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Tetralogy of Fallot: stent palliation or neonatal repair?

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Abstract

Surgical repair of Tetralogy of Fallot has excellent outcomes, with over 90% of patients alive at 30 years. The ideal time for surgical repair is between 3 and 11 months of age. However, the symptomatic neonate with Tetralogy of Fallot may require earlier intervention: either a palliative intervention (right ventricular outflow tract stent, ductal stent, balloon pulmonary valvuloplasty, or Blalock-Taussig shunt) followed by a surgical repair later on, or a complete surgical repair in the neonatal period. Indications for palliation include prematurity, complex anatomy, small pulmonary artery size, and comorbidities. Given that outcomes after right ventricular outflow tract stent palliation are particularly promising – there is low mortality and morbidity, and consistently increased oxygen saturations and increased pulmonary artery z-scores – it is now considered the first-line palliative option. Disadvantages of right ventricular outflow tract stenting include increased cardiopulmonary bypass time at later repair and the stent preventing pulmonary valve preservation. However, neonatal surgical repair is associated with increased short-term complications and hospital length of stay compared to staged repair. Both staged repair and primary repair appear to have similar long-term mortality and morbidity, but more evidence is needed assessing long-term outcomes for right ventricular outflow tract stent palliation patients.

Tetralogy of Fallot is the most common cyanotic congenital cardiac malformation, representing 7–10% of all congenital cardiac malformations and occurring in approximately 3 per 10 000 live births.[1] Tetralogy of Fallot contains a tetrad of anatomical anomalies first described by Etienne-Louis Fallot in 1888. These include a ventricular septal defect, an overriding of the ventricular septum by the aortic root, right ventricular outflow tract obstruction, and right ventricular hypertrophy.[2] Tetralogy of Fallot has a multifactorial aetiology with most cases arising sporadically with no known prenatal risk factor. Both males and females are equally affected. There is an association with genetic conditions, particularly DiGeorge Syndrome (25% will have concurrent Tetralogy of Fallot).[2] It can also be seen less commonly in Trisomy 21, 18 and 13.[1]

Tetralogy of Fallot typically presents with cyanosis, tachypnoea upon exertion, and an ejection systolic murmur. If left untreated, children may later adopt a characteristic "squatting" position to increase pulmonary blood flow in order to relieve their symptoms.[3]

Surgical timing is based upon the patients' comorbidities, degree of defect severity, and clinical manifestation. In asymptomatic patients, Tetralogy of Fallot surgical repair is usually performed between 3 and 11 months of age.[4] In symptomatic patients, management involves either an immediate complete surgical repair or a temporary palliative intervention followed by a complete repair at a later stage.[4] There is current controversy regarding the preferred method of managing the symptomatic neonate with Tetralogy of Fallot.

Clinical presentation of Tetralogy of Fallot

Presentation of Tetralogy of Fallot can vary widely based upon the degree of right ventricular outflow tract obstruction. Stenosis can range from a mild degree to complete atresia of the pulmonary valve. In infants with mild to moderate right ventricular outflow tract obstruction, oxygen saturations are not markedly decreased and so these children are pink in colour.[1] Neonates often present with a harsh systolic ejection murmur upon auscultation, often detectable from day 1 of life.[1] Growth and development may not be limited in these patients.[5] However, the right

to left shunting of blood across the ventricular septal defect can progress to congestive cardiac failure. If left unchecked, it may lead to pulmonary hypertension.[1]

In Tetralogy of Fallot with pulmonary atresia, pulmonary blood flow is supplied from either the patent ductus arteriosus or major aortopulmonary collateral arteries. Tetralogy of Fallot with pulmonary atresia typically presents in the neonatal period as the patent ductus arteriosus closes. These infants appear blue with cyanosis. In infants with this variant, the patent ductus arteriosus can be maintained with a Prostaglandin E1 infusion until definitive management can be carried out.[5]

Tetralogy of Fallot can also present with an absent pulmonary valve. This variant is presented with non-functional valve leaflets which will cause dilation of the pulmonary artery and its branches leading to airway compression, bronchomalacia, and respiratory insufficiency.[5]

