

Adult Congenital Heart Disease Right Ventricular Outflow Tract Lesions

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It has variably been estimated that between 800 000 and 1 million patients with congenital heart disease are now adults and that by 2010 more patients older than 16 years will undergo surgery for congenital heart disease than those younger than 16 years.¹ This review will focus on the clinical aspects of identifying and caring for the portion of the unique population that have right ventricular (RV) outflow tract lesions.

Clinical Morphology of the RV Outflow Tract

The left ventricle (LV) and RV both have inlet, apical, and outlet portions, although they differ considerably.² The inlet of the RV includes the tricuspid valve, and it is separated from the pulmonary valve (PV) by the crista supraventricularis. This structure results in the PV being raised upward. The apical portion of the RV has coarse trabeculations. As shown in Figure 1, the septum is home to a large septomarginal (septal) trabeculation that divides into the anterior and posterior limbs in the outflow tract. A series of septoparietal trabeculations arise along the free wall. The crista supraventricularis inserts between these limbs and is made up of 3 components: the muscular outlet septum, the ventriculoinfundibular fold, and the inner curvature of the RV.³ The small part that separates the RV and LV cavities is the outlet or conal septum. A loop including the septal trabeculation, the moderator band, septoparietal trabeculations, and the outlet septum can be conceptualized as circling the RV outflow tract. The PV is supported by the circular muscular infundibulum rising outside the RV proper. Abnormalities involving the RV outflow tract involve malpositioning of 1 or more of these structures.

Congenital Lesions That Produce RV Outflow Tract Obstruction

Obstruction to the RV outflow tract may be the result of abnormalities at the mid-RV, the infundibulum, the PV, the supravulvar region, or the branch and/or peripheral pulmonary arteries. Previous surgery may be responsible for some obstructive lesions as well. Table 1 outlines both native and postoperative congenital obstructive lesions.^{4–13}

PV Stenosis

Clinical Assessment of PV Stenosis

General Considerations

Clinically, there are 3 morphological types of congenital pulmonary stenosis (PS).¹⁴ (1) The typical dome-shaped PV is characterized by a narrow central opening but a preserved, mobile valve. Primarily because of an inherent medial abnormality, the pulmonary trunk is usually dilated. (2) The dysplastic PV is poorly mobile, and there is myxomatous thickening with no commissural fusion. The annulus and the outflow tract may be narrowed. (3) The unicuspid or bicuspid PV is generally a feature of tetralogy of Fallot, and stenosis is variable.

Many patients with PS are asymptomatic when first seen. With severe PS, RV hypertrophy develops, and symptoms of dyspnea, fatigue, chest pain, palpitations, presyncope, and decreased exercise tolerance may occur. If the right atrial (RA) pressure increases, the opening of a patent foramen ovale may occur along with cyanosis.

The dome-shaped PV is present in ≈7% to 12% of cases of congenital heart disease^{14–16} with equal sex distribution. It makes up to 80% to 90% of all congenital RV outflow tract lesions.¹⁶ Its inheritance is low, varying from 1.7% to 3.6%.^{17,18} In a study of 558 patients with microdeletions in the DiGeorge chromosomal 22q11 deletion, only 2% were found to have PS.¹⁹ Approximately 20% of patients with PS have a dysplastic valve^{20,21} and, if part of Noonan's syndrome, have an autosomal dominant trait with variable penetrance that has been mapped to chromosome 12.^{22–24}

Survival into adulthood is usual. In the Second Natural History Study of Congenital Defects,²⁵ there was no progression in patients with peak gradients <25 mm Hg, there was a 20% chance of an intervention if the gradient was between 25 and 49 mm Hg, and intervention was generally required with gradients >50 mm Hg (Figure 2).

Clinical Hemodynamics of PV Stenosis

The valvular PS jet may be directed toward the left pulmonary artery (PA), resulting in unequal distribution of blood flow in favor of the left lung.²⁶ The mobile PV creates an auscultatory ejection click that decreases with inspiration, as

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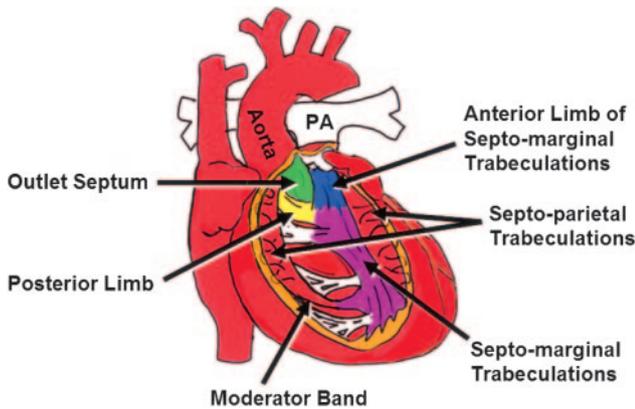


Figure 1. The anatomy of the RV outflow tract.² There is a large septomarginal (septal) trabeculation that divides into 2 limbs. The anterior limb supports the leaflets of the PV, and the posterior limb runs beneath the membranous septum. A series of trabeculations also arise along the free (parietal) wall of the RV: the septoparietal trabeculations. The crista supraventricularis is between the limbs of the septal trabeculation. The small part that separates the RV and LV cavities is the outlet or conal septum.

the right atrial kick into the stiff RV prematurely lifts the PV upward before systole (so there is less excursion of the valve in systole during inspiration compared with expiration, and therefore less click intensity). In severe PS or in patients with a dysplastic valve, there is less mobility and loss of the ejection sound altogether. The hemodynamic grading and physical examination grading of the severity of PS are outlined in Table 2.

History and Physical Examination

Most adult patients with PV or other outflow tract obstructive lesions are normal in appearance, although certain phenotypical syndromes occur that include valvular, branch, or peripheral PS. These include the rubella syndrome²⁷; Noonan syndrome,²¹ in which 60% have a dysplastic valve; Alagille syndrome²⁸ or arteriohepatic dysplasia; Williams syndrome²⁹; and Keutel syndrome.³⁰

The cardiac examination of a patient with PV stenosis is dependent on the valvular severity, the pathology of the valve, and any associated cardiac lesions. Table 2 outlines the expected findings. Pulmonary insufficiency (PI) is uncommon.

Associated Laboratory Studies

The ECG is generally normal when the RV systolic pressure is <60 mm Hg.³¹ As the lesion severity worsens, evidence of RA enlargement, right axis deviation, and RV hypertrophy may occur.³¹

The heart size on chest x-ray is normal unless there is RV failure or an associated cardiac lesion. Vascular fullness in the left lung base greater than the right (Chen's sign) is due to the preferential flow.²⁶ In severe PS, vasculature markings may be diminished. Dilatation of the main PA is common in doming but not in dysplastic PS or in subpulmonic stenosis. Calcification may be seen in older patients. The RA and RV may be enlarged if there is RV decompensation.

