

The diagnosis and management of congenital pulmonary valve stenosis

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INTRODUCTION

Pulmonary stenosis (PS) is a common congenital cardiac abnormality. Patients may present as asymptomatic with an incidental murmur due to mild PS, with advanced right ventricular dysfunction and failure due to severe PS, or even with deep cyanosis and acidosis due to critical PS. A thorough assessment is needed to determine which of the many patients born with PS need intervention and further management, and which need only routine, serial follow up.

EPIDEMIOLOGY

Congenital PS is one of the most common congenital cardiac defects found. It accounts for approximately 8 - 12% of all congenital cardiac defects, with an incidence of about 1 per 2 000 live births worldwide.⁽¹⁾ PS, as an isolated defect, is the second most common congenital cardiac defect, second only to ventricular septal defects (VSD). PS may also be found as an associated defect in up to 30% of other cardiac abnormalities, including atrial septal defect (ASD), ventricle septal defect (VSD) and patent ductus arteriosus (PDA).

There is a high incidence of congenital PS in certain genetic syndromes, including Noonan, Holt-Oram, Leopard, William and Allagile Syndromes.⁽²⁾ In most syndromes the pattern of inheritance is autosomal dominant, but rarely it may be recessively transmitted, such as in Laurence-Moon-Biedl syndrome.

ABSTRACT

Congenital pulmonary stenosis (PS) is one of the most prevalent congenital cardiac abnormalities. A thorough assessment is needed to determine which of the many patients born with PS, will need intervention and further management, and which will only need routine follow up. Accurate non-invasive assessment of the severity of the PS at transthoracic echocardiography is therefore important. This article will discuss and delineate the diagnostic approach to, and management of, a patient with congenital PS. SAHeart 2018;15:36-45

Mutations in the germlines of PTPNI and RAFI have been described to cause valvular abnormalities.⁽³⁾ Often the transmission pattern is sporadic and may be unclear. Table 1 lists the common syndromes associated with PS as well as their extra-cardiac features.

There is a slightly higher prevalence of PS in Asia when compared to Europe and the USA, with a steady increase over time;⁽¹⁾ the overall incidence in Africa has not been fully described and is unknown.

Acquired PS is rare, especially in children. Aetiologies of acquired PS, such as carcinoid syndrome, infective endocarditis and homograft dysfunction will not be covered in this review of congenital PS.⁽⁴⁾

ANATOMICAL CLASSIFICATION OF PS

PS may occur at several levels along the right ventricle outflow tract and pulmonary artery tree (see Figure 1). Valvular PS is the most common by far, however, the presence of PS at one level along the right ventricle outflow tract (RVOT) should prompt careful assessment for other, associated levels of PS such as peripheral branch pulmonary artery stenosis.

Sub-valvular PS can be infundibular or sub-infundibular (see Figure 2). Isolated infundibular PS is unusual. It is usually seen as part of tetralogy of Fallot or as a secondary phenomenon to valvular PS, where the resulting right ventricle (RV) hypertrophy causes a dynamic obstruction of the tubular RVOT. Sub-infundibular PS, also known as double chambered right ventricle (DCRV), may present in association with a small VSD. In DCRV the RV is divided into 2 cavities: a proximal (inlet) high pressure cavity and a distal (outlet) low pressure cavity. The 2 cavities are divided by anomalous muscle bundles which

TABLE I: Genetic Syndromes commonly associated with PS.

Syndrome	Cardiac findings	Extra-cardiac findings	Transmission
Noonan	Dysplastic PV with PS. Supra-valvular PS. HOCM.	Facies: bulbous nose, hypertelorism, low-set ears, down-slanting eyes, micrognathia, arched palate, deep philtrum, webbed neck. Short stature. Skeletal abnormalities	Heterogeneous trait
Williams	Supra-valvular AS. Peripheral PS.	Elfin face. Short stature. Cognitive and developmental impairment. Endocrine and GUT disorders.	Autosomal dominant trait 7q11.23 deletion
Di George	Conotruncal defects: TOF, TGA, Truncus arteriosus. Interrupted aortic arch, vascular rings. ASD/VSD.	Facies: low-set, posteriorly rotated ears, micrognathia, cleft or arched palate, hypertelorism. Developmental delay. Hypoplastic thymus with variety of immune deficiencies and hypocalcaemia.	Autosomal dominant trait 22q11 deletion
LEOPARD	ECG abnormalities. Supra-valvular PS. Valvular PS.	Lentigines/Ocular hypertelorism/Abnormal genitalia/Retardation of growth/Deafness.	Autosomal dominant trait
Allagile	Peripheral PS.	Facies: triangular face, wide nasal bridge, deep-set eyes. Intrahepatic cholestasis. Butterfly vertebrae.	Dominant trait
Congenital Rubella	Peripheral PS. PDA.	Congenital cataracts or glaucoma. Retinopathy. Short stature. Deafness.	
Keutel	Multiple peripheral PS.	Abnormal cartilage calcifications. Brachytelephalangy. Low IQ. Deafness.	Autosomal recessive trait

PV = Pulmonary valve, PS = Pulmonary Stenosis, HOCM = Hypertrophic Cardiomyopathy, AS = Aortic Stenosis, GUT = Genitourinary tract. TOF = Tetralogy of Fallot. TGA = Transposition of the Great Arteries, ASD = Atrial Septal Defect, VSD = Ventricular Septal Defect.

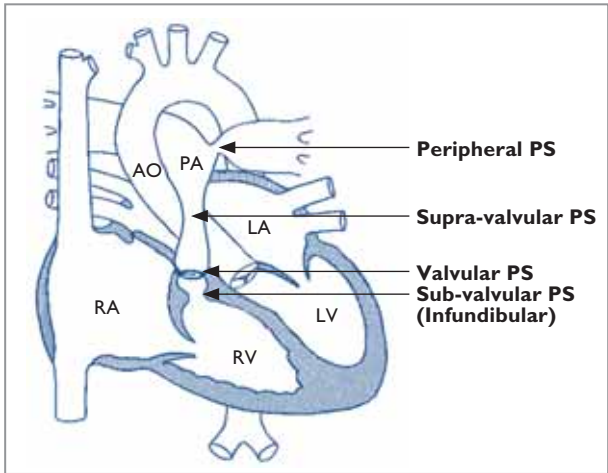


FIGURE 1: Anatomical classification of pulmonary stenosis.

may originate either from a hypertrophied moderator band or, more frequently, due to the high pressure jet of a small VSD impacting on the RV free wall and stimulating hypertrophy at that point. Sub-valvular PS may be progressive and is generally treated by surgical removal of the obstruction.

