR, 0.9-1.2 mm/kg). Neonates had significantly smaller shunts (mean size, 3.4 ± 0.4 mm vs 3.9 ± 0.7 mm; $P < .001$) and a greater shunt size-to-weight ratio (1.1 [IQR, 1.0-1.3] mm/kg vs 0.9 [IQR, 0.8-1.1] mm/kg; $P < .001$), but had comparable shunt indices (16.7 [IQR, 15.2-17.6] mm/m^2 vs 15.9 [IQR, 14.3-16.7] mm/m^2; $P = .10$) as older children. Furthermore, neonates were more likely to have a shunt size-to-weight ratio ≥1.2 mm/kg than older children (31% [16 of 52] vs 11% [8 of 70] of those with data available; $P = .01$). Patients with 3.0-mm shunts had a significantly greater shunt size-to-weight ratio than those with 5.0-mm shunts (1.1 [IQR 1.0-1.2] vs 0.9 [IQR, 0.8-1.0] mm/kg; $P = .04$). On linear regression, shunt size-to-weight ratio was inversely proportional to branch PA size ($P = .02$).

Sternotomy was performed in 66% of cases (106 of 160), including the majority of left MBTSs (82%; 14 of 17), central shunts (98%; 40 of 41), and classic BTSs (67%; 2 of 3). However, right MBTSs were evenly performed via thoracotomy (49%; 49 of 99) or sternotomy (51%; 50 of 99). Sternotomy was associated with significantly smaller shunts compared with thoracotomy (mean, 3.4 ± 0.4 mm vs 4.3 ± 0.6 mm; $P < .001$). Furthermore, proximal anastomoses to the innominate artery or ascending aorta were mostly performed via sternotomy (93%; 95 of 102), whereas anastomosis to the subclavian artery was more commonly performed via thoracotomy (80%; 41 of 51; $P < .001$). Most anastomoses to the innominate artery (82%; 51 to 62) or the ascending aorta (78%; 31 of 40) were performed with 3-mm or 3.5-mm shunts, whereas most anastomoses to the subclavian artery were performed with 4-mm or 5-mm shunts (51%; 26 of 51; $P < .001$). Central shunts were associated with a significantly smaller shunt size-to-weight ratio compared with right MBTSs (mean, 0.9 ± 0.2 mm/kg vs 1.1 ± 0.2 mm/kg; $P = .01$).

TABLE 1. Baseline patient characteristics at shunt palliation

Characteristic	Overall (N = 160)	Neonates (N = 65)	Age >30 d (N = 95)	*P* value
Age, d, median (IQR)	45 (18-84)	14 (8-21)	68 (49-113)	<.0001
Female sex, n (%)	69 (43)	26 (40)	43 (45)	.52
Weight, kg, median (IQR)	3.5 (2.7-4.4)	2.9 (2.6-3.6)	4.1 (2.9-4.6)	<.0001
BSA, m^2, median (IQR)	0.21 (0.18-0.25)	0.20 (0.18-0.22)	0.23 (0.20-0.28)	<.001
Shunt before 2007, n (%)	89 (56)	31 (48)	58 (61)	.17
Echocardiographic data, median (IQR)				
PVA, mm*	5.0 (4.2-6.0)	4.5 (3.6-5.4)	5.0 (4.5-6.0)	.03
PVA index, mm/m^2	22.2 (19.2-25.5)	22.2 (19.5-25.6)	22.3 (19.1-25.3)	.86
LPA size, mm†	3.6 (3.0-4.2)	3.3 (3.0-4.0)	3.9 (3.2-5.0)	<.01
LPA index, mm/m^2	16.4 (13.3-19.5)	18.5 (15.0-20.0)	15.8 (13.7-18.4)	.13
RPA size, mm‡	3.9 (3.3-4.5)	3.5 (3.0-4.0)	4.0 (3.5-4.9)	<.01
RPA index, mm/m^2	16.2 (14.5-20.0)	18.3 (15.0-21.0)	16.0 (14.2-18.1)	.07
RVOT peak gradient, mm Hg	64 (52-81)	52 (41-64)	75 (61-88)	<.001
Primary indication for palliation, n (%)				.01
Duct dependent	39 (24)	25 (38)	14 (15)	
Cyanotic spells	49 (31)	16 (25)	33 (35)	
Progressive cyanosis	44 (28)	16 (25)	28 (29)	
Both spells and cyanosis	26 (16)	8 (12)	18 (19)	
Hypoplastic PA	2 (1)	0 (0)	2 (2)	
Associated cardiac anomalies, n (%)				
Anomalous coronary arteries	12 (8)	5 (8)	7 (7)	.72
Bovine arch	13 (8)	6 (9)	7 (7)	.77
Discontinuous PA	4 (3)	2 (3)	2 (2)	1.00
Hypoplastic PA	58 (36)	23 (35)	35 (37)	.87
Left SVC	18 (11)	3 (5)	15 (16)	.04
PDA	78 (49)	37 (57)	41 (43)	.11
PFO	110 (69)	50 (77)	60 (63)	.08
Right aortic arch	48 (30)	21 (32)	27 (28)	.61
Extracardiac anomalies, n (%)	60 (38)	22 (34)	38 (40)	.51
Airway malacia	7 (4)	5 (8)	8 (8)	.12
Gastrointestinal	15 (9)	7 (11)	8 (8)	.78
Genetic syndrome	26 (16)	13 (20)	13 (14)	.38
Urogenital	18 (11)	4 (6)	14 (15)	.13
Comorbidities, n (%)				
Prematurity (<36 wk)	28 (18)	6 (9)	22 (23)	.03
Low birth weight (<2.5 kg)	46 (29)	18 (28)	28 (29)	.86
Preshunt support				
Mechanical circulatory support, n (%)	1 (0.6)	1 (2)	0 (0)	.42
Mechanical ventilation, n (%)	34 (21)	18 (28)	16 (17)	.17
Prostaglandin infusion, n (%)	51 (32)	37 (57)	14 (15)	<.001
Prostaglandin duration, d, median (IQR)	3 (1-11)	2 (1-8)	9 (2-22)	.04
Operative urgency, n (%)				.001
Elective	79 (49)	21 (32)	58 (61)	
Urgent	70 (44)	38 (58)	32 (34)	
Emergent	11 (7)	6 (9)	5 (5)	

IQR, Interquartile range; *BSA*, body surface area; *PVA*, pulmonary valve annulus; *LPA*, left pulmonary artery; *RPA*, right pulmonary artery; *RVOT*, right ventricular outflow tract; *PA*, pulmonary artery; *SVC*, superior vena cava; *PDA*, patent ductus arteriosus; *PFO*, patent foramen ovale. *Data available for 92 patients (36 neonates, 56 older children). †Data available for 144 patients (55 neonates, 89 older children). ‡Data available for 147 patients (57 neonates, 90 older children).

