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Congenital Heart Defects in Adults : A Field Guide for Cardiologists

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Abstract

Advances in cardiology and cardiac surgery allow a large proportion of patients with congenital heart defects to survive into adulthood. These patients frequently develop complications characteristic of the defect or its treatment. Consequently, adult cardiologists participating in the care of these patients need a working knowledge of the more common defects. Occasionally, patients with congenital heart defects such as atrial septal defect, Ebstein anomaly or physiologically corrected transposition of the great arteries present for the first time in adulthood. More often patients previously treated in pediatric cardiology centers have transitioned to adult congenital heart disease centers for ongoing care. Some of the more important defects in this category are tetralogy of Fallot, transposition of the great arteries, functionally single ventricle defects, and coarctation. Through this field guide, we provide an overview of the anatomy of selected defects commonly seen in an adult congenital practice using pathology specimens and clinical imaging studies. In addition, we describe the physiology, clinical presentation to the adult cardiologist, possible complications, treatment options, and outcomes.

Introduction

Due to improvements in surgical and medical management, the vast majority of infants born with a congenital heart defect (CHD) survive into adulthood. The current population of adults with CHD in the United States is estimated to be at least one million [1]. These patients are now transitioning from pediatric cardiology centers to the care of adult cardiologists. Adult cardiology training programs often do not emphasize the complex physiology of congenital heart defects or the details of surgical procedures that allow these patients to survive [2]. The following field guide presents an overview of the anatomy, physiology, clinical findings, surgical treatment and outcomes of many types of patients now presenting to adult congenital heart disease (ACHD) centers.

Interatrial Communications

Interatrial communications are the third most common type of congenital heart defect and the type most likely to be diagnosed in adults.

Anatomy

The anatomy of the atrial septum is more complex than apparent at first glance (Figure 1). The fossa ovalis, the central part of the atrial septum, is bounded superiorly and rightward by septum secundum or superior limbic band. The fossa is covered by the thinner and more delicate septum primum. Septum primum is more apparent from the left atrial (LA) side where the overlap with and attachments to septum secundum are clearly seen. The inferior muscular base of the atrial septum between the fossa and the coronary sinus (CS) is continuous with the Eustachian valve and contains the tendon of Todaro. The muscular portion of the atrial septum between the fossa and the atrioventricular (AV) valves is the AV canal septum [3].

A secundum atrial septal defect (ASD2) is a defect within the fossa ovalis due to deficiency of septum primum (Figure 2). It is called a secundum ASD because it represents persistence of ostium secundum or the second opening between the developing atria. There are two mechanisms for an ASD2: septum primum can be too short to overlap with septum secundum leaving a defect between the superior border of septum primum and septum secundum; or a fenestration(s) can develop in septum primum. Occasionally there can be multiple small holes in septum primum called a cribriform fossa ovalis (Figure 3).

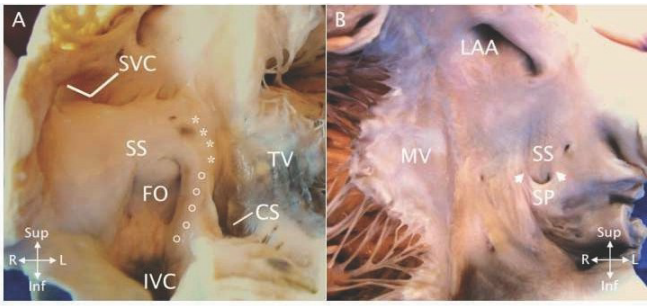

Figure 1: Anatomy of the normal atrial septum. A - Opened right atrium showing the entrance of the superior vena cava (SVC), inferior vena cava (IVC), and coronary sinus (CS). The fossa ovalis (FO) forms the central part of the atrial septum and is bounded superiorly and rightward by septum secundum (SS). Septum primum is the thin floor of the fossa. The muscular base of the atrial septum (o) is between the fossa and the coronary sinus. The AV canal septum (*) is adjacent to the tricuspid valve (TV). B - On the left atrial side, septum primum (SP) forms a hammock - shaped structure and has insertions (white arrows) on septum secundum (SS). LAA - left atrial appendage; MV - mitral valve.

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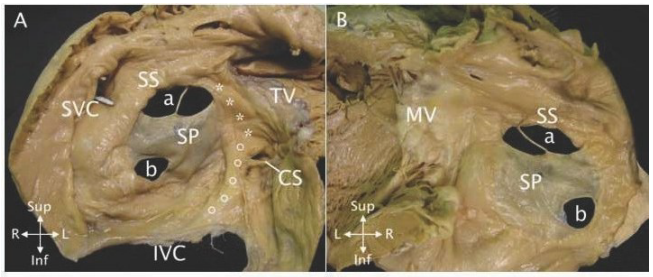

Figure 2: A. Opened right atrium showing two mechanisms for ASD2. Most frequently the defect (a) is between the superior border of septum primum (SP) and septum secundum (SS). The defect (b) can also be due to a hole in septum primum. The divided orifice of the inferior vena cava (IVC) is seen below the fossa ovalis and the orifice of the superior vena cava (SVC) above and rightward. The AV canal septum (*) is intact and the muscular floor of the atrial septum (o) is well - formed. B - The opened left atrium in the same heart showing both types of ASD2 as in A. CS coronary sinus; MV mitral valve; TV tricuspid valve.

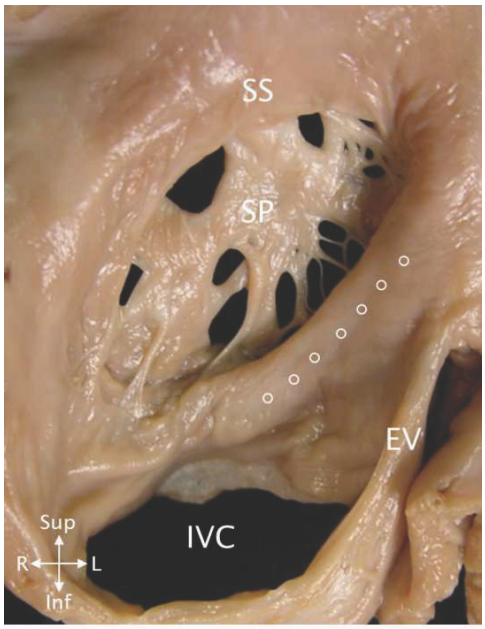

Figure 3: Multi - fenestrated septum primum (SP) or cribriform fossa ovalis. EV Eustachian valve, IVC inferior vena cava; SS septum secundum; o - muscular base of atrial septum.

While 2/3 of ASD2 are isolated, associated defects include pulmonary stenosis, partially anomalous pulmonary venous connection, and mitral valve prolapse [4].

A primum atrial septal defect (ASD1) is an AV canal or AV septal defect due to abnormal formation of the AV fibrous complex. The interatrial communication is due to failure of obliteration of ostium primum or the first hole between the atria (Figure 4). The resulting deficiency of the central part of the heart includes the inferior basal ventricular septum as well as the AV canal portion of the atrial septum. The inflow ventricular septum is shortened by the deficiency of basal muscular septum. The ASD1 is essentially always associated with abnormal development of the AV valves. The two principal AV cushions fail to fuse normally resulting in a cleft or zone of apposition between the superior and inferior components of the anterior mitral leaflet (Figure 5). The common inlet to the AV orifice is not divided because septum primum does not fuse with the AV cushions. The AV junction does not indent anteriorly because the inlet does not divide into two separate orifices. Consequently, the aorta does not become wedged between the AV valves. The AV node and penetrating bundle are more posterior than usual, lying on the crest of the muscular septum and beneath the inferior tricuspid leaflet.

Left ventricular (LV) outflow obstruction occurs 5% or so of young patients with ASD1 [5]. The mechanism is usually tethering of the superior component of the anterior mitral leaflet to the anterior

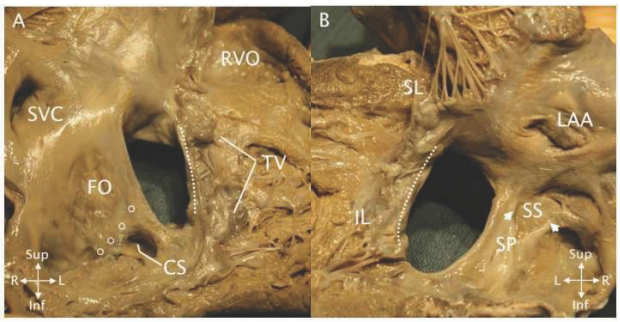

Figure 4: Opened heart with ASD1. A - The fossa ovalis (FO) is intact as seen in the opened right atrium. The ASD1 is leftward of the fossa and immediately adjacent to the TV. A tongue of AV valve tissue (.....) covers the crest of the muscular ventricular septum. B - Septum primum (SP) is seen in the left atrium inserting (arrows) onto septum secundum (SS) and continuing to the edge of the ASD1. The superior (SL) and inferior (IL) cushion components of the anterior mitral leaflet are seen in the LV. CS - coronary sinus; LAA - left atrial appendage; RVO - right ventricular outflow; SVC - superior vena cava; o - muscular base of the atrial septum.

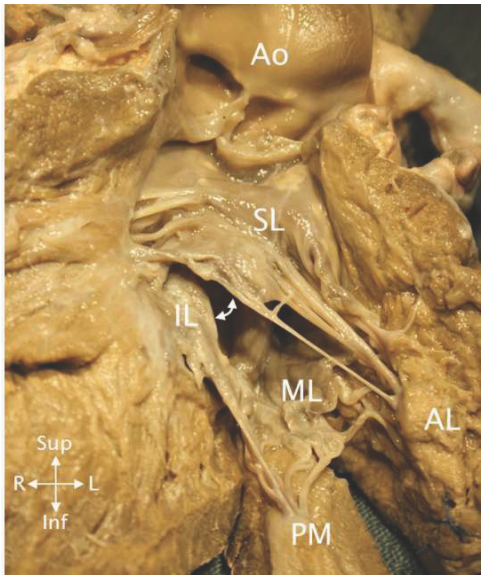

Figure 5: The superior (SL) and inferior (IL) components of the anterior mitral leaflet as well as the mural leaflet (ML) are seen in the opened LV in this heart with ASD1. The superior leaflet attaches only to the anterolateral papillary muscle (AL) and the inferior leaflet attaches only to the posteromedial papillary muscle (PM). The mural leaflet attaches to both. The cleft (white double headed arrow) is the space between the superior and inferior leaflets. Only the superior leaflet is in continuity with the aortic valve (Ao). Chordal attachments of this leaflet high in the outflow can cause subaortic stenosis.

muscular septum by short chordae. This prevents posterior motion of the leaflet out of the outflow during systole. A fibromuscular ridge or membrane contributes in some cases [6].

A sinus venosus defect (SVD) is not actually within the atrial septum (Figure 6). Rather, a superior vena cava (SVC) type of SVD is superior and rightward of the fossa ovalis, between the right cavo-atrial junction and the right upper pulmonary vein(s). The mechanism of development is unclear because these structures do not share a common wall early in development. It seems likely that SVD develop from disruption of the wall between the pulmonary veins and the SVC later in development. The SVD is always associated with anomalous drainage of one or more right pulmonary veins to the cavo-atrial junction. In some cases additional pulmonary veins connect anomalously to the SVC above the cavo-atrial junction. A rare type of SVD, the inferior or right atrial type, has been reviewed recently [7] and will not be discussed here.

The coronary sinus defect (CSD) is an opening between the CS and the LA (Figure 7). Left atrial blood traverses the CS to reach the right atrium (RA) resulting in enlargement of the CS. The size of the communication is variable, with complete unroofing of the CS in some cases. Most CSDs are associated with a persistent left SVC draining to the CS, or to the LA if unroofing is extensive. The mechanism for development of this defect is unclear because the left cardinal vein and left horn of sinus venosus do not share a common wall with the LA until later in development, suggesting that this defect also results from late disruption of the wall.

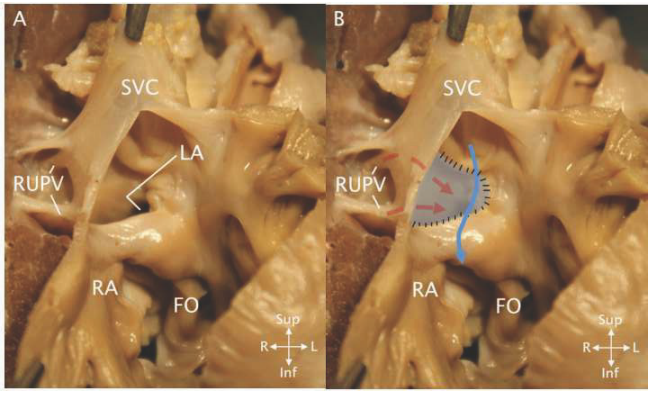

Figure 6: Superior vena cava type of SVD. A - The right atrium (RA) is opened to show the junction with the superior vena cava (SVC). The left atrium (LA) can be seen through the SVD. Two right upper pulmonary veins (RUPV) drain to the SVC - RA junction near the defect. The fossa ovalis (FO) is seen inferior and leftward of the SVD. B - The same view showing a 'patch' (gray) covering the defect. Pulmonary venous blood (dashed red arrows) flows to the LA behind the patch while the blue solid arrow indicates SVC flow to the RA in front of the patch.

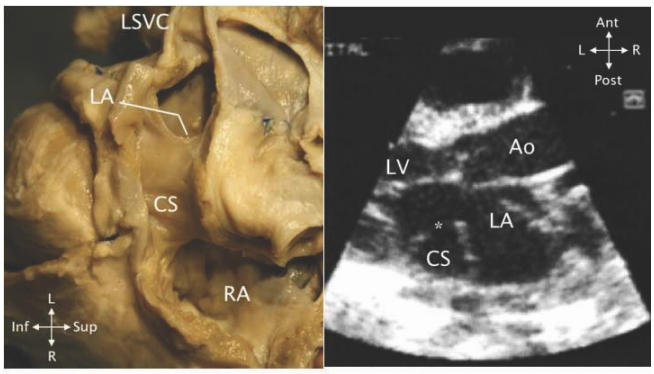

Figure 7: Posterior view of a heart with a CSD. The coronary sinus (CS) has been opened from the left superior vena cava (LSVC) to the right atrium (RA). The left atrium (LA) can be seen through the CSD, an opening in the wall between the CS and the LA. B - An echocardiogram in parasternal long - axis view showing a CSD (*) between the dilated coronary sinus (CS) and the left atrium (LA). Ao - aorta; LV - left ventricle.

All interatrial communications share a common pathophysiology and presentation.