The echocardiogram is generally definitive. A Doppler gradient is evident (Table 2), the valve mobility can be

TABLE 1. Congenitally Related Causes of RV Outflow Tract Obstruction Seen in Adult Patients

Unoperated
Valvular
Dome-shaped PV
Dysplastic PV
Unicuspid or bicuspid PV
Infundibular stenosis, usually associated with tetralogy of Fallot
Hypertrophic infundibular stenosis
Associated with PS, hypertrophic cardiomyopathy
Infundibular obstruction
Tricuspid valve tissue
Fibrous tags from inferior vena cava or coronary sinus
Aneurysm of the sinus of Valsalva
Aneurysm of the membranous septum
Subinfundibular obstruction
Double-chambered RV
Supravalvular stenosis
Hourglass deformity at valve
PA membrane
PA stenosis
PA aneurysm
Peripheral PA stenosis
Associations: rubella, Alagille, Williams, Keutel syndromes
Operated
Valvular
Native valve restenosis
Prosthetic valve stenosis
Conduit stenosis
Double-chambered RV restenosis
Peripheral or branch PS
At insertion site of prior systemic-to-pulmonary shunt
After other complex surgical repair
Infundibular stenosis after tunnel repair of double-outlet RV

assessed along with subpulmonic or supravalvular stenosis, and the size and function of the RV can be determined. Continuous, pulsed, and color-flow Doppler confirm any PI, tricuspid regurgitation, or right-to-left shunting. Saline microcavitations can also confirm a right-to-left shunt. When the PS is severe, interventricular septal flattening may occur. In patients with a dysplastic valve, the valve is thickened and immobile, and there is lack of a dilated pulmonary main trunk. Transesophageal echocardiography does not usually add additional diagnostic information.

In uncomplicated PV stenosis, the use of magnetic resonance imaging (MRI) or computed tomography is simply confirmatory. These studies provide excellent imaging of the main, branch, and peripheral PAs.

Cardiac catheterization is rarely necessary for diagnosis. Gradients above, at, and below the PV should be obtained. A peak RV systolic value of <35 mm Hg and a systolic PV gradient of <10 mm Hg are the upper limits of normal. RV function can be assessed, and shunting through any patent

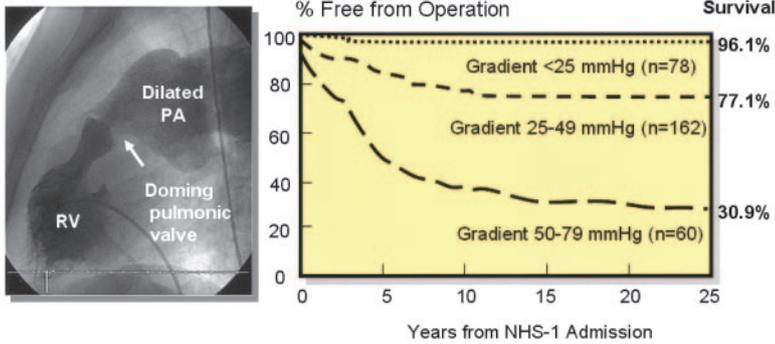


Figure 2. PV stenosis. Left, Angiography in dome-valve PV stenosis. Lateral view of classic dome PV stenosis. Note mild subpulmonic obstruction and markedly dilated main PA. Right, Outcome of medically managed patients with PS in the First Natural History Study (NHS-1). Patients with gradients >80 mm Hg were operated on. Graph reveals surgery-free survival in patients with entry gradients of <25, 25 to 49, and 50 to 79 mm Hg. Parentheses represent number of patients under observation at the 25-year anniversary. Reproduced from Hayes et al²⁵ with permission from the American Heart Association. Copyright 1993.

foramen ovale can be defined. RV angiography helps to define contractile function, the presence of infundibular obstruction, and the mobility of the PV (Figure 2). Pulmonary angiography assesses the degree of PI and any stenotic lesions in the main, branch, or peripheral PAs.

Following Up the Unoperated Patient With PV Stenosis

There is little progression in PS severity when the peak Doppler gradient is <30 mm Hg; patients can be followed up every 2 to 3 years. Those with more significant stenosis should be followed up yearly.

There is no specific medical therapy. Right heart failure is treated with diuretics. Patients with atrial arrhythmias require medical or ablation therapy. Sudden death is very rare.³² Pregnancy is well tolerated unless the lesion is extremely severe, and percutaneous valvuloplasty can be performed during pregnancy if necessary.

The 1986 American Heart Association committee report³³ recommends no restriction of activity with mild PS and nonstrenuous exercise with moderate PS and restricts only those with severe PS. For the competitive athlete, the Special Task Force report³⁴ recommends that PS patients with gradients <50 mm Hg may participate in all competitive sports; those with severe PS should only participate in low-intensity sports.

Pulmonary endocarditis is rare,³⁵ and some recommend prophylaxis only with a >25 mm Hg gradient.³⁶ The guidelines continue to endorse endocarditis prophylaxis, however,³⁷ although it is anticipated that newer revisions of the guidelines will not recommend it.

Indications for Intervention

On the basis of natural history studies of the outcomes on unoperated patients with gradients >50 mm Hg (Figure 2), patients with severe PS should undergo intervention. The recent American College of Cardiology/American Heart Association Task Force report on valvular heart disease³⁸ has extended these data, and their recommendations are summarized in Table 3.

Surgical and Percutaneous Intervention

Surgical Intervention

Surgical commissurotomies are quite effective and are now done by direct visualization. In patients with a dysplastic valve, partial or total valvectomy and valve replacement are usually required, and a transannular patch may be needed if there is annular or pulmonary trunk hypoplasia. Residual PI is commonplace with surgical procedures.³⁹

In patients with PS and significant PI, valve replacement is required. Mechanical valve replacement is used rarely be-

TABLE 2. Grading the Severity of PV Stenosis Hemodynamically³⁶ and by Physical Examination

Hemodynamic Evaluation: Degree of Obstruction	Hemodynamic Evaluation: Peak Systolic Doppler Gradient, mm Hg	Hemodynamic Evaluation: RV Systolic Pressure, mm Hg	Physical Examination
Trivial	<25	<50	...
Mild	25-49	50-74	Jugular venous pressure: Normal except mildly increased "a" wave RV palpation: No RV lift Auscultation: Ejection sound present (decreases with inspiration); systolic ejection murmur increases with inspiration and ends in mid-systole; generally grade 3/6 or less
Moderate	50-79	75-100	Jugular venous pressure: Elevated; "c-v" wave if TR present;
Severe	>80	>100	Increased "a" wave RV palpation: RV lift; generally no impulse over PA; thrill may be present Auscultation: No ejection sound; prolonged RV outflow tract systolic ejection murmur with no P2 or wide split of second sound if P2 present; murmur often 3-6/6 in intensity; right-sided S4

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TABLE 3. Recommendations for Percutaneous Balloon Valvuloplasty in Patients With PV Stenosis**Class I**

Symptomatic patients with classic PS with a peak systolic gradient >50 mm Hg and $<2+$ PI (Level of evidence: B)

Balloon valvuloplasty may be reasonable in symptomatic patients with classic PS and a peak systolic gradient >30 mm Hg and $<3+$ PI (Level of evidence: C)

Balloon valvuloplasty may be reasonable in asymptomatic patients with classic PS and a peak systolic gradient >40 mm Hg and $<3+$ PI (Level of evidence: C)

Class IIb

Balloon valvuloplasty may be reasonable in asymptomatic patients with classic PS and a peak systolic gradient between 30 and 40 mm Hg and $<3+$ PI (Level of evidence: C)

Balloon valvuloplasty may be achievable in selected symptomatic patients with a dysplastic PV and peak systolic gradient >30 mm Hg (Level of evidence: C)

Class III

Balloon valvuloplasty is not recommended for most patients with dysplastic PV disease, for patients with a peak PV gradient <30 mm Hg, or for those with concomitant $3+$ or greater pulmonary valve insufficiency (Level of evidence: C)

Adapted from Bonow RO et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease). *Circulation*. 2006;114:450–527, with permission from the American Heart Association. Copyright 2006.

cause of thrombosis issues and the possible future need for pulmonary pressure measurement. Bioprosthetic valves^{40,41} and pulmonary homografts^{40,42} have both been used with good results, the latter allowing for replacement of the main PA.⁴³ Rarely, a valved conduit is required for anatomic reasons or because of an anomalous coronary crossing the RV outflow tract that might be injured.

