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Review Article

At what age should tetralogy of Fallot be corrected?

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Abstract Tetralogy of Fallot can be corrected with very low mortality at any age, even in neonates, but this does not necessarily mean that it should be corrected in the neonatal period. Although there are many advantages to early correction, a high proportion of these neonates have residual stenosis or pulmonary regurgitation that impairs ventricular function and may require further surgery or implantation of a pulmonary valve. Before we had the ability to correct this anomaly with low mortality in small children, a variety of palliative procedures had to be performed. Today, with better understanding of the anatomy of tetralogy of Fallot, we should consider what forms of palliation will increase growth of the right ventricular outflow tract in order to reduce the complications of very early surgery.

Keywords: Pulmonary stenosis; infundibulum; balloon valvotomy; propranolol

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In the early days, open-heart surgery was seldom used in infants because anaesthetic, surgical, and postoperative techniques were inadequate; therefore, repair of a complex lesion such as tetralogy of Fallot was deferred until the child was several years old. If cyanosis was too severe, a systemic-to-pulmonary artery shunt was used as palliation. With experience, techniques improved, and eventually it became possible to perform a complete repair of tetralogy of Fallot in the neonate with very low mortality. The age distribution of total correction is shown in Figure 1, derived from the Society of Thoracic Surgeons Database.[1]

The question to be asked is "what is the optimal age for correction?".

The advantages of early correction (<3 months of age) are multiple. Restoring normal arterial oxygen saturation facilitates growth, possibly improves brain function, and avoids the occurrence of hypercyanotic spells that do not usually appear until after 3 months of age. Prolonged hypoxaemia causes polycythaemia that increases the risk of intracranial thrombosis or abscess. Early surgery also reduces the duration of severe parental anxiety. These are all worthwhile achievements, but they come at a cost. In more severe forms of the anomaly, the pulmonary annulus[1] is unusually small, and the surgeon is faced with the decision to leave some obstruction or else cut across and enlarge the pulmonary annulus – transannular patch – thereby causing pulmonary valve regurgitation and all of its late consequences, including replacing the abnormal valve. For many of these patients what we term "complete correction" is really palliation.

Shimazaki et al[2] found that the size of the pulmonary annulus in tetralogy of Fallot ranged from +3z to −12z, with a median value of −2z; z indicates the number of standard deviations from the mean.[2] The probability of requiring a transannular patch was 39% when z was −3 and up to 94% when z was −5; the probability of systolic pressure in the right ventricle being >0.7 of that of the left ventricle even if a transannular patch was used was 11% for z of −3 and 26% for z of −8.[2] With a hypoplastic right ventricle, there is little chance of having both a

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[1]The pulmonary annulus is the term used to describe the junction of the pulmonary artery and right ventricle. It is not a fibrous ring, but rather muscle with perhaps thickened endocardium.

[2]z depends on age and body size, and there are no consistent standards.[3]

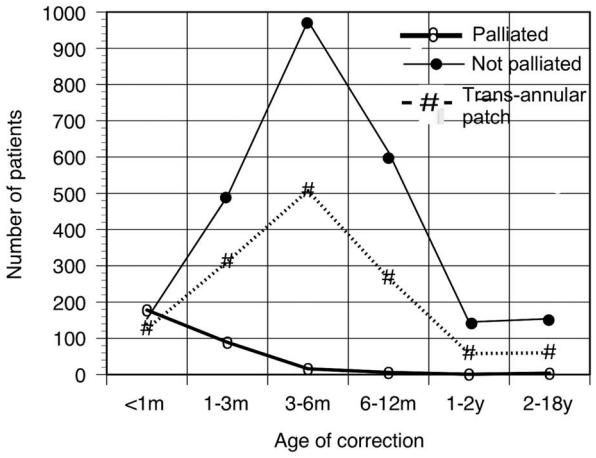

Figure 1.
The age distribution at time of corrective surgery for those with and without previous palliation, and frequency of transannular patch in those without previous palliation. The percentage needing a patch was the highest among the youngest (and smallest) children. Palliation was almost always by an arterio-pulmonary shunt. Study years 2002–2007.

normal right ventricular systolic pressure and an intact pulmonary valve. According to the Society of Thoracic Surgeons Database,[1] 52% of 2534 patients required a transannular patch without previous palliation, but 66% of 217 patients with previous palliation required a patch. This may reflect the greater severity in those who needed palliation. A more recent study by Luijten et al[4] of 453 patients with tetralogy of Fallot (median age 0.6 years) noted that 65% needed a transannular patch. In the European Association for Cardio-Thoracic Surgery Congenital Database,[5] 57.5% of patients had a transannular patch, and on average these patients were about 22 months of age, whereas those without a patch were on average 34.4 months of age.