Physiology

Flow across an interatrial communication is determined in part by the size of the defect and in part by the relative ventricular compliances [4]. Small defects (usually less than 8-10 mm) can be restrictive and limit both blood flow and pressure transmission. Flow across a large, unrestrictive defect is dependent on the difference in compliance between the right ventricle (RV) and LV rather than the pressure difference between the atria. Since the RV compliance is usually higher than LV, shunt flow is from left to right across the defect. The shunt causes volume loading of the RA and RV, resulting in chamber enlargement [8]. Increased pulmonary blood flow over time can damage the pulmonary vascular endothelium leading to an increase in pulmonary vascular resistance called pulmonary vascular obstructive disease. Comorbid conditions in adults such as ischemic and hypertensive heart disease might exacerbate the atrial left-to-right shunt by increasing LV end-diastolic pressure and decreasing compliance.

Patients with ASD1 and significant mitral regurgitation (MR) also have left heart volume overload with dilatation of the LV and LA. Subaortic stenosis can add LV pressure overload to the hemodynamic burden, with secondary LV hypertrophy and decreased compliance.

Patients with a CSD and left SVC draining to the LA have a small right-to-left shunt. Although this does not generally cause perceptible cyanosis, it does create a risk for stroke and brain abscess.

Presentation

Most interatrial communications do not cause symptoms in childhood allowing some to go undetected until adulthood [9]. Adults typically present with dyspnea, fatigue, palpitations, or atypical chest pain [10]. Alternatively, an atrial shunt might be discovered fortuitously, for example by echocardiography during evaluation for an arrhythmia.

The physical exam is characterized by a widely split and fixed second heart sound (S2) due to prolonged RV ejection which delays pulmonary valve closure. Flow across the atrial defect results in maximal filling of the RV during all phases of the respiratory cycle preventing the normal respiratory variation in the duration of RV ejection [8]. The RV apex is hyperdynamic and a pulmonary ejection murmur is usually audible due to increased RV stroke volume. If the shunt is large, a mid-diastolic tricuspid flow murmur is present as well. A holosystolic murmur at the apex indicates MR and a systolic outflow murmur at the right upper sternal edge subaortic stenosis [6].

Typical electrocardiogram (ECG) findings include rSR' pattern in the right precordial leads and first degree AV block [6]. The ECG distinguishes ASD1 from the other types by the superior QRS axis and counterclockwise frontal plane loop. The chest radiograph often shows an enlarged RA, RV and pulmonary trunk.

Diagnosis

Echocardiography is the primary diagnostic tool for interatrial communications (Figures 7, 8 and 9) [11]. Transesophageal echo is indicated in adults if the transthoracic exam is inadequate. Cardiac magnetic resonance imaging (CMR) is probably the modality of choice for SVD (Figure 10) because of its ability to detect anomalously connecting pulmonary veins [12].

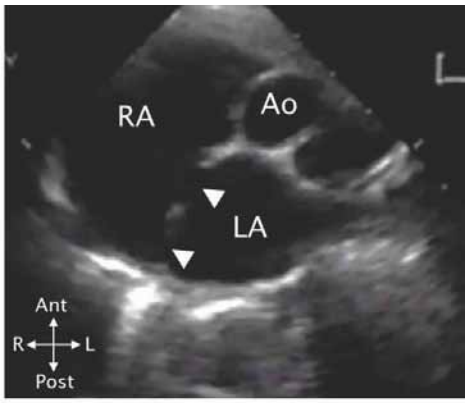

Figure 8: An echocardiogram in right sternal border view in a patient with multiple ASD2 (arrow heads). Ao - aorta; LA - left atrium; RA - right atrium.

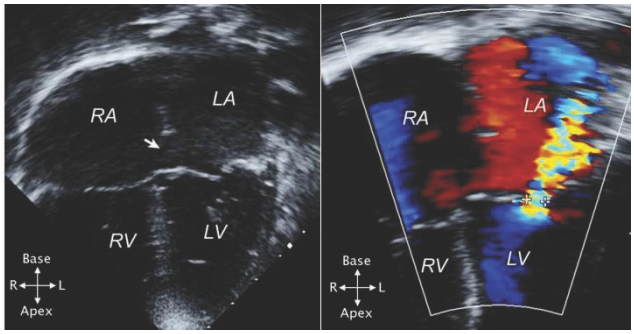

Figure 9: A - An echocardiogram in apical 4 - chamber view in a patient with ASD1 (arrow). The defect is just above the closure plane of the AV valves. B - Color Doppler exam in the same view showing mitral regurgitation (++), most likely through the cleft in the anterior mitral leaflet. LA - left atrium; LV left ventricle; RA - right atrium; RV - right ventricle. (Reprinted from Valente et al. [11] with permission).

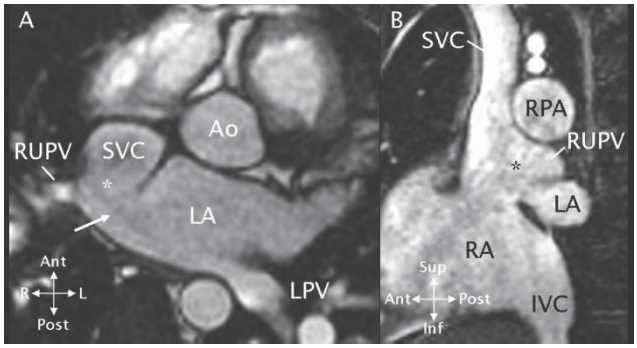

Figure 10: A - A MRI 3D SSFP axial view showing a superior vena cava (SVC) type of SVD (*). The right upper pulmonary vein (RUPV) drains to the SVC - right atrial junction near the SVD. The orifice of the RUPV into the left atrium (LA) (white arrow) is the interatrial communication. B - Sagittal projection of the same data set shows the defect (*) between the SVC - RA junction and the RUPV. Ao - aorta; IVC - inferior vena cava; LPV - left pulmonary vein; RPA - right pulmonary artery. (Reprinted from Valente et al. [11] with permission).

Catheterization is rarely indicated for diagnosis of an interatrial communication [4].

Treatment

Closure of an interatrial communication is indicated even for asymptomatic patients if the right heart is enlarged [13]. Closure of an ASD2 can be accomplished by surgery or interventional catheterization (Figure 11) [14]. Successful percutaneous closure can be achieved in 95% of patients with favorable anatomy [15]. Several series have reported a surgical success rate of 100% with a less than 1% complication rate [14-16].

ASD1, on the other hand, is a surgical defect. Repair involves patch closure of the defect and closure of the cleft or zone of apposition in the mitral valve. Failure to close the cleft in the anterior mitral leaflet often results in progressive MR and additional surgery [17]. Various techniques have been adapted to treat LV outflow obstruction, ranging from resection of fibrous tissue and removal of abnormal chordal attachments to a modified Konno procedure [18,19].

The SVD is a surgical defect as well. In most cases of SVD, the opening between the right pulmonary veins and the cavo-atrial junction can be closed using a patch, with the pulmonary veins draining to the LA behind the patch and the SVC to the RA in front of the patch (Figure 6). If there are additional pulmonary veins connecting to the SVC more superiorly, a different approach is indicated. The SVC is transected and over sewn proximally just above the superior-most pulmonary vein. The mouth of the SVC and any veins draining to the cavo-atrial junction are baffled through the defect to the LA. The distal SVC is then connected to the RA appendage. This approach is less likely to cause sinus node dysfunction [20,21].

The CSD can often be closed with a patch or by direct suture. If unroofing of the CS is extensive, then the ostium of CS can be closed with a patch and the persistent left SVC ligated or redirected to the RA. Allowing cardiac veins to drain to the LA has little effect on systemic oxygen saturation.

Complications

Atrial arrhythmias are the most frequent late complication. Patients repaired early in life have a small risk for supraventricular tachycardia and the risk increases with advancing age at repair. If repair is undertaken in adults greater than 40 years of age, pre-operative or early post-operative atrial flutter or fibrillation is an independent predictor of late recurrence of these rhythms [22]. The occurrence of atrial arrhythmias does not appear related to surgical technique [23], except in SVD where the two-patch technique is associated with a greater risk of sinus node dysfunction compared with transection of the SVC [15,16]. Atrial fibrillation appears to have an earlier age of onset (less than 30 years) in patients with ASD1 than in other atrial shunts, likely due to concomitant left AV valve regurgitation. In addition, atrial arrhythmias are a common cause of deterioration [24-27]. Late acquired heart block can be seen in ASD1, even in unrepaired patients [24]. Current guidelines recommend periodic Holter monitoring to detect AV conduction defects [13,27].

Pulmonary hypertension, another important late complication, is rare in patients operated before 25 years of age, and the risk increases

with advancing age at repair [1,11,12]. While related, in part, to increased pulmonary blood flow, the exact mechanism is unknown. Mitral regurgitation and LV outflow obstruction are other important late complications in ASD1 [13,26].

Outcomes

Patients who undergo repair of an atrial communication prior to 25 years of age appear to have a normal lifespan and low risk for pulmonary hypertension and arrhythmias [28]. Closure after 25 years but prior to 40 years increases the risk of atrial arrhythmias [22]. Repair after age 40 years reduces cardiovascular complications (Figure 12) but does not clearly provide a mortality benefit [15].

Outcomes for repair of ASD1 in adulthood are quite good with low operative risk [25-29]. Actuarial survival is significantly less than age and gender matched controls, 84% at 5 years and 77% at 10 years, respectively [29]. The freedom from reoperation for LV outflow obstruction is 70% at ten years [29].

Ebstein Anomaly

Anatomy

The primary abnormality in Ebstein anomaly is apical displacement of the functional annulus of the TV due to failure of delamination of the septal and sometimes posterior leaflets during embryological development (Figure 13). In addition, the axis of the TV is rotated from a base-apex direction to a diaphragmatic wall-outflow direction. The ventricle proximal to the functional valve annulus becomes "atrialized" with enlargement and thinning or hypertrophy [30,31], while the functional RV distal to the valve is variably hypoplastic [32]. The anterior leaflet remains attached at the anatomical tricuspid annulus, but is often large and "sail-like" while the septal leaflet is dysplastic and adherent to the underlying septum. The anterior leaflet is sometimes redundant and often has fenestrations. The leaflets are tethered to the underlying myocardium by short chordae. Papillary muscles can be attached directly to the leaflets by muscular bands [33,34]. The result most often is tricuspid regurgitation (TR) with a large, central regurgitant orifice [6], but in some cases tricuspid stenosis is predominant (Figure 14) [33].

Associated lesions include an interatrial communication, and less commonly muscular ventricular septal defect (VSD) or patent ductus arteriosus. In more complex forms of Ebstein anomaly, pulmonary stenosis or atresia or left-sided abnormalities such as mitral stenosis or regurgitation can be seen [35].

The conduction system is often abnormal, with prolonged conduction in the enlarged RA. Right bundle branch block is present in up to 95% of cases [36] and the right bundle itself might be abnormally located [6] The AV node is usually located in the triangle of Koch [32]; however, there is often discontinuity of the central fibrous body leaving accessory pathways [6,33] often located on the same side as the malformed tricuspid valve [37]. There is also prolonged infranodal conduction due to lengthening or stretching of the conduction system within the atrialized RV [36].

Physiology

Forward flow through the right heart is diminished, with right-to-left shunting across the atrial septum and/or reduced systemic cardiac output. TR reduces the forward stroke volume of the already hypoplastic functional RV. The atrialized RV balloons out during atrial systole, acting as a passive reservoir rather than participating in

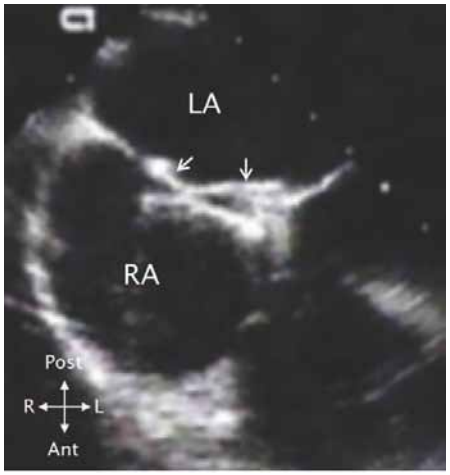

Figure 11: Transesophageal echocardiogram following device closure of an ASD 2. The left atrial arms of the device (white arrows) are seen in the left atrium (LA). RA - right atrium.

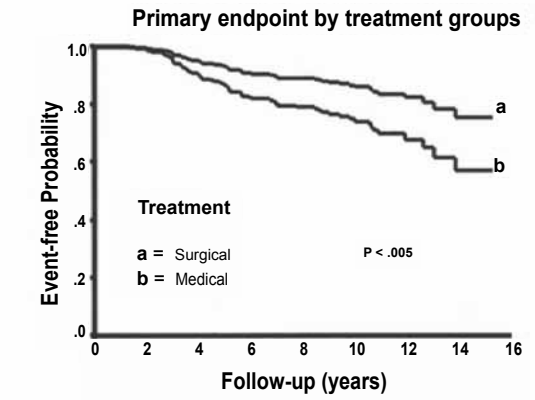

Figure 12: Kaplan Meier curve showing results of a randomized trial of surgical vs medical treatment of adults > 40 years old with ASD2 using a composite endpoint of cardiac - related death, heart failure, pulmonary or systemic embolism, recurrent pulmonary infection, sustained ventricular tachyarrhythmia and progression of pulmonary hypertension. (Reprinted from Attie et al. [16] with permission).

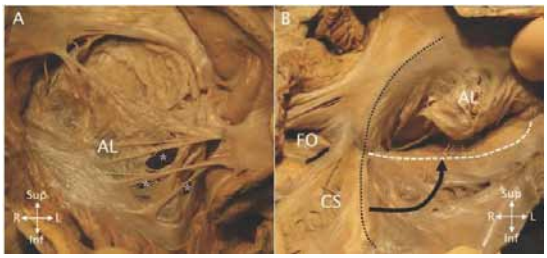

Figure 13: A heart with Ebstein anomaly. A - The right ventricle is opened showing the anterior tricuspid leaflet (AL) with multiple small fenestrations (*) and nearly continuous attachment of the anterior leaflet free edge to the RV wall. B - The right atrium and right ventricular inflow have been opened. The fossa ovalis (FO) and coronary sinus (CS) are seen in the right atrium. The black dotted line indicates the anatomic annulus of the tricuspid valve and the white dashed line the actual hinge point of the septal tricuspid leaflet. The space below the white line is the atrialized right ventricle. The black curved arrow indicates the superior rotation of the functional tricuspid annulus toward the RV outflow tract.

coordinated atrial contraction, thus impeding atriosystolic filling of the RV [38]. The small functional RV is often less compliant than the LV, favoring right-to-left atrial shunting. In patients with predominantly tricuspid stenosis, the valve directly limits forward flow and favors interatrial shunting.

The pulmonary valve (PV) and pulmonary arteries are often smaller than normal, increasing impedance to forward flow and favoring TR. Over time, there is RV dilation and thinning of the free wall, both from TR [33] and possibly from an inherent myopathy [38]. With severe RV enlargement, the ventricular septum shifts leftward adversely affecting LV filling [33]. This adverse ventricular-ventricular interaction can reduce cardiac output, especially with exercise.