Significant outflow obstruction can occur postoperatively in the pulmonary homograft with the Ross procedure. Postoperative valves, conduits, or homografts placed for other reasons can also contribute to the causes of clinical RV outflow tract obstruction. Bioprosthetic valvular degeneration is expected after ≈ 10 to 12 years,⁴⁴ and porcine valves may outlast homografts in children.⁴⁵

Percutaneous Balloon Valvuloplasty and Valve Replacement

Since the initial successful report of percutaneous balloon valvuloplasty for PV stenosis in 1982,⁴⁶ the procedure has evolved to be the treatment of choice for patients with classic domed PS. A successful procedure is defined by final peak gradient of <30 mm Hg and is obtained in $>90\%$.

Ten-year follow-up data are now available with excellent outcomes,⁴⁷ and the restenosis rate is low, generally occurring only if there was a residual gradient immediately after the procedure.⁴⁸ Rarely, dysplastic valves will respond to balloon valvuloplasty.

Several studies have compared balloon valvuloplasty with matched surgical controls^{49–51} and have found similar long-

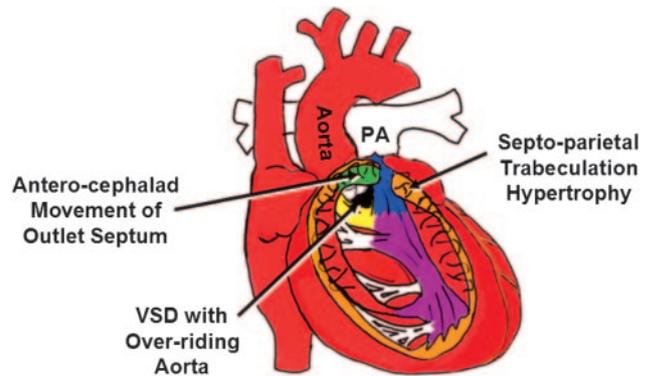


Figure 3. The anatomy of tetralogy of Fallot. The key issues are schematically shown. As noted by Anderson and Weinberg,³ components of the supraventricular crest have “sprung apart.” The cardinal feature is the anterocephalad deviation of the outlet septum. The secondary necessary feature is hypertrophy of the septoparietal trabeculations in order for subpulmonic obstruction to be present. The other classic features include RV hypertrophy, an interventricular communication (VSD), and an overriding aorta (shown through the VSD).

term results, although there appears to be more PI and ventricular ectopy in the surgical groups.⁴⁹

Recently, the use of percutaneous valve replacement has received widespread attention. Led by Khambadkone and Bonhoeffer,⁵² the procedure has been deployed successfully in RV outflow conduits⁵³ and has now been extended to include patients with native PS.

Following Up the Postoperative or Postintervention Patient

The clinical issues regarding intervention in the postoperative patient are similar to those preoperatively except for more valvular regurgitation. In the low-pressure PI setting, the diastolic gradient between the RV and PA may be small, and significant PI may be difficult to detect. Any unexplained enlargement of the RV should trigger concern that PI is more severe than noninvasive evaluation suggests.

Tetralogy of Fallot**Clinical Assessment****General Considerations**

Although actually not the first to describe this defect,⁵⁴ Etienne-Louis Arthur Fallot eloquently described the complex of 4 anatomic features that now bears his name: subpulmonary infundibular stenosis, ventricular septal defect (VSD), rightward deviation of the aortic valve with overriding of the ventricular septum, and RV hypertrophy. The range of anatomic features includes minimal overriding of the aorta and trivial PS to 95% override of the aorta and frank pulmonary atresia.

Figure 3 outlines and describes the basic anatomic features of tetralogy of Fallot.⁵⁵ The key features are the anterocephalad deviation of the outflow septum and hypertrophy of the septoparietal trabeculations. Because the outlet septum is an RV structure, malalignment of the outlet septum in this direction results in a VSD and partially commits the aorta to the RV. The VSD is large; the PV is often unicuspid or

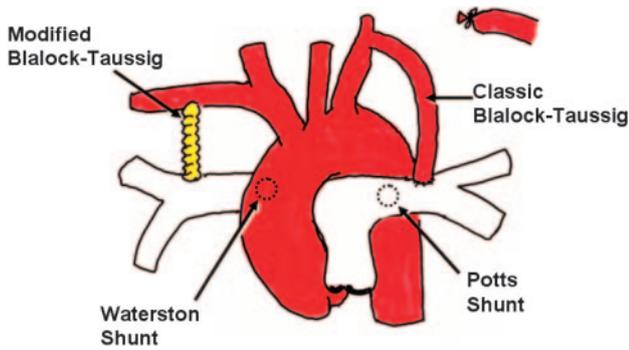


Figure 4. Palliative surgical shunts. Whenever there is inadequate pulmonary blood flow, palliative shunts may be of value before definitive correction. The sketch shows the classic subclavian artery-to-PA shunt (Blalock-Taussig), the modified Blalock procedure with the use of a tube of polytetrafluoroethylene, the Waterston shunt between the ascending aorta and right PA, and the Potts shunt between the descending aorta and left PA. See text for discussion.

bicuspid. Pulmonary branch stenosis and various degrees of PA hypoplasia may also be present, with some patients even lacking an entire main PA (most often the left branch PA, where it may hang onto the aorta via the ductus). A left PA branch coarctation in the region of the ductal insertion may also be present. The biventricular aorta is usually dilated, arises from a right-sided arch in $\approx 25\%$ of patients, and may override the septum so much that $>50\%$ comes from the RV (consistent with the definition of a double-outlet RV). The overriding aorta also tends to rotate clockwise, so that the right coronary artery is more anteriorly placed. The left anterior descending coronary artery may arise anteriorly from the right coronary artery and cross the RV outflow; when this occurs, the surgical repair may require a bridging conduit from the RV to the PA. An atrial septal defect is present in $\approx 5\%$ (sometimes called pentalogy of Fallot).

Tetralogy of Fallot is the most common cyanotic heart defect that survives to adulthood, accounting for $\approx 10\%$ of all congenital defects.⁵⁶ The recurrence rate from parent to child has been estimated at 1.2% to 8%.⁵⁷ A missense mutation for encoding a ligand expressed in the developing heart has been reported,⁵⁸ as has a mutation in the transcription factor NKX2.5.⁵⁹ In a recent study of 251 patients, 15.9% of tetralogy of Fallot patients had chromosome 22q11 microdeletions.⁶⁰

Tetralogy of Fallot is a progressive problem, and patients do poorly without surgical correction; from the Danish population study, only 4% lived to the age of 15 years.⁵⁶ By the time most reach adulthood, some palliative or corrective surgery has been performed.