Shunt characteristics according to surgical era are summarized in Table E1. We have been performing palliative shunts in younger patients in recent years (median age, 75 [IQR, 22-127] days in 1993-1999 vs 36 [IQR, 14-68] days in 2014-2021; $P < .01$), although the proportion of neonates and median weight remained similar. We also have been inserting small shunts in more patients (3 mm: 2% in 1993-99 vs 59% in 2014-21; $P < .001$), although there was no

TABLE 2. Surgical data for palliative shunt

Parameter	Overall (N = 160)	Neonates (N = 65)	Age >30 d (N = 95)	*P* value
Shunt type, n (%)				.14
Modified BTS				
Right	99 (62)	36 (55)	63 (66)	
Left	17 (11)	10 (15)	7 (7)	
Central	41 (26)	19 (29)	22 (23)	
Classic BTS	3 (2)	0 (0)	3 (3)	
Proximal anastomosis, n (%)*				<.01
Innominate	62 (41)	33 (52)	29 (33)	
Subclavian	51 (33)	12 (19)	39 (44)	
Ascending aorta	40 (26)	19 (30)	21 (24)	
Distal anastomosis, n (%)*				
Left PA	11 (7)	7 (11)	4 (4)	.08
Right PA	103 (67)	37 (58)	66 (74)	
Main PA	39 (25)	20 (31)	19 (21)	
Shunt size, n (%)†				<.001
3.0 mm	45 (30)	28 (43)	17 (20)	
3.5 mm	49 (32)	23 (35)	26 (30)	
4.0 mm	41 (27)	14 (22)	27 (31)	
5.0 mm	17 (11)	0 (0)	17 (20)	
Shunt-weight ratio, mm/kg, median (IQR)‡	1.0 (0.9-1.2)	1.1 (1.0-1.3)	0.9 (0.8-1.1)	<.001
Shunt-weight ratio ≥1.2 mm/kg, n (%)‡	24 (20)	16 (31)	8 (11)	.01
Shunt index, mm/m^2, median (IQR)	16.1 (14.8-17.4)	16.7 (15.2-17.6)	15.9 (14.3-16.7)	.10
Concomitant procedures, n (%)				
Shunt wrapped	7 (4)	2 (3)	5 (5)	.71
PA arterioplasty	11 (7)	8 (12)	3 (3)	.05
Approach, n (%)				.001
Sternotomy	106 (66)	53 (82)	53 (56)	
Lateral thoracotomy	54 (34)	12 (18)	42 (44)	
Cardiopulmonary bypass used, n (%)	67 (42)	32 (49)	35 (37)	.14
Cardiopulmonary bypass time, min, mean ± SD	64 ± 34	71 ± 40	58 ± 29	.04

BTS, Blalock–Taussig shunt; *PA*, pulmonary artery; *IQR*, interquartile range; *SD*, standard deviation. *Data available for 153 patients (64 neonates, 89 older children). †Data available for 152 patients (65 neonates, 87 older children). ‡Data available for 122 patients (52 neonates, 70 older children).

significant difference in the shunt size-to-weight ratio or shunt index. We have also been performing relatively more central shunts, more sternotomies, and using CPB more frequently in recent years, although the proportion of nonelective operations remained similar. Pulmonary overcirculation was more frequently encountered, yet hospital mortality and interstage mortality remained stable.

Outcomes of palliative shunt are reported in Table 3 and Figure 1. Hospital mortality was 3% (4 of 160) over the study period and 1% (1 of 71) since 2007. In particular, hospital mortality for neonates was 5% (3 of 65) over the study period and 3% (1 of 34) since 2007. Composite morbidity as defined occurred in 21% (33 of 160). One-fifth of the patients (19%; 30 of 160) required unplanned reoperations, mostly for shunt revision (43%; 13 of 30). Pulmonary overcirculation occurred in 13% of the patients (21 of 160), of whom 4 were managed surgically with shunt wrapping or downsizing and the remainder were managed medically. Neonates had a longer postoperative hospital stay than older children but otherwise comparable rates of hospital mortality, composite morbidity, interstage mortality, and completion of TOF repair.

Predictors of composite morbidity and hospital mortality after palliative shunt are summarized in Table 4. On ROC curve analysis, a shunt size-to-weight ratio ≥1.2 mm/kg was found to be an optimal predictive threshold for both composite morbidity and hospital mortality (Table E2). On multivariable analysis, a shunt size-to-weight ratio ≥1.2 mm/kg and prematurity were independent predictors of composite morbidity. Hospital mortality occurred in 17% of the patients (6 of 24) with a shunt size-to-weight ratio ≥1.2 mm/kg and in none of the 98 patients with a shunt size-to-weight ratio <1.2 mm/kg ($P = .001$), but no other predictor was identified.

Logistic regression analysis of predictors of shunt outcomes according to shunt characteristics are summarized in Table E3. A shunt size-to-weight ratio ≥1.2 mm/kg

