Journal of Clinical & Experimental
Cardiology

Baraona et al. J Clin Exp Cardiolog 2012, S:8
DOI: 10.4172/2155-9880.S8-006

Review Article Open Access

Coronary Arteries in Childhood Heart Disease: Implications for Management of Young Adults

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Abstract

Survival of patients with congenital heart defects has improved dramatically. Many will undergo interventional catheter or surgical procedures later in life. Others will develop atherosclerotic or post-surgical coronary heart disease. The coronary artery anatomy in patients with congenital heart disease differs substantially from that seen in the structurally normal heart. This has implications for diagnostic procedures as well as interventions. The unique epicardial course seen in some defects could impair interpretation of coronary angiograms. Interventional procedures, especially at the base of the heart, risk injuring unusually placed coronary arteries so that coronary artery anatomy must be delineated thoroughly prior to the procedure.

In this review, we will describe the variants of coronary artery anatomy and their implications for interventional and surgical treatment and for sudden death during late follow-up in several types of congenital heart defects including: tetralogy of Fallot, truncus arteriosus, transposition of the great arteries, double outlet right ventricle, congenitally corrected transposition of the great arteries and defects with functionally one ventricle. We will also discuss the coronary abnormalities seen in Kawasaki disease.

Keywords: Congenital heart disease; Adults; Coronary anatomy; Coronary pattern; Kawasaki disease; Sudden death

Introduction

A remarkable improvement in survival of patients with congenital heart defects (CHD) has occurred during the last 50 years. Now more than 90% of children born with CHD survive into adulthood. More than a decade ago the 32nd Bethesda conference reported there were more than 800,000 adults with CHD in the United States [1]. Many of these patients will undergo interventional catheter or surgical procedures for residual anatomical and hemodynamic abnormalities later in life. Others will develop atherosclerotic or post-surgical coronary heart disease. The coronary artery (CA) anatomy in patients with CHD, especially conotruncal anomalies, differs substantially from that seen in the structurally normal heart. Therefore, it is important for those caring for adult survivors with CHD to understand the variations in CA anatomy in these patients.

In this review, we will describe the variants of CA anatomy encountered in several types of CHD including: tetralogy of Fallot (TOF), truncus arteriosus (TAC), transposition of the great arteries (TGA{S,D,D}), double outlet right ventricle (DORV), congenitally corrected transposition of the great arteries (TGA{S,L,L}), and defects with functionally one ventricle (double inlet ventricle, tricuspid atresia, pulmonary atresia with intact ventricular septum, and hypoplastic left heart syndrome). We will focus on the implications of CA variants for interventional and surgical treatment and for sudden death during late follow-up.

Kawasaki disease is the most common cause of acquired heart disease in children living in developed countries. This diffuse vasculitis results in aneurysm formation, particularly in the coronary arteries. We will discuss the implications of post-Kawasaki coronary abnormalities for young adults.

Methods

We performed a literature search with the following search terms: coronary artery pattern, coronary artery anatomy, tetralogy of Fallot, double outlet right ventricle, truncus arteriosus, transposition of the great arteries, congenitally corrected transposition of the great arteries, single ventricle and Kawasaki disease. We identified those articles describing the coronary artery patterns seen in these CHD. When possible, the CA patterns were tabulated and frequencies calculated. An additional search was performed seeking examples of coronary complications of interventional procedures in subjects with CHD using the following search terms: percutaneous pulmonary valve implant, melody valve, cardiac resynchronization therapy, arterial switch operation and transcatheter aortic valve implant. Lastly, a search for sudden death in CHD survivors was completed in an effort to discover any association with CA anatomy.

Relevant heart specimens in the Cardiac Registry, Children's Hospital Boston, were examined to identify CA variants in selected CHD. We identified interventional or surgical procedures frequently performed for the defect that are known or likely to be associated with coronary complications due to usual or variant CA anatomy. We based this estimate on the proximity of CAs to structures in which an intervention is most likely and the susceptibility to compression or other damage.

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Received December 14, 2011; **Accepted** February 10, 2012; **Published** June 15, 2012

Citation: Baraona F, Valente AM, Porayette P, Pluchinotta FR, Sanders SP (2012) Coronary Arteries in Childhood Heart Disease: Implications for Management of Young Adults. J Clin Exp Cardiolog S8:006. doi:10.4172/2155-9880.S8-006

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Finally, we sought examples of variant CA anatomy demonstrated by clinical imaging studies in the imaging database of the Department of Cardiology, Children's Hospital Boston.

We labeled the aortic sinuses from which a CA arises (facing sinuses) descriptively according to patient anatomy, rather than with a number or letter [2]. There are reports of exceptional cases in which a CA arises from the non-facing sinus [3]. While one should be aware that such cases exist, they are exceedingly rare and will not be discussed here. Where possible, structures are displayed as in a short-axis plane on echocardiography or cardiac magnetic resonance (CMR).

The morphology of a CA is determined by the structures over which it courses. The major coronary arteries that we will describe here are: the right coronary artery (RCA) which passes in the atrioventricular groove between the right ventricle (RV) and its associated atrium; the circumflex coronary artery (LCx) which travels in the atrioventricular groove between the left ventricle (LV) and its associated atrium; the anterior descending artery (LAD) that parallels the interventricular septum on the anterior surface of the heart; and posterior descending artery (PDA) that parallels the interventricular septum on the inferior or posterior surface of the heart. The left main coronary artery (LCA) is usually very short and divides into the LCx and LAD. However, in some CA variants seen in CHD the LCA can be quite long (Figure 1). Other important CAs are the sinus node artery which supplies the sinoatrial node and the AV nodal artery that supplies the AV node.

Results

Among patients with congenital heart defects, CA variants occur most frequently in conotruncal anomalies. This is likely related to abnormal rotation of the outflow during development of these defects [4], and the fact that CAs develop in situ on the surface of the heart and penetrate the aortic wall to establish luminal communication [5,6]. In fact, the frequency of CA anomalies in defects with a normal outflow seems to be no higher than in normal hearts.

Tetralogy of fallot (TOF)

Young adults with repaired TOF comprise the largest single group in most adult congenital heart defect (ACHD) clinics.

Anatomy: The primary anatomical abnormality is anterior and leftward deviation of the infundibular or outlet septum, resulting in: 1) narrowing of the pulmonary outflow between the infundibular septum and the anterior wall, 2) a ventricular septal defect (VSD) because the infundibular septum fails to insert into the 'Y' of septal band, and 3) overriding of the aorta due to abnormal rotation of the outflow. RV hypertrophy is secondary to RV hypertension.

Surgical repair: Surgical treatment of TOF includes patch closure of the VSD and relief of pulmonary outflow obstruction. This can be accomplished by division or resection of muscle bundles in the outflow tract, patch augmentation of the infundibulum and/or valve annulus, or placement of a conduit between the RV and the pulmonary trunk or branches. In the majority of adults with TOF, the operative principle employed was wide patch augmentation of the RV outflow tract to avoid residual stenosis, resulting in pulmonary regurgitation. Pulmonary regurgitation is well tolerated in most patients for decades; however, RV dilation and dysfunction may ensue in later years. Therefore, more recently, the emphasis has been placed on preservation of pulmonary valve function.

Hemodynamic abnormalities encountered late after repair of TOF that can result in catheter or surgical treatment include: 1) pulmonary regurgitation, 2) residual or recurrent pulmonary stenosis, 3) branch pulmonary artery stenosis, 4) residual VSD, and 5) conduit dysfunction.

The current ACHD management guidelines recommend that CA anatomy should be determined before any intervention on the RV outflow (Class I, level of evidence C) [7].

Coronary artery anatomy: In most cases the CA anatomy in TOF is normal. However, Li et al reported that the orifice of the LCA is often located more posteriorly than in the normal heart (Figure 2) [8], possibly related to the abnormal rotation of the outflow seen in TOF [9]. In addition, a dominant LCA was found in 28% of TOF patients compared to 10 % of normal subjects.

The reported incidence of CA anomalies in patients with TOF varies widely (between 5 and 14%), [9-11] depending in part on the diagnostic modality used. Coronary variants in which a major branch crosses the RV outflow tract are potentially relevant for initial surgical repair (Figure 2-4). These include origin of the LAD from the RCA and single coronary artery arising from either the right or left coronary sinus with the LCA or the RCA, respectively, crossing the outflow (Figure 4) [12]. In such cases alternate approaches to relief of out flow obstruction might be employed such as a limited ventriculotomy below the crossing coronary artery, a transatrial-transpulmonary approach,

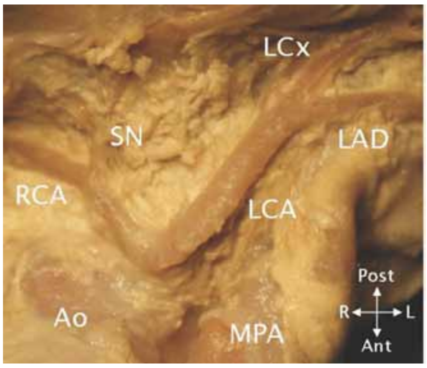

Figure 1: View of the posterior aspect of the aorta in a heart with TGA and single coronary ostium from the posterior facing sinus (single RCA, Figure 14C). The LCA is much longer than usual and passes posterior to the pulmonary artery (MPA). Ao- aorta, LAD – anterior descending artery, LCA – left coronary artery, LCx – circumflex artery, RCA – right coronary artery, SN – sinus node artery.