Clinical Hemodynamics

In the unoperated patient, there is subpulmonic obstruction with a nonrestrictive (large) VSD and variable degrees of PS. PV insufficiency is uncommon. Pulmonary hypertension occurs only if there has been inadequate RV outflow obstruction to prevent pulmonary vascular disease. With less RV outflow tract stenosis, there is minimal or no cyanosis (the so-called “pink tetralogy”) because the VSD shunt is primarily left to right. The degree of right-to-left shunting is related

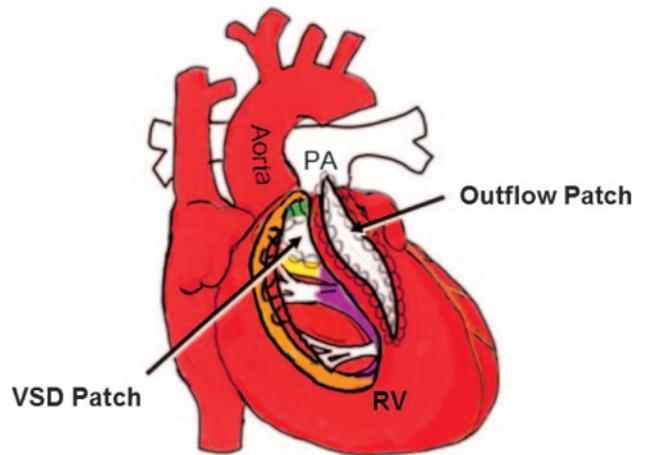


Figure 5. Classic repair in tetralogy of Fallot. An outflow patch of pericardium is used to relieve subpulmonic obstruction, and the VSD is closed with a pericardial or Dacron patch. If valvular PS is present or the main PA is hypoplastic, the outflow tract is extended into the main PA.

more to the severity of the RV outflow tract obstruction than to the degree of aortic override.⁶¹

By adulthood, the majority of surviving patients have had either palliative or more definitive repair. Palliative procedures generally include some type of systemic arterial-to-pulmonary arterial shunt (Figure 4). Palliative shunts are taken down when more definitive surgery is performed.

The classic repair includes a VSD patch, an RV outflow tract patch, and infundibular resection (Figure 5). For many patients, there is often either a concomitant surgical pulmonary valvuloplasty or a transannular patch that opens the entire RV outflow tract and crosses the PV (often resulting in PI). More recently, the problem of long-standing postoperative PI has been better appreciated, and valve replacement has been used in older children and young adults.

Varying degrees of LV dysfunction may also coexist and be a risk factor for sudden death.⁶² The cause of this associated LV dysfunction is unclear, although chronic hypoxia and long operative procedures, inherent muscle bundle abnormalities, and abnormal RV-LV interaction due to the dilated RV have all been implicated. Prolonged LV volume overload from the VSD, from palliative shunts, or from aortic insufficiency and surgical injury to the left anterior descending artery arising from the right coronary undoubtedly contribute in some cases.

History and Physical Examination

Adult patients are often asymptomatic. In the unoperated adult patient, cyanosis is common, although extreme cyanosis or a history of classic squatting (done to increase the systemic resistance and reduce systemic venous return) is uncommon. In repaired patients, late symptoms include exertional dyspnea, palpitations, right heart failure, syncope, and even sudden death.

Although a patient may present rarely with a peculiar phenotype, most look normal physically. Cyanosis and clubbing may be present. The brachial pulse on the side of a prior Blalock-Taussig shunt is often not present or markedly diminished (despite collaterals). The jugular venous pressure

is usually normal unless there is evidence for RV dysfunction, in which jugular venous distension and the presence of a large “a” wave may be noted. Tricuspid regurgitation may be present, and an RV lift is common. A right-sided arch may cause a lift below the right sternoclavicular junction. On auscultation, ejection sounds from the dilated aorta and any aortic insufficiency murmur may be present, and an RV outflow murmur is audible along with a holosystolic murmur from a residual VSD. Lesions in the pulmonary branches may create systolic or continuous murmurs along the chest wall. PI is common after transannular patching, but the intensity may be modest even in severe PI because it is usually associated with normal or low pulmonary pressures. The pulmonic second sound is usually inaudible. A right-sided S4 may be present. The LV examination is usually normal unless there is associated LV dysfunction.

Associated Laboratory Studies

The ECG is extremely important. RV hypertrophy with a right bundle-branch block is common. Postoperatively, from 0.5% to 5.5% of patients die suddenly or require therapy for ventricular arrhythmias.⁶³ Ventricular arrhythmias often originate from the surgical right ventriculotomy site or interventricular septum.

Patients at risk for sudden death include those of older age and those with persistent postoperative RV systolic hypertension.⁶⁴ A QRS duration of >180 ms, QRS prolongation over time, and increased QT dispersion of refractoriness also help to identify high-risk patients.⁶⁵ QRS duration has also been correlated with RV volume and mass and may decrease after PV replacement.⁶⁶ Atrial and ventricular arrhythmias contribute to morbidity and mortality; they are more common in those who had palliative shunts for longer periods of time, in older patients, and in those with tricuspid regurgitation,⁶⁷ pulmonary regurgitation, and progressive RV enlargement.⁶⁸ Reduced heart rate variability has also been shown to be a marker of increased risk.⁶⁹

The chest x-ray in the adult usually reveals relatively normal pulmonary vascularity. Approximately one quarter will have a right-sided aortic arch. The classic “boot-shaped” heart results from a small underfilled LV lying superior to a relatively horizontal septum, below which is the hypertrophied RV. The heart shadow in adults is confounded by volume loading from a residual VSD or palliative shunt, pulmonary regurgitation, aortic regurgitation, tricuspid regurgitation, RV and/or LV systolic dysfunction, the size of any RV outflow patch aneurysm, and a right or left aortic arch. Progressive aortic root dilatation occurs in ≈15%.⁷⁰

The Doppler/echocardiogram provides confirmation of the lesions described. The low-pressure nature of the PI makes grading the severity of the PI difficult because the pulmonary arterial diastolic pressure is often only a few mm Hg higher than the RV end-diastolic pressure. A more rapid PI pressure half-time (<100 ms) has been proposed as a better indicator of PI severity.⁷¹ Transesophageal echocardiography is not needed for the diagnosis.

Multidetector computed tomography⁷² and cardiac MR can provide a wealth of information. The RV and LV volumes and mass can be quantified along with the status of the RV

outflow tract, the PAs, the aorta, and any residual VSD.^{73,74} MRI information often obviates the need for cardiac catheterization. Delayed enhancement in the RV outflow tract has also correlated with RV dysfunction and poor outcomes⁷⁵ and provides evidence for RV-LV interaction. Radionuclide angiography is often used to quantify RV function.

The role for cardiac catheterization is diminishing as MRI and other modalities are maturing. Pulmonary angiography can semiquantify the severity of PI and note branch or peripheral PS. Coronary anomalies can be documented along with any atherosclerosis. In patients with severe RV outflow obstruction, angiography can document systemic-pulmonary collaterals. The size of residual shunts and the documentation of pulmonary hypertension are important, and the extent of pulmonary vasoactivity can be assessed.⁷⁶

Following Up the Unoperated Patient

Morbidity in unoperated patients is high and includes cyanosis, right heart failure, exercise intolerance, atrial and ventricular arrhythmias, and paradoxical emboli. Despite this, survival up to age 84 years without surgical intervention has been reported.⁷⁷ Some adults will have had only palliative shunt procedures performed. The clinical status of these patients is dependent on the severity of the RV outflow tract obstruction, the size of the VSD, and RV function. The QRS duration should be noted, and at least yearly Holter monitoring should be performed. Late repair should be considered for symptomatic patients because improved survival is afforded by surgery done even after the age of 18 years.⁷⁸