TABLE 3. Outcomes of palliative shunt

Outcome	Overall (N = 160)	Neonates (N = 65)	Age >30 d (N = 95)	*P* value
Hospital mortality, n (%)	4 (3)	3 (5)	1 (1)	.31
ICU stay, h, median (IQR)	85 (50-180)	95 (66-172)	72 (46-182)	.22
Mechanical ventilation, h, median (IQR)	60 (32-125)	64 (43-121)	46 (29-132)	.24
Postoperative hospital stay, d, median (IQR)	8 (6-14)	10 (8-17)	8 (5-12)	<.01
Early complications, n (%)				
Composite morbidity*	33 (21)	14 (22)	19 (20)	.84
Cardiac arrest	10 (6)	4 (6)	6 (6)	1.00
Mechanical circulatory support	7 (4)	1 (2)	6 (6)	.24
Unplanned reoperations	30 (19)	11 (17)	19 (20)	.68
Arrhythmias	6 (4)	5 (8)	1 (1)	.04
Cerebrovascular accident	6 (4)	2 (3)	4 (4)	1.00
Delayed chest closure	17 (11)	7 (11)	10 (11)	1.00
ICU readmission	11 (7)	3 (5)	8 (8)	.53
Low cardiac output	32 (20)	13 (20)	19 (20)	1.00
NEC	14 (9)	6 (9)	8 (8)	1.00
Abdominal surgery	4 (29)	2 (33)	2 (25)	1.00
Pulmonary overcirculation	21 (13)	8 (12)	13 (14)	1.00
Prolonged mechanical ventilation (>5 d)	32 (20)	11 (17)	21 (22)	.55
Renal replacement therapy	10 (6)	6 (9)	4 (4)	.32
Sepsis	23 (14)	10 (15)	13 (14)	.82
Shunt thrombosis/stenosis	11 (7)	4 (6)	7 (7)	1.00
Unplanned reoperation	30 (19)	11 (17)	19 (20)	.68
Shunt revision	13 (8)	4 (6)	9 (9)	
Hemothorax/pneumothorax	3 (2)	2 (3)	1 (1)	
ECMO	4 (3)	0 (0)	4 (4)	
Emergent resternotomy for clinical instability	4 (3)	2 (3)	2 (2)	
Pacemaker	3 (2)	2 (3)	1 (1)	
Wound revision	1 (0.6)	0 (0)	0 (0)	
PA arterioplasty	1 (0.6)	0 (0)	1 (1)	
Diaphragm plication	1 (0.6)	0 (0)	1 (1)	
Interstage mortality	4 (3)	2 (3)	2 (2)	.65
Interstage reintervention	13 (8)	6 (10)	7 (7)	.77
Follow-up after shunt, y, mean ± SD	12.3 ± 8.1	10.8 ± 8.4	11.3 ± 8.2	.74
Late outcome				.73
Alive after TOF repair, n (%)	147 (92)	58 (89)	89 (94)	
Death before TOF repair or palliated as not suitable for repair, n (%)	8 (5)	5 (8)	3 (3)	
Death after TOF repair, n (%)	3 (2)	1 (2)	2 (2)	
Lost to follow-up, n (%)	2 (1)	1 (2)	1 (1)	
20-y survival after shunt, % (95% CI)	90 (79-95)	90 (77-96)	89 (70-96)	.49
20-y freedom from reintervention after TOF repair, % (95% CI)	40 (28-52)	34 (16-53)	49 (32-63)	.43
RV dilation/severe PR	59 (42-72)	46 (18-70)	66 (47-80)	.66
RVOTO	74 (63-83)	76 (55-88)	74 (59-84)	.74
PA stenosis, surgical reoperation	75 (63-83)	59 (37-76)	84 (72-91)	.07
PA stenosis, catheter reintervention	82 (69-90)	82 (65-92)	82 (64-92)	.57

ICU, Intensive care unit; *IQR*, interquartile range; *NEC*, necrotizing enterocolitis; *ECMO*, extracorporeal membrane oxygenation; *PA*, pulmonary artery; *SD*, standard deviation; *TOF*, tetralogy of Fallot; *CI*, confidence interval; *RV*, right ventricular; *PR*, pulmonary regurgitation; *RVOTO*, right ventricular outflow tract obstruction. *Composite endpoint of cardiac arrest, need for mechanical circulatory support, or unplanned reoperation.

was associated with composite morbidity, hospital mortality, and shunt thrombosis/stenosis. A central shunt with a proximal anastomosis on the ascending aorta was associated with an increased risk of pulmonary overload, whereas a right MBTS with an anastomosis on the right PA was associated with reduced risk. No shunt characteristic was predictive of achieving pulmonary annulus–preserving repair (PAPR).

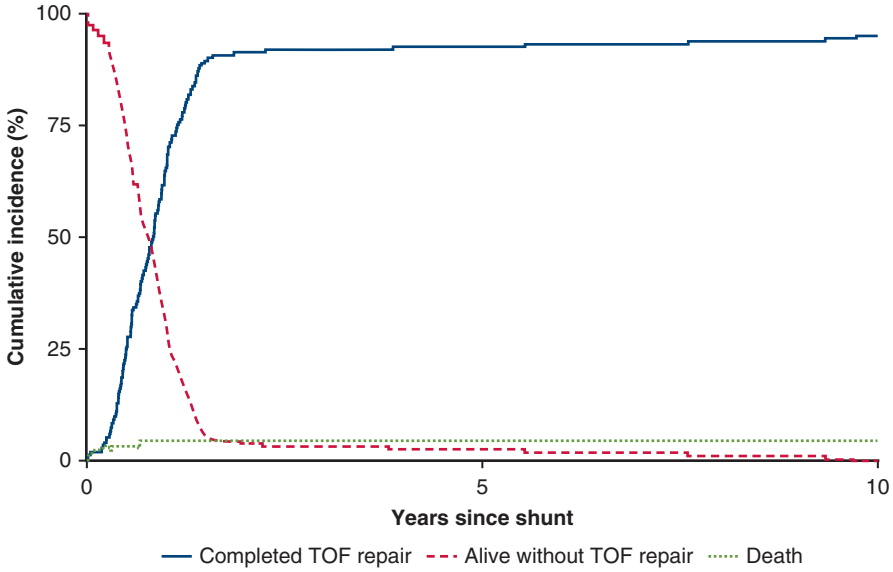


FIGURE 1. Competing risk analysis of progression to complete repair of tetralogy of Fallot in children undergoing initial shunt palliation. *TOF*, Tetralogy of Fallot.

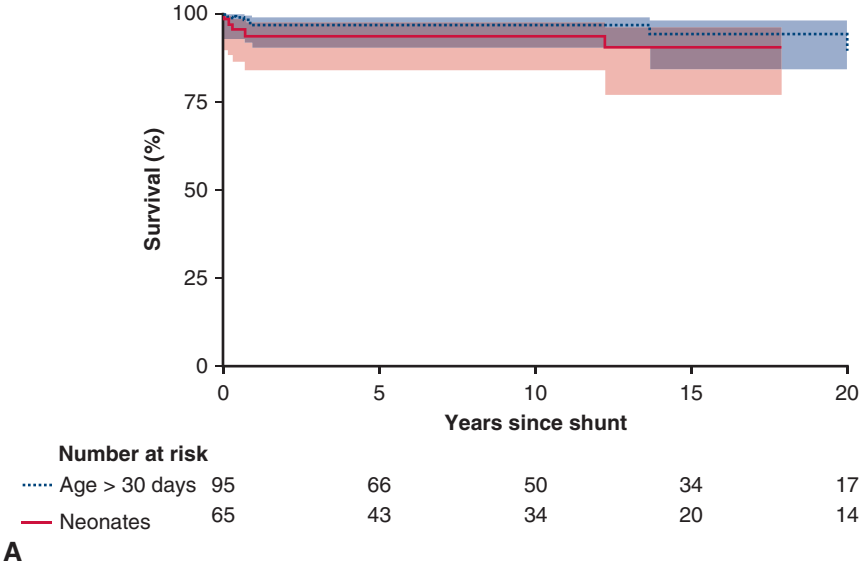
Absolute growth of PVA and branch PA sizes occurred between the time of palliative shunt and complete repair (Table E4). However, no significant improvement in the branch PA index was noted, whereas the PVA index decreased.