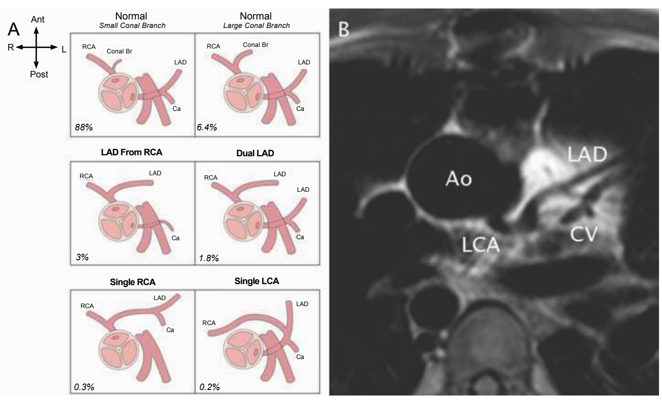

Figure 2: A – Various CA patterns seen in TOF with prevalence. (Reproduced from Geva et al. [8] with permission) B – MRI showing posterior origin of the LCA from the aortic root in a patient with TOF, CV-cardiac vein.

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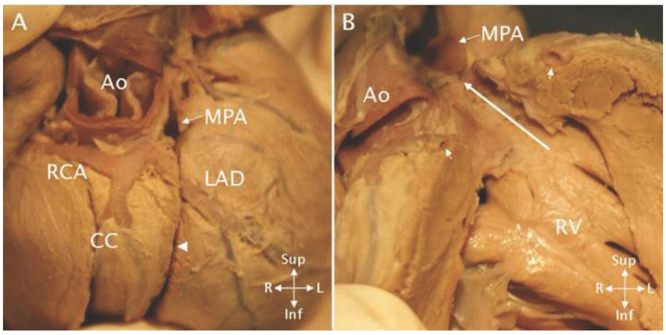

Figure 3: A – Superior frontal view of a heart with TOF showing the anomalous origin of the LAD from the RCA. The conus coronary artery (CC) originates just after the LAD. The hypoplastic main pulmonary artery (MPA) is seen to the left of the aorta (Ao). B - Frontal view with the RV opened along the cut (arrow head) indicated in A. Note the cut ends of the LAD (short arrows) divided by opening the RV outflow (long arrow).

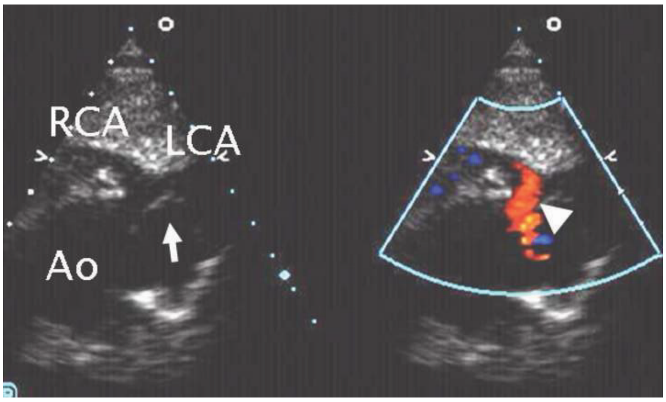

Figure 4: Parasternal short axis echocardiogram in a patient with TOF and origin of the LCA from the RCA with the LCA crossing the RV outflow (arrow). Color Doppler demonstrates flow into the single coronary orifice (arrow head).

or placement of a right ventricle-to-pulmonary artery (RV-PA) conduit. A particularly challenging anomaly to diagnose noninvasively is dual LAD, one from the LCA and one from the RCA crossing the RV outflow [12].

Another important consideration is the pattern of septal arterial supply. Hosseinpour described that the first septal artery or a large branch terminates at the base of medial papillary muscle, even in the presence of an outlet ventricular septal defect (Figure 5). Thus, the medial papillary muscle serves as a landmark to predict the site of termination of this artery, preventing arterial damage during the reparative surgery, for example, when the surgeon resects muscle to relieve the subpulmonary stenosis [13].

Chen et al. reported fair diagnostic accuracy (82.8%) using computed tomography (CT) for TOF patients of all ages with better sensitivity in older patients [14]. In comparison, coronary echocardiography has an accuracy of 98.5% in young patients (Figure 4) [10]. Consequently, the use of preoperative cardiac catheterization in TOF has declined in patients younger than 2 years of age. Cardiac CT and MR are also excellent methods for diagnosing CA anatomy.

Implications for treatment: Pulmonary regurgitation is the most frequent indication for interventional or surgical treatment late after repair of TOF. Percutaneous pulmonary valve implantation has been used with increasing frequency [15], although currently this approach is suitable only for some patients with a RV-PA conduit. During expansion of the stent in which the valve is mounted, there is a risk for compression of the normal LAD or another CA crossing the RV outflow (as described above) because it usually passes behind the conduit (Figure 6, 7), often near the site of insertion of the valve [16]. CA compression has been described after stenting the PA not only in TOF patients [17] but in other CHD as well [18,19]. Current practice includes evaluating the proximity of the LAD or crossing CA to the RV-PA conduit or homograft by simultaneous balloon inflation in the conduit and selective coronary angiography (Figure 8).

Patients with TOF and pulmonary atresia or those with an anomalous CA crossing the RV outflow have been treated most often by placement of a RV-PA homograft or conduit (Figure 6). With time, these conduits tend to become stenotic due to calcification, external compression, shrinkage or body growth. Endovascular stenting of conduits has been shown to be effective and safe [20,21]. The benefits of endovascular stenting over a repeat sternotomy must be weighed against the chance of a CA injury during conduit expansion.

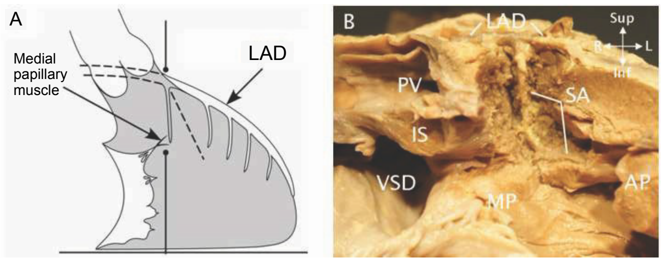

Figure 5: A – The 1st septal artery branches from the anterior descending artery (LAD) near the apical edge of the pulmonary root and passes through the anterior septum and septal band to reach the base of the medial papillary muscle (papillary muscle of the conus) (MP) According to Hosseinpour and colleagues [13], the position of the artery corresponds to a line constructed from the base of the MP perpendicular to the diaphragmatic wall. (Modified from Hosseinpour et al. [13] with permission). B – A dissection of a heart with TOF showing the position of the 1st septal artery (SA). In this case the SA is deep in the anterior septum and septal band. It veers toward the apex and supplies the anterior papillary muscle (AP). In this case the line described in A would be basal to the artery. The artery is far from the VSD or any muscle likely to be resected during relief of outflow obstruction.

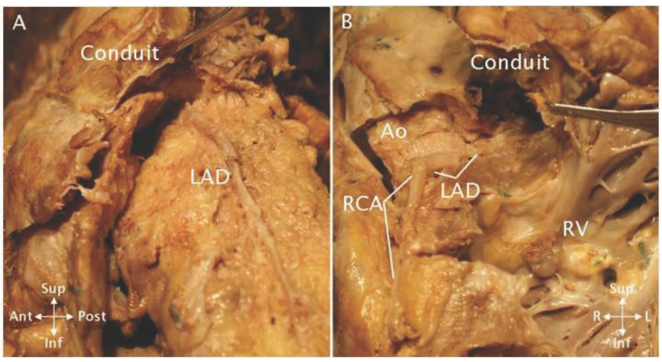

Figure 6: A – Left oblique view of a heart with TOF and pulmonary atresia. The LAD arises anomalously from the RCA and emerges from behind the RV-PA conduit (Conduit) to reach the anterior interventricular groove. B- Frontal view with the RV and RV-PA conduit (Conduit) opened showing the LAD arising from the RCA and then disappearing behind the posterior wall of the conduit.

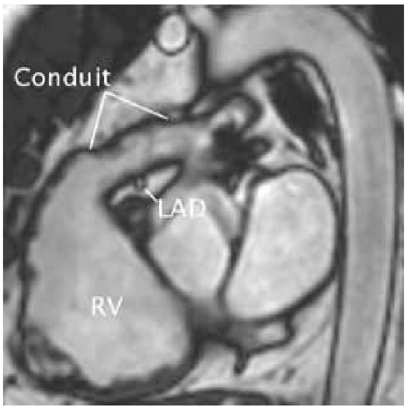

Figure 7: MRI in a patient with TOF and anomalous origin of the LAD from the RCA showing the LAD passing behind a RV-PA conduit.

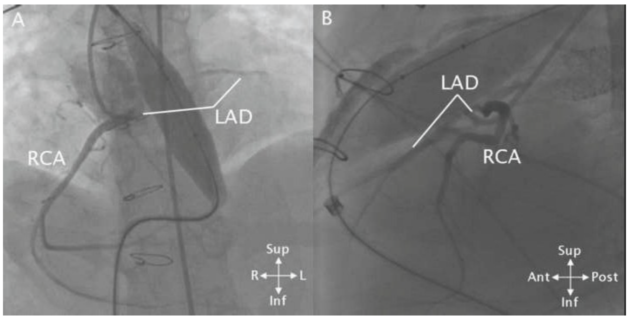

Figure 8: Right coronary angiogram in a patient with TOF and anomalous origin of the LAD from the RCA performed during inflation of a dilation balloon in the RV-PA conduit. The LAD is compressed by the balloon indicating that this patient is not a candidate for percutaneous valve implantation. This maneuver is performed routinely prior to placement of a stent or catheter implanted valve. A – AP view. B – Lateral view.

Stenosis of a branch PA is another indication for an interventional catheter procedure after repair of TOF. Common locations for branch stenosis are the site of ductal insertion in the left PA and the site of a prior Blalock-Taussig shunt in the right PA. The course of the right PA can be quite close to the LCA when it arises posteriorly (see above) (Figure 9). Expansion of a stent in the proximal right PA could obstruct the LCA.

Truncus arteriosus (TAC)

TAC is uncommon, comprising 1-4% of CHD. The natural history without intervention is poor and surgical repair is usually undertaken within the first months of life. Therefore, patients seen in adult congenital heart disease clinics have been repaired or have advanced pulmonary vascular obstructive disease.