Presentation

The severity of disease dictates when and how patients present. The most severe forms of Ebstein anomaly present with cyanosis and heart failure in the neonatal period while adults might present with only an arrhythmia associated with an accessory pathway [6]. Adult Ebstein patients also exhibit cyanosis, exercise intolerance, dyspnea, fatigue, or right-sided heart failure [39].

Despite the presence of severe TR, "V" waves are rarely seen because the capacious RA contains the increased volume with little increase in pressure [31]. The cardiac exam is often described as a musical cacophony. The first heart sound is widely split, with a loud tricuspid component due to increased excursion of the anterior tricuspid leaflet and delayed closure of the abnormal TV [6,40]. The sudden deceleration of the large anterior leaflet as it reaches the limit of its excursion produces the "sail sound" [40]. There are often ventricular filling sounds (third or fourth heart sound) due to abnormal ventricular compliance. The sum of all this is a complex quadruple rhythm. A holosystolic murmur heard best at the lower left sternal border is due to TR. Hepatomegaly from hepatic congestion usually indicates right heart failure [6].

The ECG often has tall, broad P waves with first degree AV block resulting from abnormal AV conduction in an enlarged RA [35]. The QRS is wide with a right bundle branch block pattern due to infra-Hisian conduction disturbances [35]. Up to 30% of patients have evidence of an accessory pathway (Wolf-Parkinson-White pattern). The chest radiograph typically shows cardiac enlargement with a globular contour [6,35].

Diagnosis

Echocardiography is diagnostic (Figure 15) and useful for evaluating anatomy and function of the TV, the size of the functional RV, and presence of associated defects [6,41,42].

CMR is the most reliable method for estimating RV size and function (Figure 16) [43]. It is indicated prior to surgical intervention on the valve and is probably the best method for serial evaluation of adult patients.

Pulse oximetry is useful to quantify cyanosis at rest and during exercise [13]. Exercise testing is an objective method to follow functional capacity. Extended ECG monitoring is useful to detect and diagnose arrhythmias [13].

Treatment

Medical therapy of Ebstein anomaly is limited to management of complications. Patients with refractory atrial fibrillation might benefit from pharmacologic rate control and anticoagulation [13]. Some

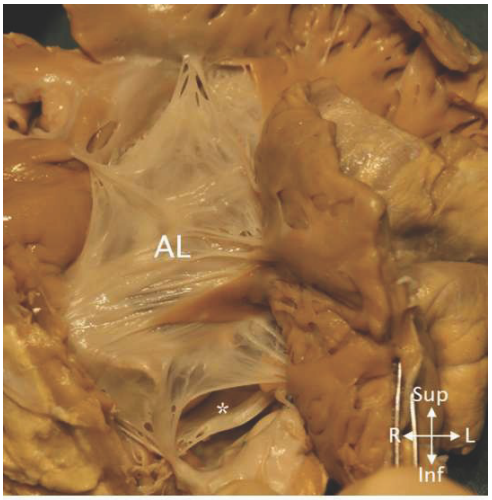

Figure 14: An obstructive form of Ebstein anomaly. The anterior tricuspid leaflet (AL) is continuously attached at the free edge to the right ventricular wall except inferiorly where there is a small orifice (*).

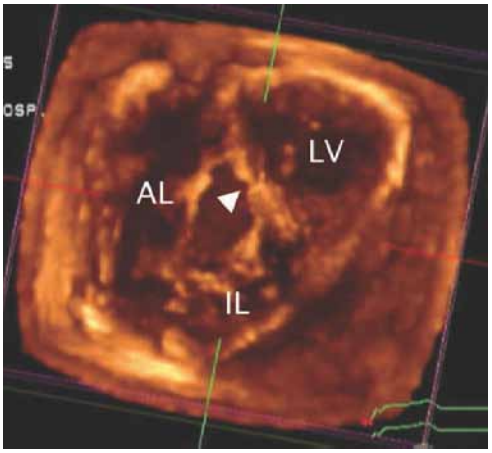

Figure 15: A 3 - dimensional echocardiogram in a patient with Ebstein anomaly viewed from the apex. The septal tricuspid leaflet did not delaminate from the septum (arrowhead) leaving a gap between the anterior (AL) and inferior (IL) leaflets. LV - left ventricle. (Image courtesy of Jerry Marx, MD, Children's Hospital Boston).

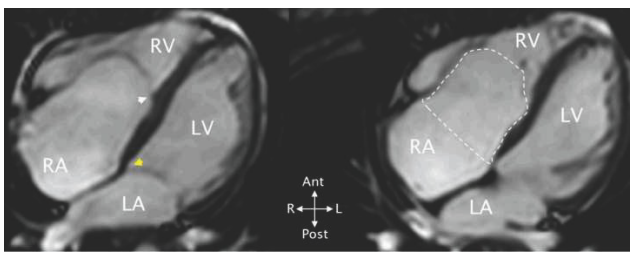

Figure 16: MRI cine SSFP 4 - chamber projection in a patient with Ebstein anomaly showing the offset between the mitral (yellow arrow)and tricuspid (white arrow) insertions. The dotted line indicates the atrialized right ventricle. The functional right ventricle (RV) is small. LA - left atrium; LV - left ventricle; RA - right atrium.

arrhythmias are controllable with medication. Diuretic therapy is useful to maintain fluid balance in heart failure.

Transcatheter ablation is the standard treatment of an accessory pathway or other arrhythmia substrate but success rates tend to be lower and recurrence rates higher than in the structurally normal heart [44].

Percutaneous closure of an ASD2 might be useful in select patients with Ebstein anomaly, although there are few supporting data. Patients with a predominately left-to-right shunt are most likely to benefit. Cyanotic patients can be harmed by ASD2 closure. If this procedure is undertaken, test occlusion of the defect must be performed to ensure that systemic blood pressure and cardiac output can be maintained [45].

TV surgery is recommended for patients with deteriorating functional capacity, cyanosis (oxygen saturation < 90%), paradoxical embolism, progressive cardiomegaly, progressive RV dilation, or a reduction of RV systolic function [13]. Prior to surgery, all patients should undergo an invasive electrophysiology study to localize and ablate any accessory pathway(s). If an arrhythmia is present and not amenable to percutaneous treatment, then arrhythmia surgery (e.g. a Maze, cryoablation of AV node reentry tachycardia, or surgical division of accessory conduction pathways) should be performed at the time of the valve procedure [13].

The objectives of surgery are to improve TV function and increase right heart output. The general strategy includes partial or complete closure of any interatrial communication, repair or replacement of the TV, and reduction of RA size. Relocating the TV to the anatomic annulus increases the size of the functional RV and decreases the size of the RA. Table 1 summarizes the surgical strategies that have been employed [46-49].

Complications

Atrial tachyarrhythmias occur in one-third of post-operative patients [50]. Catheter ablation remains a challenge with a success rate of 87% per procedure and a high recurrence rate of 29% [44]. Half of patients have multiple connections [6] and the pathways can be located in the atrialized RV with abnormal morphology of the endocardial activation potentials [51] making ablation difficult.

Recurrent hospitalizations are frequent, occurring in up to 65% of patients at 20 years postoperatively, with arrhythmia being the most common indication for readmission [50].

Sudden death is a rare late complication, occurring in about 2% of patients [52]. Identification of patients at risk is challenging [6,53-55].

Outcomes

While fetal or neonatal presentation of Ebstein anomaly is associated with a poor outcome [39, 56], adults have a much better prognosis [52,57]. Risk factors for poor outcomes in unoperated adult patients include an early age at diagnosis, male sex, severity of morbid anatomy, pulmonary outflow obstruction, and cardiothoracic ratio >0.65 [39,57]. Surprisingly, supraventricular arrhythmia does not appear to be associated with worse outcome [39,57,58]. There are no randomized trials comparing surgical and non-surgical management of Ebstein anomaly.

Surgical mortality in adult patients is low, under 3% in the current era [58]. Atrial arrhythmia is the most frequent early complication. Survival and functional status did not differ significantly between groups undergoing TV repair or replacement [50,59].

The overall freedom from late reoperation is 74% at 10 years and 46% at 20 years. Risk factors for re-operation include an arrhythmia procedure, wide complex tachycardia, at least moderate ventricular dysfunction, and age at surgery < 12 years [58].

Physiologically Corrected Transposition of the Great Arteries (CTGA)

Most patients with CTGA are now diagnosed in infancy or childhood. Some without associated defects go undetected until the 3rd to 6th decades and rare patients survive a lifetime with no symptoms [60,61]. Consequently, the population followed in most adult congenital heart disease clinics is a mix of operated and unoperated patients.

Anatomy

CTGA is a complex congenital defect with AV and ventriculo-arterial (double) discordance. There are two types of CTGA. In the most common type, the atria and the abdominal organs are in the usual locations (situs solitus). However, the ventricles are inverted so that the RA is aligned with the right-sided LV via the MV and the LA with the left-sided RV via the TV (Figure 17). Further, the great arteries are transposed so that the left-sided aorta is aligned with the RV and the right-sided pulmonary artery with the LV. At least 20% of patients have mesocardia or dextrocardia [13]. The term "corrected" is used to denote that double discordance results in physiologic correction of blood flow. Systemic venous blood reaches the pulmonary artery through the LV and pulmonary venous blood the aorta through the RV [62].

A much less common form of CTGA occurs in situs inversus and is the mirror image of the type described above. In this type, there is inversion or left-right mirror imagery of the atria and abdominal

Year of Inception	Surgeon	Effect on Tricuspid Valve	Valve Coaptation	Effect on Atrial Size	Effect on Functional RV
1958	Hunter and Lillehei [49]	Valve is brought to anatomic annulus by transverse plication of atrialized RV	Anterior and posterior leaflets function as bicuspid valve	Reduced	No effect
1972	Danielson [46]	Valve is repaired or replaced at level of functional annulus (high need for TVR[179])	Anterior leaflet functions as monocusp	Reduced (transverse plication of atrialized RV	No effect
1980	Carpentier [47]	Valve is brought to the anatomic annulus (anterior/posterior leaflets detached, annular ring)	Coaptation between leaflets and ventricular septum	Reduced (longitudinal plication of atrialized RV)	Increased
1989	Da Silva [48]	Valve is brought to anatomic annulus	Coaptation between leaflets	Reduced	Increased

RV – right ventricle; TVR – tricuspid valve replacement

Table 1: Surgical Strategies Employed in the Surgical Repair of Ebstein Anomaly.

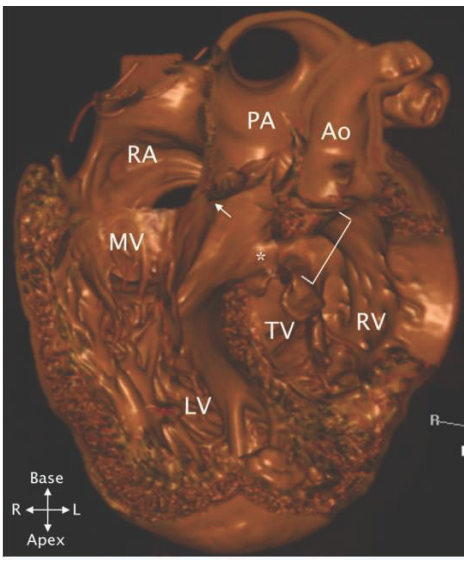

Figure 17: A 3D reconstruction of a CT scan of a waxed heart specimen with CTGA and ventricular septal defect. The right - sided right atrium (RA) is aligned with the right - sided left ventricle (LV) via the mitral valve (MV) and the left - sided left atrium with the right ventricle (RV) through the tricuspid valve (TV). The pulmonary artery (PA) is aligned with the LV and there is mitral - pulmonary fibrous continuity (white arrow). The aorta (Ao) is aligned with the RV and is separated from the tricuspid valve by subaortic conus (bracket). There is a large ventricular septal defect (*) in this specimen.

organs. Here the systemic venous blood returns to the left-sided RA, left-sided LV and left-sided and posterior pulmonary artery. Pulmonary venous blood returns to the right-sided LA, right-sided RV and right-sided and anterior aorta.

Associated lesions are frequent, with only about 16% of cases occurring in isolation [63]. The most common are VSD (60-80%), pulmonary stenosis (30-50%) and TV abnormalities (70%), including dysplasia or Ebstein anomaly (35%) [64]. Pulmonary stenosis can be valvar and/or subvalvar due to accessory AV valve tissue or a fibrous ridge [65].

The AV node (AVN) is in the anterior part of the atrial septum in CTGA in situs solitus. Often there is also an additional posterior AVN, but it is usually hypoplastic and rarely connects to a penetrating bundle [66]. This anterior location of the AVN and penetrating bundle makes them vulnerable to complete heart block [6]. The bundle branches are inverted along with the ventricles. Because of the anterior location of the node and penetrating bundle, the conduction system passes in the superior rim of a VSD [66]. In contrast, the AVN is in the usual position in CTGA in situs inversus [62].

The coronary anatomy is quite different from the normal heart. The accompanying article by Baraona et al. in this issue provides a detailed description [67].

Physiology

In the absence of associated defects, the physiology in CTGA is normal. A VSD results in shunting from the systemic RV to the pulmonary LV and produces a RV volume overload. A VSD plus pulmonary stenosis can result in a right-to-left shunt and cyanosis (like tetralogy of Fallot) or a balanced circulation with only a small shunt in one direction or the other. Isolated pulmonary stenosis causes pressure overload of the LV and if severe can cause failure of the pulmonary ventricle.

TR is like MR in the normal heart and can cause LA and pulmonary venous hypertension. The systemic RV fails sooner with associated defects and later without (Figure 18).

Presentation

Without associated defects, CTGA patients can be asymptomatic until the third to sixth decades [60,61]. Typical presenting symptoms include a murmur, cyanosis, bradycardia, heart failure, and arrhythmia [68]. In some cases the diagnosis is made incidentally by cardiac testing for other reasons.

Physical exam reveals a single, loud S2 due to the anterior location of the aorta [62] and difficulty hearing the soft closure sound of the posterior pulmonary artery [68]. A holosystolic murmur at the left sternal border, often with a thrill, indicates a VSD [69]. Pulmonary stenosis causes a systolic ejection murmur at the left or right upper sternal border [70]. Cyanosis and clubbing could be due to pulmonary stenosis with VSD (tetralogy of Fallot physiology) or to Eisenmenger syndrome [13]. A holosystolic murmur at the apex is due to TR [13].

Q waves in the inferior ECG leads are due to right-to-left septal depolarization and can be misinterpreted as a prior inferior myocardial infarction [70]. About one-half of patients have 1st degree AV block and the risk of 3rd degree AV block increases with age [69,70]. The P wave is negative in lead I in CTGA in situ sinversus because the atria are inverted; however, ventricular septal activation is normal because the ventricles are normally located [62].

Signs on the chest radiograph suggestive of CTGA are a prominent left-sided ascending aorta [62] and dextrocardia [70].

Diagnosis

Two-dimensional echocardiography is diagnostic [62,71]. CMR is the standard for assessment of ventricular size and function, and can be useful to define anatomy if echocardiographic windows are poor (Figure 19) [13].