Supra-valvular PS is a characteristic finding in several syndromes such as Williams, Noonan, DiGeorge, LEOPARD and Allagile Syndromes where it may occur as an isolated defect, or in association with other congenital abnormalities, both cardiac and non-cardiac. It is also found in congenital Rubella syndrome. The supra-valvular stenosis may be found just distal to the pulmonary valve (see Figure 3) in the main pulmonary artery (PA), at the bifurcation and origin of the branch pulmonary arteries (see Figure 4), or further along as peripheral PS. There may be a single, discrete stenosis or multiple sites of narrowing, scattered along the pulmonary artery tree. Depending on the

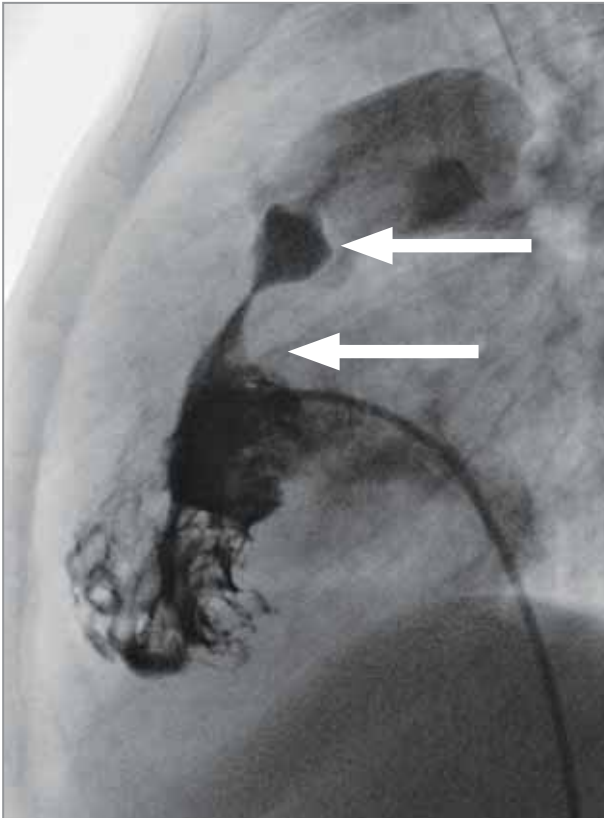


FIGURE 2: Tight sub-valvular (infundibular) and valvular PS. RV angiogram in the lateral view.

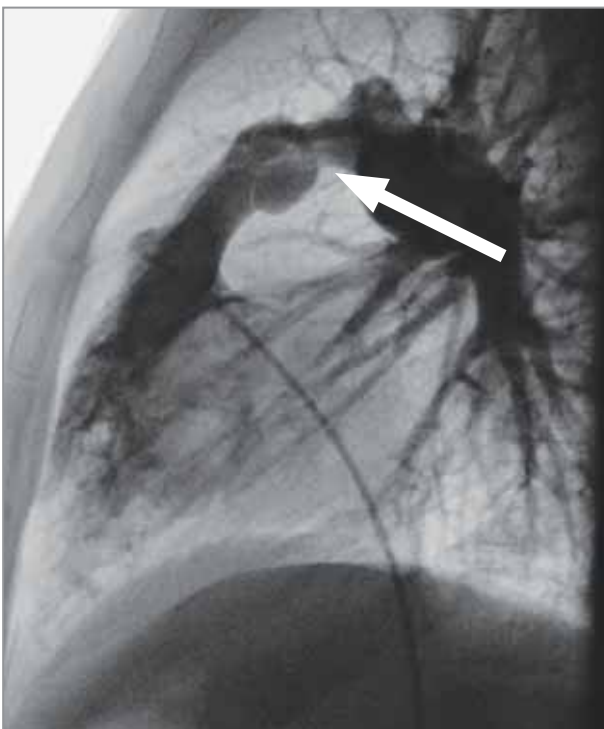


FIGURE 3: Supra-valvular pulmonary stenosis just distal to the PV. RV angiogram in the lateral view.

site and extent of PS, supra-valvular PS is often amenable to interventional relief using normal or cutting balloons or re-expandable stents that can be post-dilated as the patient grows.

Valvular PS is the most common form of PS. The PV may be only thickened and partially fused, or it may be completely dysplastic with no normal leaflets, as seen in patients with Noonan syndrome. With either type of valve, there may be secondary fixed or dynamic narrowing of the right ventricular infundibulum in moderate and severe obstruction (see Figure 2).⁽¹⁴⁾

SEVERITY CLASSIFICATION OF PS

The severity of PS is generally based on the Doppler flow gradient across the area of stenosis, as found at TTE (see Table II). The severity of PS is graded as mild, moderate, severe and critical. Whilst the first 3 are regarded as acyanotic congenital cardiac defects, critical PS causes severe cyanosis due to the associated right-to-left shunting through the patent foramen ovale (PFO) or an ASD.

EMBRYOLOGY

The pulmonary valve is formed between weeks 6 - 9 of pregnancy. The valve develops in the bulbus cordis section of the heart tube, at the junction of the conus cordis and truncus arteriosus. The heart tube wall consists of an outer layer of myocardium and an inner layer of endothelium with a thin layer of cardiac jelly between. A subset of endothelial cells undergoes specification to delaminate, differentiate and migrate into the cardiac jelly layer; a process known as endothelial-mesenchymal



FIGURE 4: Bilateral peripheral pulmonary stenosis with differential perfusion of the lungs.

TABLE II: Grading of Pulmonary Stenosis.