Anatomy: This defect results from complete failure of septation of the outflow of the heart. Both the ascending aorta and main PA (or branch pulmonary arteries) arise from a common trunk due to failure of division of the aortic sac into aortic and pulmonary components. There is a single semilunar valve, the truncal valve, which is tricuspid in 69% of cases, quadricuspid in 22% and bicuspid in 9%. As in TOF, the infundibular or outflow septum fails to insert into the 'Y' of septal band, leaving a large VSD. The rotation of the outflow also appears to be abnormal in TAC [4]. Possibly as a consequence, the truncal valve straddles the ventricular septum and has biventricular origin in 68-83% of cases. Less frequently, it arises exclusively from the RV (11-29%) or the LV (4-6%).

The classification of TAC is based on the mode of origin of the pulmonary arteries from the truncus and the integrity of the aortic arch [22].

Surgical repair: Repair of TAC includes patch closure of the VSD so that the truncal valve is aligned solely with the LV, separation of the main or branch pulmonary arteries from the truncal root and closure of the resulting defect in the wall, and establishment of continuity between the pulmonary arteries and the RV, usually by means of a conduit or homograft. If the truncal valve is dysfunctional, valvuloplasty or even replacement might be indicated.

The most frequent hemodynamic problems seen after repair of TAC include: 1) dysfunction of the conduit or homograft between the RV and PA, 2) truncal valve dysfunction, and 3) residual VSD.

Coronary artery anatomy: Proximal CA anatomy is quite variable in TAC and is associated with the number of truncal valve leaflets [23,24]. The CA pattern is most likely to be normal when 3 valve leaflets are present. The CAs do not usually arise from adjacent sinuses when 4 leaflets are present (Figure 10). A single coronary ostium has been reported in up to 18% of cases [23]. Its origin is variable but is usually from the posterior quadrant. Other recognized variants include LCx arising from the RCA (a frequent variation in TGA) in 3.6% of TAC specimens [24] and LCA arising from RCA (like in TOF) in 2.4% of cases. The RCA is dominant in about 80% of cases independent of the leaflet morphology [32].

Perhaps the most variable aspects of CA anatomy in TAC are the location and shape of coronary ostia (Figure 11) [23-25]. Suzuki et al. [24] reported a high LCA orifice (above the sinutubular junction) in 32% and a high RCA origin in 20% of cases. A mid-level position was found in 21% of cases for both the RCA and LCA. Less frequently, the coronary ostia were located low in the sinus near the functional annulus in ~2% [24]. Cases with a single coronary ostium also showed marked variability of the position. Similarly, the location around the circumference of the truncal root is unpredictable. The marked variability of CA location is a risk factor during surgical repair [26].

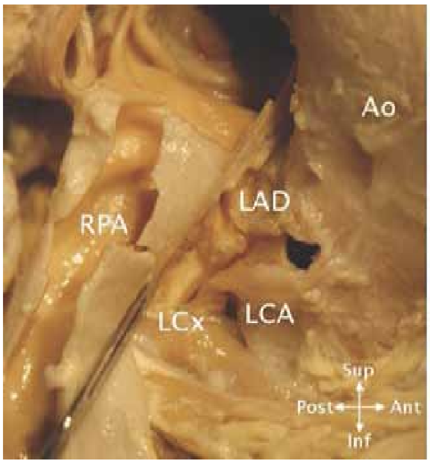

Figure 9: The LCA arises posteriorly from the aorta near the right pulmonary artery (RPA) in this heart with TOF. Stent placement in the proximal RPA could result in compression of the LCA.

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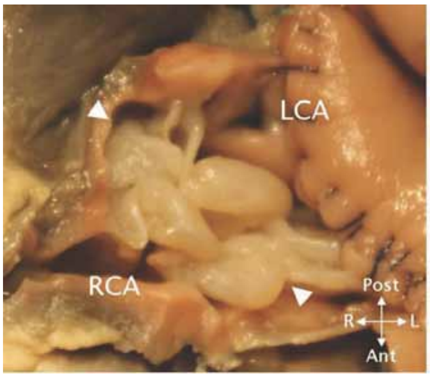

Figure 10: A quadricuspid and dysplastic truncal valve. The coronary sinuses are not adjacent but are separated by anterior and posterior non-coronary sinuses (arrow heads).

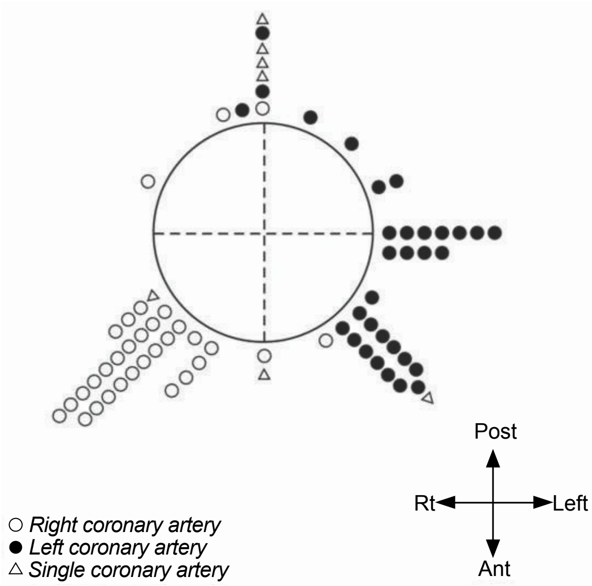

Figure 11: Marked variation in the locations of the coronary ostia in a series of patients with TAC. Facing sinuses cannot be identified in TAC because there is only a single semilunar root. (Modified from de la Cruz et al. [23] with permission).

Coronary ostial stenosis due to small size, slit-like shape, or location near or in the zone of leaflet apposition (Figure 12) [27] has been reported to cause ischemia, especially when aortic diastolic pressure is low due to run-off into the pulmonary circuit or across a regurgitant truncal valve [28].

Implications for treatment: The most frequent indications for treatment late after repair of TAC are conduit dysfunction and truncal (neo-aortic) valve dysfunction. As noted above, percutaneous valve replacement is now an established procedure for treatment of stenosis or insufficiency of a conduit or homograft. The LCA often lies adjacent to the pulmonary artery [25] or a major CA crosses the anterior surface of the RV in 13% of cases [23]. The same precautions described above for TOF to exclude coronary compression by a stent or stent-mounted valve are also appropriate for TAC patients.

The variability in CA anatomy has been associated with higher risk of perioperative complications, early death and need for adaptation of the surgical procedure [26].

Tlaskal showed that up to 44% of TAC patients have new onset or progression of truncal valve insufficiency [29]. Various methods of truncal valve reconstruction have been recommended [30,31] but valve replacement is often necessary because of dysplasia of the leaflets (Figure 10). A mechanical valve is preferred over a homograft valve because the homograft has been associated with higher early and late mortality [32,33].

Transcatheter aortic valve implantation [34,35] could be an alternative for high-risk patients with severe truncal valve stenosis or regurgitation. A small incidence of coronary obstruction has been reported with this procedure in patients with a native aortic valve [36] or a failed bioprosthesis [37]. Given the extreme variability of the location of coronary ostia in TAC, documentation of the proximal CA anatomy is indicated prior to valve implantation. CT may have a role in assessing the distance between the neo-aortic annulus and coronary ostia, for example [38].

Transposition of the great arteries (TGA)

Transposition derives from the Latin verb transponere meaning to place across. That is, the great arteries are placed across the ventricular septum: the aorta arising from the RV and the PA from the LV. TGA accounts for 5-7% of all congenital heart defects. It is lethal in infancy if no intervention is performed. Patients with TGA who have undergone an atrial or an arterial switch operation constitute another large group typically followed in ACHD clinics.

Anatomy: In the vast majority of patients with TGA the atria and ventricles are normally positioned and the abnormality is confined to the outflow. Most often the aorta is anterior and rightward of the PA. In 2/3 of cases the ventricular septum is intact. In the remainder a VSD, LV outflow obstruction, RV outflow obstruction, or coarctation might be present. Most frequently, the aorta connects to the RV via infundibular or conal muscle while the PA connects to the LV by direct mitral-pulmonary fibrous continuity. The proximal great arteries are parallel instead of crossing as in the normal heart.

Surgical repair: The first physiological correction was the atrial switch operation, reported by Senning in 1959 and Mustard in 1964. These procedures redirect venous blood within the atria so that systemic venous blood goes to the LV and pulmonary venous blood to the RV. However, the RV remains the systemic ventricle, and the tricuspid valve (TV) is the systemic atrioventricular valve. Eventual failure of these structures as systemic pump and atrioventricular valve has led

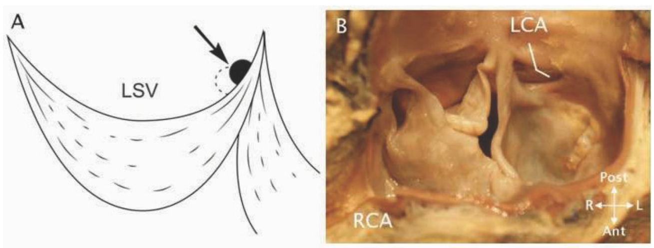

Figure 12: A - A drawing of a coronary ostium located in the zone of apposition of the truncal valve. This is one mechanism of ostial obstruction in TAC. (Modified from Van Son et al. [27] with permission) B - Slit-like orifice of the LCA. The ostium is near the left – non-coronary commissure. LSV – left sinus Valsalva.

to development of other corrective procedures. Now, the preferred procedure is the arterial switch operation (ASO), described by Jatene in 1975, which consists of transection of the aorta and PA above the sinutubular junction, movement of the PA forward while pulling the transected aorta through between the branch pulmonary arteries (Lecompte maneuver), and translocation of the coronary arteries from the anterior to the posterior root (neo-aorta). With this intervention, the LV becomes the systemic ventricle.

