Origins of Systemic to Pulmonary Collateral Arteries and their Relative Frequencies in Patients with Pulmonary Artery Atresia or Stenosis as determined using Multidetector Computed Tomography Angiography

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Thesis

Declaration

I, Mark Royden Smith, declare that this research report is my own work. The research report is being submitted for the degree of MMed (Rad Diag) at the University of Cape Town. It has not been submitted before for any degree or examination at this or any other University.

Signed by candidate

Dr Mark Royden Smith

On this the 18th day of February 2018.

Publications and presentations

This work has never been published.

It has never been presented at a congress.

Abstract-Open

INTRODUCTION:

Critical to the management of pulmonary atresia (PA) or pulmonary stenosis (PS) is accurate and comprehensive knowledge of the vascular network supplying the lungs. This vascular network can be exceedingly complex as it may include a wide variation of systemic to pulmonary collateral arteries (SPC/s).

AIM:

This study aims to guide radiologists, cardiologists and cardiothoracic surgeons in their search for SPC/s and to recommend an accurate, informative and standardised nomenclature system for SPC/s based on the relative frequency of SPC/s origins in patients with PA or PS identified using multi-detector computed tomography arteriography (MDCTA).

METHOD:

In this retrospective descriptive study a data set was created incorporating MDCTA cases performed at Red Cross War Memorial Children's Hospital, Cape Town, South Africa (RCWMCH) during the period November 2013 to November 2017. Using multiple, temporally separated readers, cases with PA or PS were identified and further analysed for systemic to pulmonary circulation collateral supply, including patent ductus arteriosus (PDA) and SPC/s with special attention given to their origins and destinations.

RESULTS:

Of 145 eligible MDCTAs, 93 demonstrated PA or PS of which 31 demonstrated systemic to pulmonary circulation collateral supply, 17 with a PDA, 19 with a single SPC/s, 5 with both a PDA and SPC/s and 14 with multiple SPC/s. The majority of SPC/s originated from the descending aorta, however, there were numerous other intra- and extrathoracic systemic arterial vessels of origin.

CONCLUSIONS:

The recommended systematic search pattern for systemic to pulmonary circulation collateral supply as determined by their relative frequencies of origin should be for a PDA first, then for SPC/s originating from the descending aorta (DA), aortic arch (AArch), left subclavian artery (LSCA) and right subclavian artery (RSCA). However, SPC/s may arise from numerous other sources and no systemic artery can be neglected.

"Systemic to pulmonary collateral artery/s" (SPC/s) is a more accurate general term than "major aortopulmonary artery/s" (MAPCA/s), as 40% of SPC/s do not originate from the aorta. The large variability in location of SPC/s makes a classification system impractical and favours descriptive characterization, the simplest form of which must include the origin and destination of each SPC/s, for example (DA to Left main pulmonary artery (LMPA)) or (AArch to right main pulmonary artery (RMPA)).

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Mr William Msemburi, biostatistician at the University of Cape Town, South Africa (Biostatistician).

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1. Rationale

Critical to the management of pulmonary atresia (PA) “absence or closure of a natural passage of the body” (Merriam-Webster, 1986) and variable degrees of pulmonary stenosis (PS) “a narrowing or constriction of the diameter of a bodily passage or orifice” (Merriam-Webster, 1986) is accurate and comprehensive knowledge of the prevailing pulmonary vasculature, including aberrations of the normal anatomical supply and collateral vascular pathways. This vascular network can be exceedingly complex as it may include a wide variation of systemic to pulmonary collateral arteries (SPC/s). Establishing the relative prevalence of different SPC/s origins will aid in developing a systematic search pattern for identifying SPC/s. This is of particular value to the involved diagnostic radiologist, cardiologist and cardiothoracic surgeon when performing and interpreting multi-detector computed tomography angiography (MDCTA) and angiographic studies in the pre-operative evaluation of PA/PS. Missed SPC/s may result in a persistent left to right shunt with progression to pulmonary hypertension, cor pulmonale and cardiopulmonary failure. Patients are also at a higher risk of developing pulmonary emboli and dysrhythmias.

Knowing the relative prevalence of different systemic to pulmonary collateral artery origins may also help to develop a standardised nomenclature system facilitating the accurate conveyance of information. Currently, the commonly used term for a systemic to pulmonary collateral artery is a “major aortopulmonary collateral artery/s” (MAPCA/s). This term has likely developed as the aorta is a frequent origin for systemic to pulmonary collateral arteries. The term MAPCA/s, however, may be a misnomer when the systemic to pulmonary collateral artery derives its origin from an artery other than the aorta,

known to include paramediastinal, bronchial and intercostal arteries. Furthermore, while performing the same function as a systemic to pulmonary collateral artery, a patent ductus arteriosus (PDA) is given special regard because of its unique role during cardiogenesis and the early postnatal period.

2. Introduction – Understanding Pulmonary Atresia and Stenosis, Commonly Related Imaging Techniques and This Study in Context

2.1. Basic Embryology of the Heart, Pulmonary Trunk and Main Pulmonary Arteries

2.1.1 Heart

Blood islands develop in the visceral layer of the lateral plate mesoderm. These blood islands become the primordial cardiovascular system, of which the endocardial tubes are a component. The endocardial tubes fuse to form the primordial heart and are subsequently surrounded by a loose, space holding tissue called cardiac jelly. Myocardium grows around this cardiac jelly, which spatially allows the myocardium to develop inward and the now single lumen fused endocardial tubes to expand outward. The primordial heart differentiates in a bulbous linear manner into the sinus venosus (which receives blood from the primordial veins), primordial atrium, primordial ventricle, bulbus cordis and aortic sac (from which the 1st aortic arch is originating and the subsequent aortic arches will originate).

The sinus venosus develops into the right atrium, vena cava and coronary sinus; the primordial atrium develops into the left atrium and right and left atrial auricles; and the

primordial ventricle develops into the left ventricle. The bulbus cordis is more complicated as it includes the conus cordis and the truncus arteriosus. The proximal third of the bulbus cordis develops into the muscular right ventricle; the conus cordis develops into the smooth outflow tracts of the right and left ventricles; and the truncus arteriosus divides into the proximal ascending aorta and proximal pulmonary trunk. The aortic sac develops into the remainder of the ascending aorta, most of the aortic arch and the brachiocephalic trunk, as well as the remainder of the pulmonary trunk (Sadler & Langman, 2010); (Moorman & Christoffels, 2003).