	Mild	Moderate	Severe
Peak Velocity (m/s)	<3	3 - 4	>4
Mean gradient (mmHg)	<20	20 - 40	>40
Peak gradient (mmHg)	<36	36 - 64	>64

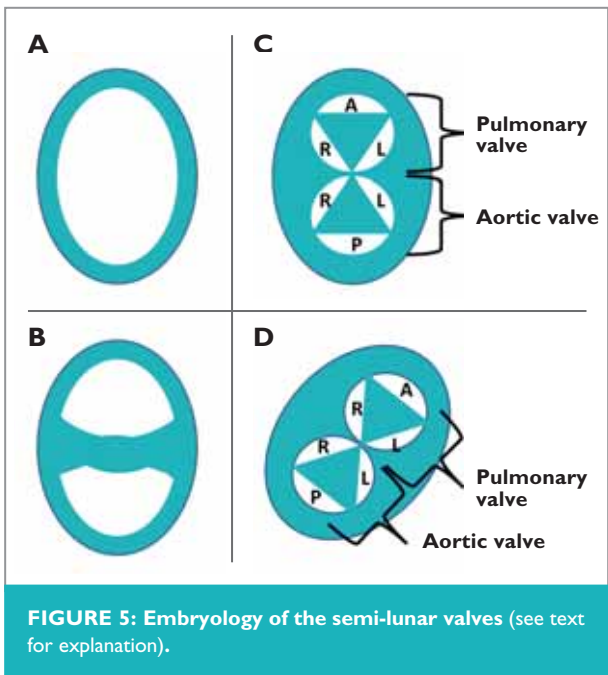


FIGURE 5: Embryology of the semi-lunar valves (see text for explanation).

transformation. The new mesenchymal cells and the cardiac jelly swell to form bulbous endocardial cushions.⁽⁵⁾

The formation of 2 separate ventricles leads to 2 separate ejection streams. These distinct streams appear to remold the cardiac jelly so that the single outflow tract (see Figure 5A) is divided into an “H-shaped” lumen. This H-shaped septum represents the accumulation of endocardial cushions into 4 mounds (see Figure 5B). During aorta-pulmonary septation, these 4 mounds are further divided to form 3 semi-lunar cusps in each separate outflow tract (see Figure 5C). The final nomenclature of each valve’s leaflets is taken from the position of the 4 early cushions (see Figure 5D). Neural crest cells migrate from the brachial crest into the semi-lunar valves to aid in aorta-pulmonary septation.⁽⁶⁾ In a complex process of further cell differentiation and apoptosis, these endocardial cushions undergo extensive delamination and remodeling from bulbous swellings to thin-walled, tapered heart valves. The 3 cusps of each valve finally consist of a single endothelial cell layer and a central matrix made up of collagen, elastin and glycosaminoglycan.⁽⁷⁾

Vascular endothelial growth factor (VEGF) is responsible for initiating the development of the endocardial cushions. Hypoxia and hyperglycemia both have regulatory effects on VEGF. There is a direct correlation between intra-partum hypoxic events and valvular disease. In addition, infants of diabetic mothers whose glucose levels are not controlled, have a 3-fold increase in cardiac defects.⁽⁵⁾

Failure of the valve to develop normally may lead to various malformations such as a single, funnel-shaped valve, fusion of 2 of the cusps, or a tri-leaflet valve that is thickened and partially fused at the commissures.⁽⁸⁾ In Noonan syndrome, overgrowth of tissue within the sinuses interferes with the normal mobility and function of the valve. The morphology of the abnormal valve will dictate what intervention or surgery will be needed to relieve the RV obstruction.

In congenital rubella and William syndrome, supra valvular and pulmonary artery branch stenoses are frequently present. An underlying intrinsic elastin abnormality leads to chaotic arrangement of the elastin fibers in the great arteries’ walls with areas of stenosis alternating with areas of aneurysmal dilatation.

APPROACH TO PS DIAGNOSIS

Overall, PS is the most benign of the valvular lesions.⁽⁹⁾ However, a good clinical examination, ECG and echocardiographic assessment are needed to quantify the severity of PS and to decide if, and when, intervention is needed. Occasionally, additional imaging such as pulmonary angiography by cardiac catheterisation or CT or MR angiography may be needed to visualise the peripheral pulmonary arteries.

Examination

The timing of presentation is dependent on the severity of the stenosis. As the greater majority of patients have only mild or moderate PS, the most common presentation of a patient with PS is one of an incidental murmur heard in a patient presenting with an unrelated complaint.⁽⁹⁾ There may be mild exercise intolerance and fatigue – symptoms often overlooked by patients and parents. In severe PS, the patient may present with episodes of chest pain or syncope due to their inability to increase their pulmonary blood flow during exercise.

The symptoms associated with PS appear to progress over time⁽⁹⁾ and long-standing, undiagnosed PS may present in adulthood as right ventricular failure.⁽¹⁰⁾ DCRV in particular is often clinically silent in childhood and only presents in adulthood with chest pain, syncope or cardiac failure.

Infants born with critical pulmonary stenosis may present immediately at birth with severe cyanosis, or a few days later when the ductus arteriosus closes. The supra-systemic RV pressure may cause RV dilatation, RV failure and severe tricuspid regurgitation (TR) with secondary cyanosis due to right-to-left shunting over the PFO or ASD.

Clinical examination should note any dysmorphic features indicating an underlying syndrome. On general assessment, the patient is typically acyanotic and well-grown. Features of RV enlargement, such as left parasternal and epigastric heave, may be present. The typical murmur is an ejection systolic murmur, loudest over the second left intercostal space, and spreading to the lung fields.⁽¹¹⁾ The degree of RV hypertrophy and the grade of the murmur are directly proportional to the severity of the PS. The first heart sound is normal, and the second heart sound is soft and may be accompanied by an opening snap.

Chest X-ray (CXR)

The CXR may be unremarkable in mild PS with a normal size heart, or it may show RV and right atrial (RA) enlargement in proportion to the severity of the PS. Right-sided enlargement is present in at least 50% of patients and results in a prominent rounded right lower heart border on frontal view and increased sternal contact on the lateral view. In addition, on frontal view the cardiac apex may appear lifted and rounded.