Coronary artery anatomy: The aorta is anterior in most cases of TGA so that the facing or coronary sinuses are posterior (near the PA) and the non-coronary sinus is anterior, the opposite of the normal heart (Figure 13). The major CAs take one of three categories of courses: usual, looping or intramural (Figure 14) [39]. Variant CA patterns are more prevalent when the great arteries are side-by-side as opposed to antero-posterior [40]. In the usual pattern, seen in 2/3 or more of patients, the left main CA arises from the left facing sinus and bifurcates into the LAD and LCx while the RCA arises from the right facing sinus [2,41]. The CAs run directly to the atrioventricular and anterior interventricular grooves, with no major arterial branch crossing either in front of or behind the vascular pedicle.

About 30% of TGA patients have a looping CA course, where one or more of the three main CAs runs in front of or behind the arterial pedicle. The most frequent looping course is the posterior loop. Two patterns comprise the majority of posterior loops: a) the LCx arising from the RCA and passing posterior to the pulmonary trunk (16%), and b) single RCA from the right facing sinus with the LCA passing posterior to the pulmonary trunk (4%). Double loops include: a) inverted RCA and LCx, that is, the LAD from the left facing sinus gives rise to the RCA which passes in front of the aorta and the circumflex arises from the right facing sinus, passing behind the pulmonary trunk (4%) and b) inverted pattern: the RCA arises from the left anterior facing sinus and passes in front of the aorta while the LCA arises from the right posterior facing sinus and passes behind the pulmonary trunk (2.5%) [2]. Note that this pattern is similar to that seen in the normal heart and is associated with side-by-side great arteries or the rare cases of TGA in which the aorta is posterior [42,43]. Anterior looping patterns are very rare and include single LCA and single RCA with anterior course of the LCA.

The intramural CA typically arises from the opposite facing sinus from normal so that both ostia are within the same sinus. It then courses within the wall of the aorta across the usually intercoronary commissure to reach its usual adventitial exit. The ostium of an intramural CA is often high above the sinotubular junction. The orifice might be oblique and stenotic as well.

Implications for treatment: The majority of adult TGA patients have undergone an atrial switch operation. Formerly the interest in the CA pattern was limited to the origin and course of the sinus node artery which can be damaged during the atrial switch operation. Injury to the sinus node artery has been blamed for the high prevalence of sinus node dysfunction and atrial arrhythmias [44]. Most frequently it reaches the sinus node via the anterior interatrial groove, passing near the superior vena cava pathway (Figure 15) [2]. Placing a stent in the superior vena caval pathway could impinge upon the sinus node artery, creating or worsening sinus node dysfunction.

Marcora et al. described a case where a stent which had been placed in the superior limb of a Mustard baffle was immediately adjacent to the LCx which arose from the RCA and had a retropulmonary course (Figure15) [45]. It is especially important to understand the CA

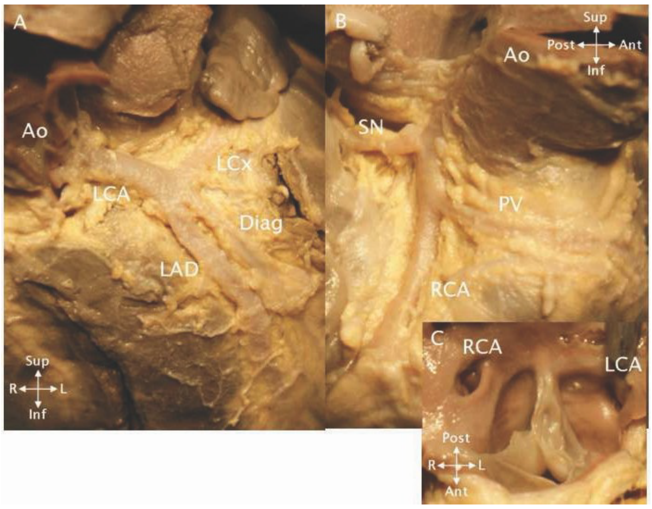

Figure 13: Usual coronary artery pattern seen in TGA. A – The LCA divides into the LAD, a diagonal branch (Diag), and the LCx. B – The RCA gives off the sinus node artery (SN) and a pre-ventricular (PV) branch before reaching the right AV groove. C – A view of the opened aortic root showing the coronary ostia from the posterior facing sinuses.

anatomy before performing interventional procedures at the base of the heart in patients with TGA.

After the atrial switch operation, both coronary ostia remain relatively posterior which can be challenging for coronary angiography (Figure 16). Marcora et al. reported excellent resolution of the epicardial CAs anatomy by CT in a series of TGA patients after the Mustard procedure. Of note, the majority of these patients had a hypoplastic left coronary system [45].

The ASO has become the treatment of choice for TGA as it restores the LV as the systemic ventricle and is associated with better mid-term outcomes. Obstruction of the neo-pulmonary outflow tract and/or branch pulmonary arteries are the most likely adverse sequelae of this intervention. A small proportion of patients develop progressive aortic regurgitation, especially those with a large subpulmonary VSD and neo-aortic root dilation [46].

Since the advent of the ASO, there has been special interest in the CA anatomy seen in TGA because it determines how the CAs are transferred during this intervention and likely influences outcomes. Pasquali et al. [47] addressed this point in a meta-analysis of 9 case series extending through the year 2000 which evaluated the relationship between CA variants and mortality after ASO. An intramural coronary artery was associated with a 6 fold increase in early mortality. In contrast to previous reports, a coronary loop was not associated with excess early mortality while a single coronary ostium carried a three-fold increase in mortality [47].

Long-term outcomes of the ASO are obviously of great interest. Reports of mid-term outcome have documented a prevalence of coronary stenosis or occlusion of ~3-8% [48,49]. Even complete occlusion of a main coronary is frequently completely asymptomatic but it has been associated with sudden death [50]. The hazard function for coronary events appears to be bimodal, with a large peak perioperatively followed by a period of low risk, followed by a rising hazard function after about 15 years [51]. Selective coronary angiography has been recommended after ASO; however there is no consensus as to when it should be performed. After the ASO, the positions of the coronary ostia are more like in the normal heart, except that the LCA ostium is more anterior than usual (Figure 16). However, in many cases, especially with variant CA anatomy, the coronary button is transferred above the aortic suture line. Recently, non-invasive methods such as CT have shown high sensitivity for detecting ostial stenosis in children [52] Therapeutic options for coronary ostial stenosis include surgery and percutaneous stent placement [53] The current ACHD guidelines recommend that adult survivors of the ASO should have noninvasive ischemia testing every 3 to 5 years (Class I, level of evidence C) [7].

A frequent indication for an interventional procedure after the ASO is branch pulmonary artery stenosis due to tension on the branches after the Lecompte maneuver. Placement of a stent in a branch pulmonary artery could impinge upon a superiorly located CA (Figure 17).

There are special considerations for replacing the aortic valve in patients after ASO and the Lecompte maneuver. In these cases, preoperative imaging (CT or CMR) to delineate coronary anatomy is essential. If aortic root replacement is planned, it is important to know the exact location of coronary arteries. Scar tissue typically obscures the translocated coronary arteries so the dissection must be conducted with caution to avoid CA injury [54]. Pasquali et al.

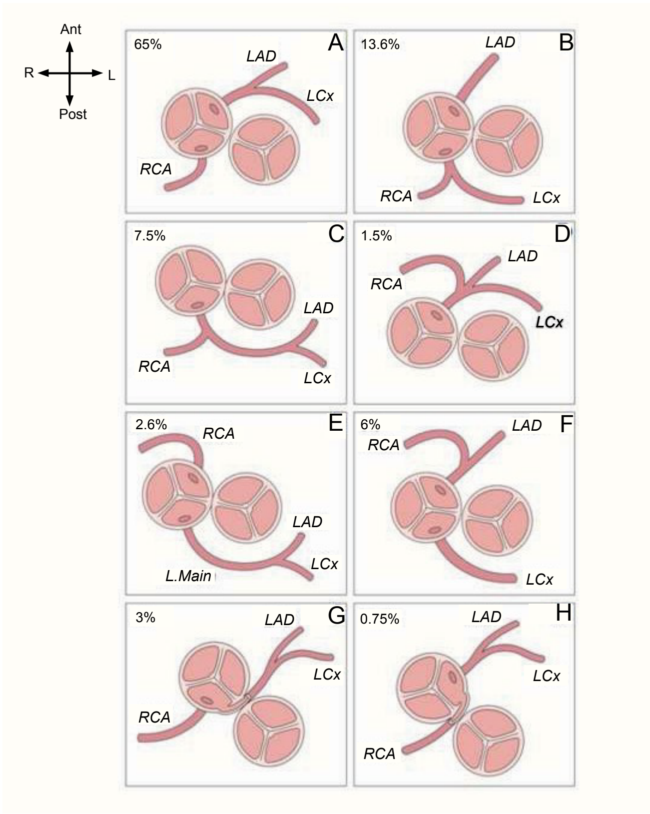

Figure 14: The most frequent coronary artery patterns seen in TGA with approximate prevalence. A – Usual pattern with the LCA from the left facing sinus and the RCA from the posterior and rightward facing sinus. B – Origin of the circumflex artery (LCx) from the RCA. C – Single RCA from the posterior facing sinus. D – Single LCA from the left facing sinus. E –Inverted arteries (note that this pattern is similar to the normal heart) F – Inverted RCA and LCx. G – Intramural LCA. H – Intramural RCA. The intramural CA in TGA usually arises from the opposite facing sinus and passes within the wall of the aorta before exiting the adventitia. The arteries share a media and do not have separate adventitia. (Reproduced from Geva et al. [8] with permission).