2.1.2 Partitioning of the Conus Cordis and Truncus Arteriosus to form the Outflow Tracts, Aorta and Pulmonary Trunk

The primitive heart has a common atrioventricular canal and a common outflow tract formed by the conus cordis and the truncus arteriosus. Subsequently the atria begin to separate and the interventricular septum starts to develop in such a manner that the common atrioventricular canal and the common outflow tract straddle the interventricular septum. Two cell conglomerates known as endocardial cushions grow to separate the common atrioventricular canal into right and left atrioventricular canals, which correspond with the right and left ventricles. The endocardial cushions also go on to form the atrioventricular, aortic and pulmonary valves. The membranous portion of the interventricular septum extends downward to meet the muscular portion, known at this stage as the septum inferius.

Simultaneously to all of these changes, the common outflow tract is being divided by the growth of four staggered swellings that fuse to form a spiralling aorticopulmonary septum.

The cells of the endocardial cushions and those of the aorticopulmonary septum are from the same neural crest cell lineage. They merge to complete the separation of the right ventricle and the now anteriorly located pulmonary trunk from the left ventricle and the posteriorly located aorta. This arrangement is made possible by the spiralling configuration of the aorticopulmonary septum (Sadler & Langman, 2010); (Moorman & Christoffels, 2003).

2.1.3. Main Pulmonary Arteries

During embryological development of the cardiovascular system there are 6 sets of primitive aortic arches.

The 1st and 2nd arches regress; the 3rd arches form the left and right common and internal carotid arteries; the right 4th arch forms part of the right subclavian artery and the left 4th arch forms part of the aortic arch; the 5th arches do not exist or regress very early in development; the right 6th arch forms the right pulmonary artery and the left 6th arch forms the left pulmonary artery and ductus arteriosus/ligamentum arteriosum.

The 6th arches send branches into the developing lung buds, which enlarge to become the pulmonary arteries. As the lungs are receiving their blood supply, partitioning of the conus cordis and truncus arteriosus into the aorta and pulmonary trunk begins to occur. On the right the communication between the 6th arch and the right dorsal aorta regresses, leaving only the right pulmonary artery. On the left, however, the communication between the 6th arch and the left dorsal aorta is retained as the ductus arteriosus (Sadler & Langman, 2010); (Moorman & Christoffels, 2003).

2.1.4 Pulmonary Valve

As mentioned the cells of the endocardial cushions also go on to form the atrioventricular, aortic and pulmonary valves (Sadler & Langman, 2010); (Moorman & Christoffels, 2003). The pulmonary valve is located at the base of the pulmonary trunk and consists of three semilunar leaflets created by endocardial folds in continuity with the cardiac skeleton. (Gross & Kugel, 1931). When the pulmonary valve has conventional anatomy it functions as a one-way valve. This allows deoxygenated blood to be pumped, unobstructed, from the right ventricular chamber into the pulmonary trunk during systole (antegrade flow) and stops backflow from the pulmonary trunk into the right ventricular chamber during diastole (regurgitation) (Gross & Kugel, 1931).

2.1.5. Pulmonary Arterial Circulation Impediment and Embryology

As can be inferred from the embryology of the heart, pulmonary trunk and main pulmonary arteries, abnormalities in development of the conus cordis, truncus arteriosus, 6^{th} arch structures, aorticopulmonary septum and the pulmonary valve can result in a spectrum of native pulmonary arterial and valve abnormalities, including atresia and various degrees of stenosis. The net result of these abnormalities, regardless of which level they occur at, is impaired peripheral pulmonary arterial circulation and increasing severity of these impediments will promote the formation of SPC/s. No publication on predictable SPC/s morphology correlating to specific sites and degrees of PA/PS was identified in the literature.

The ductus arteriosus, characterised as an aortic arch to pulmonary trunk (PT) communication, functions as a right to left shunt antenatally, allowing circulating blood to bypass the foetuses lungs. If this connection remains open antenatally it is termed a

patent ductus arteriosus (PDA) and flow reversal occurs resulting in left to right shunting, thus a PDA may be considered to be a form of SPC/s.

2.2. Congenital Anomalies featuring Pulmonary Atresia or Stenosis

Close to thirty percent of major congenital anomalies are cardiovascular (van der Linde et al., 2011). Mitchell, Korones & Berendes (1971) defined congenital heart disease (CHD) as "a gross structural abnormality of the heart or intrathoracic great vessels that is actually or potentially of functional significance". Determining the incidence of congenital heart disease and its subtypes has many confounding factors extensively elaborated on by Hoffman & Kaplan (2002) but their meta-analysis paper undertakes to "estimate its true value and provide data about the incidence of specific major forms of CHD". The more frequently encountered congenital heart diseases featuring pulmonary atresia or stenosis in accordance with Hoffman & Kaplan (2002) are briefly described below.

2.2.1 Pulmonary Valve Atresia

The incidence of pulmonary valve atresia is estimated to be 123 per million live births globally (Hoffman & Kaplan, 2002). Most commonly this arises as a congenital malformation where the pulmonary valve does not develop appropriately. Characteristically there is a dense tissue membrane in its place. Thus in pulmonary valve atresia there is no luminal continuity between the right ventricular chamber and the pulmonary trunk (Tchervenkov & Roy, 2000). Postnatally acquired causes of pulmonary stenosis such as rheumatic heart disease and infective endocarditis are extremely rare (Hoffman & Kaplan, 2002). As they are acquired after the cessation of cardiogenesis, it corresponds that they do not have associated systemic to pulmonary collateral arteries.

2.2.2 Tetralogy of Fallot

The incidence of Tetralogy of Fallot (TOF) is estimated to be 421 per million live births by (Hoffman & Kaplan, 2002). As the word tetralogy infers, TOF is the combination of four abnormalities, namely pulmonary outflow tract stenosis, right ventricular hypertrophy (RVH), ventricular septal defect (VSD) and an overriding aorta. However, it is important to understand that these abnormalities are the result of a single conus arteriosus developmental anomaly, where there is deficient expansile growth of the subvalvular infundibulum. The term "monology of Stensen" was coined by Stella van Praagh in 1970 with deference to Neils Stensen, who first described the anomaly that later became known as TOF (van Praagh, 2009); (Banderker, Pretorius, & De Decker, 2015); (Walker, Rosado-de-Christenson, Martinez-Jimenez, Kunin, & Wible, 2015); (Sheikh, Kazmi, & Syed, 2014); (Frank et al., 2010).

2.2.3 Truncus Arteriosus

The incidence of truncus arteriosus is estimated to be 107 per million live births (Hoffman & Kaplan, 2002) and is characterised by the presence of a single great artery originating from the cardiac base with a concomitant ventricular septal defect. This single great artery has only one corresponding semilunar valve and the coronary, pulmonary and systemic arteries arise from it (Collett & Edwards, 1949); (Crupi, Macartney, & Anderson, 1977). Pulmonary arterial anomalies including complete absence and stenosis are commonly associated with truncus arteriosus (Butto, Lucas, & Edwards, 1986).