Post-stenotic dilatation of the pulmonary arteries is the most characteristic finding seen on frontal view. The dilated main pulmonary artery is seen as a prominent PA knuckle on the left heart border, just below the aortic knob. The dilated left and main pulmonary arteries produce a prominent vascular shadow in the left hilum on frontal view. The right pulmonary artery is also enlarged, but due to veiling by the mediastinal opacity, it is not easily seen. Thus, in patients with severe PS, the hilar vessels appear to be of different sizes. In contrast, in patients with pulmonary hypertension, the hilar vessels are equivalent in size. This is a helpful sign in the differential diagnosis of an enlarged right heart on CXR. Post-stenotic dilatation only occurs in valvular PS, and then only if the valve is relatively normal. In infundibular and supra-valvular stenosis, as well as in the presence of a dysplastic PV, the pulmonary artery is not prominent, and the CXR may appear surprisingly normal.⁽¹²⁾

Pulmonary blood flow is normal, except in critical PS which is classified as a cyanotic cardiac defect with decreased pulmonary blood flow and oligoemic lung fields. This is due to significant right-to-left shunting through the PFO or ASD. In severe unilateral peripheral pulmonary artery stenosis, there may be obvious differential perfusion of the 2 lungs.⁽¹³⁾

ECG

The changes on the ECG vary in proportion to the degree of PS. The ECG may be completely normal, or there may be evidence of RV hypertrophy and strain such as a right deviation of the frontal axis (greater than 90°), p-pulmonale of RA enlargement and prominent R waves in VI and deep S waves in V6. In patients aged 2 - 20 years, RV pressure can be estimated by multiplying the height of the R wave in lead V4R or VI by 5.⁽¹⁴⁾ A tall R wave, the presence of a Q wave, T wave inversion or ST segment depression in VI is evidence of RV strain. It must be remembered that in children aged 1 week - 10 years, the T waves are normally inverted in VI, and thus strain will be seen as an upright T wave in VI (double inversion). Neonates also have relative right deviation of the frontal axis due to the physiological right heart dominance at birth. Thus, a normal frontal axis for a neonate is between 0 and 110°.

Echocardiography

Transthoracic echocardiography (TTE) is the investigation of choice to diagnose, localise and quantify PS. The operator needs to assess the morphology of the PV and the pulmonary arteries, measure the PV annulus, localise the site (or sites) of obstruction and evaluate the severity of the PS. Additional pulmonary valve regurgitation (PR), or tricuspid valve regurgitation (TR), must be documented and its severity assessed. Severe PR can influence the assessment of the PS Doppler gradient using Bernoulli's equation and is a contra-indication to balloon valvuloplasty. Associated cardiac defects such as ASD, VSD, PDA and tetralogy of Fallot should be sought.

2-D echocardiography in the normal parasternal short axis view can be used to assess the PV. In addition, a parasternal long axis view of the RV outflow may be obtained by rotating the probe back 90° anti-clockwise and tilting towards the right shoulder. This view is also useful in visualising PDAs.

Careful evaluation of the morphology of the valve is necessary to decide which valves will be amenable to balloon valvuloplasty. A trileaflet PV where only the commissures are fused, restricting its opening, is easily addressed with balloon dilation. The typical dysplastic PV seen in Noonan syndrome, however, will not respond to mechanical stretching with a semi-compliant balloon. This valve is usually a blob of collagenous tissue, with no discernable normal leaflet anatomy. Though the valve might stretch out well with balloon inflation, it recoils back when the balloon is deflated. Native supra-valvular PS is equally resistant to balloon dilation. The presence of post-stenotic dilatation of the main pulmonary artery (MPA) and its branches, is a reliable indicator that the PV anatomy is relatively normal. Post-stenotic dilatation of the MPA is absent with a dysplastic PV.

Continuous wave Doppler (CW) is used to measure the peak and mean gradients across the PV and RVOT. Normally, there is no systolic gradient across the pulmonic valve. With PS, however, the RV systolic pressure increases, and a pressure gradient develops between the RV and pulmonary artery.

Accurate estimation of this pressure gradient is vital in deciding which patients need intervention for their PS. Based on the gradient across the PV, the PS is graded as mild, moderate or severe (see Table II).

It is important to align the probe as closely parallel as possible to the line of the RVOT, so as to maximise the accuracy of the Doppler wave signal. The angle of the RVOT in the body is conducive to good alignment. The best position of sampling is just above the level of the PV leaflets (see Figure 6).

Pulsed wave Doppler (PW) is used to determine the peak and mean gradients at a specific point along the RVOT and pulmonary tree. It is thus useful to distinguish between sub-valvular, valvular and supra-valvular stenosis. In severe PS, however, its use is limited by the Nyquist limit of flow.

In infundibular PS or DCRV alignment may be difficult. A modified 5 chamber view where the operator rotates the probe anti-clockwise and tilts anteriorly, can usually open up the outflow tract from the RV. Similarly, the anterior angulated sub-costal or sub-xiphoid view can be useful, especially in children and neonates (see Figure7).

The TR gradient can be used to estimate the RV systolic pressure with the following formula: RV systolic pressure = TR gradient + estimated RA pressure. The right atrial pressure can be estimated by examining the size of the IVC on sub-costal view, and how it changes with respiration. With a normal RA pressure of 5mmHg, the IVC will be normal in size and collapse in respiration, with a higher pressure of 10mmHg, the IVC will be dilated but still move with respiration and in a high RA pressure of 15mmHg, the IVC will be dilated and fixed in size. The size of the IVC can be established by comparing it to the abdominal aorta on sub-costal view: the IVC is enlarged if it is bigger than the aorta at this level.

The TR gradient, in conjunction with the degree of RVH, should be correlated with the PS gradient. An isolated, high PS gradient without significant RVH or RV hypertension should prompt the operator to reassess the Doppler gradient across the PV. The reverse is also true: a low gradient in the presence of marked RVH and a high TR gradient must be followed up with repeated Doppler measurements, preferably in a few different views. An ASD with pulmonary hypertension can also present in this way and needs to be actively excluded.