What are ways around this dilemma? One possibility would be to develop procedures for reconstructing the outflow tract that do not leave residual stenosis and do not cause pulmonary regurgitation. Although several attempts have been made, none has achieved long-term success. Until that can be done, other methods are needed. At present, there are four candidates a systemic-to-pulmonary artery shunt, infundibulectomy, long-term treatment with a β-adrenergic blocking agent, and balloon dilatation of the infundibulum.

Before discussing therapy, we need to appreciate that tetralogy of Fallot covers a wide range of anatomical abnormalities.[6] In principle, the outflow tract of the right ventricle is hypoplastic, with abnormally placed muscle bands in the infundibulum, a hypoplastic pulmonary valve attachment (annulus), and a pulmonary valve that in about 75% of patients is stenotic. The main and branch pulmonary arteries are small and sometimes stenotic. Obstruction to outflow from the right ventricle can therefore occur at one or more of these sites. In some patients, the outflow tract is so hypoplastic and distorted that it is unlikely that any non-surgical approach can palliate it.

Systemic-to-pulmonary artery shunt

The Blalock–Taussig–Thomas shunt was the first attempt to palliate cyanosis in tetralogy of Fallot by anastomosing the subclavian artery to the ipsilateral pulmonary artery. Subsequently, anastomoses were created between the descending aorta and the left pulmonary artery – Potts anastomosis – or between the ascending aorta and the right pulmonary artery – Waterston anastomosis; these latter two anastomoses were difficult to make the right size, and soon dropped out of favour. More recently, a polytetrafluorene tube has been interposed between the subclavian and pulmonary arteries – modified Blalock–Taussig–Thomas shunt. The mortality for these procedures is now <10%,[7,8] quite an achievement considering that these operations are performed on the smallest and sickest children.

These shunts are usually successful in increasing arterial oxygen saturation. There is also evidence that they may increase the size of the right ventricular outflow tract and pulmonary arteries,[9–13] although whether the increase in annular diameter is more than expected from normal growth is uncertain. From the data of Al Habib et al,[1] the fact that the percentage of patients requiring a transannular patch was higher for those with palliation than without palliation suggests that the shunt did not increase growth of the right ventricular outflow tract. Even if shunts do increase annular diameter, they have a number of potential complications,[14] and make the final correction more complicated; therefore, other alternatives need to be considered.

Infundibulectomy

This surgical operation was introduced by Brock and Campbell in 1949[15] and was moderately successful. Others repeated these results, for example, Lin et al,[16] but the advent of complete correction with open-heart surgery made this operation obsolete. Now that it is possible to perform infundibulectomy with catheters with cutting blades,[17] it might be worth reconsidering using a non-surgical infundibulectomy.

β-Adrenergic blockade

Hypercyanotic spells in tetralogy of Fallot were thought to be due to spasm of the infundibular

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muscle, and it was known that the abnormal muscle in hypertrophic cardiomyopathy contracted excessively with β-adrenergic stimulation, and that a β-adrenergic blocking agent could decrease the contraction. In 1964, Honey et al[18] showed that β-adrenergic blockade with pronethalol increased arterial oxygen saturation in patients aged 14–38 years with tetralogy of Fallot, and in 1966 Singh and Gotsman[19] showed that pronethalol would abolish the hypercyanotic spells in very young children. Owing to its toxicity, pronethalol was replaced by propranolol, and in 1966 Cumming and Carr showed that it too abolished hypercyanotic spells in three infants. Many similar case reports were soon published, and in 1969 Eriksson et al[20] published the first report on the long-term successful treatment of tetralogy of Fallot in children aged 2–11 years, with success being judged by an increase in arterial oxygen saturation and a reduction or abolition of hypercyanotic spells. These children had been selected for treatment on the basis of a favourable response to propranolol during cardiac catheterisation. They were given 1 mg/kg of propranolol four times daily.