Extended ECG monitoring is used to diagnose arrhythmias and to

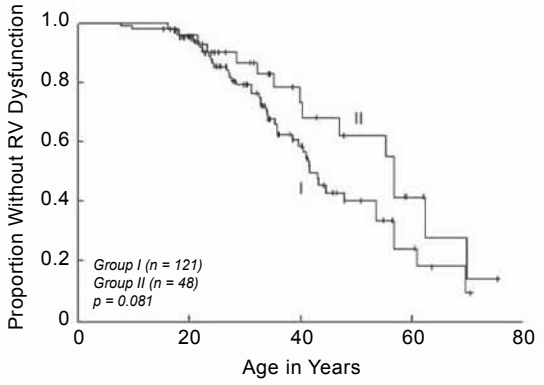

Figure 18: Kaplan Meier curve showing probability of freedom from systemic ventricular dysfunction in patients with CTGA. Group I had significant associated defects such as moderate or more tricuspid regurgitation, VSD, pulmonary stenosis. Group II had no or mild associated defects. (Reprinted from Graham et al. [63] with permission) .

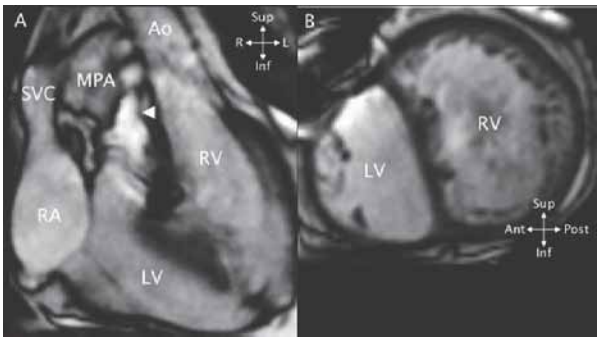

Figure 19: MRI cine SSFP frontal (A) and short - axis (B) views in a patient with CTGA. A - The right - sided right atrium (RA) is aligned with the right - sided left ventricle (LV) and the LV is aligned with the right - sided main pulmonary artery (MPA). There is dephasing in the MPA (arrowhead) due to pulmonary stenosis. The aorta (Ao) is superior and leftward and aligned with the left - sided right ventricle (RV). B - The LV, marked by the smooth septal surface and free wall papillary muscles, is anterior while the coarsely trabeculated RV is posterior. SVC superior vena cava.

estimate average and slowest heart rate in patients with heart block. Exercise testing provides an objective assessment of functional capacity.

Cardiac catheterization can be useful to obtain physiological information or if non-invasive testing is not diagnostic [13].

Treatment

Medical therapy for CTGA is useful to control arrhythmias [13] and to treat heart failure. The optimal medical strategies for treatment of systemic RV dysfunction are unknown. Diuretic therapy is effective for management of fluid balance. In a small study of 28 CTGA patients, afterload reduction with ACE inhibitors did not improve exercise capacity [72]. It is unclear if renin-angiotensin activation plays a role in systemic RV dysfunction [73]. On the other hand, a small pilot study of carvedilol in CTGA patients with RV dysfunction showed positive remodeling and increased exercise duration [74].

Invasive electrophysiology treatment is indicated for atrial tachyarrhythmias (catheter ablation) and for bradycardia due to heart block (pacemaker therapy). Single site pacing can induce dyssynchrony and rightward septal shift can worsen TR [13]. Biventricular pacing in CTGA is difficult due to the unusual cardiac venous anatomy [75].

In adolescent and adult patients, surgical therapy is usually directed to a specific hemodynamic abnormality. Patients with severe or progressive TR are candidates for TV replacement [13]. Timing of surgery should avoid deterioration of RV function [76]. Closure of a VSD should be considered if the RV is dilated and pulmonary vascular resistance is not significantly elevated. Severe aortic regurgitation (likely from progressive root dilation) with RV dilation should be addressed before RV function deteriorates. Relief of isolated pulmonary stenosis has been advocated, but it is not clear that this is beneficial unless LV pressure is suprasystemic. In fact, the septal shift toward the LV that follows lowering LV pressure can provoke or worsen TR [77].

Some highly select adult patients with CTGA are candidates for an anatomic correction. The success of anatomic repair is dependent on the LV being adequately prepared to generate systemic blood pressure [69]. Included are patients with severe, but remediable, pulmonary stenosis and those with a large outlet VSD. The procedure switches both venous inflow (Mustard) and arterial outflow (arterial switch or Rastelli operation, that is baffling the LV to the aorta through the VSD and placement of a RV to pulmonary artery conduit) [13]. Adult patients with symptomatic RV failure are candidates for heart transplantation because re-training the LV to perform systemic work after years of functioning as the pulmonary ventricle has been mostly unsuccessful [78].

Previously operated CTGA patients might also undergo surgery for various reasons including replacement of a dysfunctional LV- or RV-to-pulmonary artery conduit and aortic valve surgery for aortic regurgitation [13].

Complications

Presbitero et al. categorized the onset of complications by decade in a group of patients with CTGA without associated lesions. The percentage of patients with complete AV block was fairly constant from decade to decade and ranged from 25 to 30%. TR begins in the second decade, becomes moderate or more in the third decade, and increases in severity and prevalence thereafter. Supraventricular arrhythmias appear in the fifth decade, and can result from increasing LA pressure due to progressive TR and/or a failing systemic RV. Progressive TR begets more dilation of the systemic RV, which in turn contributes to more regurgitation [70]. Congestive heart failure with pulmonary edema often ensues between the fourth and sixth decades [60]. Aortic regurgitation, not previously reported in CTGA, is now known to be a frequent problem in this population [69].

Outcome

Outcomes for conventional repair have improved from lessons learned over the past three decades. The outcomes for various cohorts are shown in (Table 2) [79-83]. Earlier referral for surgery before deterioration of RV function [79,80], replacement of the TV for even mild to moderate regurgitation during surgery for other indications [83], and use of techniques to avoid heart block have resulted in current operative mortality of about 6%. However, medium to long-term outcomes are disappointing, with a 69% survival at 10 years for patients undergoing repair of VSD +/- pulmonary stenosis or atresia [82]. Graham et al. found that by age 45 years 67% of patients with associated lesions and 25% with isolated CTGA had symptoms of heart failure (Figure 18) [63].

Transposition of the Great Arteries (DTGA)

Infants with DTGA present with cyanosis in the first days of life. Without treatment at least 90% die by one year of age [84]. Consequently, patients presenting to an ACHD center have had corrective surgery in infancy or childhood.

Anatomy

The primary abnormality in DTGA is ventriculo-arterial discordance. The atria and ventricles are normally located but the great arteries are aligned with the incorrect ventricle, that is, the aorta is aligned with the RV and the pulmonary artery with the LV [62]. The aorta is usually anterior and rightward of the pulmonary artery but the great arteries can be side-by-side and rarely the aorta is posterior or anterior and leftward [6].

Associated defects include a VSD (40%), LV outflow tract obstruction (20%), and coarctation of the aorta (5%) [6]. Coronary artery anatomy is variable and important for the arterial switch operation (ASO) [85]. The article by Baraona et al. in this issue provides details [67].

Patients born before the early 1980s most likely underwent an atrial switch operation (Mustard [86] or Senning [87]) or a Rastelli

Lead Author	Year	Patients	Outcomes
Lundstrom [83]	1990	111 patients from Hospital for Sick Children and National Heart Hospital of whom 51 underwent surgery	• Operative mortality: 11/51 (22%) • Dilated systemic ventricle is a risk factor for a poor outcome
Termignon [79]	1996	52 patients from Laennec Hospital, Paris	• Operative mortality: 15% • Survival: 83% at 1 year, 55% at 10 years (for patients with associated VSD/LVOTO) while those with only associated VSD had 71% survival at 10 years
Van Son [80]	1995	40 patients from Mayo Clinic	• Operative mortality 10% • Survival: 78% at 5 years, 61% at 10 years • RVEF > 44% favored survival
Yeh [81]	1999	127 patients underwent surgery at Hospital for Sick Children, median age at operation was 8 years	• Operative mortality 6% • Survival: 48% at 20 years
Hraska [82]	2005	123 patients underwent surgery at Children's Hospital Boston, median age at operation was 7.9 years	• Survival: 84% at 1 year, 75% at 5 years; 68% at 10 years, and 61% at 15 years • Freedom from RV dysfunction (2V repair) 43% at 15 years • Ebstein malformation of the tricuspid valve is a risk factor for RV dysfunction

VSD – Ventricular septal defect; LVOTO – Left Ventricular Outflow Tract Obstruction; RVEF – Right Ventricular Ejection Fraction; V – Ventricle; TVR – Tricuspid Valve Replacement; RV – Right Ventricle

Table 2: Outcomes for Surgical Repair for CTGA.

[88] operation. Patients born after the late 1980s were most likely repaired using the ASO (Figure 20). After an atrial switch operation the ventricular and arterial anatomy are unchanged. A baffle is placed in the atria to redirect systemic venous blood to the MV and pulmonary venous blood to the TV (Figures 20, 21). In contrast, after the ASO [89] the great arteries are inverted so that the aorta connects with the posterior root (previously pulmonary root) and the pulmonary artery with the anterior root (Figures 20, 22). The aorta is pulled through between the branch pulmonary arteries allowing the branches to straddle the aorta. The coronary arteries are translocated from the anterior to the posterior root (Figure 22).

A Rastelli operation has been used in patients with a large VSD and severe pulmonary stenosis (Figure 23). Here the LV is baffled to the aorta through the VSD, the pulmonary trunk is closed, and a conduit is placed from the RV to the distal pulmonary artery [88]. There are alternative operations that accomplish the same type of repair and might have advantages in specific cases [90].

Physiology

Prior to corrective surgery, the systemic and pulmonary circulations are in parallel instead of in series. Consequently, desaturated blood from the systemic veins is returned to the body and saturated blood from the pulmonary veins is returned to the lungs. This is incompatible with life for more than few minutes without some mixing of the circulations, which usually occurs across the foramen ovale, a VSD, and/or the ductus arteriosus [62]. At repair, the circulations are placed in series either by switching the inflow sources (atrial switch operation) or by switching the outflows (arterial switch operation and Rastelli). After an atrial switch operation, the RV remains the systemic ventricle while after an ASO the LV becomes the systemic ventricle.

Presentation

In addition to routine care, patients after atrial switch operation might present with fatigue, arrhythmia, venous congestion, or symptoms of heart failure. Patients are also referred during pregnancy for more intensive surveillance. The clinical examination after an atrial switch shows a forceful and sustained RV impulse and a loud, single S2 (as explained for CTGA). A holosystolic murmur at the left sternal border could be TR or a residual VSD [69]. Subpulmonary stenosis, a frequent finding, is indicated by an ejection murmur higher up the left sternal border. Venous congestion or hepatomegaly could signal systemic venous pathway obstruction or heart failure.

Patients who have had an ASO are usually asymptomatic but might complain of chest pain or exercise limitation. The physical exam is usually unremarkable but a pulmonary outflow murmur or a diastolic murmur of pulmonary or aortic insufficiency might be audible.

After an atrial switch operation the ECG continues to show right-axis deviation and RV hypertrophy. Various rhythm abnormalities

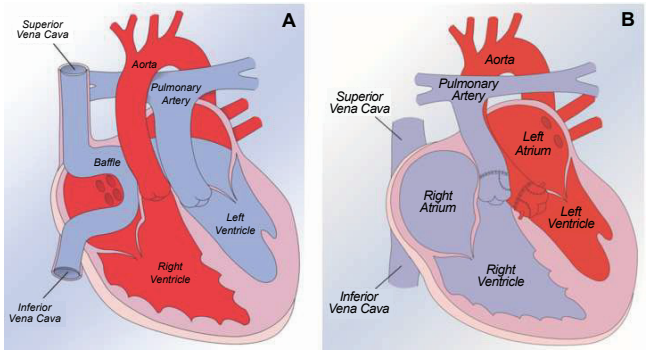

Figure 20: Cartoons illustrating the atrial switch operation (A), and the arterial switch operation (B). (Reprinted from Valente et al. [11] with permission).

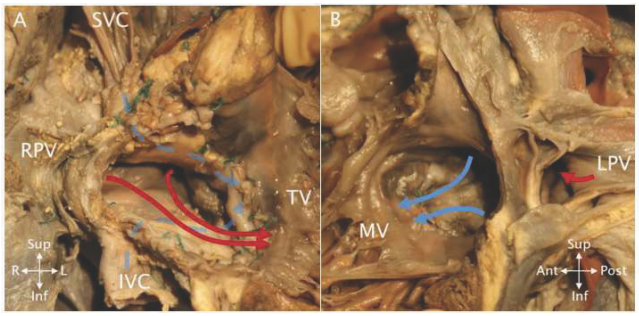

Figure 21: A - The opened pulmonary venous atrium in a heart after a Mustard atrial switch operation. The red curved arrows indicate flow from the right (RPV) and left pulmonary veins toward the tricuspid valve (TV) and right ventricle. The dashed blue curved arrows indicate flow from the superior vena cava (SVC) and inferior vena cava (IVC) behind the limbs of the baffle toward the mitral valve and left ventricle. B - The opened systemic venous atrium in the same heart showing the other side of the baffle with SVC and IVC flow (blue curved arrows) toward the mitral valve (MV). The left pulmonary veins (LPV) are seen posterior to the systemic venous atrium.

might be evident including bradycardia, junctional rhythm, or complete heart block [13]. The chest radiograph often shows cardiac enlargement. After an ASO, the ECG and chest radiograph are usually normal.

Diagnosis

The echocardiogram might not demonstrate the atrial baffle and venous pathways adequately after an atrial switch operation. CMR is excellent for anatomic evaluation, measurement of ventricular size and function and myocardial characterization (Figures 24, 25). CT angiography can be used for functional assessment in patients with an implantable device such as a permanent pacemaker or automated defibrillator and is excellent for coronary artery anatomy [91]. Extended ECG monitoring is useful to detect and diagnose arrhythmias. Exercise testing is an excellent method to follow functional capacity or detect ischemia from coronary artery abnormalities.

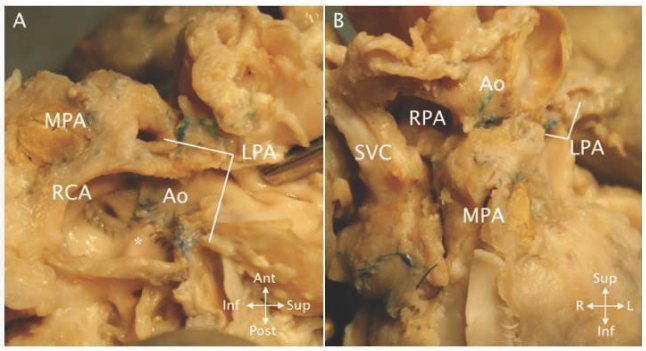

Figure 22: A - Left lateral view of the great arteries after an arterial switch operation. The main pulmonary artery (MPA) is anterior to the aorta (Ao). The left pulmonary artery (LPA) has been divided to show the inside of the aorta. The suture line (blue sutures) is evident between the ascending aorta (Ao) and the pulmonary root (*). The right coronary artery ostium (RCA) with surrounding button of aortic wall is seen on the right side of the aorta. B - A frontal view of the same heart showing the MPA and branches. The right pulmonary artery (RPA) passes posteriorly between the Ao and the superior vena cava (SVC). The divided LPA is to the left of the aorta (Ao).