Tetralogy of Fallot cases are often complicated by hypercyanotic spells, a sudden decrease in oxygen saturations triggered by acutely increased right ventricular outflow tract obstruction.[1] During these spells, the amplified pulmonary vascular resistance increases the right to left shunting of deoxygenated blood across the ventricular septal defect. Patients are commonly irritable, tachypnoeic, profoundly cyanotic, and have reduced consciousness.[1] The systolic ejection murmur is often absent during these spells. Frequent hypercyanotic spells are an indicator for urgent surgical intervention.[1]

Diagnosis and investigations

Tetralogy of Fallot is now prenatally diagnosed in up to 60% of patients.[6] In the United Kingdom, this high rate of prenatal detection is a result of the Foetal Anomaly Screening Programme. Guidelines recommend ultrasound scanning in every pregnancy to screen for foetal anomalies between 18- and 20-weeks gestation. This includes echocardiographic assessment of multiple views of the heart, including the four-chamber view, right and left outflow tracts, and the 'three vessels and trachea' view.[7]

Tetralogy of Fallot patients can be further investigated prenatally through pulmonary valve measurements, monitoring aorta and pulmonary trunk growth, and Doppler assessment of the great arteries.[8] Prenatal diagnosis and investigations facilitate early intervention: features such as reversal of flow in the arterial duct, and failure of growth of the pulmonary trunk, prompt urgent surgical intervention in the neonatal period.[8]

Transthoracic echocardiography (Echo) is currently the most common mode of imaging in Tetralogy of Fallot patients postnatally. Although advances in Doppler Echo have reduced the requirement for cardiac catheterisation and angiography, impaired image quality sometimes limits its use.[9] Thus, cardiac catheterisation is sometimes used to visualise the pulmonary arteries and major aortopulmonary collateral arteries prior to surgical intervention.[10] Cardiac catheterisation can also be used to assess the reversibility of pulmonary hypertension and the degree of pulmonary vascular resistance. In some instances, cardiac catheterisation is diagnostic for infants with complex pulmonary atresia, when other methods of identifying major aortopulmonary collateral arteries and pulmonary artery anatomy are less reliable.[11]

CT and cardiovascular MRI are also used to elucidate details regarding patent ductus arteriosus-pulmonary artery morphology and coronary artery anatomy before surgical repair.[10,11] They are advantageous in producing a detailed image of the whole heart and its vascular structures through non-invasive means. In the case of cardiovascular MRI, this is also without exposure to radiation.[9,12] Use of cardiovascular MRI is routinely considered for procedural planning of Tetralogy of Fallot patients with complex morphology that cannot be adequately assessed by echocardiography alone. Cardiovascular MRI's unique ability to detect myocardial fibrosis and scarring is useful in the post-operative period, particularly for detecting signs of post-operative right ventricle restrictive physiology.[13] However, the routine use of cardiovascular MRI is limited by cost, availability, and need for anaesthesia or sedation.[14]

Management options

Palliation

There are a number of palliative options for cyanotic Tetralogy of Fallot neonates that augment their pulmonary blood flow.[15] These include the modified Blalock-Taussig shunt, ductal stent, balloon pulmonary valvuloplasty, and right ventricular outflow tract stent. The modified version of the Blalock-Taussig shunt entails the insertion of a graft which connects the subclavian artery to the pulmonary artery.[16] In cases of duct-dependent Tetralogy of Fallot with pulmonary atresia, a stent is introduced into the patent ductus arteriosus, adopting either the femoral artery or the transvenous approach depending on the specific anatomy of the duct.[17] A pulmonary balloon dilation is carried out for patients with valve stenosis of the pulmonary artery.[18] The newest procedure is the right ventricular outflow tract stent.[19] In this procedure, which is commonly transfemoral, the pulmonary valve is balloon dilated after which a pre-mounted coronary stent is implanted across the pulmonary valve.[19] Simplified illustrations of these palliative techniques are illustrated in Figure 1.

Some studies favour use of palliative intervention for symptomatic neonates with Tetralogy of Fallot over neonatal surgical repair.[20,21] The palliative approach does not reduce the success of a definitive repair at a later stage.[20,21] The sub-group of Tetralogy of Fallot patients in which the two-stage approach is preferred is those suffering from hypercyanotic spells, born premature, weighing <4 kg, or is <3 months of age at intervention. Palliation is also preferred in patients with anatomical variants such as atrio-ventricular septal defect or pulmonary atresia, a pulmonary artery z-score <−2, or extracardiac conditions such as necrotising enterocolitis, tracheoesophageal fistula, sepsis, or respiratory compromise that can increase the risks of single stage repair.[21–24] The majority of patients who have a palliation procedure undergo definitive repair by 6 months of age.[24]