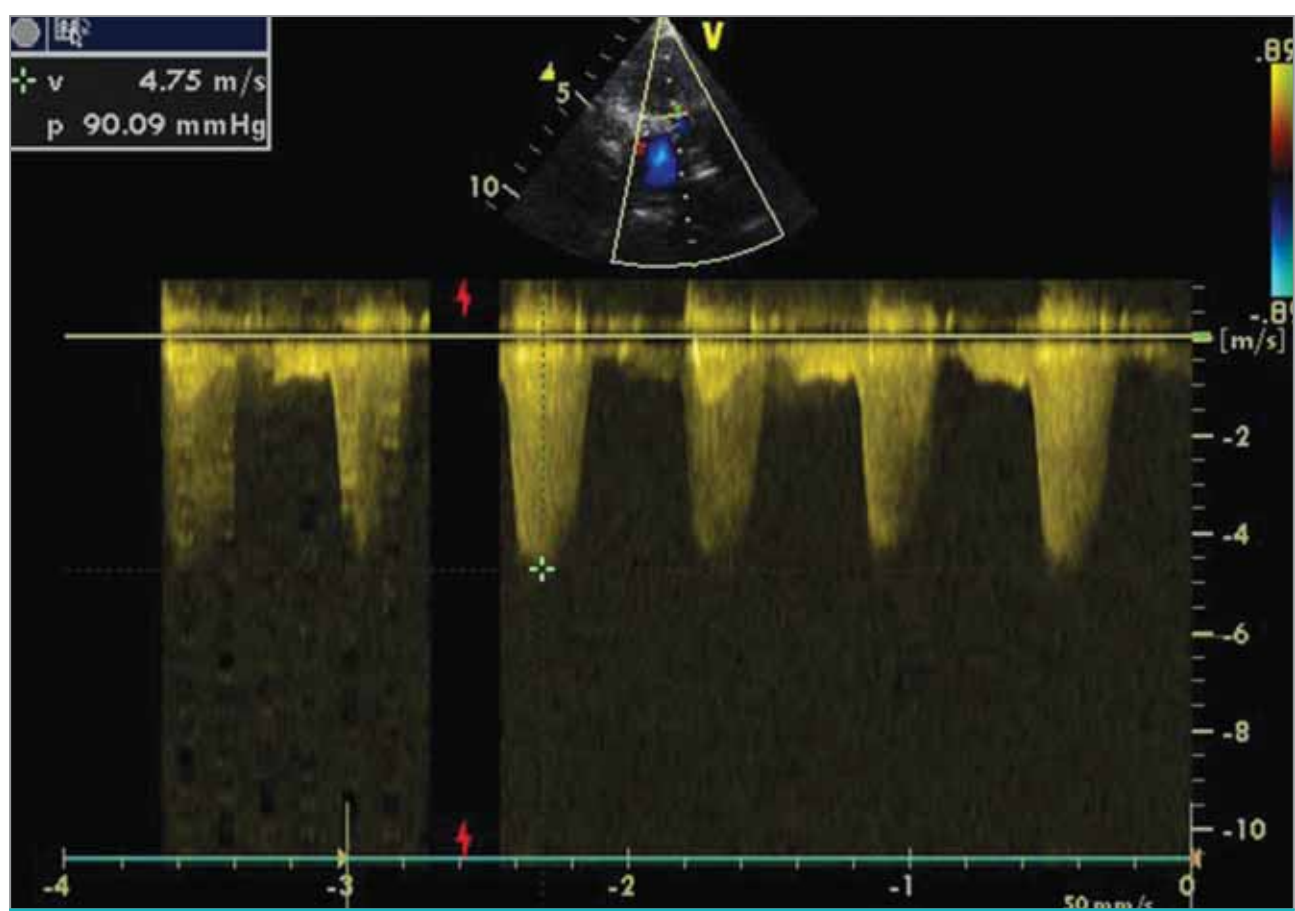


FIGURE 6: TTE short axis: Doppler gradient across the PV. Severe PS.