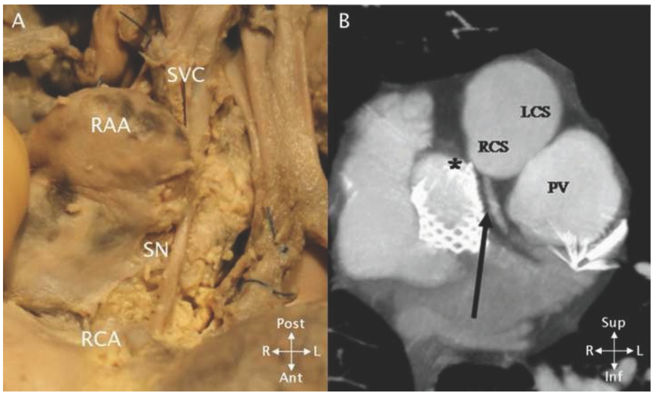

Figure 15: A -Superior view of a heart with TGA after a Mustard operation. The aorta is folded anteriorly showing the sinus node artery (SN) close to the superior vena cava pathway (SVC) as the artery courses from the proximal RCA toward the crista terminalis. Stent placement in the SVC pathway could compress the sinus node artery. B – A stent (*) has been placed in the SVC pathway because of obstruction after a Mustard operation. The stent is very close to the LCx (arrow), which arises from the RCA, but does not compress it. (Reproduced from Marcora et al. [45] with permission). RCS- right coronary sinus, LCS- left coronary sinus, RAA- right atrium appendix. PV- pulmonary valve.

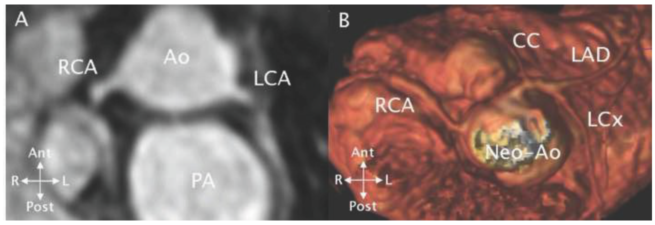

Figure 16: A – CA origins in TGA after an atrial switch operation. The RCA ostium is relatively posterior while the LCA ostium is near the usual location, although in the anterior vessel. B – CAs after an arterial switch operation. The RCA ostium is near the usual location but the LCA ostium is much more anterior than usual.

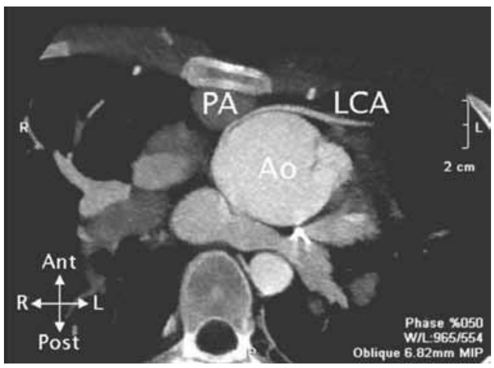

Figure 17: Proximity of the PA to the superiorly located LCA after an ASO in a patient with single RCA (Figure 14C). Placement of a stent in the PA could compress the LCA.

reported chronotropic impairment late after ASO especially in patients with variant CA patterns [41]. One hypothesis is that more extensive dissection is needed to mobilize and transfer variant CAs, impeding reinnervation of the heart. Chronotropic incompetence appears to be related to decreased exercise performance after the ASO [55].

Double outlet right ventricle (DORV)

This defect is characterized by an abnormal ventriculo-arterial alignment in which both great arteries are completely or nearly completely aligned with the RV. DORV can occur with virtually the full spectrum of congenital heart defects.

Anatomy: There are many variations in the anatomy of DORV and the physiology depends largely on the relationship between the VSD and the great arteries as well as associated defects. The VSD is usually large and located within the 'Y' of septal band; although in unusual cases it is remote from the outflow. The orientation of the infundibular septum and the position of the great arteries are mostly responsible for the relationship between the VSD and the great arteries. The variable rotation of the outflow during development that explains the variations in anatomy and physiology also likely produces the highly variable CA anatomy.

Surgical repair: Choice of surgical correction requires a complete understanding of the relationship between the VSD and the great arteries, the size of the VSD, adequacy of the ventricles, and associated defects such as pulmonary stenosis, straddling AV valve, etc. In general, surgical repairs include: 1) VSD closure directing the LV to the aorta with or without relief of RV outflow obstruction, 2) VSD closure to the pulmonary artery with atrial or arterial switch operation 3) staged single-ventricle palliation (Fontan procedure).

Coronary artery anatomy: The CA pattern in DORV follows the position of the great arteries. In a series of 44 DORV hearts, the pattern seen in the normal heart was the most frequently observed (34%). This pattern is usually present when the aorta is relatively posterior and rightward and the physiology is like a large VSD or TOF. In cases with a rightward and anterior aorta the CA pattern is similar to the usual pattern seen in TGA (25%). As in TGA, variant CA patterns are often seen in side-by-side great arteries (27%) [56]. When the aorta is anterior and leftward, the RCA crosses in front of the RV outflow (Figure 19).

Implications for treatment: The potential difficulties with assessment of CA anatomy and of interventional treatment of residual abnormalities in DORV are similar to those described above for TOF and TGA. A leftward, anterior aorta in DORV with normally positioned atria and ventricles (DORV {S,D,L}) is usually associated with pulmonary stenosis (right-sided). The RCA crossing the pulmonary outflow (Figure 18) often precludes patch augmentation, requiring a RV-PA conduit or homograft. Stent augmentation or percutaneous placement of a valve in the conduit could compress the underlying RCA.

Congenitally corrected transposition of the great arteries (C-TGA)

C-TGA is one of the few CHD that presents in adulthood. While most cases are diagnosed in infancy and childhood, a few without associated defects present late with arrhythmia or heart failure.

Anatomy: As with TGA, the great arteries arise from the opposite ventricle from normal hence the name transposition. The ventricles are inverted with atrioventricular discordance; the right atrium drains to the right-sided LV and the left atrium to the left-sided RV. Only the atria are in the normal position in C-TGA. The PA is right-sided, posterior and aligned with the LV while the aorta is anterior, left-sided and aligned with the RV. In the absence of other defects the physiology is normal because systemic venous blood reaches the PA via the LV and pulmonary venous blood the aorta via the RV. This is why some patients reach adulthood without detection. Like TGA after an atrial switch, the weak links in the systemic circulation are the RV and TV. Frequently associated defects include TV dysplasia (Ebstein malformation), VSD and pulmonary stenosis.

Surgical treatment: Tricuspid regurgitation is probably the most frequent indication for surgical treatment in adults with CTGA. The results of a plastic procedure on the TV have been disappointing so that replacement is usually performed [57]. Closure of a large VSD has been performed in some patients with no or mild associated abnormalities. In some patients with extreme pulmonary stenosis or pulmonary atresia, a conduit has been placed between the LV and the PA with closure of the VSD. In the last 20 years the double switch operation has become the procedure of choice in children with more complicated forms of C-TGA [58,59]. This procedure entails performing an atrial switch operation (Mustard) and an ASO to achieve anatomic correction. This approach places the LV and mitral valve in the systemic circulation while correcting any associated defects. Not surprisingly, the complications of the double switch include atrial baffle obstruction, pulmonary outflow obstruction, and CA complications.

Occasional patients do not have two adequate ventricles and undergo Fontan palliation.

Coronary artery anatomy: As in TGA, the aorta is anterior in C-TGA so that the facing sinuses are posterior. Unlike TGA, however, the ventricles are inverted in C-TGA and the CA pattern generally follows the ventricular position. Consequently the morphologically LCA originates from the rightward and posterior sinus and the morphologically RCA from the leftward and posterior sinus (Figure 19). The LCA bifurcates into the LAD, which runs in the anterior interventricular groove, and the LCx in the right AV groove. Various reports have indicated that the CA pattern is relatively uniform in C-TGA [60-62]. McKay et al. reported that the sinus node artery consistently arises anteriorly from the LCx [60]. Although documented in few cases, the AV nodal artery (to the anterior node) derives from a branch of the LCA that passes along the medial side of the right atrial wall [60]. Both nodal arteries could be at risk for damage during construction of the atrial baffle as part of the double switch repair.

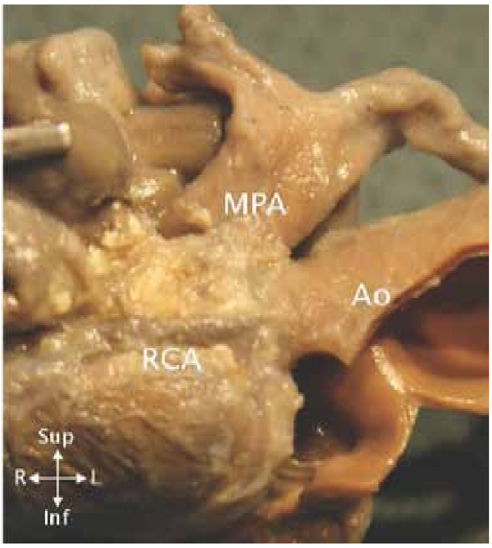

Figure 18: Frontal view of a heart with dextrocardia and DORV {S,D,L}. The RCA crosses in front of the right-sided pulmonary artery (MPA).

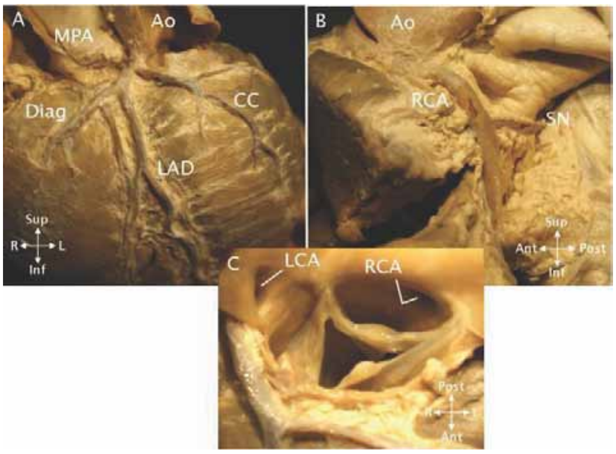

Figure 19: CA anatomy in CTGA. A – The LCA arises from the right posterior sinus and gives rise to a large conus coronary artery (CC), the LAD, and a large diagonal branch (Diag). Usually the circumflex coronary arises from the LCA but is absent in this case. Cardiac veins are seen paralleling the CAs. B – Left lateral view showing the origin of the RCA from the left posterior sinus. The sinus node artery (SN) arises from the RCA in this case instead of the LCx which is absent. C – The LCA ostium is just above the right posterior sinus and the RCA ostium is in the left posterior sinus. The anterior leftward sinus is the non-coronary sinus.