Right ventricular outflow tract stent

Right ventricular outflow tract stenting is now seen as the first-line option for Tetralogy of Fallot palliation by leading centres globally in comparison to the modified Blalock-Taussig shunt alternative.[23–25] It is preferred due to higher morbidity (such as pulmonary stenosis, pulmonary congestion requiring diuretic use, seroma formation, or Horner's syndrome) associated with Blalock-Taussig shunt operation.[26,27] Quandt et al[25] also reported superior pulmonary artery growth in their right ventricular outflow tract stent patients in comparison to their Blalock-Taussig shunt patients.[25]

Carrying out a right ventricular outflow tract stent procedure can be difficult in patients with a short infundibulum, right ventricular outflow tract muscular atresia, or non-confluent central pulmonary arteries.[24,25] These patients require an alternative form of palliation such as a Blalock-Taussig shunt, or an early primary repair. Early primary repair is also preferred to right ventricular

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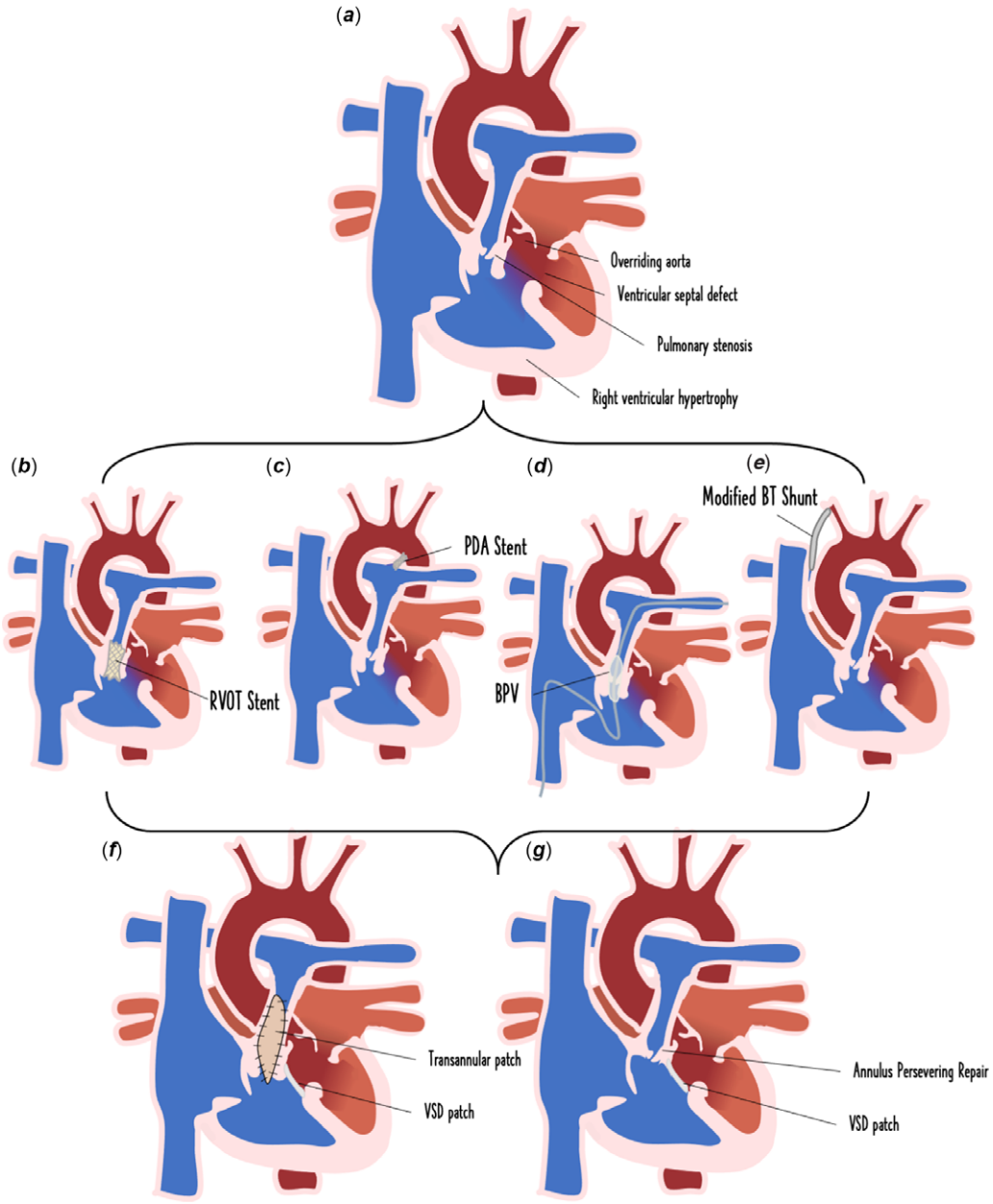