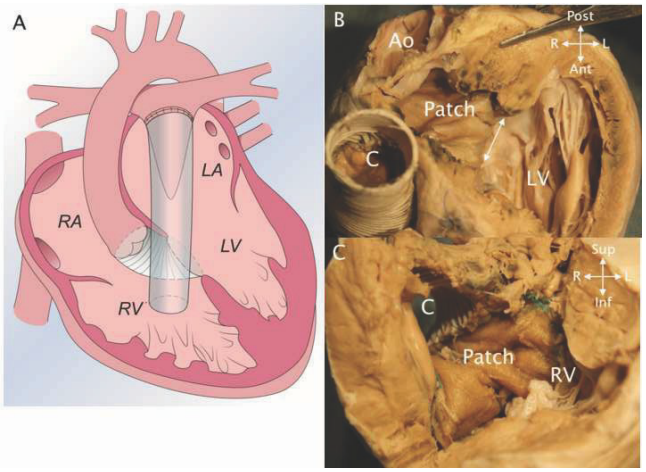

Figure 23: A - a cartoon depicting the Rastelli operation for DTGA with ventricular septal defect (VSD) and pulmonary stenosis. The left ventricle (LV) is baffled to the aorta through the VSD and a conduit is placed from the right ventricle (RV) to the pulmonary artery. (Modified from Valente et al. [11] with permission). B - A heart specimen after a Rastelli operation shows the ventricular septal defect (double headed arrow) and the patch (Patch) directing the LV to the aorta (Ao). C - The opened RV showing the other side of the patch (Patch) and the junction of the conduit (C) with the RV.

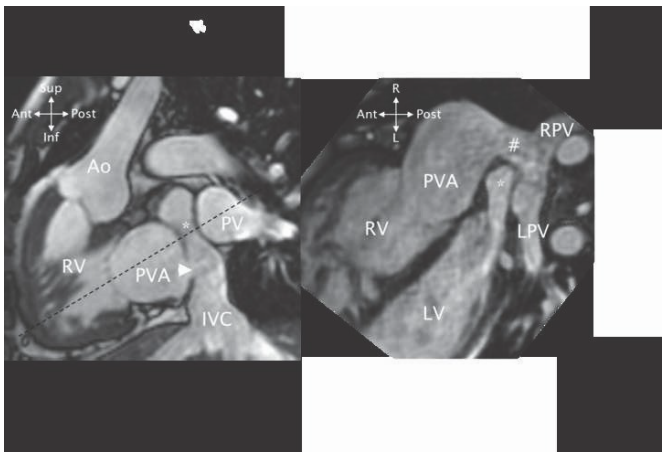

Figure 24: MRI cine SSFP images in a patient after a Senning atrial switch operation. A - Right ventricular (RV) 2 - chamber view showing the two parts of the pulmonary venous atrium (PVA, PV) separated by the systemic venous atrium (*). The arrowhead indicates a baffle leak, a break in the interatrial baffle, allowing communication between the systemic and pulmonary venous atria. B - A 4 - chamber view in the plane indicated by the black dashed line in A. The connection (#) between the component of the pulmonary venous atrium (PV) that receives the pulmonary veins (RPV, LPV) and the supra - tricuspid portion (PVA) is seen in this view. (Reprinted from Valente et al. [11] with permission).

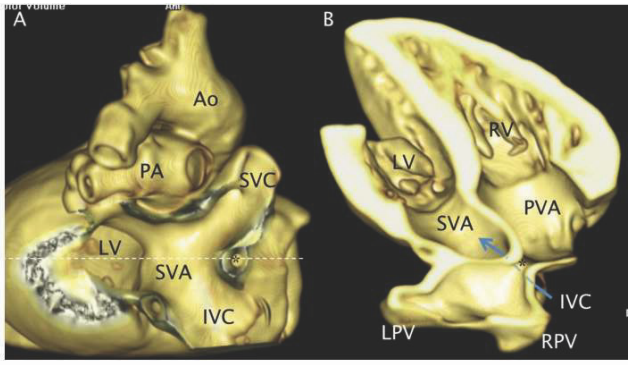

Figure 25: 3D reconstruction of a CT exam of a waxed human heart with severe pulmonary venous pathway obstruction (*) after a Senning atrial switch operation. A - posterior view with the pulmonary veins removed to show the superior vena cava (SVC) and inferior vena cava (IVC) pathways joining the systemic venous atrium (SVA). The junction (*) between the portion of the pulmonary venous atrium that receives the right (RPV) and left (LPV) pulmonary veins and the supra - tricuspid portion of the pulmonary venous atrium (PVA) is severely stenosed. B - A cut in the plane indicated by the dashed white line in A showing the two portions of the pulmonary venous atrium. The IVC pathway (blue arrow) passes beneath the narrowed junction.

After an ASO the echocardiogram shows the anterior pulmonary artery paralleling the aorta and the branch pulmonary arteries passing posteriorly on either side of the ascending aorta. CMR demonstrates overall anatomy, coronary artery anatomy, and ventricular size and function (Figure 26). CT angiography is also useful for assessment of the coronary arteries. CMR provides anatomic evaluation as well as functional assessment after the Rastelli operation (Figures 27, 28).

Complications

Atrial switch procedure: Sinus node dysfunction is the most

frequent complication of an atrial switch operation. Loss of sinus node function is progressive and by 20 years only 40% of patients remain in sinus rhythm [92]. Tachy-brady syndrome is common in this setting as is atrial flutter. Atrial tachyarrhythmias during the operative period, permanent heart block, and small size at surgery are independent risk factors for sudden death [92]. Arrhythmia-free survival is better in patients without concomitant lesions such as VSD or LVOT obstruction [93].

By 25 years after surgery, 61% of Mustard patients had moderate or severe RV dysfunction [93,94]. Risk factors are unclear, but excess hypertrophy is likely to be important [6,95]. Recurrent ischemia contributes to ventricular dysfunction as evidenced by regional wall motion abnormalities, perfusion defects and late gadolinium enhancement documented decades after a Mustard procedure [96]. TR usually accompanies RV dysfunction and can contribute to further deterioration [93].

Other late complications include venous pathway obstruction and baffle leaks (Figures 24, 25). The SVC pathway is most often involved and usually decompresses via the azygos vein so that adults are rarely symptomatic [97]. It is usually discovered during placement of a transvenous pacemaker for sinus node dysfunction. Inferior vena cava pathway obstruction is rare [13]. Baffle leaks are more frequent but usually small. These persistent communications can be a source of paradoxical embolization especially if a transvenous pacemaker is in place [97]. Obstruction of the pulmonary venous pathway (Figure 25) is more likely with the Senning operation but is rare late after surgery [97].

Pulmonary vascular disease is a late complication in 5-7% of patients after the atrial switch procedure, particular if a large VSD or persistent ductus arteriosus was present prior to repair [6]. Pulmonary venous pathway obstruction is another cause of elevated pulmonary artery pressure [98].

Rastelli operation: Complications are mainly conduit obstruction and subaortic stenosis from inadequate enlargement of the VSD [99]. LV dysfunction has been described mostly in the setting of severe subaortic stenosis. There is a small but persistent incidence of sudden death, presumed to be arrhythmic in nature [99].

Arterial switch operation: Pulmonary artery stenosis is the most frequent complication following the ASO. Mechanisms include inadequate growth of the suture line, scarring and retraction of the material used to fill the coronary artery button sites, and tension at the anastomotic site if there is inadequate mobilization of the distal pulmonary arteries [100]. Arrhythmia is infrequent and sudden death is rare [6]. The LV in the systemic position maintains good function over time.

There is a modest risk for neo-aortic valve regurgitation related in part to neo-aortic root dilatation. Patients with a VSD tend to be at higher risk for neo-aortic valve regurgitation [100].

Coronary stenosis or occlusion has been discovered in 5-7% of patients after the ASO and has been associated with ventricular dysfunction and sudden death [101].

Although pulmonary hypertension after the ASO is infrequent, it was a cause of late death in one study [102].

Treatment

Atrial switch: Arrhythmia management is the most common

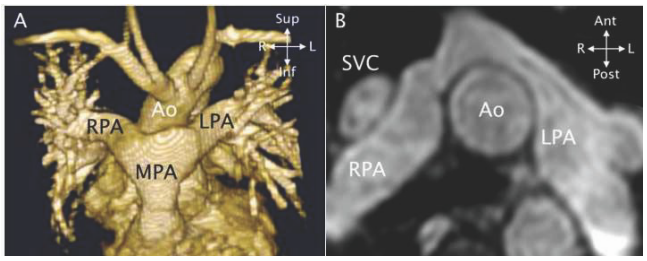

Figure 26: CMR exam in two patients after an arterial switch operation. A - Frontal view of a 3 - D reconstruction from a MRA showing the anterior pulmonary artery (MPA) with the branch pulmonary arteries (RPA, LPA) on either side of the ascending aorta. (Reprinted from Valente et al. [11] with permission). B - A 3D SSFP in axial projection showing the distorted contours and proximal narrowing of the branch pulmonary arteries (RPA, LPA). The ascending aorta (Ao) is seen between the branch pulmonary arteries and the superior vena cava (SVC) in front of the RPA.

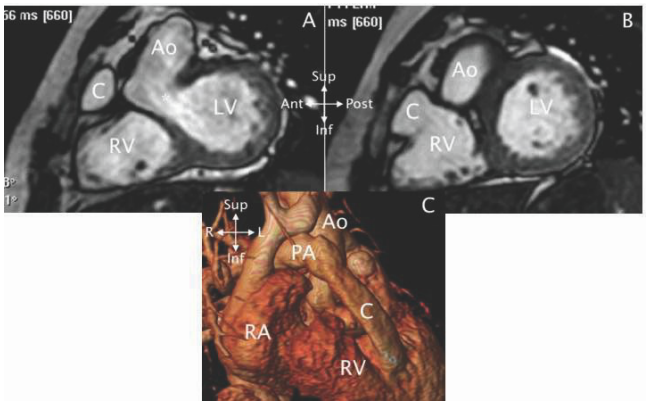

Figure 27: CMR exam in a patient after a Rastelli operation. A - A cine SSFP short - axis cut through the ventricular septal defect (*) showing the flow path from the left ventricle (LV) to the aorta (Ao). B - A more apical cut showing the junction of the conduit (C) with the right ventricle (RV). C - A 3 - D reconstruction from the MRA showing the RV - pulmonary artery (PA) conduit (C) to the right of the Ao. The conduit is flattened by the chest wall.

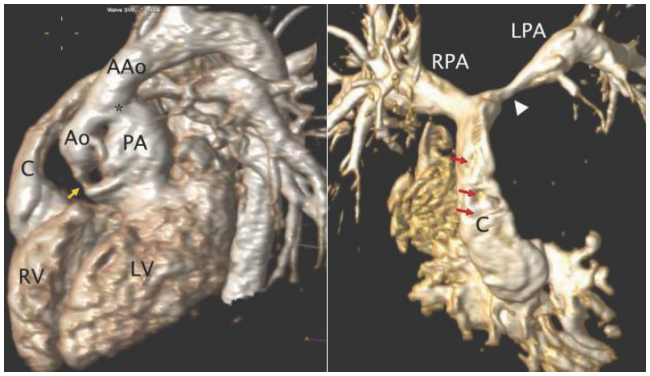

Figure 28: 3D reconstructions from a MRA performed in an adult patient with complex double outlet right ventricle who underwent repair in childhood. A - Left lateral view showing a Damus - Kaye - Stansel anastomosis (*) between the pulmonary root (PA) and the ascending aorta (AAo) because of severe subaortic stenosis (yellow arrow). The left ventricle (LV) was baffled to the pulmonary root (PA) through the ventricular septal defect. B - A conduit (C) was placed between the right ventricle (RV) and the pulmonary arteries. There is severe proximal left pulmonary artery (LPA) stenosis (white arrowhead). The irregularities in the anterior wall of the conduit (red arrows) are artifacts from sternal wires. RPA - right pulmonary artery.

treatment. Medical or transcatheter treatment of atrial tachyarrhythmia can be challenging. Ablation of arrhythmia substrates after an atrial switch operation has a success rate of 70% at best because of the complex atrial anatomy [103]. Sinus node dysfunction with tachy-brady syndrome is an indication for pacemaker therapy.

SVC pathway obstruction can be treated by stent placement, but it is important to define the coronary artery anatomy before undertaking an interventional procedure at the base of the heart [67]. A baffle leak can often be closed percutaneously with a device.

Heart failure symptoms are usually treated with an ACE inhibitor and beta blockade but there is little evidence of efficacy [104]. Diuretic therapy can be used to maintain fluid balance. Heart transplantation should be considered for end-stage heart failure in atrial switch patients.

Rastelli operation: Replacement of the RV-PA conduit or homograft is the most frequent re-operation after the Rastelli operation. Enlargement of the VSD to alleviate subaortic stenosis is a less frequent secondary procedure. A residual VSD can often be closed with a device, especially 'intramural' defects between the edge of the baffle and the anterior RV wall [105].

Arterial Switch Operation: Treatment of neo-pulmonary outflow obstruction or of branch pulmonary stenosis is undertaken in about 8-10% of patients following the ASO. Stent placement is usually effective for branch pulmonary artery stenosis. Dense scarring of the proximal outflow renders it less amenable to percutaneous therapy and usually requires re-operation.

Outcomes

Late outcomes for the various procedures for DTGA are listed in (Table 3) [106]. Survival for the atrial switch operations is 75-80% at 25 years [13,107]. Long-term survival (20 years) for the Rastelli operation has been disappointing at 50-60% [108,109], but more recent reports are more encouraging, [99,110] The late survival for the arterial switch operation is 85% overall at 15 years and 95% for hospital survivors [111].

The late survival is higher for the ASO compared with the atrial switch procedures, with fewer long-term complications [106].

Tetralogy of Fallot (TOF)

Anatomy

TOF results from leftward and superior displacement of the infundibular or outlet septum, apparently related to abnormal rotation of the outflow during embryogenesis. This causes RV outflow obstruction, a VSD in the 'Y' of septal band, aortic overriding through the VSD, and secondary RV hypertrophy [112]. The pulmonary valve (PV) is often small and/or stenotic and the pulmonary artery branches can be diffusely hypoplastic, often with discrete stenoses. In extreme cases the RV outflow and even the pulmonary trunk are atretic [62]. Associated lesions include a right aortic arch in 25% of cases, an ASD 2 (often called pentalogy of Fallot), or rarely, an AV canal defect [13]. Coronary artery anomalies occur in about 5% of patients and can be important for surgical repair [6]. The accompanying article in this issue by Baraona et al. describes these variants in detail [67].