The mean duration of follow-up after palliative shunt was 12.3 ± 8.1 years. Actuarial survival at 20 years after shunt palliation was similar between neonates (90%; 95% confidence interval [CI], 77%-96%) and older children (89%; 95% CI, 70%-96%; $P = .49$) (Figure 2, *A*).

TABLE 4. Logistic regression analysis of predictors of early morbidity and hospital mortality after shunt

Predictor	Early morbidity*		Hospital mortality	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Univariable analysis				
Shunt-weight ratio ≥1.2 mm/kg	3.90 (1.53-9.97)	<.01	—†	
Neonate	1.10 (0.51-2.39)	.81	4.55 (0.46-44.73)	.19
Age (per 1-d increase)	0.99 (0.98-1.00)	.05	0.99 (0.97-1.02)	.54
Prematurity (<36 wk)	3.96 (1.64-9.58)	<.01	5.00 (0.67-37.12)	.12
Urgent/emergent surgery	2.31 (1.03-5.15)	.04	0.97 (0.13-7.09)	.98
Preoperative mechanical ventilation	3.10 (1.33-7.18)	<.01	1.18 (0.12-11.74)	.89
Pulmonary overcirculation	2.81 (1.05-7.49)	.04	—‡	-
Cyanotic spells	0.90 (0.42-1.94)	.79	1.11 (0.15-8.07)	.92
Preoperative prostaglandin	1.52 (0.69-3.37)	.30	2.18 (0.30-15.96)	.44
Prostaglandin duration (per 1-d increase)	1.05 (1.01-1.10)	.03	1.04 (0.98-1.12)	.21
Central shunt	1.93 (0.85-4.39)	.12	3.00 (0.41-22.02)	.28
Concomitant PA arterioplasty	1.49 (0.37-5.95)	.57	—§	
Extracardiac anomalies	0.94 (0.42-2.08)	.88	1.69 (0.23-12.32)	.61
Multivariable analysis				
Shunt-weight ratio ≥ 1.2 mm/kg	3.12 (1.07-9.15)	.04		
Prematurity (<36 wk)	3.91 (1.25-12.17)	.02		
Urgent/emergent surgery	2.46 (0.86-7.07)	.09		
Pulmonary overcirculation	2.94 (0.92-9.40)	.07		
Age (per 1-d increase)	1.00 (0.98-1.01)	.46		
Preoperative mechanical ventilation	1.42 (0.49-4.09)	.51		

OR, Odds ratio; *CI*, confidence interval; *PA*, pulmonary artery. *Early morbidity was defined as any of cardiac arrest, need for postoperative mechanical circulatory support, or unplanned reoperations. †Hospital mortality occurred in 17% (4/24) of patients with a shunt-to-weight ratio ≥1.2 mm/kg, versus 0% (0/98) of patients with a shunt-to-weight ratio <1.2 mm/kg ($P = .001$, Fisher exact test). ‡None of the patients who had pulmonary overcirculation had hospital mortality. §None of the patients who had concomitant PA arterioplasty had hospital mortality.



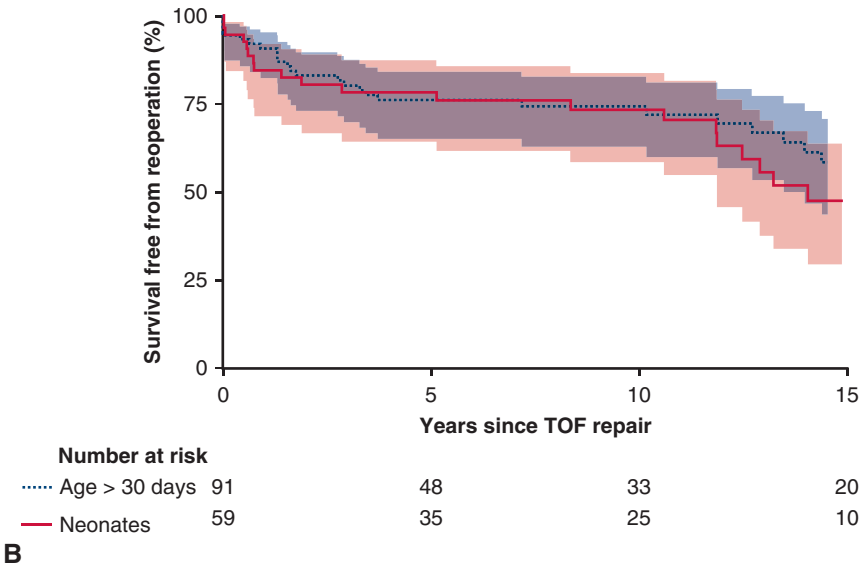


FIGURE 2. A, Survival after shunt, comparing neonates and those age >30 days at the time of shunt palliation for tetralogy of Fallot (*TOF*). B, Reoperation-free survival after complete repair of TOF, comparing neonates and those aged over 30 days at the time of shunt palliation. *Shaded area* defines 95% confidence interval.

TOF Repair

One hundred and fifty of the 160 patients (94%) completed TOF repair, including 21% (32 of 150) with PAPR. The median age was 10.8 (IQR, 6.9-15.3) months, and the median weight was 7.9 (IQR, 6.7-9.0) kg. The median interval since palliative shunt was 9.6 (IQR, 6.0-12.6) months. There was no in-hospital mortality. In recent years, we have been performing TOF repair in younger patients (median age, 15.1 [IQR, 12.5-18.0] months in 1993-1999 vs 7.3 [IQR, 5.8-9.1] months in 2014-2021; $P < .001$) and at shorter interstage intervals (median, 12.0 [IQR, 10.3-14.8] months in 1993-1999 vs 5.8 [IQR, 4.1-7.1] months in 2014-2021; $P < .001$) (Table E1).

Operative data on TOF repair are summarized in Table 5, comparing patients who achieved PAPR (n = 32) with those who required TAP (n = 113) or an RV-PA conduit (n = 5). The PAPR group had significantly larger PVA size than the other groups before both palliative shunt and TOF repair. In particular, the PAPR group had a similar PVA index as other patients before shunt palliation yet a significantly higher PVA index before TOF repair (22.7 [IQR, 17.6-25.0] mm/m^2 vs 17.1 [IQR, 14.0-20.3] mm/m^2; $P = .04$). Age, weight, and shunt type and size had no associations with PAPR.