Figure 1. Palliative intervention options for the symptomatic neonate with Tetralogy of Fallot. Symptomatic neonate with Tetralogy of Fallot demonstrating tetrad of malformations: pulmonary stenosis, ventricular septal defect, overriding aorta, right ventricular hypertrophy (***a***), right ventricular outflow tract (RVOT) stent palliation (***b***), ductal stent palliation (***c***), balloon pulmonary valvuloplasty palliation (***d***), and modified Blalock-Taussig (BT) shunt surgical palliation (***e***), afterwards patients undergo complete surgical repair which can involves a ventricular septal defect (VSD) patch with either the transannular patch approach (***f***) or an annulus-preserving repair (***g***).

outflow tract stenting in patients with potential for pulmonary valve preservation.[24] Outcomes of palliative intervention are summarised in Table 1.

Right ventricular outflow tract stenting is an effective method of palliation for Tetralogy of Fallot patients, with reported success rates as high as 93.6%.[28] Oxygen saturations and pulmonary artery z-scores are consistently increased after right ventricular outflow tract stenting. Oxygen saturations increased by 20.1% across 10 studies,[28] and pulmonary artery z-score increased from −2.68 to −0.92 across one cohort.[23]

The procedural death rate of right ventricular outflow tract stenting is 3.7% across 10 studies.[28] Paediatric ICU length of stay ranges from 24 to 120 hours.[28] Re-intervention rates in right ventricular outflow tract stent patients are significant, with one trial reporting up to 54% of right ventricular outflow tract stent patients require a re-intervention before complete repair.[24] Common re-interventions include repeat dilatation of the right ventricular outflow tract stent, or implantation of a second or third stent.[24]

During the subsequent complete repair, 95/265 (36%) of right ventricular outflow tract patients require a transannular patch.[28] Fewer patients with staged repair require a transannular patch compared to primary repair.[29] Cardiopulmonary bypass time for complete repair ranges from 95 to 165 minutes in patients who first have right ventricular outflow tract stent palliation. One study found that average cardiopulmonary bypass time is longer in

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Table 1. Outcomes of palliative intervention

Outcomes	Palliative intervention
Cardiopulmonary bypass time	***Right Ventricular Outflow Stent***
	Ranged from 95 to 165 minutes (average of 101.7 minutes).[22]
Length of PICU stay	***Right Ventricular Outflow Stent***
	Ranged from 24 to 120 hours across 6 studies (average 88 hours).[28]
	Average after complete repair was 5 days in RVOT stent patients. This was slightly shorter than early repair groups (PS = 6, PA = 7).[24]
	Ductal Stent
	Median PICU LOS was 4.2 days, and hospital LOS 12 days.[30]
Short-term outcomes	***Right Ventricular Outflow Stent***
	Success rate of 93.6% across 10 studies assessing the outcome of 265 patients.[28]
	The procedural death rate of RVOT stenting was 3.7% across the ten studies.[28]
	Cumulative increase of 20.1% in oxygen saturations after RVOT stenting.[28]
	Increase of pulmonary artery z-score from −2.68 to −0.92.[23]
	Ductal Stent
	Superior to BT shunt in terms of risk of procedural-related complications.
	Procedural complications such as arrhythmia (3.8%), vascular injury during access (9.4%), and DS failure (15.7%).[30]
	Balloon Pump Valvuloplasty
	Increase in pulmonary artery z-scores and oxygen saturations. One recent study reports a z-score increase from −3.56 to −1.82 after BPV.[33]
	Another reports average O^2 saturation increased from 63 to 87% (+24%).[32]
Long-term outcomes	***Right Ventricular Outflow Stent***
	After a median 2.1 years follow-up:
	40% of patients with initial RVOT stent palliation have persistently elevated RV pressures
	40% required multiple re-interventions such as left pulmonary artery dilatations to increase pulmonary blood flow.[20]
	Balloon Pump Valvuloplasty
	Re-intervention rates were noticeably higher versus aforementioned palliation techniques.[33–35]