Since then, propranolol has been used by many centres.[21,22] It is not always effective.[23] At times ineffectiveness may be due to too small a dose; Garson et al[22] observed that failure was more likely in patients given doses of 1.2 versus 2.6 mg/kg. Adrenergic blockade would also be ineffective if the major sites of obstruction were at the pulmonary valve or pulmonary artery. Today, it would be easy using pulse oximetry to determine which patients respond to propranolol and what dose is needed.

Studies have shown that patients on long-term propranolol at the time of corrective surgery are not at a disadvantage,[24,25] although Barazzone et al[26] demonstrated that the effects of isoproterenol were blunted but could be overcome by giving higher doses of the adrenergic agent. To avoid intraoperative problems, Garson et al[22] discontinued propranolol 4 days before surgery, but this risks having hypercyanotic spells before or even during surgery.

There are potential complications with long-term propranolol. Occasionally with higher doses, patients may develop congestive heart failure.[22] The possibility of severe hypoglycaemia must always be considered and checked,[27,28] and occasionally severe bradycardia leads to withdrawal of the drug.[29] Apart from these problems, in a minority of patients, propranolol does improve arterial oxygen saturation and reduces or abolishes hypercyanotic spells. The big unanswered question is whether the added months of growth make reconstruction of the outflow tract easier. Is body growth accompanied by annular growth?

Balloon dilatation and stenting

A second approach would be to dilate the stenotic pulmonary valve and/or infundibulum with a balloon, thus allowing more flow and time for growth to occur – Brock[30] had shown that surgical valvotomy relieved cyanosis, but balloon valvotomy is much more convenient. Qureshi et al[31] used an atherectomy catheter to perform a myomectomy. Several groups used stents to keep the outflow tract wide.[32–39]

Most of these studies showed an improvement in arterial oxygen saturation and a growth of the pulmonary arteries.[32–39] The effect on the pulmonary annulus was mixed. Almost all studies that reported changes in the annulus used z values. As the annulus tends to increase in size with age, even in tetralogy of Fallot, the z value indicates whether the increased size is proportional to age – z value unchanged – or has increased beyond what is expected from ageing – less negative z value. Some studies related the size of the pulmonary annulus to the aorta, but this is less well validated. Several investigators described improved growth of the annulus by 2 SD or more,[40–46] and Kreutzer et al[47] found that z increased from −4.0 to −3.3.

In a series of 19 infants studied by Sluysmans et al,[45] a transannular patch was avoided in 69%, representing a 30–40% reduction from their usual practice; on the other hand, Battistessa et al[48] found that balloon dilatation caused no improvement, and Piechaud et al[49] had mixed results that on average were disappointing. Sreeram et al[50] noted that after balloon dilatation the annulus enlarged by an average of 29%, but this was no more than what occurred because of growth in those without dilatation. Although arterial oxygen saturations increased, the frequency of annular patching was unchanged.

As with all procedures, there is some risk of damage. Lamb et al[51] observed that at surgery 15 months after the balloon dilatation there was linear tear in the main pulmonary artery. Ugurlu et al[52] noted at surgery two pseudoaneurysms in the outflow tract.

Conclusion

The final decision about the optimal timing of repair of tetralogy of Fallot that will leave minimal distortion of the right ventricular outflow tract cannot be determined with the information discussed above; it will take years of clinical trials to do that. What I have tried to do is to show that some forms of palliation should be reconsidered.

Given the wide variety of pathological findings in tetralogy of Fallot, no one treatment is likely to be effective in all these patients; the "one-size-fits-all"

approach is doomed to failure. Failure to improve may be due to selecting the wrong form of treatment for the anatomy; valvotomy will not help the patient if the main obstruction is infundibular, and propranolol will not be useful if obstruction is mainly at the valve level; therefore, it is first necessary to determine the anatomy of the right ventricular outflow tract and to base therapy on the findings. If the main obstruction is at the pulmonary valve, then balloon dilatation of the valve is a reasonable choice. If the main obstruction is at the infundibulum, then propranolol is the first choice. Sometimes relief of an obstructive pulmonary valve may be associated with an increase in infundibular obstruction when the distending ventricular pressure is decreased, and as obstruction may occur at more than one site in any patient there is no reason why a patient should not get propranolol and balloon dilatation, with perhaps stenting of the outflow tract if the infundibulum remains obstructive. Infundibulectomy remains a possible treatment if other methods do not work.

There is no guarantee that palliation will improve outcomes, but if palliation appropriate to the abnormal anatomy is successful in many patients, subsequent repair may be easier and more successful.

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Conflicts of Interest

None.

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