Patients presenting to an ACHD center have undergone repair in infancy or childhood. Repair includes patch closure of the VSD and relief of RV outflow obstruction [6]. Patch augmentation of the RV outflow, division or resection of obstructing muscle, and bypass of obstruction using a RV-pulmonary artery conduit are typical approaches to repair. Until the last 2-3 decades wide patch augmentation of the outflow was standard treatment to avoid any residual stenosis, at the expense of creation of free pulmonary regurgitation (PR) (Figure 29). More recently, the emphasis has shifted to preservation of PV function as the late deleterious effects of chronic PR have become apparent. Patients repaired in the last 2 decades are likely to have had a transatrial-transpulmonary approach with limited or no infundubulotomy. Efforts are now made to avoid a trans-annular patch [62] or to place the patch in such a way as to preserve valve function as much as possible. In patients with pulmonary atresia or with a major coronary artery crossing the RVOT, an RV-to-pulmonary artery conduit is used (Figure 30). Additional defects such as ASD2 are closed at the time of complete repair and any previously constructed shunt (Figure 31) taken down [6].

Physiology

The physiology of TOF depends on the severity of outflow obstruction and can vary from absence of cyanosis (pink tetralogy)

Type of Surgery	Era	Early mortality	Late Survival	Major Complications and Incidence	Reoperations
Arterial Switch [106]	1980	3.8%	88% (10 and 15 years)	Pulmonary stenosis (3.9%) Aortic regurgitation (3.8%) Coronary lesions (2%)	4.5-18%
Atrial Switch (Mustard/ Senning) [106]	1960	16.5%	77.7% at 10 years 67.2% at 30 years	Arrhythmia (47.6 – 64.3%) Tricuspid Regurgitation (34.9%) Systemic Ventricular Dysfunction (11.5 – 14.6%) Baffle related problems (5.6%)	5.1%
Rastelli [106]	1969	7%	80% at 10 years	RVOTO (65%) Arrhythmias (24%) LVOTO (16%)	44%

RVOTO – Right Ventricular Outflow Tract Obstruction; LVOTO – Left Ventricular Outflow Tract Obstruction

Table 3: Comparison of corrective surgery for DTGA (adapted from [106]).

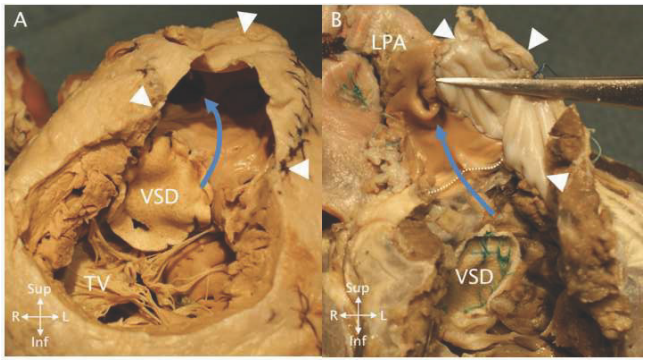

Figure 29: Two hearts after repair of TOF with the right ventricle opened. A - This heart was operated in an earlier era when wide patch plasty of the right ventricular outflow was the standard. Note the large patch defined by the arrowheads over the outflow (blue curved arrow). The ventricular septal defect patch (VSD) is seen between the tricuspid valve (TV) and the outflow. B - The outflow patch (arrowheads) is much smaller in a heart operated more recently. The patch crosses the pulmonary annulus (white dotted line) and extends onto the left pulmonary artery (LPA).

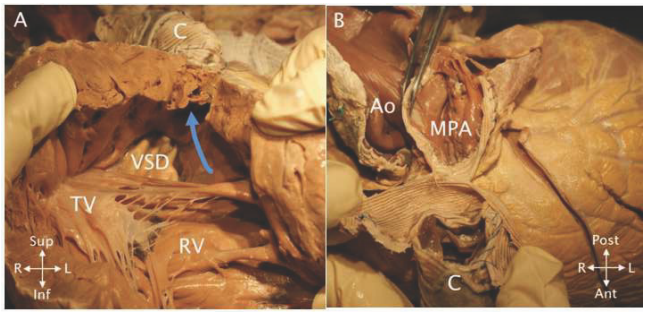

Figure 30: A - Opened right ventricle (RV) in a patient with TOF and pulmonary atresia who underwent repair using a valved conduit. The RV outflow (blue curved arrow) was created from the ventriculotomy to which the conduit (C) was sewn. The ventricular septal defect patch (VSD) is seen extending above the tricuspid valve (TV). B - An anterior superior view of the same heart showing the connection of the valved conduit (C) to the main pulmonary artery (MPA) to the left of the aorta (Ao).

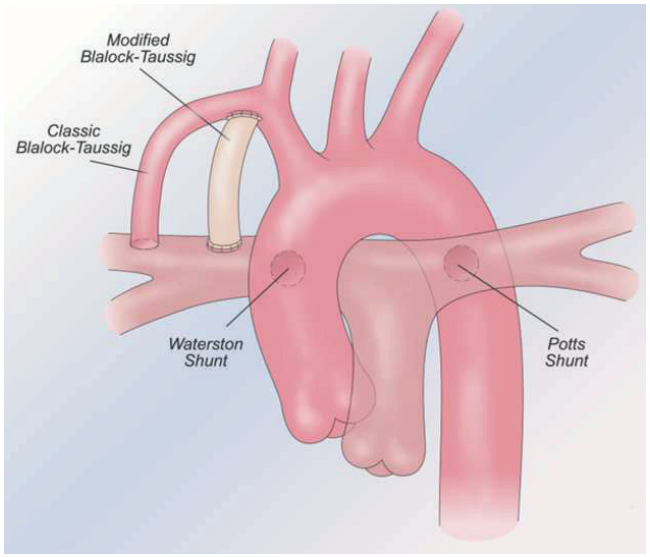

Figure 31: Cartoon showing the various types of aorto - pulmonary shunts that have been used over the past half century. The classical Blalock - Taussig shunt connects the subclavian artery opposite the side of the aortic arch end - to - side to the ipsilateral pulmonary artery. The modified Blalock - Taussig shunt is constructed by inserting a tube graft between the innominate artery or the proximal subclavian artery and the ipsilateral pulmonary artery. The Potts shunt is a side - to - side connection of the left pulmonary artery to the descending aorta. A Waterston shunt is a connection of the ascending aorta side - to - side to the right pulmonary artery. (Modified from Valente et al. [11] with permission).

to ductus arteriosus-dependent pulmonary circulation in cases with pulmonary atresia.

After repair the majority of patients have normal oxygen saturation and no residual shunt. The predominant physiology is RV volume overload from moderate or more PR. Few patients have residual pulmonary stenosis. TR from damage to the tricuspid valve during VSD closure or due to annular dilation compounds the effects of PR. Residual VSD is uncommon in the current era but can contribute to LV dilation.

RV dysfunction and failure as a consequence of chronic volume overload are seen late after repair. LV dysfunction is also seen late after repair, even in the absence of a residual VSD or other volume overload [113]. The mechanism remains unclear.

Presentation

The unoperated adult with TOF is rarely encountered in developed countries but is less rare where access to health care is more limited. Cyanotic and clubbed, these patients present with exercise limitation, secondary erythrocytosis, stroke or heart failure. S2 is usually single and patients with a patent RV outflow have a systolic ejection murmur in the pulmonary area while those with pulmonary atresia have continuous murmurs over the chest and back due to aorto-pulmonary collaterals [13].

Most patients remain asymptomatic for years after repair of TOF. Some complain of exercise limitation, arrhythmia, or heart failure symptoms. Physical exam of the chest provides clues to the treatment history. A lateral thoracotomy scar indicates initial palliation with an aorto-pulmonary shunt. An absent or weak radial pulse on the side of the thoracotomy suggests a classical Blalock-Taussig shunt. A sternotomy scar usually indicates complete repair. S2 is single because the PV has been damaged or even removed at repair. There is often a low-to-medium pitched systolic ejection murmur at the left sternal border due to residual pulmonary stenosis. A diastolic decrescendo murmur in the same area indicates PR. There might be concomitant aortic regurgitation, resulting from aortic root dilation. An aortic regurgitation murmur is high-pitched in contrast to the low-pitched PR murmur. A residual VSD is indicated by a holosystolic murmur at the lower sternal border. Patients who have undergone only palliation with an aorto-pulmonary shunt have a continuous murmur (Figure 31).

Right bundle branch block is seen routinely on ECG, especially following a trans-ventricular approach to repair (common before 1990). Atrial fibrillation or flutter might also be present and is more common with increasing age [114]. The chest radiograph often shows a large heart due to RV enlargement.

Diagnosis

Echocardiography is used in the routine evaluation of repaired TOF patients [3].

CMR has emerged as the modality of choice for evaluating ventricular size and function. In addition, the anatomy of the RV outflow (Figure 32), pulmonary arteries, aorta and aorto-pulmonary collaterals can be seen in detail, which is necessary for surgical planning. The severity of PR can be quantified (Figure 33), as can any residual shunt. Lastly, myocardial viability can be assessed using late gadolinium enhancement (Figure 34) [113]. If there are contraindications to CMR, CT is also excellent for evaluation of TOF [13], however, this procedure exposes the patient to ionizing radiation.

Complications

The most common late complication is chronic PR. Residual RV outflow obstruction and branch pulmonary artery stenosis (Figure 35) [13] are less frequent but important late complications. Conduit dysfunction is expected and virtually all conduits undergo replacement or interventional treatment at some point. TR can be progressive and compounds the RV dilation. Late RV dilation and dysfunction are common [115]. Progressive aortic regurgitation, usually associated

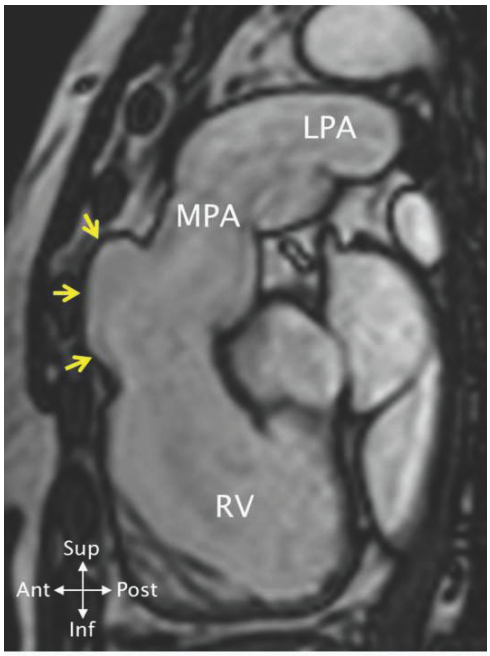

Figure 32: MRI 3D SSFP sagittal plane image in a patient late after repair of TOF. The right ventricle (RV) is dilated and an outflow tract aneurysm (yellow arrows) has formed. LPA - left pulmonary artery; MPA - main pulmonary artery. (Reprinted from Valente et al. [11] with permission).

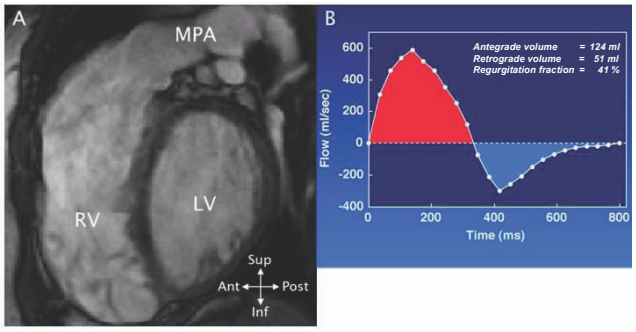

Figure 33: A - MRI cine SSFP short - axis image in a patient late after repair of TOF. The RV is dilated due to severe pulmonary insufficiency from wide patch plasty of the RV outflow. B - Graph of instantaneous flow velocity vs time calculated from a phase contrast MR sequence prescribed across the right ventricular outflow. Antegrade flow is shown above baseline (red) and retrograde or regurgitant flow below (blue). The area under each portion of the curve indicates volume flow which is used to calculate the regurgitant fraction.

with aortic root dilation, has been reported to occur in 15-18% of patients [116,117].

Arrhythmias are another important late complication. The most frequent are atrial flutter or fibrillation, seen mostly in patients > 55 years old. Prevalence of ventricular arrhythmias increases with age and is associated with LV dysfunction [114]. Patients who present with arrhythmias should undergo evaluation for a hemodynamic cause [13].

LV dysfunction late after repair of TOF is likely due to adverse ventricular-ventricular interaction with the dilated, often dysfunctional RV and appears to be at least as significant a risk factor for arrhythmia and sudden death as RV dysfunction [113].

Treatment

PV replacement is the treatment for chronic PR (Figure 36) but the timing and method remain key management questions. PV replacement is usually recommended for patients with severe PR and symptoms or decreased exercise performance. Replacement is also reasonable for patients with severe PR and RV dysfunction, or with symptomatic or sustained atrial or ventricular arrhythmias.

Surgical valve replacement is the only option currently available for the native RV outflow tract. Operative mortality for PV replacement is low [118] and exercise performance improves [119]. Although RV volume decreases it often does not normalize, especially if the RV was severely dilated preoperatively [120,121]. While the question of operating too late has been raised [122], performing PV replacement too early is also an issue, as all prosthetic valves have a limited life span.

RV outflow reconstruction or RV remodeling surgery [123] might be considered in conjunction with PV replacement. The anterior wall of the RV is often thin and poorly contractile (Figure 36) [123],

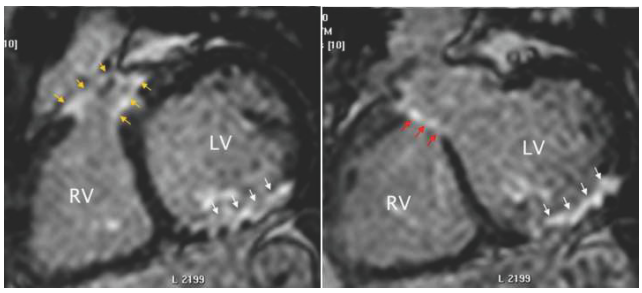

Figure 34: MRI short - axis images showing delayed gadolinium enhancement in a patient after repair of TOF. A - A cut at the level of the right ventricular (RV) outflow showing delayed enhancement of the outflow patch (yellow arrows). The patient suffered a perioperative inferior infarction of the left ventricle (LV) indicated by delayed enhancement (white arrows). B - A cut through the LV outflow showing delayed enhancement of the patch closing the ventricular septal defect (red arrows). The LV inferior infarction is seen in this cut as well (white arrows).