PICU, Paediatric ICU; RVOT, right ventricular outflow tract; PS, Pulmonary Stenosis; PA, Pulmonary Atresia; LOS, length of stay; DS, Ductal stents; RV, right ventricle.

patients with right ventricular outflow tract stent palliation compared to those with primary repair;[24] however, in another study, this difference lacked statistical significance.[25] Sandoval et al[24] found that no patients with a right ventricular outflow tract stent had pulmonary valve preservation after complete repair, compared to 41% of early repair patients. Accordingly, right ventricular outflow tract stent palliation is usually not considered in patients with potential for pulmonary valve preservation.[24]

One study found average post-operative Paediatric ICU length of stay after complete repair was an average of 5 days in right ventricular outflow tract stent palliation patients. This was slightly shorter than early repair groups (Pulmonary Stenosis = 6, Pulmonary Atresia = 7). Average post-operative hospital length of stay was reported as an average of 11 days for the stent group, also slightly shorter than early repair groups (Pulmonary Stenosis = 13, Pulmonary Atresia = 14).[24]

There are varied medium-term outcomes reported for Tetralogy of Fallot patients with right ventricular outflow tract stent palliation before complete repair. One study found after 2.1 median years, 40% of patients have persistently elevated right ventricle pressures and 40% require multiple re-interventions such as left pulmonary artery dilatations to increase pulmonary blood flow.[19] Another study similarly reports high re-intervention rates (25%), but no deaths by 3.2 median years.[24] There is limited evidence describing long-term outcomes in Tetralogy of Fallot patients with stent palliation.

Ductal stent

Ductal stents are typically performed for duct-dependent lesions with compromised patency of right ventricular outflow tract.[17,24] There are various approaches to inserting this type of stent depending on the relationship of the patent ductus arteriosus to aorta.[17] An advantage of ductal stent is a reduction of complications commonly associated with the Blalock-Taussig shunts.[30]

A meta-analysis[30] comparing ductal stent to Blalock-Taussig shunt in neonates with duct-dependent lesions (not exclusively Tetralogy of Fallot) found ductal stent to be superior to Blalock-Taussig shunt in terms of risk for procedural-related complications. Ductal stent patients had complications such as arrhythmia (3.8%), vascular injury during access (9.4%), and ductal stent failure (15.7%).[30] Median Paediatric ICU length of stay was 4.2 days, and hospital length of stay 12 days. There was no significant difference in 30-day mortality between patients who had a ductal stent and those who had a Blalock-Taussig shunt; however, ductal stent

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patients had better medium mortality rates.[30] Forty-four percentage of patients who underwent ductal stent had re-interventions, including balloon angioplasty of ductal stent, re-stenting, and pulmonary valvuloplasty.[30] Ductal stent can have negative impacts at time of complete repair, such as pulmonary artery distortion complicating surgery, and need for stent removal[30] and should thus only be undertaken after careful consideration. Further studies looking at both short- and long-term outcomes of ductal stent in exclusive Tetralogy of Fallot cohorts would be beneficial.

Balloon pulmonary valvuloplasty

Balloon pulmonary valvuloplasty is best suited for patients with pulmonary artery valvular stenosis rather than infundibular obstruction.[31] In this cohort, it can be used to delay early surgical repair in symptomatic neonates by enhancing blood flow through the pulmonary arteries, promoting pulmonary annulus growth and increasing oxygen saturations.[31] However, balloon pulmonary valvuloplasty is less effective in cases with an hypertrophied infundibulum[32], and these patients often require early re-intervention with a Blalock-Taussig shunt before definitive repair.[33]

After balloon pulmonary valvuloplasty, studies report an increase in pulmonary artery z-scores and oxygen saturations. One recent study reports a z-score increase from −3.56 to −1.82 after balloon pulmonary valvuloplasty.[33] Another study states that the average oxygen saturations increased from 63 to 87% (+24%).[32]