The mean duration of follow-up after TOF repair was 10.8 ± 7.8 years. Actuarial 25-year survival was 94% (95% CI, 81%-98%), with no late mortality in the PAPR

TABLE 5. Surgical data and outcomes of TOF repair

Characteristic	Overall (N = 150)	PAPR (N = 32)	TAP (N = 113) or RV-PA conduit (N = 5)	*P* value
Data at shunt				
Age, d	48 (18-86)	45 (17-100)	45 (20-83)	.98
Neonate, n (%)	59 (39)	12 (38)	47 (40)	.84
Weight, kg, median (IQR)	3.5 (2.8-4.4)	3.6 (3.0-4.4)	3.4 (2.7-4.4)	.58
PVA, mm, median (IQR)*	5.0 (4.2-6.0)	5.7 (5.0-6.8)	4.8 (4.1-5.8)	.04
PVA index, mm/m^2, median (IQR)	22.2 (19.2-25.5)	25.7 (23.2-26.6)	22.0 (19.0-25.3)	.28
Shunt type, n (%)				.43
Right MBTS	95 (63)	24 (75)	71 (60)	
Left MBTS	15 (10)	3 (9)	12 (10)	
Central	38 (25)	5 (16)	33 (28)	
Classic BTS	2 (1)	0 (0)	2 (2)	
Shunt-weight ratio, mm/kg†	1.0 (0.9-1.2)	1.0 (0.9-1.1)	1.0 (0.8-1.2)	.60
Shunt index, mm/m^2	16.1 (14.6-17.4)	16.0 (15.2-16.7)	16.4 (14.6-17.5)	.72
Data at TOF repair				
Age, mo	10.8 (6.9-15.3)	11.7 (7.3-15.4)	10.3 (6.7-15.1)	.32
Weight, kg	7.9 (6.7-9.0)	8.2 (6.8-9.0)	7.8 (6.6-9.2)	.64
BSA, mm^2	0.37 (0.32-0.43)	0.38 (0.33-0.41)	0.37 (0.32-0.43)	.98
Interstage interval, mo	9.6 (6.0-12.6)	10.5 (6.8-13.6)	9.1 (5.7-12.4)	.36
Echocardiographic data before TOF repair				
PVA, mm‡	6.6 (5.3-9.0)	10.1 (9.0-12.0)	6.0 (5.0-8.0)	<.001
PVA index, mm/m^2	17.5 (15.0-21.2)	22.7 (17.6-25.0)	17.1 (14.0-20.3)	.04
LPA size, mm§	7.0 (5.2-8.0)	6.7 (5.5-8.0)	7.0 (5.0-8.1)	.98
LPA index, mm/m^2	17.1 (14.2-21.1)	18.0 (15.1-20.2)	17.0 (14.0-22.2)	.97
RPA size, mm‖	6.5 (5.5-8.0)	6.3 (5.9-8.0)	6.6 (5.3-8.0)	.69
RPA index, mm/m^2	17.1 (14.2-19.5)	17.4 (15.6-19.0)	17.1 (14.2-19.5)	.79
RVOT peak gradient, mm Hg	74 (64-88)	71 (56-81)	77 (64-91)	.06
Intraoperative data				
Cross-clamp time, min, mean ± SD	87 ± 30	84 ± 32	88 ± 29	.57
Bypass time, min, mean ± SD	151 ± 53	137 ± 44	155 ± 55	.10
Postoperative data				
RVOT peak gradient >40 mm Hg, n (%)	26 (17)	9 (28)	17 (15)	.25
ICU stay, h, mean ± SD	77 ± 112	81 ± 126	77 ± 109	.89
Mechanical ventilation, h, mean ± SD	47 ± 86	55 ± 105	46 ± 82	.65
Hospital stay, d, mean ± SD	12 ± 19	12 ± 14	12 ± 20	.98
Mortality, n (%)				
Hospital mortality	0 (0)	0 (0)	0 (0)	-
Late mortality	3 (2)	0 (0)	3 (3)	1.00
Follow-up after TOF repair, y, mean ± SD	10.8 ± 7.8	12.3 ± 8.7	10.4 ± 7.6	.22
Reoperation, n (%)				
Any indication	51 (34)	10 (31)	41 (35)	.83
RV dilation/severe PR	25 (17)	1 (3)	24 (20)	.02
RVOTO	26 (17)	7 (22)	19 (16)	.44
PA stenosis	25 (17)	2 (6)	23 (19)	.11
20-y survival, % (95% CI)	94 (81-98)	100	92 (74-98)	-
20-y freedom from reintervention, % (95% CI)	40 (28-52)	62 (41-78)	31 (17-45)	.21
Balloon angioplasty for branch PA	82 (69-90)	100	86 (73-92)	-
Surgical reoperation				
Any indication	43 (31-55)	62 (41-78)	35 (21-49)	.42
RV dilation/severe PR	59 (42-72)	94 (67-99)	43 (23-61)	.01
RVOTO	74 (63-83)	74 (53-87)	73 (58-83)	.52
PA stenosis	75 (63-83)	93 (74-98)	67 (52-78)	.07

PAPR, Pulmonary annulus-preserving repair; *TAP*, transannular patch; *RV*, right ventricle; *PA*, pulmonary artery; *IQR*, interquartile range; *PVA*, pulmonary valve annulus; *MBTS*, modified Blalock–Taussig shunt; *BTS*, Blalock–Taussig shunt; *TOF*, tetralogy of Fallot; *BSA*, body surface area; *LPA*, left pulmonary artery; *RPA*, right pulmonary artery; *PR*, pulmonary regurgitation; *RVOT*, right ventricular outflow tract; *ICU*, intensive care unit; *RVOTO*, right ventricular outflow tract obstruction; *CI*, confidence interval. *Data available for 87 patients (22 with PAPR, 65 others). †Data available for 116 patients (25 with PAPR, 91 others). ‡Data available for 53 patients (9 with PAPR, 44 others). §Data available for 130 patients (25 with PAPR, 105 others). ‖Data available for 130 patients (27 with PAPR, 107 others).

group. The PAPR group had significantly greater actuarial 20-year freedom from pulmonary regurgitation (PR)-related reoperation (94% [95% CI, 67%-99%] vs 43% [95% CI, 23%-61%]; $P = .01$), although the overall reoperation rate was not significantly different. Patients who underwent shunt palliation as neonates had comparable risks of reoperation (Table 3) and 15-year reoperation-free survival as older children (48% [95% CI, 29%-64%] vs 59% [95% CI, 44%-71%]; $P = .33$) (Figure 2, *B*). On Cox regression analysis, PAPR was an independent protective factor from reoperations for severe PR (hazard ratio, 0.08; 95% CI, 0.01-0.58), whereas a residual RVOT peak gradient >40 mm Hg after TOF repair was an independent predictor for reoperations for RVOT obstruction (hazard ratio, 3.27; 95% CI, 1.35-7.94) (Table E5). We could not identify any predictor of reoperation-free survival.