Indications for Intervention or Reintervention

Most adult patients will have undergone classic repair, usually including VSD closure and an RV outflow patch. PI is inevitable after transannular patching. Symptomatic patients require reoperation, but the indications are still controversial in the asymptomatic patient. The result of chronic PI is RV dilatation and eventual RV failure, and surgical intervention is often delayed unnecessarily.^{79,80} Once there is any evidence for RV dysfunction, PV replacement should be performed. Exercise capacity often remains reduced after repair of tetralogy of Fallot. Indications for reoperation are outlined in Table 4.⁶⁸

Surgical or Percutaneous Intervention

Palliative Surgical Interventions

Figure 4 schematically displays the types of arterial-to-pulmonary shunts used to increase pulmonary blood flow. The

TABLE 4. Indications for Reintervention in Tetralogy of Fallot

Symptoms of right heart failure
RV enlargement or evidence for RV dysfunction, especially if PI present
Clinically significant arrhythmias (atrial or ventricular)
Progressive aneurysmal dilation of an RV outflow tract patch
Onset or progression of tricuspid regurgitation
Residual VSD with shunt >1.5:1
Residual patent arterial-pulmonary shunts leading to LV volume overload
Residual RV outflow tract or PS with systolic RV/LV 0.67
Significant aortic insufficiency with evidence for LV dysfunction
Dilated aortic root >5.5 cm

Data derived from Freedom and Shi-Joon⁵⁷ and Gatzoulis.⁶⁸

classic Blalock-Taussig shunt attaches the subclavian artery to the branch PA. The modified Blalock-Taussig approach, now the preferred method, uses a polytetrafluoroethylene (Gore-Tex) tube for shunt creation. Other approaches utilize surgical windows between the descending aorta and the left PA (the Potts shunt) and between the right PA and ascending aorta (the Waterston-Cookey shunt). The higher mortality, the problem of distortion of the small PAs, and the evidence for pulmonary hypertension after >5 years⁸¹ have resulted in the latter 2 central procedures being abandoned. There are still adult patients who have survived with only these shunts, however.

Total Repair of Tetralogy of Fallot

Primary repair for tetralogy of Fallot (Figure 5) was facilitated greatly by the development of prostaglandin therapy that allowed the ductus arteriosus to remain patent to stabilize these infants. The timing of complete repair in the neonate remains controversial,^{82,83} with some groups still favoring a staged procedure and others favoring primary early repair. If the left anterior descending coronary artery crosses the RV outflow tract, then a RV to PA conduit may be used.

The risk of surgical repair of tetralogy of Fallot is remarkably low at <5%.⁵⁷ Nollert and colleagues⁸⁴ reported actuarial 10-, 20-, 30-, and 36-year survival rates at 97%, 94%, 89%, and 85%, respectively. Death was most commonly due to heart failure or was sudden (presumably arrhythmic). Others have reported similar data.⁸⁵ In a Mayo Clinic series,⁶⁴ the overall 32-year actuarial survival was 86%. The most common cause of death was sudden.

Late PV Replacement

When there are indications for late PV replacement (Table 4), the procedure can also be done with low morbidity and mortality.⁸⁶ Several studies have noted that RV diastolic dysfunction persists in some patients after either repair⁸⁷ or PV replacement.⁸⁸ These data have led many to conclude that we are waiting too long for PV replacement.^{80,89}

Percutaneous Intervention

Percutaneous methods for repair of tetralogy of Fallot and its complications are still in development. Balloon angioplasty and/or stents have been used when there is valvular, branch, or peripheral PS. In a patient with branch stenosis and a patent Waterston shunt, a covered stent has been used to reduce the stenosis and close the shunt.⁹⁰ Cutting balloons have been successful in opening both the RV infundibulum and a stenotic PV.⁹¹ Recently, repair of postoperative pulmonary homograft or conduit stenosis and/or regurgitation has been tackled with the use of a percutaneous PV with good initial success,^{92,93} although the dilation of the RV outflow due to the surgical patch presents a problem for seating of a percutaneous valve.

Following Up the Postoperative Patient

The patients should be followed up for any indication for reintervention (Table 4). The ECG QRS width should be followed up. The risk of pregnancy in unrepaired tetralogy is high, but the risk is much less in patients who have undergone repair. In a study⁹⁴ of 29 patients after 63 pregnancies, complications of congestive heart failure or arrhythmias

occurred in 19%. In another study,⁹⁵ 43 patients had 112 pregnancies, but 40 miscarried. Patients who developed symptoms during the pregnancy had LV dysfunction, pulmonary hypertension, or severe PI with baseline RV dysfunction. Six percent of the offspring had congenital cardiac lesions. For these reasons, the search for 22q11 chromosomal microdeletions and fetal echocardiography should be considered.

Endocarditis prophylaxis is recommended in all patients. Patients who have had a good surgical result can generally participate in athletic competition without restriction.

The role for invasive arrhythmia management and automatic implantable cardioverter-defibrillator use remains controversial. Arrhythmias are often harbingers of hemodynamic derangement, and these should be addressed before one assumes that the arrhythmia is primary. Unfortunately, arrhythmias may still occur even in those not considered at highest risk.⁹⁶

Double-Chambered RV

Clinical Assessment

General Considerations

In this disorder, the RV is divided into a high-pressure proximal chamber and lower-pressure distal chamber by anomalous muscle bundles, creating a double-chambered RV. The morphological features may be very diverse, and the particular muscle bands involved vary from an anomalous septoparietal band, an anomalous apical shelf, or an abnormal moderator band.⁹⁷ The distance between the moderator band and the PA may be abnormally short.⁹⁸ The RV outflow tract obstruction is generally believed to be an acquired one and to be progressive over time, although the basic anatomic features are congenital. In ≈75% of cases, it is associated with a perimembranous VSD that is usually, but not always, below the level of the muscular obstruction. In some instances, there is greater RV dysfunction when the VSD is restrictive or closes. Other associations include valvular PS, tetralogy of Fallot, and double-outlet RV. There is subaortic obstruction in a variable number of these patients, up to 88% in 1 study.⁹⁹ Subaortic obstruction is very uncommon in patients with tetralogy of Fallot.

The anomaly is rare, occurring in ≈1% of patients with congenital heart disease.¹⁰⁰ No genetic pattern has been identified. It has been reported to develop in ≈3% of patients with repaired tetralogy of Fallot¹⁰¹ and in 3% to 10% of patients with a VSD.¹⁰²

Clinical Hemodynamics and Physical Examination

The obstruction may be marked at times. The resulting hypertrophy results in an RV heave, and the murmur across the obstruction is often accompanied by a thrill. The murmur of an associated VSD may be present. If there is an interatrial connection or the VSD is proximal to the obstruction, cyanosis may occur. Rarely, RV failure and tricuspid regurgitation become evident.

Associated Laboratory Studies

The ECG usually suggests RV hypertrophy. Right-sided leads may help to confirm the diagnosis, with upright T waves in R_{V_3} in 40%.¹⁰³



Figure 6. MRI of double-chambered RV, revealing the MRI anatomy of a double-chambered RV. pRV indicates proximal right ventricle; dRV, distal right ventricle. Reproduced from Ibrahim et al¹⁰⁴ with permission from the American Heart Association. Copyright 2002.

The chest wall echocardiogram is diagnostic with demonstration of hypertrophy and Doppler/color flow evidence for midventricular gradient. The presence of the VSD will be noted. Transesophageal echocardiography is not necessary for the diagnosis.