Transannular patching is required less often after balloon pulmonary valvuloplasty when compared to Blalock-Taussig shunt.[31] One study reported only 29% of patients with balloon pulmonary valvuloplasty required transannular patch; this is compared to 90% with Blalock-Taussig shunt.[31] This is because the balloon pulmonary valvuloplasty technique successfully promotes pulmonary annular growth in most patients.[34] Muneuchi et al[33] found that 48% (15/31) of patients who had a balloon pulmonary valvuloplasty still required another palliative surgical repair, an aortopulmonary shunt, before complete repair. The patients who required an aortopulmonary shunt before complete repair had greater infundibular obstruction.[33]

Complete repair

The surgical management of Tetralogy of Fallot has had significant advances; the majority of centres now opt for a transatrial or transatrial–transpulmonary approach with excellent long-term results.[35] This is an improvement from the original operation requiring a ventriculotomy. A ventriculotomy required a longer incision through the ventricle, pre-disposing the patient to a higher rate of complications.[36]

The two main objectives for open repair are closing the ventricular septal defect and correcting the right ventricular outflow tract obstruction. Once the ventricular septal defect has been patched, the aorta will no longer receive deoxygenated blood from the right ventricle, removing the overriding aorta.[37] Once the right ventricular outflow tract obstruction is repaired, afterload on the right ventricle reduces, leading to lower contractility and reducing right ventricular hypertrophy.[38] A popular technique to repair the ventricular septal defect involves a polytetrafluoroethylene patch using a single continuous stitch through the tricuspid valve.[39]

The need for neonatal primary repair is dependent on the severity of the condition. If the patient is experiencing end organ damage from cyanosis, increased cyanotic episodes, pulmonary valve atresia, or requiring administration of PGE1, neonatal repair is preferred over a delayed repair.[37,40] Neonatal repair more often requires transannular patch compared to a delayed repair.[41] Indications are summarised in Table 2.

Table 2. Indications for palliation versus neonatal open repair

Palliation[21–24]	Early open repair[37,40]
Increased cyanotic episodes	
Pulmonary valvular atresia	
Duct-dependent circulations (e.g. PGE1-dependent)	
Pulmonary artery z-score <−2	Potential for PV preservation
Prematurity	
Birth weight < 4kg	
Anatomical variants (e.g. AVSD or major aortopulmonary collateral arteries [MAPCAs])	
<3 months	
Extracardiac conditions (e.g. sepsis, necrotizing enterocolitis, tracheoesophageal fistula, respiratory compromise)	

PV, pulmonary valve.

Transannular patch versus annulus preserving repair

Repair of the right ventricular outflow tract obstruction involves either a transannular patch or annulus-preserving repair.[34,42,43] The optimum treatment for Tetralogy of Fallot involves limiting both residual post-operative pulmonary regurgitation and pulmonary stenosis, so selecting the correct procedure is imperative.[43,44] Many valve-sparing surgical techniques have been described, such as balloon pulmonary valvuloplasty, pulmonary cusp patch reconstruction, pulmonary valve commissurotomy +/− rigid bougie dilatation, and complete resection of sub-valvular and supravalvular areas of obstruction.[13] An annulus-preserving repair is preferable over a transannular patch due to reduced incidence of future valve replacement, lower rates of severe right ventricle dilation and pulmonary regurgitation, and better right ventricle function at first adult follow-up.[34] Annulus-preserving repairs are described as up to 6 times less likely than transannular patch to undergo pulmonary valve replacement indicating that transannular patch should only be done if necessary.[34]

A transannular patch procedure is commonly considered if the pulmonary annulus does not reach a threshold size,[45] a finding more frequent in neonatal repairs compared to later repairs. The long-term complications of arrhythmias and ventricular dysfunction mean that transannular patch are avoided when possible.[46] Moreover, abnormal coronary arteries or a distinctly small pulmonary artery may require a conduit rather than a transannular patch.[45]

Due to anatomical variation of pulmonary valves in Tetralogy of Fallot, it is not always possible to preserve the pulmonary valve. One study discovered 10% of their patient cohort had monocuspid valves which are not suitable for pulmonary valve preservation.[47] Promisingly, 90% of their patient cohort had bicuspid or tricuspid pulmonary valves. Of those 90%, in 48.7%, they were thickened and dysplastic and not able to be preserved, leaving 56% of the original cohort morphologically suitable for pulmonary valve preservation.[47]

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Pulmonary valve replacement

Pulmonary valve replacement is indicated in patients with significant pulmonary regurgitation; other indications include presence of heart failure or new arrhythmias due to right ventricle dilatation.[48] Pulmonary valve replacement is usually given in adulthood (ranging from 12 to 31 years after complete repair).[49] Interestingly, recent evidence suggests that pulmonary valve replacement does not have significant clinical outcomes in comparison to conservative management of pulmonary regurgitation. Both a meta-analysis and multicentre observational study found that pulmonary valve replacement did not significantly impact right ventricle ejection fraction, atrial tachycardia, sustained ventricular tachycardia, heart failure, or death.[50,51] Instead, the meta-analysis only found significant impact on NYHA class and right ventricle volumes.[50] Both studies highlighted a need for more evidence comparing outcomes of pulmonary valve replacement with conservative management.