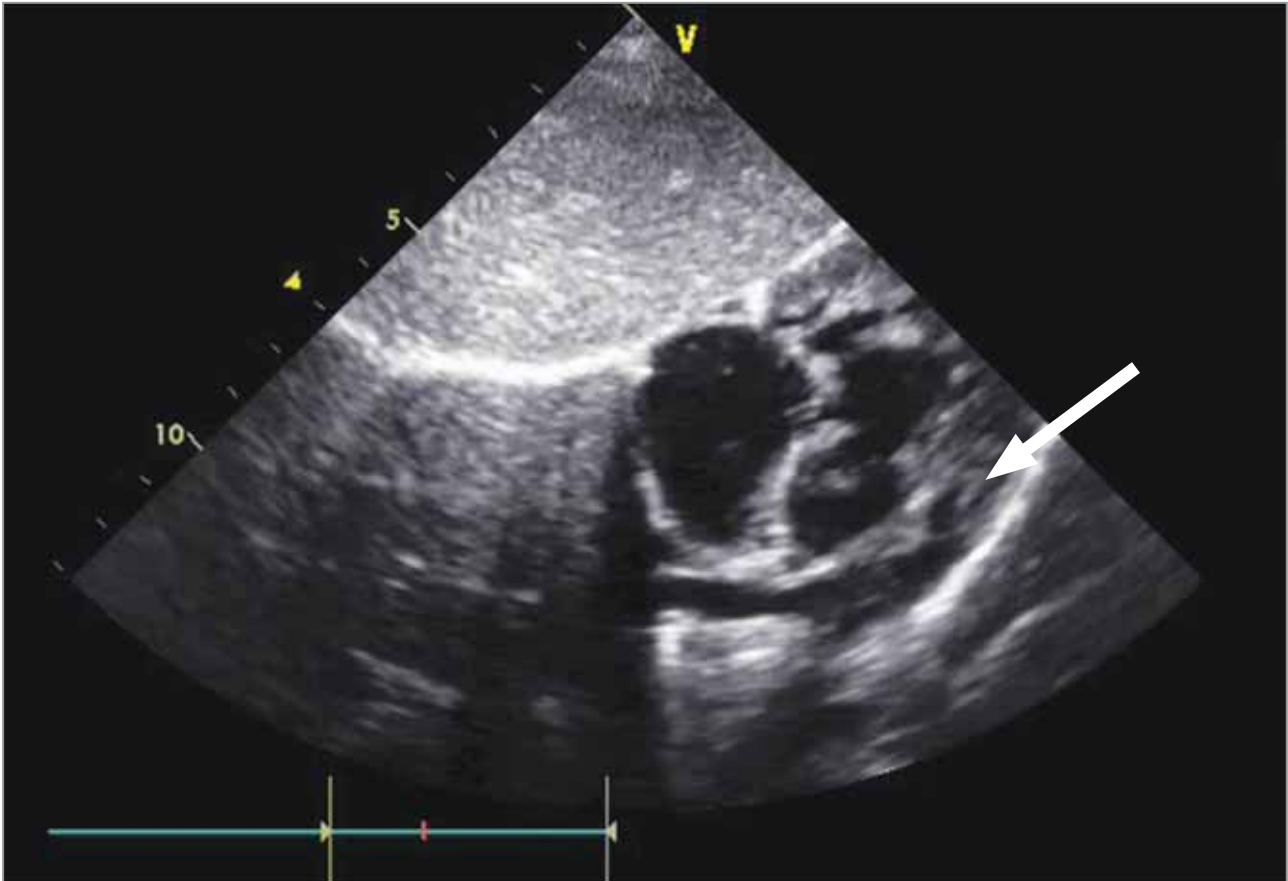


FIGURE 7: TTE Subcostal view showing a tight infundibular stenosis (arrow).

The PS gradient can be over-estimated if there are multiple levels of stenosis or moderate to severe PR. The severity of the PR can be assessed by the PR jet's length and width in relation to the size of the annulus and the RVOT. An eccentric jet of PR, as seen with some dysplastic valves, can make estimation difficult, however, if the PR flow starts in the branch pulmonary arteries, the PR is always severe. A PR pressure half time $<100\text{ms}$ is an additional indicator of significant PR as well as prolonged duration of the PR flow in diastole on PW Doppler. A PR index (PR Index = PR duration/diastolic duration) <0.77 has 100% sensitivity and 85% specificity in identifying patients with severe PR.⁽¹⁵⁾ Although the RV end-diastolic pressures increase with severe PR, this may eventually have a beneficial effect on maintaining forward flow over the pulmonary valve and also limit the amount of PR. In all situations, the TR gradient can be used to give a superior estimation of the real PS gradient.

Transoesophageal echo (TOE) is seldom used to routinely assess the severity of the PS, as most information may be derived from normal TTE views. The RVOT can be easily visualised at TOE but seeing the superficial, anterior-lying PV and pulmonary arteries is often challenging and offers little additional information.

Computed tomography (CT)

The usefulness of CT scanning in congenital heart disease is often limited by the inability to scan in multiple planes as well as the radiation exposure and the need for a contrast medium in CT angiography.⁽¹⁶⁾ Most pulmonary valve morphology can be adequately visualised on TTE.

Magnetic resonance imaging (MRI)

The role of MRI is usually to supplement the information obtained at echocardiography. It is, however, the examination of choice for the accurate determination of right ventricular function.⁽¹⁷⁾ Velocity-flow mapping can be used to calculate the volumes of shunts and pressure gradients across valves and conduits, as well as interrogation of valvular function.⁽¹⁸⁾

Cardiac catheterisation

The usual indication for cardiac catheterisation is to intervene and relieve the RVOT obstruction. However, it may also be used to localise the site (or sites) of the obstruction, to establish its severity, and to document any additional cardiac defects. The peak-to-peak gradient between the pulmonary artery and the RV is obtained by direct catheter pull-back. Alternatively, a multi-lumen catheter can be used for simultaneous pressure recordings.

TREATMENT

The goal of treatment is to relieve the pressure overload of the RV by relieving the RVOT obstruction.

Mild PS can be observed and followed up every year or 2 to assess for worsening stenosis. A constant Doppler gradient <30mmHg has little risk of progression. Moderate PS should be followed up at least annually and if any RV enlargement or symptoms develop, should be treated. Severe PS should be addressed promptly. Critical PS is a cardiac emergency and needs immediate intervention.

Balloon valvuloplasty

Since the 1980s, balloon valvuloplasty has mostly replaced surgery as the treatment of choice for valvular PS. Rare complications include bradycardia, hypotension and desaturation during balloon inflation, right bundle branch or atrio-ventricular block, balloon rupture and damage to the tricuspid and pulmonary valves. Perforation of the RVOT is possible, especially in small children.⁽¹⁹⁾ The risk of death or major complications is low: 0.24% and 0.35%, respectively.⁽²⁰⁾

Femoral venous access is attained and the pre-procedure RV pressure is noted. A RV angiogram is performed with an

angiographic catheter such as the NIH or Pigtail catheter. The morphology and size of the PV and pulmonary artery tree is visualised. Careful attention must be paid to assess for additional sites of stenosis that might also need intervention. Useful fluoroscopy views include: frontal view with RAO angulation to assess the RVOT, frontal view with cranial angulation to assess the PA bifurcation and origins of the branch PA, and straight lateral view to assess the RVOT and measure the PV annulus.

A semi-compliant balloon is chosen that is maximally 1.2 times the annulus' measurement (see Figure 8). Aggressive over-dilation of the PV with oversized balloons should be avoided as there is a higher risk of vascular rupture and dissection, as well as severe post-balloon dilation PR, which is poorly tolerated by the hypertrophied RV. The length of the balloon should be chosen carefully. A longer balloon will give greater stability during inflation, however, it might impinge on, and damage, adjacent structures such as the TV.