MRI (Figure 6) is the best imaging modality.¹⁰⁴ A photon deficit along the obstructing bundle has been noted on thallium-201 single photon emission computed tomography imaging¹⁰⁵ as well as increased uptake on Tc-99m tetrofosmin single photon emission computed tomography.¹⁰⁶

Cardiac catheterization and angiography are confirmatory and provide important imaging and hemodynamic and shunt information.

Following Up the Unoperated Patient

Although most patients undergo repair before adulthood, some present much later. Symptoms in the adult may mimic coronary disease (angina) or LV dysfunction (dyspnea). Dizziness and syncope occur occasionally. Echocardiography or cardiac MRI should be followed up. In patients with anginal symptoms, cardiac catheterization to exclude coronary disease may be warranted. Because there may be some dynamic obstruction contributing to the gradient, β -blockers and calcium channel blockers are often tried along with diuretics. There are few data regarding their effectiveness. In a study of patients without repair, the midventricular gradients increased an average of 6.2 ± 3 mm Hg each year.¹⁰⁷

Surgical and Percutaneous Intervention

Surgical Intervention

The midventricular obstruction is a mechanical problem. Surgical intervention should be considered in all patients who are symptomatic or have peak gradients >50 mm Hg. The surgical approach resects the muscle bundles and repairs any associated lesions. Surgical risk is low,^{108,109} and the results quite good. In 1 report, of 20 patients with a mean follow-up of 19 years, 17 were in New York Heart Association class I at follow-up. Of interest, 25% developed aortic insufficiency.

Percutaneous Intervention

There have been isolated attempts at percutaneous alcohol ablation of the conal branch from the right coronary artery

and the use of balloon dilatation. These options may be considered in patients who are not otherwise surgical candidates.

Following Up the Postoperative Patient

Most patients do well after surgical intervention and lead fairly unrestricted lives. There is little recurrence of obstruction after adequate surgical repair, and follow-up of associated congenital defects usually takes precedent. There are case reports of patients developing a double-chambered RV after repair of either tetralogy of Fallot¹⁰¹ or a perimembranous VSD.¹¹⁰ Activity for most is not limited after surgery, although endocarditis prophylaxis is still recommended.

Uncommon RV Outflow Tract Lesions

Double-Outlet RV

Clinical Assessment

General Considerations

Double-outlet RV requires at least 50% of each great vessel to arise from the morphological RV. This broad definition covers lesions from tetralogy of Fallot to those with single-ventricle physiology. The VSD is typically large and has 4 potential locations: subaortic, subpulmonic, doubly committed, or remote. The insertion and location of the outlet septum define which great vessel is related to the VSD. In Figure 7A, the outlet septum may be attached to the anterior limb of the septomarginalis muscle, leaving the VSD in the subaortic position. There is often subpulmonic narrowing, and the lesion resembles tetralogy of Fallot. In Figure 7B, the outlet septum may be attached to the posterior limb of the septomarginalis muscle, leaving the VSD in a subpulmonic position. The subaortic infundibulum is often narrowed, resulting in subaortic obstruction. In Figure 7C, there is no or a trivial outlet septum, and the VSD is doubly committed to each great vessel. In Figure 7D, the VSD is not related to either great vessel and is remote from the outflow tract. These latter VSDs can be in the inlet or in the muscular septum and are often very large.

The arterial trunks may vary in location, with the aorta generally to the right of the pulmonary trunk. If the trunks spiral as they leave the base of the heart, the VSD is usually subaortic. If the trunks are parallel with the aorta anterior and rightward, the VSD is usually subpulmonic; when the VSD is only under the pulmonary trunk, the configuration is called the Taussig-Bing heart.¹¹¹

Other anomalies, such as valvular PS, may also be present in many patients. Atrioventricular valve tissue may attach to the infundibular septum or may straddle the VSD, creating surgical challenges. Coronary anomalies include the left anterior descending from the right coronary artery (much as in tetralogy of Fallot).

Clinical Hemodynamics

The clinical hemodynamics reflect the location of the VSD, outlet septum, and any subvalvular or valvular stenosis. Patients with a subaortic VSD most resemble those with tetralogy of Fallot. The degree of subpulmonic or valvular stenosis determines whether the lungs are protected from the VSD flow and how much cyanosis occurs. Patients with a

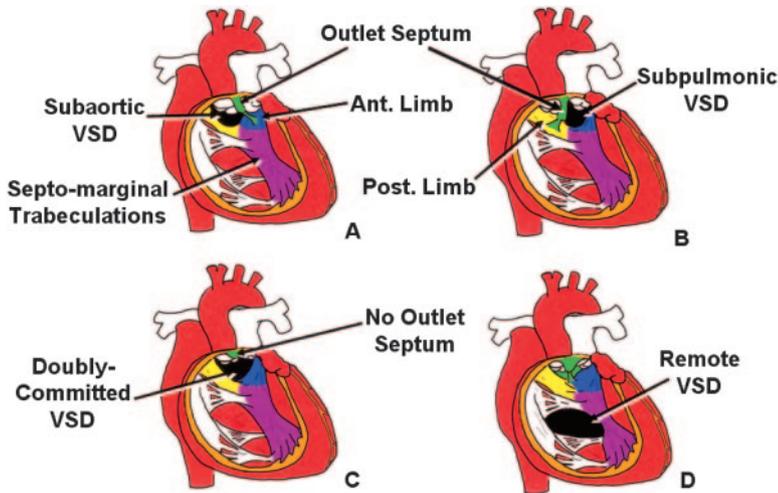


Figure 7. The variations in the double-outlet RV complex. The outlet septal location defines the location of the VSD. In those with a subaortic VSD, the outlet septal attaches to the anterior (Ant.) limb of the septal band. In those with a subpulmonic VSD, the outlet septal attaches to the posterior (Post.) limb of the septal band. In the doubly committed VSD, there is absence of the outlet septal. A remote VSD is often so large that the patient functionally has a single ventricle. Adapted from van Arsdell¹¹² with permission from Elsevier Ltd. Copyright 2003.

subpulmonic VSD often have subaortic stenosis, resulting in much of the blood from the heart being shunted toward the lung, so that cyanosis becomes a major issue early in the course. Unrepaired adult survivors generally have Eisenmenger's physiology. Approximately 50% of patients also have aortic coarctation or aortic arch hypoplasia.¹¹² A doubly committed VSD is uncommon, and the ventricles can vary in regard to how much of the cardiac output from each ventricle each great vessel receives. A remote or noncommitted VSD is usually so large that the physiology resembles that of a single ventricle.

Because the anatomy of double-outlet RV is so diverse, outcome studies are difficult to interpret. With few exceptions, adult patients will have undergone some surgical repair in infancy. A biventricular repair is possible in most patients. In remote VSD patients, often the only surgical therapy is the Fontan procedure.

Associated Laboratory Studies

The ECG usually reflects the presence of RV and/or LV hypertrophy. Right bundle-branch block is common. Operated patients with double-outlet RV are susceptible to both atrial and ventricular arrhythmias. In the postoperative period, ventricular ectopy has been found to be related to a longer QRS duration, a longer QTc, and a shorter J to T_{max}.¹¹³ Sudden death has been found to be more common in patients operated on later in life, those with perioperative and postoperative ventricular ectopy, and those with third-degree atrioventricular block.¹¹⁴

The chest x-ray is consistent with expected chamber enlargement and pulmonary flow and pressure. Diminished pulmonary vasculature and a concave left heart border suggest severe PS and a subaortic VSD (similar to tetralogy). In the absence of PS, the PA is enlarged, and increased pulmonary vascularity and cardiomegaly occur. Malposition of the aorta may be evident.