Immediate post-operative outcomes

Evidence highlights that early repair increases ICU and hospital length of stay, and risk of post-operative cardiac events.[43,52] Bailey et al[52] report that ICU length of stay was increased by 90% to an average of 6 days in those having an early primary repair in comparison to a staged approach.[52] One study reported infants >90 days old undergoing complete repair had both a lower rate of post-operative complications and a shorter hospital length of stay compared to neonates.[53] Moreover, neonatal Tetralogy of Fallot repairs had the highest mortality rate (9.82%) compared to those >180 days old (0.85%) with the same open repair procedure.[53]

In comparison to staged repair, a retrospective study analysing 2,363 patients noted a higher risk of mortality in those with complete neonatal repair during hospital stay, at 30-day follow-up, and 2-year follow-up.[54] Patients with neonatal repair had increased cardiac complications (ECMO, Pleural effusion, need for CPR) and longer hospital stay.[54] This study also adjusted for confounders, such as patient, hospital, and systematic factors.

There are common complications immediately following a complete neonatal Tetralogy of Fallot repair that require further intervention, investigation, and monitoring. These complications include: residual ventricular septal defect, residual and persistent right ventricular outflow tract obstruction, arrhythmias (ventricular tachycardia or atrial fibrillation/flutter), right bundle branch block, or sudden cardiac death.[55] Other commonly reported immediate post-operative complications include pericardial effusion requiring draining, pleural effusion requiring drainage, chylothorax, bleeding requiring re-operation, superficial wound infection, and junctional ectopic tachycardia.[56] In patients with transannular patch repair, right ventricle restrictive physiology is commonly reported due to poor diastolic relaxation, which can contribute to a low cardiac output state.[57] This is commonly managed by optimising the ventricular preload through fluid resuscitation or by mechanical circulatory support if necessary.[58] While timing of the repair is a significant risk factor for increased mortality and morbidity in Tetralogy of Fallot patients, frequency of complications also depends largely on the severity of Tetralogy of Fallot. Important factors include pre-operative size of the pulmonary valve and pulmonary arteries, right ventricular – pulmonary artery pressure gradient, and oxygen saturation.[46]

Long-term complications

Long-term survival after Tetralogy of Fallot repair is generally very good, with >90% of patients surviving after close to 30-year follow-up.[35,59] While staged repair increased risk of mortality in the first 6 years following repair, there was no significant difference after this period.[59] Pulmonary regurgitation is the most common long-term complication in patients who survive Tetralogy of Fallot repair; 20 years after complete repair, up to 64% of patients have pulmonary regurgitation.[60] Risk factors for pulmonary regurgitation include a larger transannular patch and prolonged post-operative ventilator support.[61] Pulmonary regurgitation contributes to right ventricle dilatation in Tetralogy of Fallot patients, which reduces exercise tolerance and increases risk of right ventricle dysfunction, heart failure, and sudden cardiac death.[62]

Smith et al[59] also report the frequency of repaired Tetralogy of Fallot complications, such as arrhythmia (n = 12 [8.3%]), cardiac arrest (n = 34 [23.5%]), and congestive heart failure (n = 26 [17.9%]).[59] Factors contributing to heart failure in repaired Tetralogy of Fallot include damage to the myocardium (due to multiple cardiac surgeries, insufficient myocardial protection during cardiopulmonary bypass, or long-standing palliative shunts), chronic volume overload (due to pulmonary regurgitation), and size of transannular patch (which can cause large segments of the right ventricular outflow tract to be akinetic or dyskinetic).[63] Outcomes of early primary surgical repair are summarised in Table 3.