2.2.4 DiGeorge Syndrome

DiGeorge syndrome is a subcategory of 22q11.2 deletion syndrome, with the presence of immune compromise being the primary differentiator from the other subcategories.

Cardiovascular, facial, intellectual, immunological and endocrine abnormalities are recognised features of DiGeorge syndrome. Of the cardiovascular abnormalities, conotruncal anomalies including TOF and truncus arteriosus are the most common (Chen et al., 2016); (De Decker et al., 2016).

2.2.5 Congenital Rubella

Rubella is a well-known teratogenic virus. Infection during the first trimester may give rise to a wide variety of congenital abnormalities with the frequent inclusion of pulmonary arterial stenosis (Yazigi et al., 2017).

2.3. Pulmonary Atresia Classification and Basic Surgical Principles

According to Leonard, Derrick, O'Sullivan & Wren (2000) pulmonary atresia may broadly be divided into pulmonary atresia with intact ventricular septum (PA-IVS); pulmonary atresia with ventricular septal defect (PA-VSD); and pulmonary atresia accompanied by more complex anomalies. PA-IVS is described as having conventional atria and atrioventricular concordance and a complete interventricular septum; PA-VSD is described as having normal atria and atrioventricular concordance but an incomplete interventricular septum; and pulmonary atresia accompanied by more complicated deformities includes cases that do not comply with the first two categories such as those with tricuspid valve atresia or a double outlet right ventricle.

The management of pulmonary atresia with ventricular septal defect is principally influenced by the architecture of the pulmonary circulation and to a lesser extent the intracardiac anatomy (Tchervenkov & Roy, 2000); (Hayabuchi, Mori, Kitagawa, Inoue, & Kagami, 2007); (Fang et al., 2011).

SPC/s, as the nomenclature implies, arise from the systemic circulation and supply the lungs. SPC/s include MAPCA/s, which classically stem from the descending thoracic aorta and more rarely from the aortic arch or abdominal aorta. Infrequently SPC/s derive their origin from the subclavian, carotid or coronary arteries. Pulmonary blood flow, especially in cases of PA-VSD, may also be derived from an augmented system of bronchial arteries. Even paramediastinal and intercostal arteries are known to occasionally contribute to the pulmonary circulation (Maeda et al., 2006). Consequently, pulmonary blood supply in cases of pulmonary atresia may be exceedingly complex and is further complicated by the natural progression of the disorder, as these vessels routinely develop pulmonary hypertension or stenose, resulting in pulmonary hypoperfusion and incapacitating hypoxaemia (Brown, Eyskens, Mertens, Dumoulin, & Gewillig, 1998). There is a theory that SPC/s are bronchial arteries that would normally regress but have instead dilated to supplement or provide pulmonary blood flow. This is supported by the morphological similarities between SPC/s and bronchial arteries and the lack of normal native bronchial arteries in patients with SPC/s (Norgaard et al., 2006); (Walker et al., 2015). It is postulated that the cellular programming for primitive bronchial arteries to involute is impaired by the altered pulmonary haemodynamic requirement and hence these vessels persist as stenosed vessels of pulmonary supply. Palliative endovascular intervention in the form of balloon dilation or stenting is known to result in acceptable clinical improvement in pulmonary blood flow in cases of stenosis (Brown et al., 1998).

Tchervenkov & Roy (2000) proposed a type A, B and C classification system premised on pulmonary circulation morphology. Ostensibly the term MAPCA/s in this and the

following classification systems is used to incorporate all SPC/s and will not be altered in the interest of accurate reference.

In Type A, pulmonary blood flow is solely via native pulmonary arteries and MAPCA/s are not present.

In Type B, a combination of native pulmonary arteries and MAPCA/s exist.

In Type C, pulmonary blood flow is solely via MAPCA/s and native pulmonary arteries are not present.

A comparable classification system had already been published by Barbero-Marcial & Jatene (1990) also categorizing pulmonary circulation in the presence of pulmonary atresia with ventricular septal defect into types A, B and C, and Mace et al. (1996) reiterated and further elaborated on the Barbero-Marcial & Jatene (1990) classification.

In Type A, the central pulmonary arteries supply every bronchopulmonary segment and the primary surgical concern is whether the existing pulmonary arteries offer the potential for definitive correction. Type A is further subdivided into A1 where the pulmonary arteries range from normal to hypoplastic and A2 where the pulmonary arteries are stenotic or non-confluent.

In Type B there is a combination of branch central pulmonary arteries and MAPCA/s, blood flow to each bronchopulmonary segment being provided by one or the other. When this configuration occurs, the primary surgical undertaking is to join (“unifocalise”) the MAPCA/s to the existing pulmonary arteries, thus amalgamating the entire pulmonary circulation and promoting conventional growth with a view to subsequent definitive repair.

In Type C, only MAPCA/s provide blood flow to all of the bronchopulmonary segments, as the central pulmonary arteries are completely atretic. In this instance, the primary surgical undertaking is to join the MAPCA/s to existing lobar arteries and fashion an interposed connecting pulmonary artery and an accompanying systemic to pulmonary artery shunt, also with a view to subsequent definitive repair.

Allowing for the clear similarities between the proposed classifications, the Tchervenkov & Roy (2000) classification claims to be a simpler, more encompassing and applicable to both recent management trends, including "primary repair in type A and the single stage unifocalization ± repair in types B and C", as well as customary multistage management techniques.

Maeda et al. (2006) emphasizes that it is critical to describe all vasculature comprising the pulmonary circulation prior to operative intervention. Any available collateral arteries, including MAPCA/s, bronchial and non-bronchial collateral systemic vessels, may be utilized for surgical reconstruction (Kouchoukos & Kirklin, 2003). Furthermore, any missed MAPCA/s that should be tied off may result in a detrimental persistent "left to right" shunt.

Quantitative indices including the McGoon ratio, Pulmonary Arterial Index (PAI) and Total Neopulmonary Arterial Index (TNPAI) are frequently employed to determine the necessity for surgical intervention.

The McGoon ratio is the summation of the diameters of the left and right main pulmonary arteries just prior to their first order division divided by the diameter of the

aorta at the level of the diaphragm; the PAI is the summation of the cross-sectional areas of the left and right main pulmonary arteries just prior to their first order division divided by the body surface area; and the TNPAI is the summation of the cross-sectional areas of the left and right main pulmonary arteries just prior to their first order division as well as the cross-sectional area of SPC/s divided by the body surface area (Yin et al., 2011). These indices were proposed based on vessel parameters determined by invasive angiography (IA) and influence the necessity, type and timing of repair. However, MDCTA has effectively superseded IA to determine these indices.

While variations in utilitarian classification of pulmonary atresia and pulmonary blood supply persist, the uniform thread is that acute, on-going and definitive surgical management is dependent on accurately elucidating the prevailing pulmonary vascular anatomy.