DISCUSSION

The optimal management strategy for infants younger than 3 months of age with symptomatic TOF who require early surgery remains controversial. In recent years, early complete repair has been favored by some, but this strategy may result in higher rates of early morbidity and postoperative complications.[5,13] Importantly, a recent large multi-institutional study of neonates demonstrated superior survival with a staged approach compared with primary complete repair.[6] In light of these findings, we aimed to review our results with a systematic approach of staged repair.

Early Outcomes

Our hospital mortality of 4.6% (3 of 65) after neonatal palliation was consistent with that of 6.2% (11 of 178) reported in the Society of Thoracic Surgeons (STS) database. Importantly, it compared favorably to the discharge mortality rate of 7.8% (12 of 154) after neonatal primary repair.[1] For patients older than 1 month, our hospital mortality was 1.1% (1 of 95), which again compared favorably to that of 8.6% (9 of 105) in the STS database for patients aged 30 days to 6 months.

Importantly, we observed that shunt size mismatch was associated with adverse outcomes, with shunt size-to-weight ratio $\geq$1.2 mm/kg being an independent predictor of post-shunt morbidity and mortality. This is consistent with previous findings in patients undergoing MBTS in general.[14-16] Shunt size mismatch was particularly prevalent among neonates, who were also more likely to be duct dependent preoperatively. Oversized shunts may contribute to pulmonary overload and systemic hypoperfusion. Furthermore, discrepancy in size between the branch PA and the rigid prosthetic conduit is known to cause distortion of the branch PA and stenosis of the anastomotic site.[17] Much of the early morbidity associated with shunt-weight mismatch in our cohort was related to unplanned reoperations for shunt revision. To minimize the risk of shunt size mismatch, we tend to aim for a shunt diameter-to-weight ratio of just over 1 mm/kg. Given the smallest currently available shunt is 3.0 mm in diameter, we aim to defer operating on patients under 2.5 kg, preferring to support them on prostaglandin infusion until they reach 2.5 kg. As we have increasingly used smaller shunts, we have also observed a reduction in the interstage period, likely reflecting the need for earlier surgery to maintain adequate pulmonary blood flow.

Late Mortality

It remains unclear whether there is any long-term survival difference between symptomatic young infants undergoing shunt palliation and those undergoing early complete repair. Survival of 90% to 93% at 5-years following symptomatic neonatal TOF repair has been reported,[18-20] but scarce data is available for the long-term. The survival of our entire cohort was 95% at 1-year, 5-years and 10-years, 93% at 15-years, and 90% at 20-years after shunt palliation, with neonates having comparable survival to older children. This is consistent with previous studies reporting 94% to 97% survival at two to five years and 93% survival at 10 years after staged TOF repair.[19,21,22] The long-term survival of the currently reported palliated cohort appears to be slightly lower than our previously reported overall TOF cohort, which had 96% survival at 25-years.[7] This is unsurprising, given that patients with the smallest PAs or the narrowest RVOT were selected for palliation. However, patients who survived to complete TOF repair appeared to have comparable late survival to other patients who underwent primary repair at our institution, with 94% survival at 25-years. On the other hand, although neonatal TOF repair appears to yield equivalent mid-term survival to staged repair,[3,19] their baseline demographics may not be comparable given that most centers select patients with operative risk factors, such as hypoplastic PAs and coronary artery anomalies, for staged palliation rather than early repair.[3] Furthermore, a recent analysis of the US multicenter database demonstrated that neonatal TOF repair was in fact associated with significantly higher risk of early and 2-year mortality as compared to staged repair.[6]

Late Reinterventions

The risk of late reinterventions after staged palliation versus neonatal TOF repair is also currently unclear. There appears to be a 20% to 40% reintervention rate at 5-years after neonatal TOF repair,[19,23-25] but only limited follow-up is reported. Some studies demonstrated no difference in late reintervention rate between patients who had prior palliation versus primary repair.[26,27] However, we have previously reported that prior palliation was a significant risk factor for late reoperations for RV dilation or RVOTO.[7] In the current study, freedom from reoperation after staged

TOF repair was 89% at 1-year, 76% at 5-years and 74% at 10-years, which was comparable to previous reports.[19,21,22] However, we also found a high risk of reinterventions beyond 10-years, mainly attributed to reoperations for RV dilation, such that freedom from any reintervention was only 40% at 20-years. This was lower than that previously reported with our overall TOF cohort, who had a 25-year freedom from reintervention of 75%.[7] In particular, close to 25% of our palliated cohort would require reoperations for RVOTO and as much as 40% would require reoperations for RV dilation at 20-years. Again, this likely reflects the fact that palliated patients were selected for their small PAs and narrow RVOT. These patients likely required more extensive resection at the time of TOF repair, and their smaller PAs might have resulted in persistently high RV afterload that precipitated progressive RV dilation.

Importantly, we found that patients who required shunt palliation as neonates were not at increased risk of late reinterventions as compared to older infants, despite more frequently requiring concomitant PA reconstructions at TOF repair. Some studies of primary TOF repair have similarly found no increased risk of reinterventions among neonates as compared to older children.[25,26]

Alternative Palliative Strategies

In recent years, transcatheter palliation via RVOT or ductus arteriosus stenting has emerged as viable alternatives to systemic-to-pulmonary shunt in high-risk patients deemed not yet suitable for complete repair. Both RVOT and ductal stents have been found to promote better and more uniform growth of branch PAs, result in less morbidity, and allow shorter interstage interval to complete repair.[28,29] However, both procedures have also been associated with increased need for transcatheter reinterventions.[29-31] Furthermore, RVOT stenting may result in increased need for a TAP at the time of complete repair as it necessitates partial or complete destruction of the pulmonary valve.[31,32] although not all studies came to this conclusion.[28,30]

It is worth noting that all currently available data come from nonrandomized, retrospective studies that are subject to selection and reporting bias. Data are lacking on patients who have failed attempts at transcatheter palliation or who were deemed not suitable based on preprocedural anatomy. Furthermore, expertise is currently limited to selected centers, and the long-term outcomes of these strategies are unclear. In comparison, we have long-term data available on the outcomes of systemic-to-pulmonary shunt, which remains the most prevalent palliative procedure practiced worldwide.[1] Indeed, transcatheter palliation offers promising prospects for the management of symptomatic young infants with TOF, but further experience in its practice is needed before it can be widely adopted as an alternative to a systemic-to-pulmonary shunt.