The coronary sinus (CS) ostium has a predictable location in patients with C-TGA because the atria develop normally [63,64]. However, the venous branches (e.g. the great cardiac vein, lateral branches) draining to the CS develop with the ventricles which are inverted [63].

Implications for treatment: Other than arrhythmia, RV dysfunction and tricuspid regurgitation are the most frequent late complications [65,66]. As noted, TV replacement is favored over repair [67] and should be considered prior to deterioration of RV function (RVEF <40%) [57]. The RCA runs in the left atrioventricular groove and, as in the normal heart, is at risk for injury during valve replacement.

Obstruction of the intraatrial baffle constructed as part of the double switch operation is a known complication of this procedure. Stent placement in the SVC limb can result in obstruction of either or both nodal arteries.

An important cause of RV dysfunction appears to be repeated episodes of ischemia and micro infarction. Coronary flow reserve is reduced [68] and, in the face of RV hypertrophy necessary to support the systemic circulation, can result in inadequate perfusion due to supply-demand mismatch. Myocardial fibrosis, visualized by CMR as areas of delayed gadolinium enhancement, is predictive of reduced ejection fraction, poor exercise tolerance, and progressive clinical deterioration [69]. Coronary angiography is indicated for patients in whom RV dysfunction is not well explained (class IIa, level of evidence C) [7].

Coronary stenosis or occlusion can occur following the arterial switch portion of the double switch operation as described above for TGA. The prevalence of this complication following the double switch has not been reported but is likely to be similar to that for the ASO for TGA. It is likely to be a risk factor for sudden death as well, but this is not known. As for TGA following the ASO, there are no clear guidelines for when and how often coronary angiography should be performed.

Some C-TGA patients with heart failure secondary to RV dysfunction benefit from cardiac resynchronization therapy [70,71]. The coronary sinus ostium location is usually normal but has been reported to be on the same side of the Eustachian valve as the IVC in some patients [72]. Although cannulation is usually possible, stimulation of the RV may be difficult due to small and short lateral epicardial veins. In such cases, large collateral veins draining into the interventricular vein might be used [63].

Single ventricle (SV)

Patients with functionally one ventricle comprise a heterogeneous group. The common feature is the presence of only one ventricle capable of supporting the systemic circulation. This group represents about 1-2% of congenital heart defects.

Double inlet left ventricle (DILV): In DILV, both atrioventricular valves are aligned with the dominant LV. There is a hypoplastic infundibular or outflow chamber that usually supports the aorta, with the PA aligned with the LV (transposition).

Anatomy: The atrial anatomy is usually normal in DILV. In the majority of cases the LV and outflow chamber are inverted and great arteries are transposed (DILV with TGA {S,L,L}). The infundibular chamber is small and usually left-sided. Occasionally the LV and outflow chamber are in the usual position (DILV with TGA {S,D,D}). Here the infundibular chamber is right-sided. Rarely in cases with normal ventricular arrangement the great arteries are normally related (DILV with normally related great arteries {S,D,S}) – also known as the Holmes heart.

The communication between the LV and the outflow chamber – variously called a bulboventricular foramen, interventricular foramen, or VSD - can be restrictive causing subaortic stenosis – or subpulmonary stenosis in the case of the Holmes heart. Subaortic stenosis is often associated with coarctation of the aorta. Pulmonary stenosis (valvar and subvalvar) or even atresia is frequent. Atrioventricular valve anomalies are also prevalent including leaflet hypoplasia, dysplasia and clefts, as well as straddling into the outlet chamber.

Surgical repair: Although septation and biventricular repair of DILV was tried in the past, it was uniformly unsuccessful and has been abandoned [73]. As with other functionally single ventricle defects, the treatment of DILV is a staged Fontan palliative procedure. The exact sequence of stages depends on the underlying anatomy.

Coronary artery anatomy: The CAs arise from the two facing aortic sinus – usually the posterior sinuses - irrespective of the great artery relations or the position of the ventricle. However, the pattern of epicardial coronary arteries is a function of the underlying ventricular anatomy as described above for CTGA. Anterior and posterior delimiting arteries mark the position of the septum and indicate the size of the outflow chamber (Figure 20) [74].

Tricuspid atresia

Tricuspid atresia (TA) encompasses a spectrum of anomalies with variable ventriculo-arterial alignments. The size of the VSD is also variable and is an important determinant of the physiology and clinical presentation.

Anatomy: The TV is atretic so there is no direct connection between the right atrium and RV. Systemic venous blood returning to the right atrium must traverse the foramen ovale or an atrial septal defect to reach the left atrium. The LV contains the only atrioventricular valve,

Citation: Baraona F, Valente AM, Porayette P, Pluchinotta FR, Sanders SP (2012) Coronary Arteries in Childhood Heart Disease: Implications for Management of Young Adults. J Clin Exp Cardiolog S8:006. doi:10.4172/2155-9880.S8-006

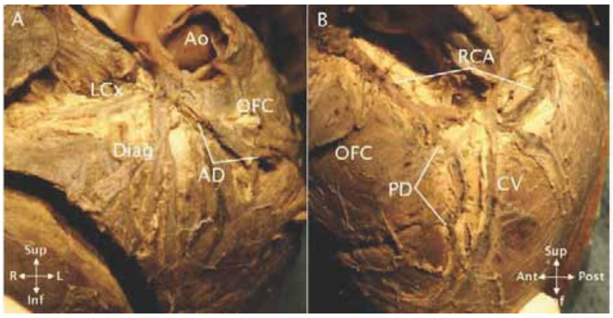

Figure 20: Coronary artery pattern in DILV with TGA{S,L,L}. A - The right-sided morphologically LCA gives rise to the LCx in the right AV groove, a large diagonal artery (Diag), and a small anterior delimiting artery (AD) that marks the anterior septum. B – The left-sided RCA gives off the posterior delimiting artery (PD) before passing into the posterior left AV groove where it gives rise to a variable number of branches supplying the posterior LV wall. CV- cardiac vein, OFC – outflow chamber.

the mitral valve. The outlet chamber or rudimentary RV lacks most or the entire inflow portion and communicates with the LV via a VSD. The great arteries are normally related in 70% of cases and transposed in most of the remainder. Pulmonary outflow obstruction is frequent in normally related great arteries due mostly to a restrictive VSD. When the great arteries are transposed, subaortic stenosis is frequent due to a small VSD and is often associated with coarctation of the aorta.

Surgical repair: Current surgical strategy is staged Fontan palliation. As for DILV, the palliative stages depend on the anatomy.

Coronary artery anatomy: The coronary ostia are in the anterior facing sinuses when the great arteries are normally related, and the posterior facing sinuses in transposition. Deanfield reported the epicardial coronary pattern in 48 TA specimens. The artery demarcating the posterior septum descended at the acute margin of the ventricular mass rather than at the crux. The two arteries in the anterior and posterior interventricular grooves meet at the apex of the rudimentary RV in about 1/2 of cases (Figure 21). An additional artery descends from the crux in 75% of specimens and ~90% have parallel arteries descending from the atrioventricular groove between the delimiting acute marginal coronary artery and the crux when no artery is visible at the crux [75].

Pulmonary atresia with intact ventricular septum (PA/IVS)

This is a rare congenital heart defect. Pulmonary atresia is usually valvar and associated with variable hypoplasia of the TV and RV. Invariably, there are concordant atrioventricular and ventriculo-arterial alignments.

Anatomy: The TV is small and often dysplastic with stenosis or regurgitation, and in 10% of cases there is Ebstein malformation [76]. The RV is small but usually contains both inflow and outflow portions. The PV is usually formed but atretic. The pulmonary trunk extends to the atretic valve and the normal-sized branch pulmonary arteries are continuous with the pulmonary trunk.

Surgical repair: Management of PA/IVS depends on the size of the RV and TV as well as the CA anatomy. A biventricular repair is achievable in about ½ of cases [77]. The procedure includes patch plasty of the RV outflow and creation of a systemic-to-pulmonary shunt. With RV growth, the shunt can be taken down and, if necessary, the atrial communication closed. Factors incompatible with a biventricular repair include absence of a RV outflow, diminutive RV and TV valve, and RV dependent coronary circulation (see below). In such cases a staged Fontan palliation is performed. Mortality after right ventricular decompression seems to depend on the amount of LV myocardium at risk of ischemia with this intervention [77].

Coronary artery anatomy: Abnormal communication between one or more CA and the RV is seen in 30-60% of cases [78]. The suprasystemic RV pressure during development appears to cause preexisting channels or sinusoids in the developing fetal myocardium to remain patent. Fistulous connections are usually tortuous and variable in size, number and site and are more frequent in smaller ventricles. Most commonly involved are the RCA, the PDA and the LAD [79].

Coronary stenoses often result from endothelial injury sustained as a result of turbulent flow generated by retrograde coronary perfusion from the RV [79]. When present, stenosis or occlusion of the CA is usually located between the fistulous connection with the RV and the origin from the aorta (Figure 22). Right ventricular-dependent coronary circulation is present when stenosis or atresia of one or more CAs results in part of the myocardium being dependent upon RV ejection into the CA for adequate perfusion. Calder et al. reported the CA anatomy in 35 PA/IVS specimens. A single coronary ostium was

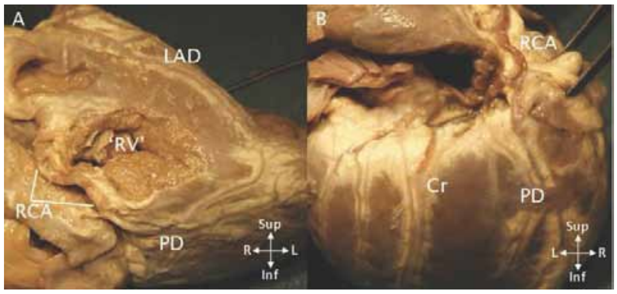

Figure 21: A – The hypoplastic RV ('RV') in a heart with tricuspid atresia is demarcated by the LAD anteriorly and a posterior delimiting artery (PD) at the acute margin of the heart. B – The posterior aspect of the heart in another case of tricuspid atresia. In addition to the delimiting artery (PD) at the acute margin there is a large branch that descends from the crux (Cr) of the heart.