2.4. Pulmonary Circulation Imaging Techniques

Echocardiography, magnetic resonance imaging (MRI), multidetector computed tomography angiography (MDCTA) and invasive angiography (IA) will be discussed as modalities employed in evaluation of the pulmonary circulation. It is important to consider the limited availability of some or all of these resources, both in terms of facilities and expertise.

2.4.1. Echocardiography

It has been demonstrated in infants that the morphology of central pulmonary arteries can be reliably determined using echocardiography (Smyllie, Sutherland, & Keeton, 1989); (Acherman, Smallhorn, & Freedom, 1996); (Mackie, Gauvreau, Perry, del Nido, & Geva, 2003). Operator dependence does, however, play a major role in this form of imaging and while echocardiography may hint at the presence of SPC/s, acoustic window constraints often preclude comprehensive evaluation of their course and precise morphology. The difficulties of echocardiography in older/bigger children are also well established (Rajeshkannan et al., 2010). Despite these limitations, echocardiography remains the principal modality in the initial evaluation of CHD because it is commonly available, portable, cost-effective and has no radiation burden.

The use of additional or alternative imaging modalities is thought necessary in only a minority of cases where the information that echocardiography elicits is regarded as incomplete (Banderker et al., 2015).

2.4.2. Cardiovascular Magnetic Resonance Imaging

Advances in magnetic resonance imaging (MRI) such as ECG-gated cardiovascular MRI (CMR) and contrast enhanced MRI angiography (MRA) provide exceptionally good quality images with comprehensive morphological and functional cardiac and extra-cardiac information without the dangers of ionizing radiation and iodinated contrast agents (Prasad et al., 2004); (Geva, Greil, Marshall, Landzberg, & Powell, 2002); (Boechat et al., 2005); (Banderker et al., 2015). Limited availability especially in the South Africa public

sector, expense, non-portability, lengthy sedation or anaesthesia, MRI incompatibility of anaesthetic and ICU equipment and certain metallic implants, suboptimal airway and lung depiction, gadolinium induced risk for nephrogenic systemic sclerosis (NSF) and lengthy post processing demands, present major deterrents to the use of these imaging techniques (Rajeshkannan et al., 2010); (Banderker et al., 2015).

2.4.3. Multidetector Computed Tomography Angiography vs. Invasive Angiography

Invasive angiography, traditionally recognised as the gold standard for the preoperative assessment of pulmonary circulation morphology (Maeda et al., 2006); (Hayabuchi et al., 2007), has, over the past two and a half decades, largely been superseded by the increasing value of computed tomography angiography as a suitable means of mapping vascular anatomy.

Rubin, Armerding, Dake & Napel (2000) reported that CTA had become a significant method for assessing vascular morphology, having even better diagnostic capability than IA in certain instances, as well as being more cost effective. This opinion was reiterated by Lawler & Fishman (2001) Siegel (2003) and Remy-Jardin (2004).

Griel et al. (2006) found that there was a high inter-observer correlation when specifically comparing MDCTA to traditional angiography for the visualization of MAPCA/s and their morphology, concluding that MDCTA can be employed as an accurate “alternative to diagnostic cardiac catheterization and selective angiography.”

Hayabuchi et al. (2007) concluded similarly in a study specifically evaluating the size and morphology of the pulmonary arteries, and Hayabuchi et al. (2010) also demonstrated strong correlation between MDCTA and IA.

The manipulation of volumetric data sets obtained by MDCTA into multiplanar and three-dimensional reconstructions allows for vascular anatomy to be evaluated from any direction and facilitates quantification not achievable by projection methods like IA (Rubin, Dake, Napel, McDonnell, & Jeffrey, 1993); (Rubin, Paik, Johnston, & Napel, 1998). Lawler and Fishman (2001) established along similar lines that MDCTA could differentiate vessels overlying one another (especially the aorta), which is difficult on projection imaging. Other advantages of MDCTA over IA include being less invasive (IA may be entirely precluded due to a patient's critically ill condition) and more cost effective (Rubin, Armerding, et al., 2000), as well as having the ability to demonstrate extracardiac and nonvascular thoracic pathology (Katz, Jorgensen, & Rubin, 1999). Maeda et al. (2006) added that information on the spatial relations of vessels supplying non-vascular pathology would be detailed by MDCTA. Maeda et al. (2006) also purported that MDCTA detailed all vasculature within the obtainable spatial resolution and scanned volume within a single acquisition, whereas multiple selective catheterizations are necessary in IA to describe different vessels. With regard to comparative radiation exposure, Chandrashekhar, Sodhi, Saxena, Rohit & Khandelwal (2012) reported doses when using MDCTA that were considerably less than doses described in cardiac catheterization angiography.

While both IA and MDCTA allow for functional assessment of flow, IA also allows for measurement of intravascular pressures, important in the presence of SPC/s as they can cause pulmonary hypertension. Furthermore, MDCTA functional assessment comes at the expense of the dose penalty imposed by ECG gating.

A further advantage of IA is that direct conversion to endovascular intervention is possible if needed (Maeda et al., 2006); (Hayabuchi et al., 2007). Remy-Jardin et al. (2004) and Hayabuchi et al. (2007) do, however, demonstrate that MDCTA studies done prior to endovascular procedures, aid in the ease of direct selective catheterization as well as shortening theatre time and iatrogenic complications.

2.4.4. Evolution of Multi Detector Computed Tomography and the Relevance of Improved Capabilities

Rubin et al. (1999) demonstrated that MDCT scanners are more efficient than single detector computed tomography (SDCT) scanners in terms of acquisition speed and longitudinal spatial resolution when performing computed tomography angiography (CTA).

Rubin et al. (2000) (Rubin, Shiau, et al., 2000) specifically compared 4-MDCT to SDCT and concluded that 4-MDCT presented considerable advantages not only in terms of acquisition speed and longitudinal spatial resolution but also in markedly reducing the volume of contrast material necessary for adequate imaging quality.

Maeda et al. (2006) compared the 16-MDCT to 4-MDCT with particular interest in

assessment of bronchial systemic collateral arteries. The bronchial systemic collateral arteries were thought to be inadequately depicted by 4-MDCT as their average diameter is 1,5 mm (Pump, 1972), rendering 2 mm collimation insufficient. 16-MDCT augmented the previously discussed benefits of MDCT, allowing a greater area to be scanned with narrower 1 mm collimation over a briefer period of time. It was found that MAPCA/s, bronchial and non-bronchial systemic collateral arteries were consistently and accurately depicted in terms of their 'numbers and sites of origin, their varying diameters, their courses, and the areas of the lungs they supply' (Maeda et al., 2006).

Greil et al. (2006), Hayabuchi et al. (2007) and Hyabuchi et al. (2010) using 16-MDCT in their studies, both demonstrated strong correlation between MDCT and IA findings.