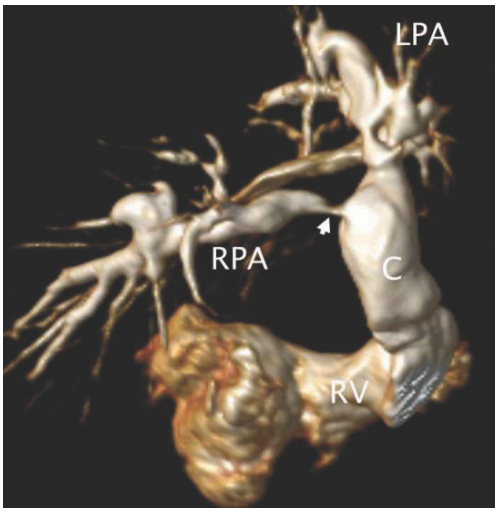

Figure 35: 3D reconstruction of a MRA in an adult patient after repair of TOF with pulmonary atresia. Multiple collateral arteries were unifocalized with the central pulmonary arteries and connected to the right ventricle (RV) using a conduit (C). There is severe proximal stenosis (white arrowhead) of the right pulmonary artery (RPA). LPA left pulmonary artery.

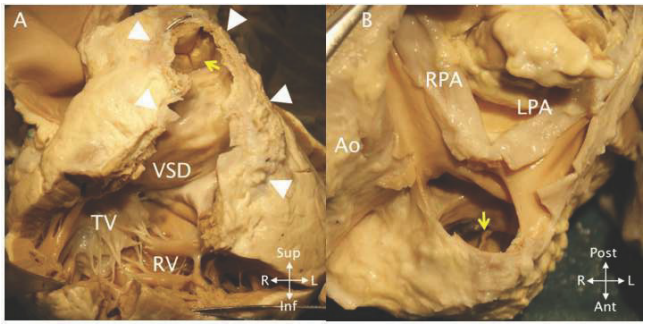

Figure 36: A - The opened right ventricle (RV) in a heart following repair of TOF and implantation of a bioprosthesis (yellow arrow) in the pulmonary position. The ventricular septal defect patch (VSD) is completely endothelialized. The RV anterior wall (white arrowheads) is thin and fibrotic. This tissue is often removed when RV remodeling is performed during valve implantation. B - The bifurcation of the pulmonary artery showing the branches (RPA, LPA) and the arterial surface of the bioprosthesis (yellow arrow).

with akinesia or dyskinesia in up to 38% of patients undergoing PV replacement. Abnormally contracting segments can stem from infundibular resection or perioperative ischemic insult [124]. Tricuspid valve annuloplasty can also be performed for moderate or severe TR [6].

Treatment options for failure of a RV-to-pulmonary artery conduit include replacement of the conduit, stent implantation to treat stenosis, and percutaneous valve implantation to treat regurgitation [125].

Residual VSD with Qp/Qs > 1.5:1 should be repaired, either surgically or by device placement [13]. Late aortic root dilation is common [116] and might require intervention, although the indications are not clear. Balloon dilation or stenting should be considered for branch PA stenosis if flow in the artery is reduced and especially when accompanied by PR [6].

Atrial arrhythmias can be addressed by a Maze procedure at the time of PV replacement [6]. Patients with documented sustained VT or aborted sudden cardiac death should receive an ICD for secondary prevention [126]. While there remains no consensus on the management of non-sustained VT found on surveillance monitoring [13], programmed ventricular stimulation can be of use in risk stratifying the asymptomatic patient. A score based on six clinical variables (prior shunt, sustained VT, QRS > 180 ms, ventriculotomy at original repair, nonsustained VT, and LVEDP > 12 mm Hg) has also been shown to be useful for risk stratification [127].

Outcomes

Survival after repair of TOF is less than expected for the general population at all times and the rate of attrition increases sharply 25 years after surgery (Figure 37) [128]. The similarity of the survival curve shown in (Figure 37) to that for congenital PR [129] strongly suggests a role for chronic RV volume overload in late mortality. Sudden death due to ventricular arrhythmia is the most common cause of death after surgical repair of TOF [128]. The risk for sudden death is 3-6% over the 25-30 year follow-up period [13]. Older age at complete repair, a prior Waterston or Potts shunt, placement of an outflow tract patch, and earlier year of surgery were found to be risk factors for late mortality in patients operated during the 1950s-1970s [128,130]. QRS duration > 180 milliseconds is a sensitive predictor of life-threatening ventricular arrhythmia [131].

The underlying hemodynamic abnormality found most frequently in patients who had ventricular tachycardia and/or sudden death was PR. Peripheral pulmonary stenosis and TR were also associated with ventricular tachycardia [132]. Moderate or more TR was associated with late atrial flutter/fibrillation.

As a result of these late complications, current surgical approaches focus on preserving the PV annulus, accompanied by aggressive resection of RVOT obstruction [133]. Only short to mid-terms results are available but this approach seems to produce less RV dilation [133].

Fontan Circulation

Hearts with one functional ventricle are rare, comprising 1-2% of all congenital heart defects. The prognosis without surgical intervention in childhood is poor, although rare patients with well-balanced circulations survive into adulthood with reasonable functional capacity [134]. The physiology in infancy depends on several factors, including Qp/Qs ratio, systemic outflow obstruction, pulmonary venous anomalies, and AV valve function. Long-term palliation involves several staged procedures leading to the Fontan circulation. Congenital heart defects typically staged toward this type of palliation include tricuspid atresia, double-inlet LV, hypoplastic left heart syndrome, hypoplastic right heart syndrome, and other more rare defects.

Clinical use of complete right heart bypass was first reported by Fontan and Baudet in 1971 as palliation for tricuspid atresia [135]. Since then, several modifications of the original procedure have been devised, always with the goal of separating the circulations by directing systemic venous return to the pulmonary arteries without an interposed ventricle, and using the one functional ventricle in the systemic circulation. The evolution of the Fontan operation over the last 40 years has been reviewed recently [136].

Anatomy

Virtually all adults with functionally one ventricle followed in adult congenital heart disease centers have undergone some variant of the Fontan operation (Figure 38). Most patients operated before the 1990s had connection of the RA to the pulmonary arteries, either directly or by means of a conduit, and closure of any communication between the RA and the systemic circulation (Figure 39). More recent modifications

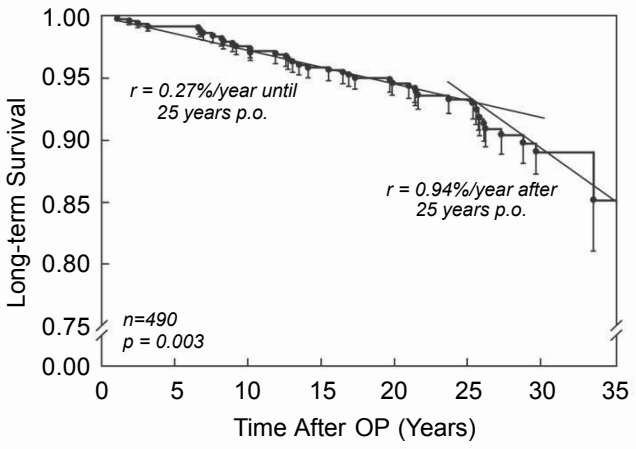

Figure 37: Kaplan Meier survival curve for hospital survivors of TOF repair. Note the inflection in the curve at about 25 years. The late attrition rate is nearly 4 times the early rate. (Reprinted from Nollert et al. [128] with permission).

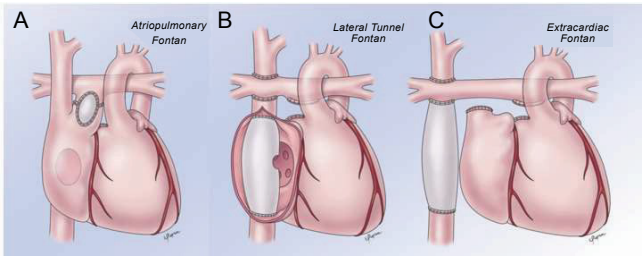

Figure 38: Types of Fontan operations likely to be seen in adult congenital centers today. A - The atriopulmonary connection was abandoned in the mid - 1980s because of dilatation of the right atrium predisposing to thrombosis and atrial arrhythmias. B - lateral tunnel is used widely in part because of the ease of fenestration of this type. C - extracardiac conduit is also widely used because it can be performed without bypass and does not create extensive atrial suture lines. This type is more difficult to fenestrate. (Modified from Valente et al. [11] with permission).

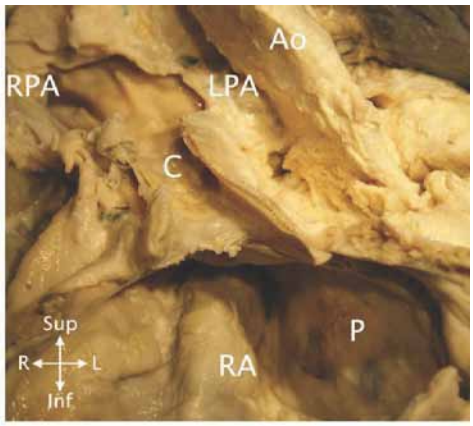

Figure 39: Frontal view of a heart after an atriopulmonary Fontan operation. A conduit (C) was used to join the right atrium (RA) and the pulmonary arteries. The right (RPA) and left (LPA) branches are seen arising from the junction with the conduit. The aorta (Ao) is anterior and leftward in this heart with Double Inlet Left Ventricle (DILV). There is a calcified patch (P) on the right AV valve to prevent flow of venous blood from the RA into the systemic ventricle.

include the lateral tunnel connection [137,138] and the extracardiac conduit connection [139,140]. These modifications have superior flow characteristics and little or none of the RA is exposed to high venous pressure [138]. The extracardiac conduit also avoids extensive suture lines in the RA. The benefits of these modifications include better hemodynamics and less potential for arrhythmias [141,142].

An atrial septal defect or fenestration is often created in the baffle to reduce systemic venous pressure and increase preload to the systemic ventricle (Figure 38B) [143]. Although the fenestration allows a small right-to-left shunt and causes mild arterial desaturation, it increases cardiac output early postoperatively and reduces the duration of pleural drainage following surgery [144,145]. The fenestration can usually be closed percutaneously later in life to eliminate residual cyanosis [146].

Physiology

Pulmonary blood flow is dependent on systemic venous pressure, a measure of the residual energy imparted to the blood by the systemic ventricle. To maintain cardiac output, the mean systemic venous pressure must approximate the mean pulmonary artery pressure in the normal circulation. This means that systemic venous pressure is chronically elevated (at least 10-12 mm Hg). Even with low pulmonary vascular resistance the resting cardiac output in Fontan patients is only about 70% of normal [141]. Further, the capacity to increase systemic venous pressure, and subsequently pulmonary blood flow, is quite limited. Systemic ventricular preload is determined by the pulmonary blood flow. At rest the systemic ventricle is preload deprived because the pulmonary blood flow is limiting. Under these circumstances preload is the major determinant of cardiac output [147]. Modest changes in inotropy and heart rate have little effect on cardiac output. After load reduction also has little effect on cardiac output but can cause hypotension because of the limitations imposed by preload deprivation. During exercise, pulmonary blood flow increases approximately linearly with mean systemic venous pressure. Consequently, doubling cardiac output requires a mean venous pressure of 20-25 mmHg, which is sustainable only for short periods of time. This fits with the empirical finding that during exercise, Fontan patients can only increase cardiac output 1½ - 2 times [148]. Chronic preload deprivation appears to have deleterious effects on systemic ventricular diastolic and systolic function and might explain the relentless deterioration of function observed in these patients. In summary, cardiac output is dependent on systemic ventricular preload while inotropic state, heart rate and after load have minor effects except at extremes. Preload is a function of pulmonary blood flow which is determined by total pulmonary resistance (pulmonary vascular resistance plus any gradient in the Fontan pathway), probably the most important determinant of functionality of the Fontan circulation.

Presentation

Adult Fontan patients are followed at regular intervals in adult congenital heart centers. Symptoms might include limited functional capacity, arrhythmia, edema, serous effusions, heart failure symptoms, diarrhea, and stroke. Physical exam findings include prominent veins, hepatomegaly, and edema. S2 is single because there is only a systemic arterial circulation. A stenotic murmur indicates systemic outflow obstruction while a holosystolic murmur means AV valve regurgitation or rarely a communication between the ventricle and the pulmonary circulation. A continuous murmur is usually due to a persistent aorto-pulmonary connection such as a shunt or collateral vessel.

Diagnosis

The echocardiogram is used routinely for follow-up but it has limitations. Useful for valvar and ventricular function and for detection of outflow obstruction, echo often produces poor images of the Fontan pathway, has a poor sensitivity for detecting thrombus in the venous pathway, and generally cannot image the branch pulmonary arteries. Conversely, CMR is excellent for anatomic and functional evaluation (Figures 40, 41) and fair for detection of thrombus. Extended ECG monitoring is essential for detection and diagnosis of arrhythmia. Monitoring of blood chemistry is important to detect renal or hepatic dysfunction.

Complications

Adult patients with Fontan physiology are at risk for multiple complications. Those with an atriopulmonary connection are at particularly high risk for RA dilation with thrombus formation and atrial arrhythmias [149]. Both problems lead to diminished cardiac output, reduced exercise capacity and diminished quality of life. The prevalence of thrombosis in the venous pathway is unknown. Approximately 50% of Fontan patients experience atrial tachycardia by 20 years post-operatively [149].

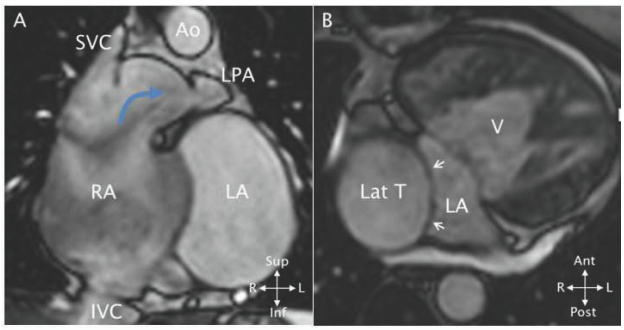

Figure 40: A - MRI cine SSFP coronal view in a patient with an atriopulmonary connection (blue curved arrow). The right atrium (RA) is dilated and the atrial septum bulges into the left atrium (LA). B - MRI 3D SSFP axial view in a patient with functionally one ventricle (V) after a lateral tunnel Fontan operation. The lateral tunnel (Lat T) is seen in cross - section within the atrium. A patch (white arrows) separates the tunnel from the remainder of the atrium (LA). IVC - inferior vena cava; LPA - left pulmonary artery; SVC - superior vena cava. (Reprinted from Valente et al. [11] with permission).