The chest wall echocardiogram can define the underlying conditions and the status of the surgical repair. Transesophageal echocardiography is particularly helpful in assessing chordal attachments. The presence of residual subvalvular and valvular stenosis or regurgitation, a residual VSD, pul-

monary hypertension, and the status of conduits or surgical baffles can also be addressed.

MRI not only provides the data observed by echocardiography but also helps to identify the size of the great arteries and their relationship to the VSD.

Cardiac catheterization and contrast angiography are confirmatory for the most part. Defining the presence of pulmonary hypertension and its causes (pulmonary vascular disease or left heart disease) is important.

Surgical Intervention

Biventricular repair (leaving the patient with both a functioning RV and LV) is the goal when possible. The orientation of the VSD is critical to the surgical approach to avoid obstructing newly created subaortic or subpulmonic outflow channels. Numerous approaches in the past have been taken to anatomically correct the defects, including initial palliation with pulmonary banding to prevent pulmonary hypertension if the pulmonary circuit is unprotected or the use of systemic-to-pulmonary shunts if there is pulmonary underperfusion. Closure of the VSD and the use of atrial switch operations (Mustard or Senning) or the Damus-Kaye-Stansel modification of the Fontan procedure (creation of a single ventricle by attaching the RA to the right PA and attaching the main PA end to side directly to the aorta) have been used but are no longer in vogue. Some of these patients are still being followed up as adults, however.

Repair of double-outlet RV with subaortic VSD is dependent on the proximity of the VSD to the aorta. In most cases, an intraventricular tunnel made of a Gore-Tex patch can baffle blood from the LV through the VSD to the aorta (Figure 8). If the VSD is small, obstruction of the tunnel is avoided by enlarging the VSD. RV outflow obstruction may require an RV outflow resection or patch. Most of these repairs are done in the first year of life.

Repair of double-outlet RV with subpulmonic VSD is now accomplished with the arterial switch procedure and a VSD patch (Figure 9). Alternatively, when the great vessels are side by side and there is enough space between the tricuspid annulus and the PV, a tunnel can be created under the PV connecting the aortic valve to the LV outflow. If the space is too restrictive, an anterior baffle can be created (the Ka-

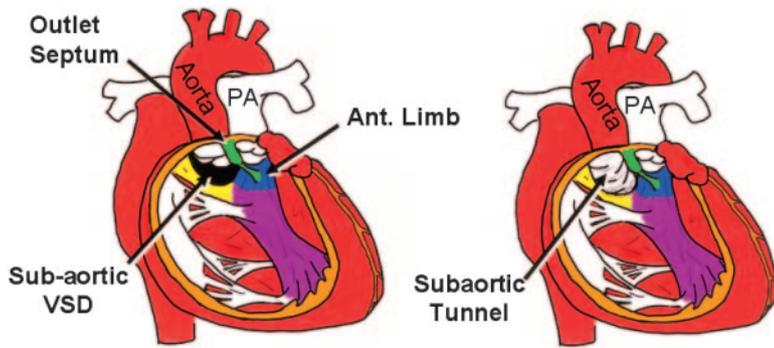


Figure 8. Repair of double-outlet RV with subaortic VSD. The basic anatomy is shown on the left. A tunnel is constructed to baffle the LV to the aorta. Os indicates outlet septal. Adapted from van Arsdell¹¹² with permission from Elsevier Ltd. Copyright 2003.

washima repair). Any associated aortic coarctation or hypoplasia is repaired at the same time.

Repair of double-outlet RV with doubly committed VSD is often not dissimilar to repair of a large VSD. At times, the VSD may be more related to the PA, and an arterial switch may be required, or it may be related to the aorta, and interventricular tunneling may be preferred.

Repair of double-outlet RV with a remote VSD can be very complex. These are rare lesions, and most patients get single-ventricle palliation with pulmonary banding as an infant, then a Fontan procedure later in early childhood. In a few patients, biventricular repair can be accomplished with long tunnel construction, resection of infundibular muscle, and even use of arterial switch procedures.

Following Up the Postoperative Patient

Most patients followed up as adults will have undergone surgical intervention. An ECG should also be part of the evaluation given the aforementioned issues regarding conduction disease and risk for sudden death. Complications to be anticipated are dependent on the underlying anatomy and the type of surgery performed. Issues that should be followed up include the status of both ventricles, any evidence for residual valvular or subvalvular stenosis or insufficiency (especially searching for subaortic or subpulmonary obstruction if a tunnel-type operation has been performed), the presence of a residual VSD, evidence for coarctation or recoarctation, evidence for conduit stenosis or regurgitation (if a conduit had been used), heart block,

or other atrial and/or ventricular arrhythmias. If a Fontan procedure was performed, RA size and evidence of thrombus are relevant, along with evidence of an elevated pulmonary pressure that would negate the effectiveness of the Fontan physiology.

If the physiology is similar to tetralogy of Fallot, the risk of pregnancy is low as long as the patient is asymptomatic and does not have severe PI, pulmonary hypertension, or LV dysfunction.^{94,115} Most patients with double-outlet RV who have had successful biventricular repair can carry a pregnancy to term. The risk increases in those requiring a Fontan procedure, but there are many reports of successful pregnancies in this situation as well.^{116,117} Lifelong endocarditis prophylaxis is generally recommended but may be less important in those with tetralogy-type repair with no residual intraventricular communication.¹¹²

Truncus Arteriosus or Common Arterial Trunk

General Considerations

Truncus arteriosus or common arterial trunk is a very uncommon lesion in adults, and essentially all adult patients will have had surgical intervention. It consists of a single arterial trunk giving origin to the PAs, coronary arteries, and the systemic circulation. It is rare even among congenital heart lesions, occurring in only $\approx 1\%$.¹¹⁸ Several classifications of the common trunk have been proposed on the basis of the origins of the pulmonary arteries. These include the Collett and Edwards,¹¹⁹ the van Praagh and van Praagh,¹²⁰ and the

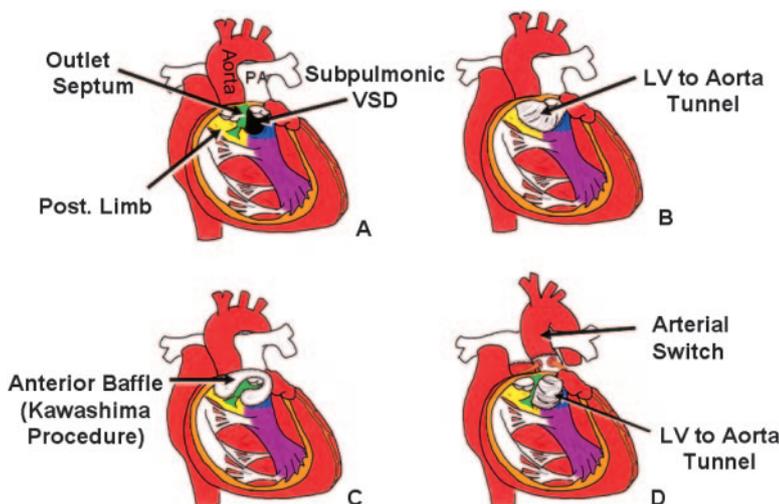


Figure 9. Repair of double-outlet RV with subpulmonic VSD. The anatomic situation is shown in A. If the distance between the tricuspid valve and PA is great enough, an intraventricular tunnel may be created (B). When the tricuspid valve and PV are too close, a baffle may be created around the anterosuperior margin of the PV (C), or an arterial switch procedure may be done with a much shorter intraventricular tunnel being needed (D). Adapted from van Arsdell¹¹² (with permission from Elsevier Ltd, copyright 2003) and from Freedom et al¹³⁸ (with permission from Blackwell Publishing, copyright 2004).