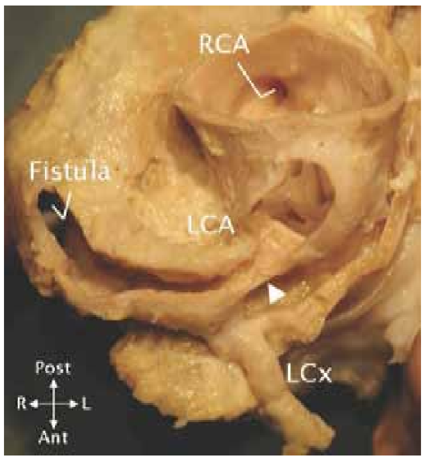

Figure 22: LCA-RV fistula in pulmonary atresia with intact ventricular septum. The ostium of the LCA is dilated but the LCA narrows rapidly (arrow head) to an area of severe stenosis due to marked thickening of the vessel wall. After the origin of the LCx, the coronary dilates and forms a large fistulous connection with the RV.

present in 20% of cases: the RCA arose from the LAD in 3 cases, the LCA from the RCA in 1 case, and the RCA from the LCA in 1 case [80]. Atresia of a coronary ostium is associated with a high mortality [79].

Double inlet right ventricle (DIRV)

This is a very rare congenital heart defect. Here, both atrioventricular valves are exclusively committed to the RV. The atrioventricular valves are separate in ~35% of cases and a common valve is present in the remainder.

Anatomy: Girod described the morphology in DIRV specimens according to AV valve anatomy. In cases with separate AV valves entering the RV, the rudimentary LV was located posteriorly and to the left or was absent. Straddling of the left atrioventricular valve into the rudimentary LV can be seen in some cases [81]. In cases with a common AV valve, it entered the morphologic RV exclusively and a rudimentary LV was always present. Both great arteries arise from the RV. The aorta is most often anterior. Stenosis of either outflow can occur.

Surgical repair: Staged Fontan palliation is the only treatment option. Initial palliative maneuvers are determined by the exact anatomy.

Coronary artery anatomy: The aorta is usually anterior so that the CAs arise from the posterior facing sinuses. The anterior and posterior descending arteries delineate the position of the rudimentary LV. There are no prominent interventricular branches in DIRV, rather a wreath of smaller arteries descend toward the apex randomly around the atrioventricular junction (Figure 23) [74].

Hypoplastic left heart syndrome (HLHS)

This heterogeneous group of congenital heart anomalies is characterized by left heart structures that are, in aggregate, too small to support the systemic circulation at an acceptable filling pressure.

Anatomy: HLHS can be divided into three anatomic groups: 1) mitral and aortic stenosis, 2) mitral stenosis and aortic atresia, 3) mitral and aortic atresia. The first is really one end of the spectrum of critical aortic stenosis. The second, analogous to PA/IVS, might carry a worse prognosis than the other types [82]. The ascending aorta size is variable and related to the amount of anterograde flow through the aortic valve. If the aortic valve is atretic the ascending aorta is markedly hypoplastic and functions as a "common coronary artery". The transverse aortic arch size is variable and coarctation is almost universal.

Coronary anatomy: The CAs usually have normal ostia, arising normally from the aortic sinuses, and follow a normal epicardial course (Figure 24). Anterior and posterior delimiting arteries usually define the hypoplastic LV irrespective of the degree of hypoplasia. The major epicardial coronary arteries usually occupy the atrioventricular and interventricular grooves. Sometimes these arteries are distended and tortuous, especially the distal portions, having a "corkscrew" configuration [83]. Lloyd et al. measured the diameters of the orifices and the proximal courses of the CA and showed no difference from normal hearts [84]. Baffa reported a normal ratio between wall thickness and lumen diameter of the main CAs in children with HLHS [85]. Fistulous communications with the LV are less frequent than in PA/IVS but do occur in the subset with aortic atresia and mitral stenosis. There is some debate about the significance of coronary anomalies in HLHS. They could impact the blood supply to the RV which is the systemic ventricle [86,87]. Coronary anomalies are more prevalent the smaller the LV.

Implications for treatment: The techniques used today for Fontan palliation involve an extracardiac conduit or a lateral tunnel in the right atrium. Consequently, CA variations do not seem to have major implications when a Fontan procedure is planned. The Fontan patient population is young and few have developed coronary artery disease, so there is still limited experience. Placement of a stent in a pulmonary branch could impinge upon a coronary artery but we know of no reports of this complication. The main challenge in these patients is likely to be interpretation of CA imaging due to the variable and often unpredictable anatomy.

Kawasaki disease

Kawasaki disease is a diffuse vasculitis that affects primarily infants and children from about 6 months to 4 years of age. The clinical presentation, diagnostic criteria, treatment, and short-to-midterm follow-up have been extensively documented [88] and will not be discussed here.

The arteritis causes aneurysms of medium sized transitional arteries, especially the coronary arteries. The intense inflammatory

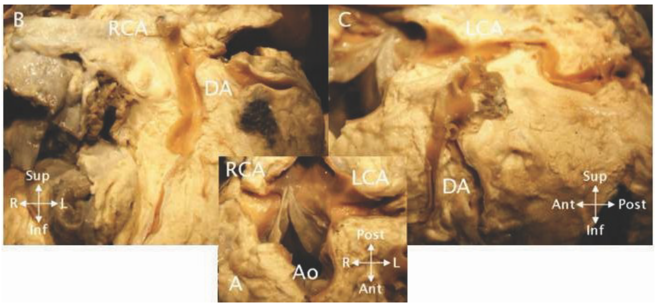

Figure 23: In hearts with DIRV the coronary arteries arise from the posterior facing sinuses (A) and encircle the AV groove, giving of a number of variably placed descending branches (DA) (B & C).

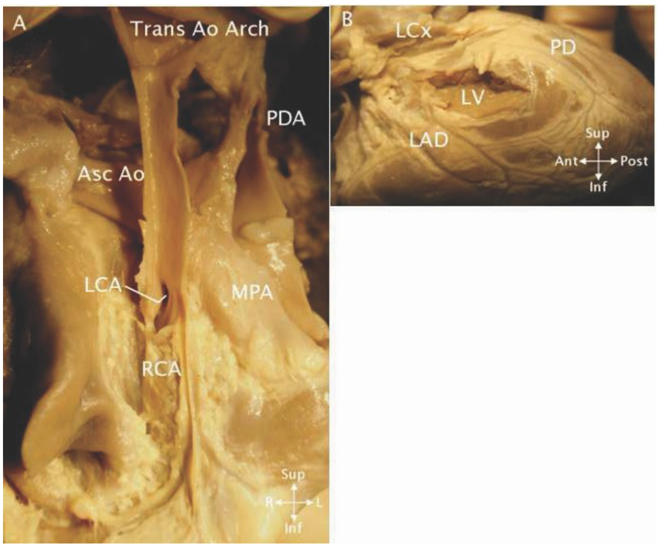

Figure 24: The coronary arteries arise from the hypoplastic ascending aorta in HLHS. The aortic valve is atretic in this heart. Coronary blood flow derives from retrograde flow in the ascending aorta. The course of the RCA is normal. The LCA gives off both the LAD and the posterior delimiting artery (PD) that demarcates the hypoplastic LV.

process appears to be a response to a superantigen-producing infectious agent enhanced by dysregulation of the normal T-cell response [89]. The process is most marked in CAs where it is maintained by a cascade of inflammatory mediators including TNFα and working in part through Toll-like receptor 2 which is disproportionately expressed in CAs [89]. Matrix metalloproteinase 9, induced by TNFα, disrupts elastic fibers and other structural proteins in the vessel wall causing aneurysm formation (Figure 25). Genetics plays a significant role in the risk for development of Kawasaki disease and in outcome [89]. First, there is a marked variation in the prevalence of the disease based on ethnicity. The prevalence in Asian populations is 4-20 times higher than in populations in North America and Europe [89]. In addition, gene variants in pathways regulating T-cell response and vascular biology have been identified by genome-wide association studies that are associated with increased risk for and/or increased severity of Kawasaki disease [89].

Coronary aneurysms develop during the second and third weeks of the disease in 20-25% of untreated patients. Treatment with immune globulin can prevent aneurysm formation in most cases, with about 5% of treated patients developing aneurysms [88]. Smaller aneurysms usually resolve but giant ones (> 8 mm diameter) rarely do (Figure 26). Slow blood flow within the aneurysm predisposes to thrombus formation which can precipitate an acute coronary syndrome (Figure 27) [90].

Aneurysms heal by intimal hyperplasia and by thrombosis and remodeling [91]. In more than 50% of aneurysms, the angiographic appearance of the coronary artery normalizes [92]. However, the vessel wall remains grossly abnormal (Figure 28). Intravascular ultrasound studies show marked intimal-medial thickening in the previously aneurismal part of the vessel [93]. Pathological studies have confirmed marked intimal thickening due largely to smooth muscle proliferation [91]. Coronary artery calcification is often present in areas with severe intimal thickening [90]. Coronary aneurysms, especially giant aneurysms, progress to stenosis or occlusion in 4-5% of patients (Figure 26) [94].