Leber et al. (2006) stated that the advent of 64-MDCT would inevitably improve imaging precision and that MDCTA would further supersede IA as the vascular imaging method of choice.

A study by Rajeshkannan et al. (2010) using 64-MDCT concluded that MDCTA and its data post processing capabilities such as multiplanar and 3D reconstruction are critical to the diagnosis and management planning of PA-VSD, increasingly replacing IA.

Yin et al. (2011) demonstrated that dual source computed tomography (DSCT) was better at identifying and describing MAPCAs and native pulmonary arteries than IA. This was thought to be largely attributable to the ability of multiplanar and 3D reconstruction to eliminate the superimposition of vessels experienced with IA. It was also formally

reported by Yin et al. (2011) that DSCT quantitative measurements strongly correlated with IA, allowing for accurate calculation of the McGoon ratio, PAI and TNPAI, which, as discussed, play a critical role in surgical decision-making.

2.5. Our Study in Context

In our study we used 64-MDCTA to evaluate the cardiovascular system with specific reference to PA and SPC/s.

Accurate imaging is critical to the management of pulmonary atresia/stenosis and MDCTA with 16 rows and above is comparable to the conventionally accepted gold standard of IA, both in terms of demonstrating the pulmonary arterial morphology and quantitative functional analyses. Furthermore, MDCTA is emerging as the imaging modality of choice in when employed in isolation or in combination with other modalities due to its many additional advantages, such as having less exposure to ionizing radiation, being less invasive, less time consuming, more cost effective and depicting potentially influential nonvascular thoracic pathology. In addition, MDCTA has the major benefits of multiplanar reconstruction and three-dimensional reconstruction that further aids in ease of information conveyance to the involved clinicians and surgeons.

Several studies discuss SPC/s in patients with PA/PS but little emphasis is placed on their relative frequencies and standardised nomenclature. Knowing the relative frequencies of specific SPC/s will help to direct the investigating radiologists, cardiologists and cardiothoracic surgeons in a systematic search for these vessels.

Identifying the various sites of origin other than from the aorta will support using the term “systemic to pulmonary collateral artery/s” (SPC/s) rather than “major aortopulmonary collateral artery” (MAPCA/s) as the broader term, with the term MAPCA/s being reserved for use as a specific subdivision of SPC/s. Knowing possible sites of non-aortic origin SPC/s and their frequency may give insight into further suitable subdivisions and help to develop an accurate, informative and standardised nomenclature system.

3. Aims

This study aims to guide radiologists, cardiologists and cardiothoracic surgeons in their search for systemic to pulmonary collateral arteries and to recommend an accurate, informative and standardised nomenclature system for systemic to pulmonary collateral arteries by establishing the relative frequencies of origin of systemic to pulmonary collateral arteries in patients with pulmonary atresia/stenosis using multidetector computed tomography angiography.

4. Objectives

1. To create a sample group of patients from the cohort of thoracic cardiovascular cases scanned using multidetector computed tomography angiography at Red Cross War Memorial Children’s Hospital between November 2013 and November 2017 that were found to have pulmonary atresia/stenosis with a patent ductus arteriosus and/or systemic to pulmonary collateral arteries

2. To identify the various origins of systemic to pulmonary collateral arteries within the sample group, using multidetector computed tomography angiography.

3. To evaluate the relative frequencies of the identified systemic to pulmonary collateral artery origins within the sample group.

5. Study Procedure

5.1. Research Paradigm

In conjunction with the University of Cape Town biostatistician, William Msemburi, the research paradigm was determined to be a retrospective descriptive study.

5.2. Sample

The sample group for this study was selected from patients who had undergone thoracic cardiovascular MDCTA at Red Cross War Memorial Children's Hospital, Cape Town, South Africa (RCWMCH) during the period November 2013 to November 2017. RCWMCH is the largest dedicated paediatric hospital in Southern Africa with 300 beds and accommodating an estimated 260 000 patient visits annually. It is a government run public service hospital affiliated to both the University of Cape Town and the University of Stellenbosch providing a near full spectrum of paediatric health care services and training at secondary, tertiary and quaternary levels. RCWMCH is a referral centre not only for South Africa but also for the entire sub-continent.

5.2.1. Inclusion criteria

All patients where the thoracic cardiovascular MDCTAs demonstrated PA/PS with a PDA and/or SPC/s were included in the study. Whilst the admissions age range of RCWMH is birth to 13 years, the age range included patients outside of the institutional age limit by special managerial consent.

5.2.2. Exclusion criteria

All patients where the SPC/s origin could not be determined on both first and second readings of the thoracic cardiovascular MDCTAs were excluded from the study.

5.3. Materials and Methods

Despite the retrospective nature of this study, the MDCTA acquisition technique was standardised over the period of investigation.

5.3.1. Hardware and Software

5.3.1.1. Multi-detector Computed Tomography Scanner

Philips Brilliance CT 64 slice: NCTB422; software version 2.4.5 – configurations as listed in Appendix 1.

5.3.1.2. Multi-detector Computed Tomography Scanner Workspace

Philips Workspace: NCTA440; software version 4.0.0 – configurations as listed in Appendix 2.

5.3.1.3. Injection System for Computed Tomography Investigations

Bayer Medran Stellant CT Injection System: SCT 212 – system and mechanical specifications as listed in Appendix 3.

5.3.1.4. Reporting Station

Hardware: Two diagnostic monitors; tower; navigation monitor.

Software: Xiris booking platform; ISITE viewing platform; XRE2 reporting platform.

System and mechanical specifications as listed in Appendix 4.

5.3.2. Standard Multi-detector Computed Tomography Angiography Acquisition Protocols at Red Cross War Memorial Children's Hospital

5.3.2.1. Non-ECG-Synchronised Cardiac and Chest MDCTA RCWMCH Protocol

Personnel appropriately skilled in paediatric sedation or anaesthesia and in the management of cardiac emergencies were present during the time of imaging acquisition. Iodine allergy was excluded. A large bore intra-venous (IV) cannula was sited in the antecubital fossa contralateral to the aortic arch. A 20 -22 gauge IV cannula was deemed to be acceptable for the procedure with a preference for a 20 gauge IV cannula in patients older than three years or where ECG-synchronised MDCTA was performed. Non-ionic iodinated contrast with a volume of 2ml/kg bodyweight was administered at a rate of 2ml/second using a CT specific automated injecting system. A bolus tracking technique was used with the scan trigger set at 150 Hounsfield unit (HU) using a region of interest (ROI) in the descending thoracic aorta at the level of the carina. For the non-ECG-synchronised cardiac protocol a 10-15 ml chasing bolus of 50% dilution contrast-saline solution was administered (Banderker et al., 2015).