The RVOT and PV is crossed using a multi-purpose catheter. With severe stenosis, crossing the PV directly may be difficult, and a soft guidewire can be used to facilitate advancing the catheter into the MPA. The pressure in the MPA and branch

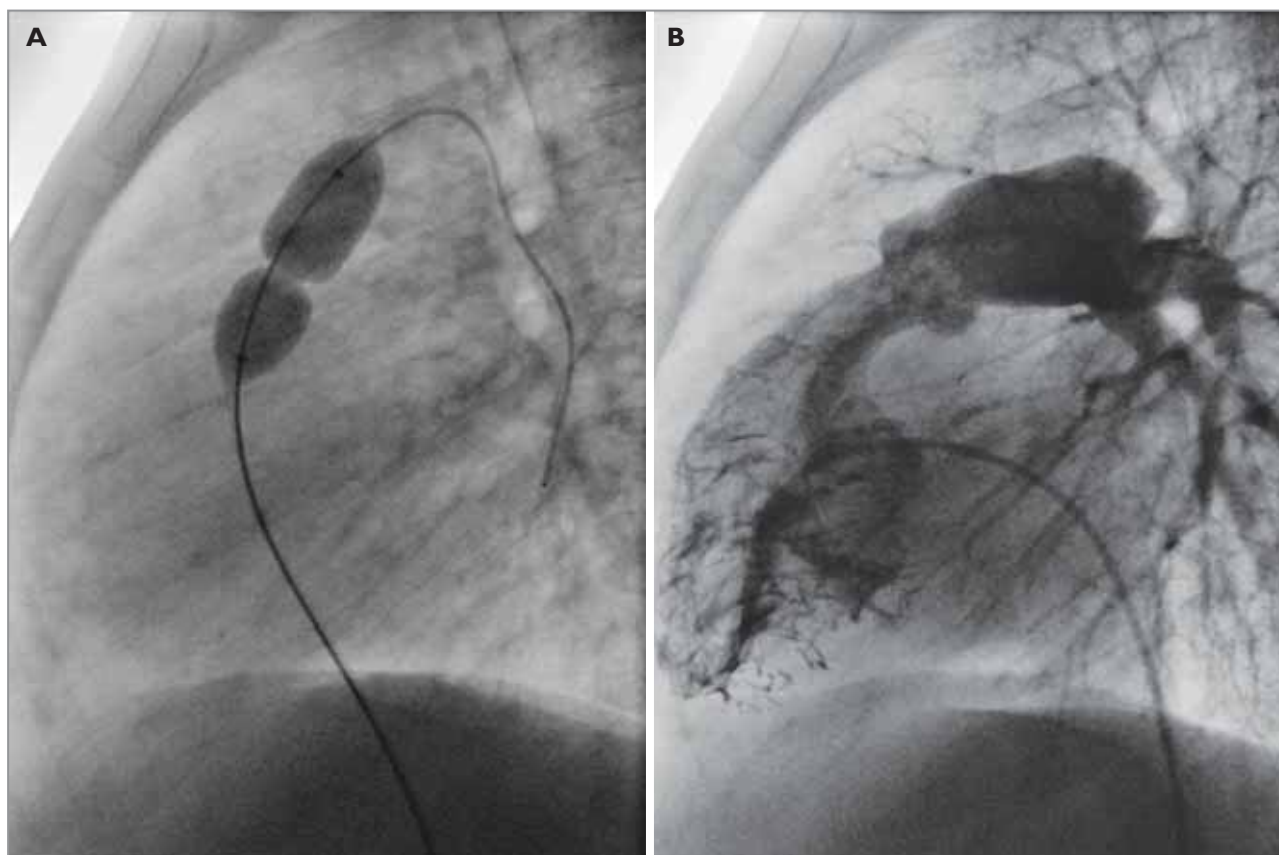


FIGURE 8: Images taken during balloon dilatation of the PV in a patient with critical valvular PS.

A: Tyshak II 10 mm balloon inflated showing clear waist at level of valvular PS.

B: Post-valvuloplasty RV angiogram shows good opening of the PV and filling of the MPA.

PAs is measured. Although a direct pull-back gradient across the narrowed PV is preferable, in cases where access across tight stenosis was tricky, the distal pressure is simply subtracted from the previously noted RV pressure to calculate the stenotic gradient, rather than losing the hard-won catheter position. The multi-purpose catheter is advanced to the LPA and a firm support wire is placed as distally in the LPA as possible. The LPA is preferred as it usually offers a superior angle of approach for the balloon to cross the RVOT. The balloon is prepared and advanced along the firm guidewire across the area of narrowing. It is inflated using an inflation device, containing a 1:2 mixture of contrast solution and saline, to the recommended nominal pressure. Fluoroscopy during inflation will note whether the area of constraint on the balloon formed by the stenosis is eliminated during inflation, or if the “waist” formed persists. A significant residual waist may be an indication to up-size to a larger balloon – whilst not exceeding the maximum of 1.2 times the PV annular size. It is also useful to capture fluoroscopy during deflation of the balloon, to see if there is any recoil of the balloon waist. This is often seen if the PV is dysplastic or severely fibrotic, and may be an indication for using a less compliant balloon for subsequent dilations. The pressure gradient across the PV is measured again after valvuloplasty – the procedure is considered successful if the gradient obtained by direct pull-back from the MPA to the RV is reduced to <30mmHg. If further dilations are anticipated, this pull-back gradient can be performed using a multi-track catheter, whilst maintaining the guidewire position in the LPA.

Critical PS is a cardiac emergency. In the neonatal period, the PDA may be re-opened, using a prostaglandin infusion at 0.01 - 0.1 µg/kg/min, to augment the pulmonary blood flow. In the older child, the PDA has fibrosed to form the ligamentum arteriosus, and prostaglandin administration is ineffective. The patient must be taken for an urgent valvuloplasty to relieve the RVOTO. Access across the valve is usually obtained using a right coronary catheter with a soft 0.014” wire. During the procedure, prolonged occlusion of the tiny stenotic valve opening with catheters or wires must be avoided. It is advisable to prepare the chosen balloon and have it on the table so that it can be rapidly advanced across the PV as soon as the guidewire is in position. The balloon is inflated with a more dilute mixture (1:3) of contrast to saline. This lower viscosity solution aids to rapidly deflate the balloon, thus quickly restoring pulmonary bloodflow. Some neonatal valves may be so stenotic that serial balloon inflations may be necessary to adequately open the PV, starting with a small coronary balloon and gradually working up to the appropriate size final balloon. In long-standing critical PS, the patient may develop acute pulmonary oedema after the obstruction is relieved, and treatment with diuretics and ventilatory support may be needed in the short term until the lungs adapt to their new, increased blood flow.