Future innovations

New methods are constantly being explored to improve outcomes for patients with Tetralogy of Fallot. With advancing technology within surgery, this is increasingly possible. Technology such as 3D-printing enhances both surgeons' practical skills and their detailed knowledge of specific patient's anatomy, which can improve procedural planning.[64] Another innovation is the use of virtual reality for training and enhancing the surgeon's perception of anatomy. A Cambridge hospital currently uses a number of virtual reality headsets for surgical training and preparation prior to complex surgery.[65]

Other future innovations involve using new technology to intervene in Tetralogy of Fallot patients as an alternative to the traditional surgical repair. These innovations include high-frequency ultrasound to ablate muscle mass – a potential solution for infundibular stenosis with supporting evidence for use in hypertrophic cardiomyopathy.[66] Use of new generation stents that can either mimic growth or biodegrade may alter right ventricular outflow tract stenting as a permanent alternative to surgical repair.[67] Furthermore, use of new perimembranous ventricular septal defect closure devices may provide an alternative to surgical ventricular septal defect closure.[66] While risk of damage to the aorta or conduction problems may be higher using device ventricular septal defect closure, randomised control trials report similar results in comparison to surgical closure – however, these are often in older and larger children.[66]

Another innovation is use of percutaneous pulmonary valve implantation as an alternative to surgical pulmonary valve replacement . One model predicts that three pulmonary valve replacements would be required throughout adult Tetralogy of Fallot life: an initial percutaneous pulmonary valve implantation in young adulthood, followed by one in middle age and another closer to old age.[68] The subsequent percutaneous pulmonary valve implantation would utilise the valve-in-valve percutaneous method, which involves inserting the valve using a catheter. This would limit patients to only one surgical intervention after Tetralogy of Fallot repair.[68] While applying this model in real life might prove challenging, studies have established that

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Table 3. Outcomes of early primary repair

Outcomes	Early Repair
Cardiopulmonary Bypass Time	Earlier neonatal repair (average of 23 days): average of 137 minutes.[43]
Length of PICU stay	Average of 6 days in those having an open repair at under 6 months of age. 90% increase in PICU length of stay compared to a staged approach.[52]
	Earlier neonatal repair (average age of 23 days): PICU length of stay 5 days and a total hospital stay of 10 days.[43]
Short-term outcomes	Higher risk of mortality in those with complete neonatal repair during hospital stay, at 30 day follow-up, and 2-year follow-up.[54]
	Patients with neonatal repair had increased cardiac complications (ECMO, Pleural effusion, need for CPR).[54]
	Common complications include: residual ventricular septal wall defects, residual and persistent RVOTO, arrhythmias (ventricular tachycardia or atrial fibrillation/flutter), RBBB, or sudden cardiac death and Pericardial effusion requiring draining.[55,61]
Long-term outcomes	Long-term survival after TOF repair is generally very good, with >90% of patients surviving after close to 30 years follow-up.[35,59]
	Pulmonary regurgitation (PR) is the most common long-term complication in patients who survive TOF repair; 20 years after complete repair up to 64% of patients have pulmonary regurgitation.[60]
	PR contributes dilatation in TOF patients, which reduces exercise tolerance and increases risk of RV dysfunction, heart failure, and sudden cardiac death.[62]
	Frequency of repaired TOF complications, such as arrhythmia (n = 12 [8.3%]), cardiac arrest (n = 34 [23.5%]), and congestive heart failure (n = 26 [17.9%]).[59]

PICU, Paediatric ICU; RVOTO, right ventricular outflow tract obstruction; RBBB, right bundle branch block; TOF, Tetralogy of Fallot; RV, right ventricle.

percutaneous pulmonary valve implantation can reduce the number of surgeries in a patient with Tetralogy of Fallot.[69] However, use of innovations which may worsen outcomes is controversial, particularly because outcomes following surgical Tetralogy of Fallot repair are generally very good.

Conclusion

Tetralogy of Fallot repair has very good outcomes overall, with >90% survival at 30 years. The ideal time for intervention is around 6 months. However, in the symptomatic neonate with insufficient pulmonary blood flow, early intervention is required. In some patients, a staged repair with stent palliation is preferable to early primary repair. This is often in patients with small size, complex anatomy, or comorbidities. Long-term survival between staged repair and primary repair appears to be similar. There is lack of studies that compares long-term survival of newer stent palliation methods to neonatal complete repair. This highlights a need for further evidence, particularly as these options become more popular in comparison to the traditional option of a Blalock-Taussig shunt.

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