Limitations

This study was limited by its lack of randomization and its retrospective nature. We were unable to determine the rationales behind the surgical decisions for individual patients. Although our institution adopted a uniform policy during the study period of palliative shunting for all symptomatic infants under 4 months of age, the specific surgical management has changed over time, as demonstrated by our findings. The primary endpoints occurred relatively infrequently, which might have limited the statistical power of our analyses. We also had incomplete data available on several key variables, including the length of shunt, PVA size, and branch PA size, which were not universally reported at our institution.

CONCLUSIONS

Staged repair of TOF in symptomatic young infants allows 95% of patients to achieve complete repair and results in low mortality but a high rate of reintervention at long-term follow-up. A shunt size-to-weight ratio $\geq$1.2 mm/kg is associated with mortality and morbidity before complete repair. Neonates undergoing shunt insertion have comparable late outcomes to those of older children.

Conflict of Interest Statement

Dr Ye is recipient of a Postgraduate Scholarship from the National Health and Medical Research Council (1190479) and a Doctor in Training Research Scholarship from Avant. Dr Brizard has served on the advisory board of Admedus. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: tetralogy of Fallot, shunt, staged repair, neonates

TABLE E1. Operative data according to surgical era

Characteristic	1993-1999 (N = 48)	2000-2006 (N = 41)	2007-2013 (N = 42)	2014-2021 (N = 29)	*P* value
Age, d, median (IQR)	75 (22-127)	39 (22-63)	27 (14-55)	36 (14-68)	<.01
Neonate, n (%)	14 (29)	17 (41)	22 (52)	12 (41)	.17
Weight, kg, median (IQR)	4.3 (3.0-5.4)	2.9 (2.6-4.1)	3.5 (2.7-4.2)	3.2 (2.8-4.0)	.08
Shunt size, n (%)					
3.0 mm	1 (2)	7 (17)	20 (48)	17 (59)	<.001
3.5 mm	8 (17)	12 (29)	19 (45)	10 (34)	
4.0 mm	19 (40)	18 (44)	2 (5)	2 (7)	
5.0 mm	16 (33)	1 (2)	0 (0)	0 (0)	
Shunt-to-weight ratio, mm/kg, median (IQR)	1.1 (0.9-1.3)	1.1 (0.9-1.3)	1.0 (0.8-1.1)	1.0 (0.9-1.1)	.08
Shunt index, mm/m^2, median (IQR)	16.1 (13.4-17.6)	16.7 (14.8-18.1)	15.8 (14.6-17.1)	16.7 (15.0-16.7)	.86
Shunt type, n (%)					<.001
Modified BTS					
Right	42 (88)	30 (73)	16 (38)	11 (38)	
Left	3 (6)	4 (10)	2 (5)	8 (28)	
Central	3 (6)	5 (12)	23 (55)	10 (34)	
Classic BTS	0 (0)	2 (5)	1 (2)	0 (0)	
Approach, n (%)					<.001
Sternotomy	12 (25)	24 (59)	41 (98)	29 (100)	
Lateral thoracotomy	36 (75)	17 (41)	1 (2)	0 (0)	
Urgent/emergent surgery, n (%)	23 (48)	17 (41)	25 (60)	16 (55)	.39
Cardiopulmonary bypass used, n (%)	4 (8)	8 (20)	34 (81)	21 (72)	<.001
Composite morbidity, n (%)	3 (6)	12 (29)	10 (24)	8 (28)	.02
Pulmonary overcirculation, n (%)	3 (6)	2 (5)	9 (21)	7 (24)	.02
Hospital mortality, n (%)	0 (0)	3 (7)	1 (2)	0 (0)	.10
Neonatal hospital mortality, n/N (%)	0/14 (0)	2/17 (12)	1/22 (5)	0/12 (0)	.53
Interstage mortality, n/N (%)	1/48 (2)	2/38 (5)	1/41 (2)	0/29 (0)	.77
Interstage time to TOF repair, mo, median (IQR)	12.0 (10.3-14.8)	11.5 (8.7-15.1)	6.7 (4.6-9.1)	5.8 (4.1-7.1)	<.001
Age at TOF repair, mo, median (IQR)	15.1 (12.5-18.0)	13.0 (10.8-15.6)	7.0 (4.6-9.7)	7.3 (5.8-9.1)	<.001

IQR, Interquartile range; *BTS*, Blalock–Taussig shunt; *TOF*, tetralogy of Fallot.

TABLE E2. Receiver operating characteristic curve analysis of shunt-to-weight ratio in predicting early morbidity and hospital mortality

Shunt-to-weight ratio, mm/kg	Early morbidity			Hospital mortality		
	Sensitivity	Specificity	Youden index*	Sensitivity	Specificity	Youden index*
≥1.00	0.719	0.522	0.241	1.000	0.475	0.475
≥1.10	0.594	0.711	0.305	1.000	0.653	0.653
≥1.20	**0.438**	**0.889**	**0.327**	**1.000**	**0.831**	**0.831**
≥1.30	0.250	0.922	0.172	0.250	0.873	0.123
≥1.40	0.094	0.944	0.038	0.250	0.941	0.191

Early morbidity area under the curve (AUC) = 0.670 (95% confidence interval [CI], 0.553-0.786); hospital mortality AUC = 0.893 (95% CI, 0.820-0.966). Early morbidity defined as a composite endpoint of any of cardiac arrest, need for postoperative mechanical circulatory support, or unplanned reoperations. Bold indicates that a shunt-to-weight ratio cut-off of 1.2 mm/kg results in the highest Youden index for both early morbidity and hospital mortality. *Youden index = sensitivity + specificity − 1.