Endothelial function in areas of healed aneurysm remains abnormal for years (possibly permanently) after the acute episode (Figure 29) [93]. In contrast, CA segments that appeared normal by echo during the acute illness exhibit normal endothelial function [93]. Peripheral vascular endothelial function also appears normal late after the acute

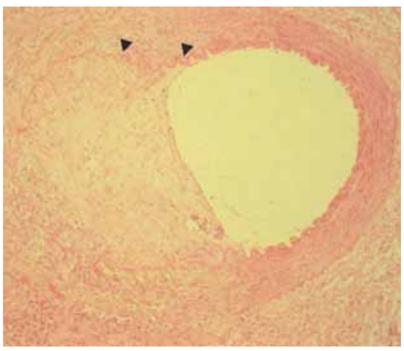

Figure 25: A developing coronary artery aneurysm in a patient dying of Kawasaki disease. The portion of the vessel wall to the right is intact. On the left the vessel wall has been dissolved by lytic enzymes. The internal elastic lamina (arrow head) is disrupted. Disruption of the vessel wall allows the aneurysm to develop. Photomicrograph courtesy of Dr. Jane C. Burns, Director, Kawasaki Disease Research Center University of California San Diego.

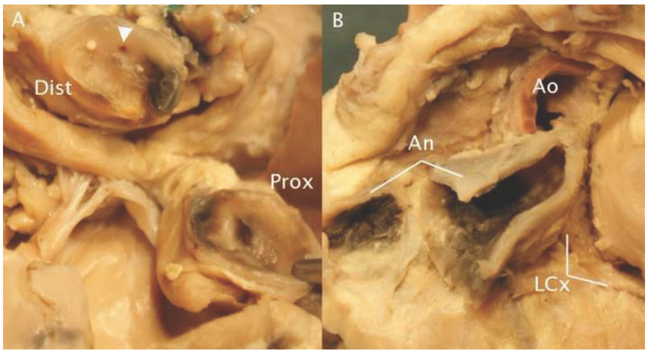

Figure 26: A - Proximal (Prox) and distal (Dist) ends of a giant aneurysm of the RCA in a patient with Kawasaki disease. The mid portion of the aneurysm was removed for histology. Note the severe stenosis of the RCA at the exit from the distal end of the aneurysm (arrow head). B – Giant aneurysm of the distal LCA and LAD. The aneurysm has been opened lengthwise and divided transversly. The LCx is not involved.

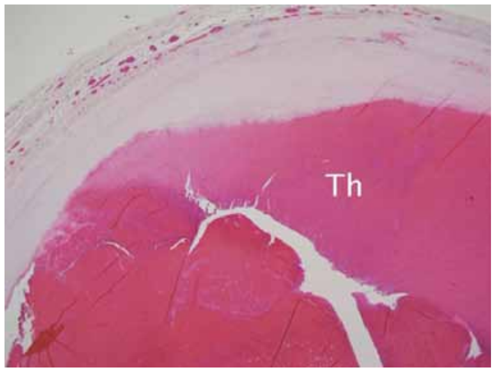

Figure 27: Giant aneurysm of the RCA in a patient with Kawasaki disease. The artery is markedly dilated with intimal hyperplasia. A clot adherent to part of the arterial wall produces subtotal occlusion and caused a lethal myocardial infarction.

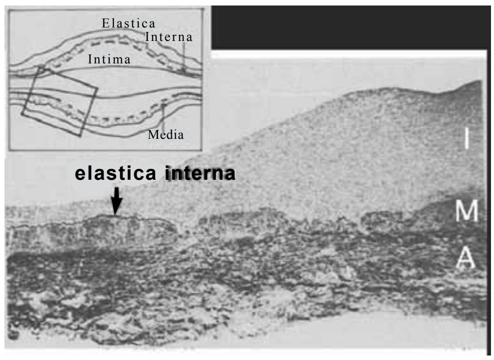

Figure 28: Healed aneurysm after Kawasaki disease. The inset indicates where the section was taken in the aneurysm. Note the marked hyperplasia of the intima (I) to the right side. The elastic lamina is disrupted and the media (M) is irregular in the healed aneurysm. A – adventitia (Modified from Sasaguri & Kato [91] with permission).

illness irrespective of coronary artery involvement [95]. Kawasaki disease results in ischemic heart disease during short-to-midterm follow-up in 1-2% of patients [96]. Consequently, small numbers of children and adolescents have been treated by bypass grafting or by

Citation: Baraona F, Valente AM, Porayette P, Pluchinotta FR, Sanders SP (2012) Coronary Arteries in Childhood Heart Disease: Implications for Management of Young Adults. J Clin Exp Cardiolog S8:006. doi:10.4172/2155-9880.S8-006

interventional catheter procedures. A late follow-up study showed a patency rate of 78% for arterial grafts and a 70% freedom from coronary events at 10 years [97]. Balloon angioplasty has yielded poor results, particularly later than 2 years after the acute illness, because of marked fibrosis and calcification of the vessel wall [98]. The combination of rotary ablation and stent placement seems to be the most successful approach [99].

The clinical course of young adults who suffered an episode of Kawasaki disease in childhood is not well understood. Long-term follow-up studies including adolescents and some young adults with persistent coronary artery abnormalities have shown that existing stenotic lesions tend to progress in severity and that the prevalence of coronary stenosis increases progressively [100]. Burns and colleagues found 74 cases in the literature of young adults presenting with coronary heart disease likely attributable to Kawasaki disease [101]. The mean age at presentation was about 25 years and 85% were of Asian ethnicity. Kato and colleagues surveyed hospitals in Japan and found 130 adult patients with coronary aneurysms possibly related to a prior episode of Kawasaki disease (Figure 30) [102]. Involvement of the LCA is about 10 times more frequent (42% vs. 4%) in post-Kawasaki CA disease compared to atherosclerotic coronary disease [103]. In addition, more than 1/3 of post-Kawasaki patients had evidence of coronary calcification on chest x-ray. Guidelines were recently published (Table 1) for follow-up of young adults with a history of Kawasaki disease although, as the authors point out, there is a lack of supporting evidence [104].

Conclusion

CA patterns in patients with CHD often differ from those seen in the structurally normal heart. This has implications for diagnostic procedures as well as interventions. Unusual location of the coronary ostia can complicate cannulation for angiography. The unique epicardial course seen in some defects, especially single ventricle defects, could impair interpretation of coronary angiograms. CMR and/or CT might be the methods of choice for delineation of the epicardial coronary anatomy because of the 3D nature of the data sets.

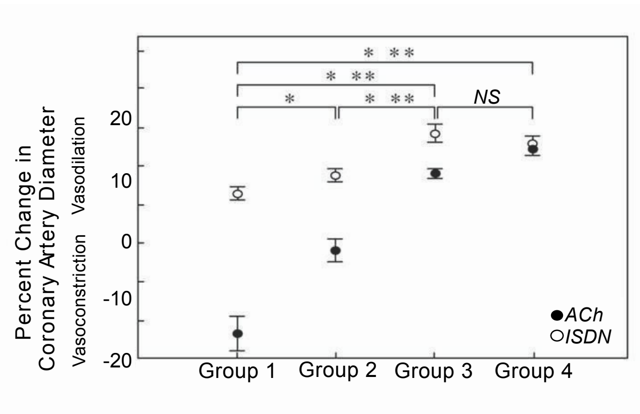

Figure 29: Response to acetylcholine (ACh) and isosorbide dinitrate (ISDN) in patients > 10 years after acute Kawasaki syndrome. Aneurysms were present in Groups 1 (≥4 mm) and 2 (< 4mm) during the acute illness but had completely resolved at the time of testing. Group 3 did not have aneurysms during the acute illness and Group 4 were controls with CHD but no history of Kawasaki disease. In both groups with healed aneurysms the endothelium-dependent response to acetylcholine is constriction indicating severe endothelial dysfunction. Also dilation in response to ISDN is less than in controls. Error bars = SEM. *p < 0.05 (ACh);***p < 0.05 (ISDN)*. (Modified from Iemura et al. [93] with permission).

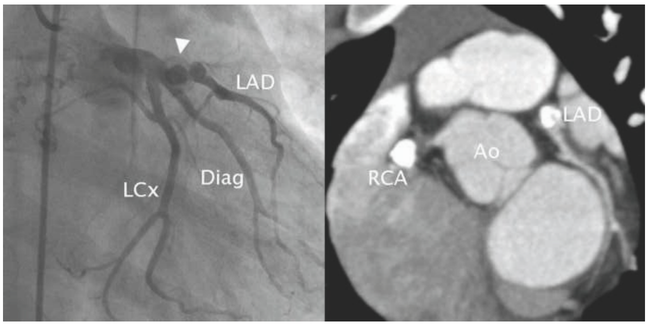

Figure 30: A - Coronary angiogram in a patient late after Kawasaki disease showing a calcified aneurysm (arrow head) of the proximal LAD.
B - CT angiogram in a patient after Kawasaki disease. There is heavy calcification of both the RCA and LAD

	Recommended Follow-up	Coronary imaging
No CA abnormality during acute illness	Every several years	No
Asymptomatic with persistent aneurysm(s)	Semiannual	Every several years
Symptoms of ischemia	Quarterly or more	As indicated

Recommended follow-up of adults with a history of Kawasaki disease during childhood [102].

Table 1: Follow-up of Kawasaki adult patients

Interventional procedures, especially at the base of the heart, risk injuring unusually placed coronary arteries so that coronary artery anatomy must be delineated thoroughly prior to the procedure.

Kawasaki disease is now known to be a cause of premature coronary heart disease but its prevalence and clinical course in young adults are poorly understood. Careful follow-up of these patients is important for their clinical care and is essential to further the understanding of this disease.

Acknowledgement

We are grateful to Emily Harris for her contribution to this article and Anne Marie Valente is currently NIH funded (NHLBI 1RC4HL104831-01).

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This article was originally published in a special issue, **Congenital Heart Disease-Recent Discoveries and Innovations** handled by Editor(s). Dr. Georg Hansmann, Children's Hospital Boston, USA; Dr. Matthias Sigler, Georg-August University Goettingen, Germany