5.3.2.2. Utility of Electrocardiogram-Synchronised Cardiac Multidetector Computed Tomography Red Cross War Memorial Hospital Protocol

As a rule studies were performed without electrocardiogram (ECG) gating due to the requirement of pharmacological heart rate manipulation in often critically ill patients, the dose penalty incurred and technical difficulties experienced when using ECG-synchronised MDCTA. Only retrospective ECG-gating is available at RCWMCH whilst the more expensive but radiation-sparing prospective gating software is as yet not available. ECG-gated MDCTA is only utilized in specific indications where coronary artery anomalies are suspected, based on echocardiographic findings. For example, a large conus branch of the right coronary artery overlying the right ventricular outflow tract is at risk of being transected during augmentation surgery of the outflow tract and must be confirmed prior to surgical intervention.

5.3.3. Case Creation

Patients requiring cardiac MDCTA were scheduled on the RCWMCH booking platform (XIRIS).

A 64-MDCT scanner (Philips Brilliance) was used in accordance with either the standard RCWMCH cardiac MDCTA protocol or using the less frequently employed retrospective ECG-synchronised MDCTA protocol.

Patient details and history, was transferred from the booking platform to the reporting platform (XRE2) in each case. The images were linked to each case and transferred to the viewing platform (Philips ISITE).

5.3.4 Interpretation and Reporting

The images were interpreted by a radiology registrar and a specialist radiologist on the viewing platform (Philips ISITE) using the source images, maximum intensity projection (MIP), slice thickness manipulation, multiplanar reconstruction and three-dimensional reconstruction. A provisional report was then generated on the reporting platform (XRE2). This was regarded as the first reading. A further reading prior to the issuing of a final report was performed with the involved cardiologists and cardiothoracic surgeons in attendance.

5.4. Data Collection, Analysis and Statistics

Detailed consultation with the University of Cape Town biostatistician, William Msemburi, determined the research paradigm to be a retrospective descriptive study. The statistical analysis appropriate to the objectives of this study will be proportions and percentages.

An Excel spreadsheet of all cardiac CTA cases done at RCWMCH from November 2013 to November 2017 was created by the principle investigator. This was done by applying the filters for data selection of 'CTA, cardiac and CTA' to the RCWMCH Picture, Archiving and Communication system (PACS) database for the time period November 2013 to November 2017. These cases were anonymised by allocating a randomized number code to each. A second reading of these cases was done by a radiology registrar and a specialist radiologist and correlated with the findings of the first reading. Where there was discordance between the first and second readings, the second reading was regarded as definitive as it was done by the most experienced RCWMCH paediatric radiologist in cardiovascular imaging. Additional information, the presence of PA/PS, the presence of a

PDA and/or SPC/s and the artery of origin of each SPC/s was added to each case and recorded on the Excel spreadsheet (Appendix 5).

An Excel spreadsheet was created for the totals of the number of cases requiring cardiac MDCTA; the number of cases with and without PA/PS; the number of cases determined to have PA/PS with and without collateral supply, the number of cases with a PDA and/or SPC/s; the number of cases with a PDA only; the number of cases with SPC/s only; the number of cases with both a PDA and SPC/s; the number of cases with a single SPC/s, and the number of cases with multiple SPC/s. (Appendix 6).

An Excel spreadsheet was created of the numbers of certain congenital heart diseases (CHD) and related additional information, their percentage of the total MDCTA/s performed; their percentage of the total cases with pulmonary atresia/stenosis; the number of that CHD with collateral supply and percentage of total cases with collateral supply; the number of that CHD with a PDA, percentage of total cases with a PDA and percentage of that CHD with collateral supply; the number of that CHD with SPC/s, percentage of total cases with SPC/s and percentage of that CHD with collateral supply; the number of that CHD with a PDA and SPC/s, percentage of total cases with a PDA and SPC/s and percentage of that CHD with collateral supply. (Appendix 7).

An Excel spreadsheet was created of the named arteries of SPC/s origin, the total number of cases with SPC/s arising from that named artery of origin; the total number of SPC/s arising from that named artery of origin; the percentage of the total number of SPC/s; number of cases with multiple SPC/s originating from the same named artery of origin; and the percentage of that named artery of origin with multiple SPC/s. (Appendix 8)

Using Excel, these spreadsheets were further represented as tables and/or graphs to facilitate ease of understanding.

5.5. Reliability and validity

Steps taken to establish reliability include multidisciplinary, multiple observer readings performed on separate occasions of each MDCTA ensuring interobserver and temporal agreement on the origin of each SPC/s.

Validity was established by ensuring that each vessel determined to be a SPC/s fulfilled specific defining criteria - SPC/s must originate from a systemic artery and supply pulmonary tissue with the exclusion of conventional bronchial arteries.

6. Departmental Research and Ethics

6.1. Departmental Research Committee Approval

Approval was obtained from the Department of Radiation Medicine, Faculty of Health Sciences, University of Cape Town and the Department of Paediatrics and Child Health, Faculty of Health Sciences, University of Cape Town.

6.2. Ethics Approval

Ethics approval was obtained from the Human Research Ethics Committee, Faculty of Health Sciences, University of Cape Town, HREC REF: 855/2017.

6.3. Consent forms

Consent is null and void as this is a retrospective observational study and has no potential to influence the management and outcomes of the sample group involved. The patients' cases were also randomised and anonomised.

6.4. Data safety

Data was stored on a private password protected laptop. Access was restricted to the primary investigator and involved supervisors. Furthermore the patients' cases were anonomised by allocating a randomised number code to each case. Access to the key was again restricted to the primary investigator and involved supervisors.

7. Results

7.1. Note on PDA Subcategory

Please note that PDA, while included in the dissertation because it is a systemic to pulmonary arterial connection, is given it's own subcategory designation differentiating it from other SPC/s.

7.2. Tables, Figures and Written Results

Table 1. Cardiac CTA Inclusion Cases

Case	Additional Information	Pulmonary Atresia/Stenosis (Yes or No)	Patent Ductus Arteriosus (Yes or No)	Systemic to Pulmonary Collateral Artery (Yes or No)
1		No	No	No
2	TOF	Yes	No	No
3	PA	Yes	No	No
4	TOF	Yes	No	No
5	TOF	Yes	No	No
6	TOF	Yes	No	No
7		No	No	No
8	TOF	Yes	No	No
9	TOF	Yes	No	No
10	PA and VSD	Yes	No	Yes: Single: 1 from AArch with a branch to the RMPA and a branch to the RLL
11	TOF	Yes	No	No
12		No	No	No
13	PA and AVSD	Yes	No	No
14	Interrupted Aortic Arch	No	No	No
15	Tricuspid atresia	Yes	No	No
16		No	No	No
17	Di George	Yes	Yes to LMPA	Yes: Multiple: 1 from LSCA to RML-PA; 1 from RSCA to RUL-PA; 1 from AArch to LMPA