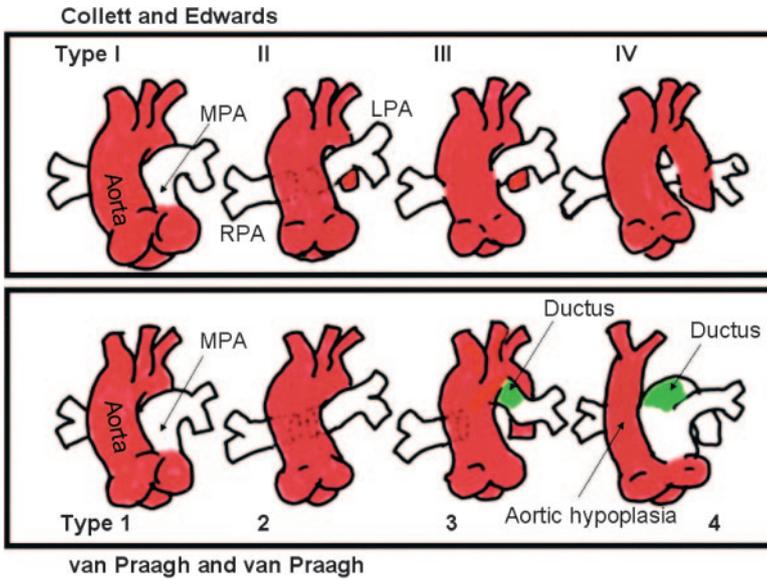


Figure 10. Classification schemes for common arterial trunk. The top panel outlines the Collett and Edwards scheme,¹¹⁹ and the bottom panel outlines the one proposed by van Praagh and van Praagh.¹³⁹ MPA indicates main PA; RPA, right PA; and LPA, left PA. Adapted from Connelly¹²⁸ (with permission from Elsevier, copyright 2003) and from Freedom and Yoo¹²⁷ (with permission from Blackwell Publishing, copyright 2004). See text for discussion.

Jacobs' modification from the Society of Thoracic Surgeons.¹²¹ Figure 10 schematically outlines the Collett and Edwards and the Van Praagh and Van Praagh classifications. The Society of Thoracic Surgeons' classification simply combines types 1 and 2.

The common trunk is large, and cystic medial necrosis is usually present, resulting in further dilatation as the patient ages. There is a strong association between common arterial trunk and microdeletions of 22q11.2,^{60,122} occurring in up to 40% of patients.

The common trunk usually overrides the VSD and is committed to both ventricles, although exceptions occur.¹²³ The VSD is large and nonrestrictive and results from absence of the infundibular septum. It lies between the 2 limbs of the septomarginal trabeculation. The truncal valve may have from 1 to 6 cusps. In 1 study, 61% had a tricuspid truncal valve, 31% a quadricuspid valve, and 8% a bicuspid valve.¹²⁴ Poor valve function (mostly incompetence) usually results in early heart failure and death in infancy. The coronary arteries may arise above the truncal leaflets in a variety of positions, although many are normally located. The left anterior descending artery may be small, with large infundibular and septal branches originating from the right coronary artery, placing them in danger of injury during surgical ventriculotomy when a conduit is used.¹²⁵ Other coronary anomalies may also coexist.¹²⁶

A patent ductus arteriosus is present in half of all patients, and its size is inversely related to the size of the residual common trunk.¹²⁷ Other common anomalies include an interrupted aortic arch or coarctation in 10% to 20% (often associated with the Di George syndrome), an atrial septal defect, a persistent left superior vena cava, aberrant subclavian arteries or mirror-image arch vessels, or skeletal, bowel, or bladder abnormalities.¹²⁸

Surgical Intervention

Previously, initial surgical repair involved banding of the PAs to protect the lungs. Currently, complete repair is attempted at an early age. The basic repair involves closing the VSD

through a right ventriculotomy, then separating the PAs and attaching them to a valved conduit sewn into the RV outflow tract (Figure 11).

Following Up the Postoperative Patient

The successful repair of this lesion was first reported in 1968,¹²⁹ and few patients have survived to adulthood. Among hospital survivors, Rajasinghe and colleagues¹³⁰ reported an actuarial survival rate of 83% at 15-year follow-up. Virtually all the patients had reoperation by 10 to 12 years, however, with a median time to reoperation of 5.1 years. Reoperation was primarily for conduit replacement (usually because of the small size of the original conduit) or truncal valve replacement because of valvular insufficiency.

Patients require at least yearly follow-up, with focus on any evidence of conduit stenosis or regurgitation, aortic root dilatation, branch PA stenosis or a residual VSD, ventricular

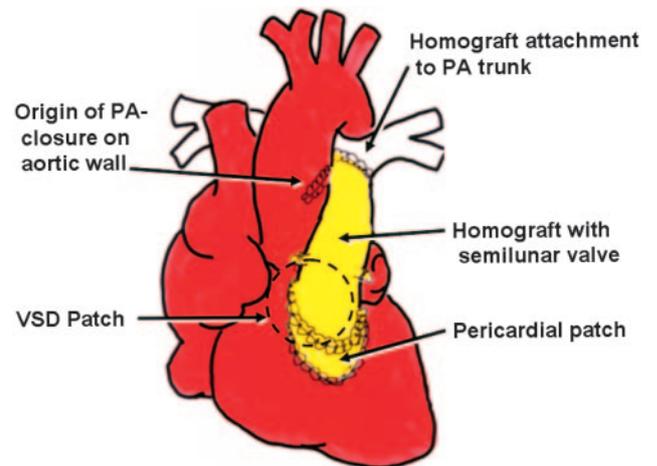


Figure 11. Surgical repair of common arterial trunk. In complete repair, after closure of the VSD, the PA is detached from the aorta and connected to the RV outflow with the use of a conduit (a homograft is shown here). Sketch modified from Connelly¹²⁸ (with permission from Elsevier, copyright 2003) and from Parson et al¹⁴⁰ (with permission from Icon, Inc, copyright 2004).

dysfunction, truncal valve stenosis or regurgitation, arrhythmias, or pulmonary hypertension and right heart failure. Some catheter-based approaches have been used to palliate complications, including conduit valvuloplasty,^{131,132} stenting,¹³³ or percutaneous conduit valve replacement.⁵³ Stenting of pulmonary branch stenosis is also feasible.¹³⁴ Otherwise, most reintervention is surgical.¹³⁵

Adult patients with good surgical results and no complications often have minimal symptoms,¹³⁰ and some can be active. Successful pregnancy has been reported, although it is discouraged given the high incidence of chromosomal 22q11 deletions in this patient population.^{60,136} For that reason, chromosomal analysis should be done in patients who are contemplating a pregnancy.¹²⁸ Fetal echocardiography may be able to detect a common arterial trunk and may be important in the decision of whether to prematurely terminate an ongoing pregnancy.¹³⁷ Endocarditis prophylaxis is recommended in all.

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Disclosures

None.

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KEY WORDS: heart diseases ■ ventricles ■ heart defects, congenital ■ heart septal defects ■ pulmonary valve stenosis ■ tetralogy of Fallot ■ truncus arteriosus

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