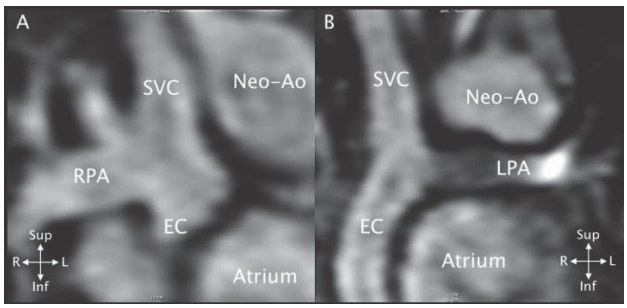

Figure 41: MRI 3D SSFP frontal views in a patient with hypoplastic left heart syndrome after extracardiac conduit Fontan operation. A - The Glenn anastomosis between the superior vena cava (SVC) and the right pulmonary artery (RPA) is seen. The junction of the extracardiac conduit (EC) with the inferior aspect of the RPA is seen but the rest of the conduit is out of the plane. The neo - aorta (Neo - Ao) is to the left of the SVC. B - The conduit (EC), SVC and left pulmonary artery (LPA) are seen but the RPA is out of plane. As frequently seen the LPA is smaller than the RPA. Note that the conduit is separate from the atrium.

Systemic ventricular outflow obstruction causes hypertrophy and increased ventricular end-diastolic pressure. Examples include sub-aortic stenosis due to restriction of the VSD or bulboventricular foramen in patients with double-inlet LV or recurrent aortic coarctation in those with hypoplastic left heart syndrome. Abnormal AV valve morphology puts patients at risk for valvar regurgitation. Examples include Ebstein anomaly of the TV in CTGA and common AV canal in heterotaxy syndrome. Chronic AV valve regurgitation is associated with increased Fontan pathway pressure, diminished ventricular compliance, systolic and diastolic dysfunction, as well as significant arrhythmias [150]. Other less common complications include protein-losing enteropathy, plastic bronchitis, liver dysfunction, and stroke.

Treatment

Closure of a fenestration or other interatrial communication has been undertaken to treat cyanosis or systemic embolization, usually by percutaneous device placement [10]. Cardiac output tends to decrease following closure of the fenestration likely due to reduction of systemic ventricular preload [151].

Obstruction of the Fontan pathway or of the pulmonary arteries can be treated by stent placement or by surgery.

The Fontan conversion was proposed in the 1990s to improve outcomes of adult survivors of atriopulmonary connection [152]. This procedure involves revision of the original Fontan pathway to an extracardiac conduit, with branch pulmonary artery reconstruction and RA reduction when necessary. This is accompanied by a Maze type of arrhythmia surgery and placement of a permanent pacemaker [153]. Residual associated anatomical lesions such as systemic outflow obstruction or AV valve regurgitation can be addressed at the time of surgery [154]. Additional surgery of this sort must be balanced with risk of prolonged ischemic time.

Heart transplantation is effective in Fontan patients with intractable arrhythmias, advanced heart failure, and protein-losing enteropathy. Survival is worse compared to patients with other forms of congenital heart disease or with cardiomyopathy. Protein-losing enteropathy usually improves following transplantation [155].

Outcome

Actuarial survival without transplantation after a Fontan operation for patients born before 1985 was 89.9% at 10 yrs, 82.6% at 20 years and 69.6% at 25 years. The principal causes of death were thromboembolic, heart failure related, and sudden death [156]. Adult Fontan patients often live with low cardiac output, which drops further with atrial arrhythmias. Almost universal functional limitation is related to limited capacity for augmentation of cardiac output with activity. Multi-system dysfunction related to high venous pressure is distressingly common, and includes hepatic dysfunction, [157-159] renal dysfunction [160], endothelial dysfunction [159], lower extremity venous insufficiency and venous reflux [161], and coagulation abnormalities [162].

Fontan conversion surgery can be carried out with relatively low mortality (5.9% in one series [7]) but is not applicable to the majority of Fontan patients. The causes of mortality in this series were multiple, and included intractable heart failure and coronary artery disease. The overall arrhythmia recurrence rate was 12.8% during a mean follow-up of 56 months [141,154].

Although the Fontan operation provides good palliation to most patients with functionally one ventricle, it has serious long-term limitations. It seems likely that most, if not all, Fontan patients will become transplant candidates because of heart failure. Novel approaches are needed to this complex problem.

Actuarial survival following transplantation for failed Fontan was 76% at 1 year, 70% at 3 years, and 68% at 5 years [155]. Survival at 1 year was 8% lower than for patients with other forms of CHD and 14% lower than for cardiomyopathy.

Coarctation of the Aorta

Anatomy

Aortic coarctation is a discrete, shelf-like narrowing of the aorta at the site of insertion of the ductus arteriosus or ligamentum arteriosum (Figure 42) [163]. The shelf is typically in the superior and leftward wall of the aorta and is produced by ductus tissue that abnormally encircles the aorta [164]. When the ductus arteriosus constricts, it pulls the opposite wall of the aorta inward. Often discrete coarctation is associated with tubular hypoplasia of the isthmus and/or aortic arch.

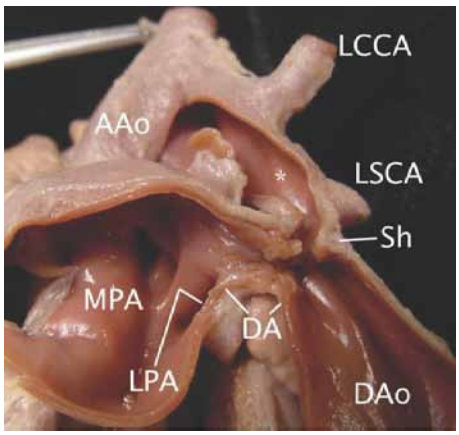

Figure 42: Discrete juxtaductal coarctation. The posterior shelf (Sh) is seen just distal to the left subclavian artery (LSCA). The ductus arteriosus (DA) is opposite the posterior shelf. Note the fleshy, corrugated appearance of the ductus tissue, completely different from either the main pulmonary artery (MPA) or the descending aorta (DAo). The distal arch (*) is mildly narrow. AAo - ascending aorta; LPA - left pulmonary artery.

The left subclavian artery can arise from the descending aorta distal to the coarctation. Occasionally the right subclavian artery arises anomalously from the descending aorta distal to the coarctation. Associated lesions include bicommissural (bicuspid) aortic valve, VSD, intracranial (berry) aneurysm, and MV abnormalities [6].

After repair, the anatomy at the coarctation site depends on the treatment strategy used. Following resection and end-to-end or extended end-to-end anastomosis, the abnormal ductal tissue and covering ridge of fibrous tissue have been removed but replaced by a circular or elliptical suture line. The ductal tissue and fibrous ridge remain extending into the aortic lumen following either subclavian flap plasty or patch plasty while the lumen has been enlarged with a gusset of autologous arterial tissue or prosthetic material. A prosthetic tube graft joins the proximal and distal aortic segments bypassing, but not altering, the coarcted segment. Balloon dilation enlarges the lumen by creating tears in the intima and media which then heal with remodeling of the arterial wall. The fibrous reaction can again encroach on the lumen. Stent placement maintains the enlarged vessel in a distended state and prevents recoil. Neo-intima covers the stent and, if extensive, can cause in-stent stenosis.

Physiology

Obstruction of the arch causes hypertension proximal to the obstruction and reduced blood flow and pressure distal. In adults, large collateral vessels develop that bypass the obstruction and maintain adequate resting flow to the lower body (Figure 43). Flow might not be sufficient for activity resulting in claudication or postprandial abdominal pain. Hypertension in the proximal aorta induces LV hypertrophy, premature development of atherosclerosis, and contributes to rupture of intracranial aneurysms and stroke.

Endothelial dysfunction has been described in the pre-coarctation vessels even after successful repair of coarctation in childhood [165]. The abnormal vascular biology seen even after successful repair likely contributes to persistence of hypertension and the high prevalence of vascular events.

Presentation

The rare unrepaired adult presents with hypertension and/or a murmur. Chronic complaints may include headache, leg claudication, and rarely abdominal angina. The blood pressure in the right arm is elevated and higher than leg blood pressure. Pulses are prominent in the right arm and neck but diminished and delayed in the legs [13]. The apical impulse is often sustained and a harsh systolic murmur that can extend into diastole is audible in the interscapular region due to the coarctation. Large collaterals that bypass the coarctation produce continuous murmurs heard variously over the chest [69].

Repaired patients with recurrence of coarctation can have similar symptoms. Either can present with symptoms related to late complications such as hypertension, stroke, and chest pain due to aortic dissection or coronary artery disease [166]. Important points in the history include age at repair and the operative technique used because both have bearing on anticipated long-term complications [167]. In addition to the physical exam features noted above, the type of chest scar is informative. A left thoracotomy scar suggests a standard repair of isolated coarctation. A subclavian flap plasty was most likely the technique used if the left arm pulse is diminished or absent. A median sternotomy scar suggests more extensive arch reconstruction or repair of accompanying lesions such as a VSD [168].

ECG findings include LV hypertrophy, LV repolarization abnormalities, and occasionally RV conduction delay. The chest X-ray might show a dilated ascending aorta, the "3-sign" representing indentation of the aorta at the coarctation site, and rib notching from collateral vessels [13].

Diagnosis

Echocardiography of the aortic arch is often limited in adults. Suprasternal notch and high left parasternal views are used to display the aortic arch, isthmus, and proximal descending aorta. The gradient is estimated based on peak systolic Doppler velocity. A particularly useful echo finding is an abnormal flow pattern in the descending aorta which reveals decreased pulsatility and absence of early diastolic flow reversal. Other important features include aortic valve morphology and function, LV size and function, and other associated defects [13].

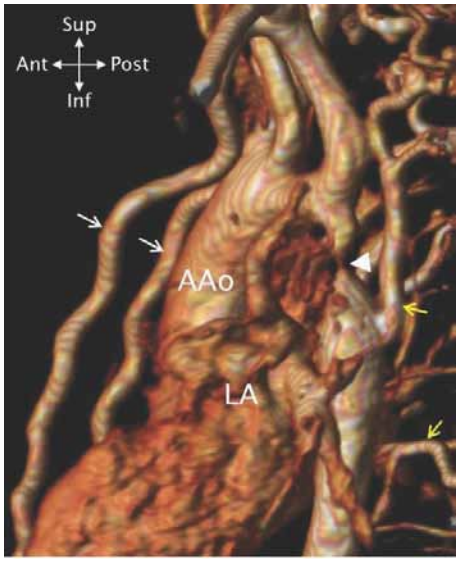

Figure 43: Left lateral view of a 3D reconstruction from a MRA in an adult with severe coarctation (white arrowhead). Note the large collateral vessels (yellow arrow) and the dilated internal mammary arteries (white arrows). AAo - ascending aorta; LA - left atrium.

CMR provides far superior images of the aorta and of collateral vessels and is usually indicated in adults with native or recurrent coarctation prior to intervention (Figure 43) [169] and CMR or CT evaluation of the thoracic aorta is recommended at least every five years following intervention [13].

Complications

Late complications include systemic hypertension, premature coronary atherosclerosis, stroke, recurrence of coarctation, aortic aneurysm formation or dissection, and endocarditis [166,170]. Hypertension persists in up to 1/3 of patients after successful resolution of coarctation [171]. The causes are complex and include arch morphology, endothelial dysfunction, and recurrent coarctation [172]. Premature atherosclerosis, including coronary artery disease and stroke, are leading causes of death late after repair of coarctation [173].

Some late problems stem from the type of repair employed. For example, the rate of aneurysm formation is much higher after Dacron patch aortopasty [174,175]. Aneurysm formation at prior balloon dilation sites remains a long-term concern [176].

Treatment

There is general agreement that native or recurrent coarctation in an adult should be treated if the peak-to-peak gradient is >20 mm Hg. However, a lower gradient is not sufficient to exclude the need for treatment because of collateral flow [13]. Indications for intervention with a low gradient include exercise-induced gradient/hypertension, anatomic narrowing, and elevated LVEDP [177]. Percutaneous balloon dilation is indicated for recurrent and or native coarctation in some adult patients with discrete lesions (Figure 44). However, the availability of covered stents and stent grafts has made stent placement the treatment of choice for most adult patients with native or recurrent coarctation [172].

Outcome

The survival for unrepaired coarctation of the aorta is poor, with an average age at death of 34 years [178]. Ninety percent of deaths among patients with coarctation occurred before the age of 50 years, whereas in normal subjects, ninety percent of deaths occurred after age 50 years. The causes of death included congestive heart failure, aortic rupture, bacterial endocarditis and intracranial hemorrhage [178].

Survival data after repair of coarctation in the early surgical era between1946 and 1981 are sobering. The estimated survival was 92% at 10 years, 84% at 20 years, and 72% at 30 years after initial repair. The mean age at death was 38 years, an improvement of only 4 years over the natural history. The most common cause of late death was premature coronary artery disease, followed by sudden death, heart failure, cerebrovascular accidents, and ruptured aortic aneurysm. Age at initial repair predicted survival, with patients younger than 9 years at repair faring best [167]. After the age of 6 years, arterial hypertension persists in 25-50% of patients despite surgery [6].

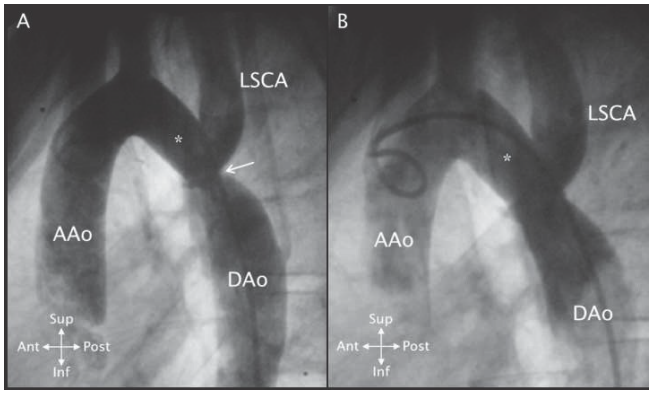

Figure 44: Left lateral angiograms in an adult patient with recurrent coarctation (white arrow) before (A) and after (B) balloon dilation.

More recent survival data are similarly disappointing. A review of reported series including nearly 1000 patients with coarctation repaired in childhood found a 22 year survival of 87% [173].

Outcomes for balloon angioplasty of discrete native coarctation in adults are good with a low risk of re-coarctation and aneurysm [179,180]. Risk factors for a suboptimal outcome include a higher pre-angioplasty systolic pressure gradient, earlier procedure date, older patient age and the presence of recurrent obstruction. The risk of acute procedural complications is low and obstruction is relieved in the majority of patients [176]. When angioplasty was compared with surgery, the gradient reduction was similar but with an increased incidence of aneurysm formation and restenosis with balloon angioplasty [181]. Results of balloon angioplasty for recurrent coarctation are not as favorable [182]. Placement of a covered stent is now the preferred treatment for adult coarctation at many institutions because of the low recurrence rate, low probability of aortic wall injury and near absence of aneurysm formation [172].

Conclusion

In conclusion, the number of adults with congenital heart disease presenting for cardiology care is increasing each year. Successful surgical, interventional, and intensive care strategies have resulted in more living adults with CHD than children. Cardiologists caring for these patients must have a working knowledge of congenital heart defects, their treatment, complications and outcomes. This illustrated guide is presented as an aid for understanding and managing these complex and difficult patients.

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