18	TOF	Yes	Yes	No
19	Situs Inversus with DORV	No	No	No
20		No	No	No
21	VACTERL; agenesis of the R lung, RPA, RPVs and R MB	Yes	No	No
22	PA and VSD	Yes	No	No
23		No	No	No
24	TOF	Yes	No	No
25	TOF	Yes	No	No
26	No	No	No	No
27	PA and VSD	Yes	No	No
28	TOF	Yes	No	No
29	TOF	Yes	No	No
30	Truncus Arteriosus	No	No	No
31	TOF	Yes	Yes to LMPA	No
32		No	No	No
33		No	No	No
34	Aortic Coarctation	No	No	No
35	Dextrocardia with Right Isomerism	Yes	Yes to RMPA (Right sided AArch)	No
36	PA and VSD	Yes	No	Yes: Multiple: 3 from DA forming a plexus supplying the RLL and LLL
37		No	No	No
38	TOF	Yes	Yes to LMPA	Yes: Multiple: 1 from Right Vertebral Artery to RUL; 1 from DA to posterior and medial basal segments of the RLL
39		No	No	No
40	TOF	Yes	No	Yes: Multiple: 1 from Arch to LMPA; 1 from DA to RMPA
41	TOF	Yes	No	No
42	TOF	Yes	No	No
43		No	No	No
44	TOF	Yes	No	No
45	PA and VSD	Yes	No	Yes: Multiple: 1 from LSCA to LMPA; 1 from DA to RUL; 1 DA to RML
46	Absent Pulmonary Valve Syndrome	Yes	No	Yes: Multiple: 1 from DA to RUL; 1 from DA to RML and RLL
47	TOF	Yes	No	No
48	TOF	Yes	No	No
49		No	No	No
50	TOF	Yes	No	No
51		No	No	No
52	Truncus Arteriosus	Yes	No	No

53	Multiple Abnormalities	Yes	Yes to LMPA	Yes: Single: 1 from Infradiaphragmatic to Right Lung
54	Situs Inversus Totalis	No	No	No
55	Congenital Rubella	Yes	Yes to LMPA	No
56		No	No	No
57	Aortic Coarctation	No	No	No
58	TOF	Yes	No	No
59	Truncus Arteriosus	Yes	No	No
60		No	No	No
61	TOF	Yes	No	Yes: Single: 1 from DA to LMPA
62	TOF	Yes	No	No
63	Truncus Arteriosus	Yes	Yes	No
64		No	No	No
65	TOF	Yes	No	No
66		No	No	No
67		No	No	No
68	TOF	Yes	No	No
69	No	No	No	No
70	TOF	Yes	No	No
71	PA and VSD	Yes	No	No
72		No	No	No
73		No	No	No
74	TOF Downs	Yes	No	No
75	TOF	Yes	No	No
76		No	No	No
77	TOF	Yes	No	No
78		No	No	No
79	Truncus Arteriosus	Yes	Yes to LMPA	No
80		Yes	No	No
81	Truncus Arteriosus	No	No	No
82	TOF	Yes	Yes to LMPA	Yes: Multiple: 2 From DA to RMPA
83	No	No	No	No
84	TOF	Yes	Yes to LMPA	No
85	TOF	Yes	No	Yes: Single: 1 from Left Brachiocephalic/LSCA to LMPA
86	TOF	Yes	No	No
87	DORV	Yes	No	No
88	No	No	No	No
89	Congenital Rubella	Yes	Yes to LMPA	No
90	Multiple Abnormalities	Yes	No	Yes: Multiple: 1 from RSCA to RULPA; 1 from LSCA to LMPA
91	TOF	Yes	No	No
92		No	No	No
93	TOF	Yes	Yes to LMPA	No
94		Yes	No	No

95	TOF	Yes	No	No
96	TOF	Yes	Yes to LMPA	Yes: Multiple: 2 From DA to RMPA
97		No	No	No
98	Truncus Arteriosus	Yes	No	No
99	TOF	Yes	Yes to LMPA	No
100	PA	Yes	No	No
101		No	No	No
102		Yes	No	No
103	TOF	Yes	No	No
104	TOF	Yes	No	Yes: Single: 1 from RSCA to Right Lung
105		No	No	No
106	Truncus Arteriosus	Yes	No	No
107	LPA stenosis	Yes	No	No
108		No	No	No
109		No	No	No
110		No	No	No
111		No	No	No
112	TOF	Yes	No	No
113	TOF	Yes	No	No
114	TOF	Yes	Yes to LMPA	No
115	TOF	Yes	No	No
116		No	No	No
117		No	No	No
118	TOF	Yes	No	No
119	TOF	Yes	No	No
120	TOF	Yes	No	Yes: Multiple: 1 from RSCA to RUL-PA; 1 from LSCA to LMPA
121	TOF	Yes	No	Yes: Multiple: 1 from Left Thyrocervical Trunk to LMPA; 1 from AArch to LMPA; 1 from Infradiaphragmatic arterial system (?Coeliac Trunk, Left Gastric or direct Aortic) to LMPA
123		No	No	No
124		No	No	No
125	TOF	Yes	No	Yes: Multiple: 1 from LSCA; 1 from AArch; 1 from Left 6th Intercostal Artery - forming an arterial plexus supplying the Left Lung
126		No	No	No
127	TOF	Yes	No	No
128	TOF	Yes	No	Yes: Multiple: 2 from AArch to plexus; 1 from Right Bronchial Artery to plexus; 1 from Left Inferior Bronchial Artery to Plexus - to Left Lung
129	PA and VSD	Yes	Yes to LMPA	No

130	TOF	Yes	No	No
131	TOF	Yes	No	No
132	TOF	Yes	No	No
133	TOF	Yes	No	No
134	TOF	Yes	No	No
135		No	No	No
136		No	No	No
137	PA and AVSD	Yes	No	No
138	TOF	Yes	No	No
139	PA and VSD	Yes	No	Yes: Multiple: 3 from DA - 1 to Left Interlobar Artery; 1 to LUL apicoposterior segment; 1 to LLL superior segment
140	TOF Downs	Yes	No	No
141	TOF	Yes	No	No
142	TOF	Yes	No	No
143		No	No	No
144		No	No	No
145		No	No	No

TOF (tetralogy of Fallot); PA + VSD (pulmonary atresia and ventricular septal defect); LMPA (left main pulmonary artery); RMPA (right main pulmonary artery); RUL-PA (right upper lobe pulmonary artery); RML-PA (right middle lobe pulmonary artery); AArch (aortic arch); DA (descending aorta); LSCA (left subclavian artery); RSCA (right subclavian artery); LLL (Left lower lobe); RUL (right upper lobe); RML (right middle lobe); RLL (right lower lobe)