TABLE E3. Logistic regression analysis of predictors of shunt outcomes, according to shunt characteristics

Shunt characteristic	Composite morbidity*		Hospital mortality		Shunt thrombosis/stenosis		Pulmonary overcirculation		Pulmonary annulus-preserving TOF repair	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Shunt type										
Modified BTS										
Right (n = 99)	0.58 (0.27-1.26)	.17	0.20 (0.02-.94)	.16	1.08 (0.30-3.87)	.90	0.32 (0.13-0.84)	**.02**	1.99 (0.82-4.79)	.13
Left (n = 17)	0.81 (0.22-2.99)	.75	2.91 (0.29-29.72)	.37	Nil	-	1.48 (0.39-5.69)	.56	0.91 (0.24-3.46)	.89
Central (n = 41)	1.93 (0.85-4.39)	.12	3.00 (0.41-22.02)	.28	1.72 (0.48-6.24)	.40	3.16 (1.23-8.15)	**.02**	0.48 (0.17-1.34)	.16
Classic BTS (n = 3)	1.95 (0.17-22.22)	.59	Nil	-	Nil	-	Nil	-	Nil	-
Proximal anastomosis										
Innominate (n = 62)	1.51 (0.70-3.29)	.30	Nil	-	1.24 (0.36-4.27)	.73	0.89 (0.34-2.29)	.81	0.71 (0.31-1.61)	.41
Subclavian (n = 51)	0.47 (0.19-1.16)	.10	2.04 (0.28-14.92)	.48	0.42 (0.09-2.03)	.28	0.29 (0.08-1.04)	.06	2.06 (0.91-4.66)	.08
Ascending aorta (n = 40)	1.30 (0.56-3.05)	.54	2.92 (0.40-21.46)	.29	1.68 (0.47-6.08)	.43	3.09 (1.20-7.98)	**.02**	0.63 (0.23-1.68)	.35
Distal anastomosis										
Right PA (n = 103)	0.96 (0.42-2.18)	.93	0.48 (0.06-3.48)	.46	0.84 (0.23-3.01)	.79	0.38 (0.15-0.97)	**.04**	1.83 (0.72-4.63)	.20
Left PA (n = 11)	0.80 (0.16-3.87)	.78	Nil	-	Nil	-	2.58 (0.63-10.64)	.19	1.03 (0.20-5.25)	.97
Main PA (n = 39)	1.39 (0.66-2.92)	.39	2.05 (0.46-9.09)	.34	1.46 (0.49-4.37)	.50	1.62 (0.70-3.73)	.26	0.48 (0.17-1.33)	.16
Shunt size										
3.0 mm (n = 45)	1.32 (0.58-3.04)	.51	0.79 (0.08-7.78)	.84	3.13 (0.91-10.87)	.07	1.98 (0.77-5.09)	.16	0.56 (0.22-1.41)	.22
3.5 mm (n = 49)	2.23 (1.01-3.97)	**.049**	6.65 (0.67-65.66)	.11	1.22 (0.34-4.38)	.76	1.35 (0.52-3.51)	.54	1.24 (0.54-2.85)	.62
4.0 mm (n = 41)	0.56 (0.21-1.48)	.24	Nil	-	0.25 (0.03-2.04)	.20	0.41 (0.11-1.47)	.17	0.86 (0.35-2.12)	.74
5.0 mm (n = 17)	Nil	-	Nil	-	Nil	-	0.36 (0.05-2.86)	.33	2.33 (0.78-7.00)	.13
Shunt-to-weight ratio†										
≥1.2 mm/kg (n = 25)	3.90 (1.53-9.97)	**<.01**	‡	‡	4.04 (1.12-14.59)	**.03**	0.79 (0.21-2.99)	.73	1.27 (0.41-3.90)	.68

Significant *P* values (<.05) are in bold type. *TOF*, Tetralogy of Fallot; *OR*, odds ratio; *CI*, confidence interval; *BTS*, Blalock–Taussig shunt; *PA*, pulmonary artery. *Composite endpoint of cardiac arrest, postoperative mechanical circulatory support, or unplanned reoperations. †Data available for 122 patients (52 neonates, 70 older children) ‡Hospital mortality occurred in 17% (4/24) of patients with shunt-weight ratio ≥ 1.2 mm/kg, versus 0% (0/98) of patients with shunt-weight ratio < 1.2 mm/kg (*P* = .001 on Fisher's exact test).

TABLE E4. Interval growth of pulmonary valve annulus and branch pulmonary artery size between shunt and TOF repair

Variable	Before shunt, mean ± SD	Before TOF repair, mean ± SD	*P* value
PVA, mm	4.9 ± 1.3*	7.0 ± 2.3†	<.001
PVA index, mm/m^2	22.2 ± 5.6	17.4 ± 5.2	<.001
LPA, mm	3.8 ± 1.1‡	6.6 ± 2.2§	<.001
LPA index, mm/m^2	16.7 ± 4.4	17.6 ± 6.0	.31
RPA, mm	4.1 ± 1.3‖	6.5 ± 2.0¶	<.001
RPA index, mm/m^2	17.2 ± 4.4	17.2 ± 5.0	.99

TOF, Tetralogy of Fallot; *SD*, standard deviation; *PVA*, pulmonary valve annulus; *LPA*, left pulmonary artery; *RPA*, right pulmonary artery. *Data available for 92 patients (36 neonates, 56 older children). †Data available for 87 patients (22 with pulmonary annulus–preserving repair [PAPR], 65 others). ‡Data available for 144 patients (55 neonates, 89 older children). §Data available for 130 patients (25 with PAPR, 105 others). ‖Data available for 147 patients (57 neonates, 90 older children). ¶Data available for 130 patients (27 with PAPR, 107 others).

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TABLE E5. Cox regression analysis of predictors of adverse outcomes after TOF repair

	Death or any reoperation		Reoperation for PR/RV dilatation		Reoperation for RVOTO		Reoperation for PA stenosis	
Variable	Univariable *P* value	Multivariable *P* value	Univariable *P* value	Multivariable *P* value	Univariable *P* value	Multivariable *P* value	Univariable *P* value	Multivariable *P* value
Female	.55		.25		.50		.51	
Low birth weight	.22		.33		.24		.33	
Prematurity	.23		.69		.43		.49	
Genetic syndrome	.15	.49	.22		.36		.85	
Neonate at shunt	.33		.66		.74		.10	.77
Age at initial shunt	.29		.81		.19		.08	.35
Weight at initial shunt	.46		.93		.92		.54	
PVA index before shunt	.60		.98		.62		.38	
Shunt-to-weight ratio >1.2 mm/kg	.93		.56		.57		.78	
PA arterioplasty required at shunt	.82		.27		.21		.05	.21
Age at TOF repair	.24		.91		<.01	.07	.95	
Weight at TOF repair	.09	.73	.64		.15		.58	
PAPR	.36		**.01***		.52		.07	.10
RVOT peak gradient >40 mm Hg after repair	.33		.49		.02	**<.01**†	.55	

Variables with a *P* value < .20 on univariable analysis were included in the multivariable analysis. Significant *P* values are in bold type. *PR*, Pulmonary regurgitation; *RV*, right ventricle; *RVOTO*, right ventricular outflow tract obstruction; *PA*, pulmonary artery; *PVA*, pulmonary valve annulus; *TOF*, tetralogy of Fallot; *PAPR*, pulmonary annulus-preserving repair. *Hazard ratio [HR], .08; 95% confidence interval [CI], .01-.58. †HR, 3.27; 95% CI, 1.35-7.94.