Supra-valvular and peripheral PS are usually resistant to balloon dilatation. Pre-dilatation with cutting balloons may be needed to score the endothelium so that it can be stretched out.

Alternatively, re-expandable stents may be placed to relieve severe areas of obstruction. In children, these will need to be post-dilated serially as they grow.

Cardiac surgery

Surgery is indicated where valvuloplasty has failed to adequately reduce RVOT obstruction or where it is unlikely to be effective; for example in a hypoplastic PV annulus or obviously dysplastic valve, infundibular stenosis or peripheral stenosis. It is also indicated where there are associated defects that need surgical repair. Surgical valvotomy of the PV should be performed if the RVSP exceeds 80mmHg (TR velocity >4.3m/s). If a commissurotomy is unsuccessful and there is still severe PS and/or PR, a valve replacement may be needed. A non-mechanical valve, such as a homograft or other bioprosthetic valve is preferable as the risk of thrombosis in pulmonary mechanical valves is higher than in aortic mechanical valves, and long-term anti-coagulation therapy has its own associated morbidities. The longevity of these conduits is, however, limited in children, with stenosis and/or regurgitation developing rapidly due to graft calcification. In these patients, serial conduit placements may be needed until the child has grown enough for a percutaneous pulmonary valve implantation (PPVI). Although PPVI valves are currently not freely available in all sectors due to their prohibitive pricing, it is hoped that they will be in the future.

PROPHYLAXIS AGAINST INFECTIVE ENDOCARDITIS

The turbulent bloodflow across any area of stenosis can expose underlying cardiac collagen. This will then activate the coagulation cascade with formation of sterile clots along the lines of turbulence. If the patient then develops a bacteremia, for example after a dental extraction, these clots can then be colonised by bacteria to form septic vegetations with resultant Infective Endocarditis (IE). The latest AHA guidelines do not classify isolated PS as a risk factor for IE.⁽²¹⁾ However, we have seen IE cause severe destruction of the PV with subsequent right heart failure. The patient is left with a non-functional PV, with residual PS, and free PR. In our population, many professionals would still advocate prophylaxis against IE for congenital valvulopathies.

CONCLUSION

Pulmonary valve stenosis is a common congenital heart defect with a variable presentation. The majority of patients have a mild grade of PS and can be observed only. More severe PS can be treated well with little risk. Balloon valvuloplasty is the treatment of choice for valvular PS, and in experienced hands, has little morbidity or mortality. Many patients, however, may have some degree of residual PS or PR and must therefore be followed up long term.

Conflict of interest: none declared.

REFERENCES

1. Van der Linde D, Konings EE, Slager MA, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J Am Coll Cardiol* 2011;58:2241-7.
2. Libby P, Bonow RO, Mann DL, et al. *Braunwal's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Saunders Inc; 2007.
3. Jorge AA, Malaquias AC, Amhold IJ, et al. Noonan syndrome and related disorders: A review of clinical features and mutations in genes of the RAS/MAPK pathway. *Horm Res*. 2009;71(4):185-93.
4. Inglessis I, Landzberg MJ. Interventional catheterisation in adult congenital heart disease. *Circulation*. 2007;115(12):1622-33.
5. Armstrong EJ, Bischoff J. Heart valve development: Endothelial cell signaling and differentiation. *Circ Res*. 2004;95(5):459-70.
6. Kirby ML, Gale TF, Stewart DE. Neural crest cells contribute to normal aorticopulmonary septation. *Science*. 1983;220:1059-1061.
7. Maron BJ, Hutchins GM. The development of the semilunar valves in the human heart. *Am J Pathol*. 1974;74:331-344.
8. Moore K, Persaud T. *The Developing Human. Clinically Oriented Embryology*. 1998.
9. Nishimura RA, Gersony, et al. Second Natural History Study of Congenital Heart Defects. *Circulation*. 1993;87:89-137.
10. Libby P, Bonow RO, Mann DL, et al. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Saunders Inc; 2007.
11. Crawford. *Pulmonic stenosis*. *Cardiology*. 3rd ed. Mosby Inc; 2009.
12. D'Alfonso A, Sciotti G, Milano A. Images in cardiovascular medicine. Combined aortic and pulmonary stenosis in a 79-year-old man. *Ital Heart J*. 2000;(12):848.
13. Danford DA, Gumbiner CH, Martin AB. Effects of electrocardiography and chest radiography on the accuracy of preliminary diagnosis of common congenital cardiac defects. *Pediatr Cardiol*. 2000;21(4):334-40.
14. Vibhuti N Singh. *Imaging in Pulmonic Stenosis*. *E-medicine* 2015.
15. Cuypers JAAE, et al. *Heart* 2013;99:339-347.
16. Tenisch EV, Alamo LT, Sekarski N, et al. MR and CT imaging of pulmonary valved conduits in children and adolescents: Normal appearance and complications. *Pediatr Radiol*. 2014;(12):1518-31.
17. Geva T, Greil GF, Marshall AC. Gadolinium-enhanced 3-dimensional magnetic resonance angiography of pulmonary blood supply in patients with complex pulmonary stenosis or atresia: Comparison with x-ray angiography. *Circulation*. 2002;106(4):473-8.
18. Rajiah P, Nazarian J, Vogelius E, et al. CT and MRI of pulmonary valvular abnormalities. *Clin Radiol*. 2014;69(6):630-8.
19. Voet A, Rega F, de Bruaene AV, et al. Long-term outcome after treatment of isolated pulmonary valve stenosis. *Int J Cardiol* 2012;156:11-15.
20. McCrindle BW. Independent predictors of long-term results after balloon pulmonary valvuloplasty. *Valvuloplasty and Angioplasty of Congenital Anomalies (VACA) Registry Investigators*. *Circulation* 1994;89:1751-9.
21. AHA Statement: Infective Endocarditis in Children. *Circulation*. 2015; 132:1487-1515.