Table 2. Totals and Percentages

	No. of Cases	% of total MDCTAs	% of cases with PA/PS	% of cases with Collateral Supply	% of cases with PDA	% of cases with SPC/s
Total Cardiac MDCTAs	145					
Total without PA/PS	52	37%				
Total with PA/PS	93	63%				
PA/PS without Collateral Supply	62	43%	67%			
PA/PS with Collateral Supply	31	21%	33%			
PDA cases Total	17	12%	18%	55%		
SPC/s cases Total	19	13%	20%	61%		
PDA only cases	12	8%	13%	39%		
SPC/s only cases	14	10%	15%	45%		
Both SPCs and PDA cases	5	3%	5%	16%	29%	26%
Number of Cases with single SPC/s	5	3%	5%	16%		26%
Number of Cases with Multiple SPC/s	14	10%	15%	61%		74%

Figure 1. MDCTA Cases Totals and Percentages

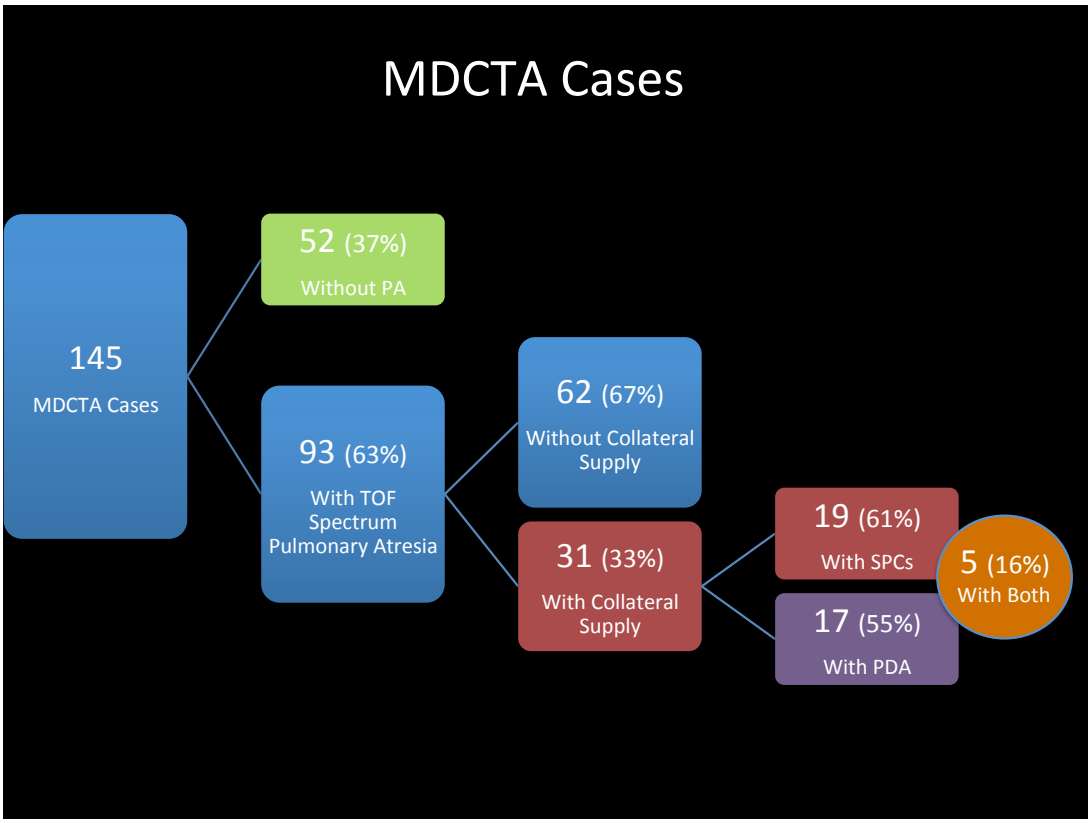
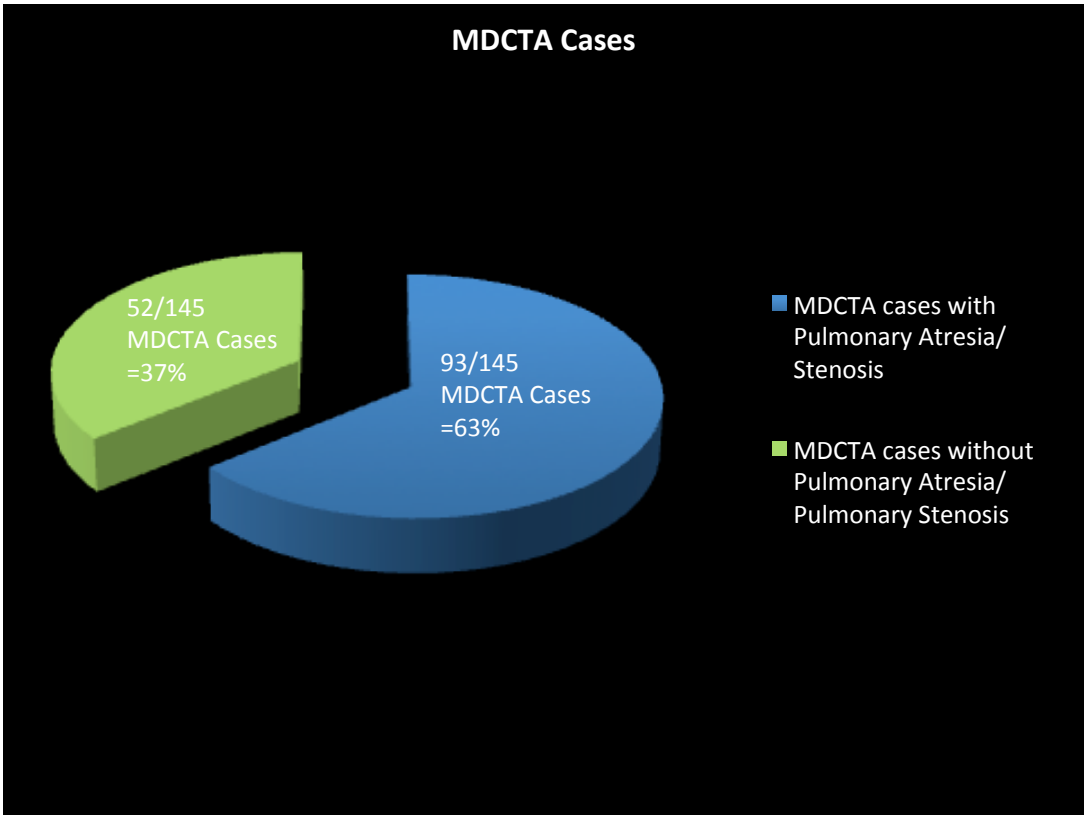


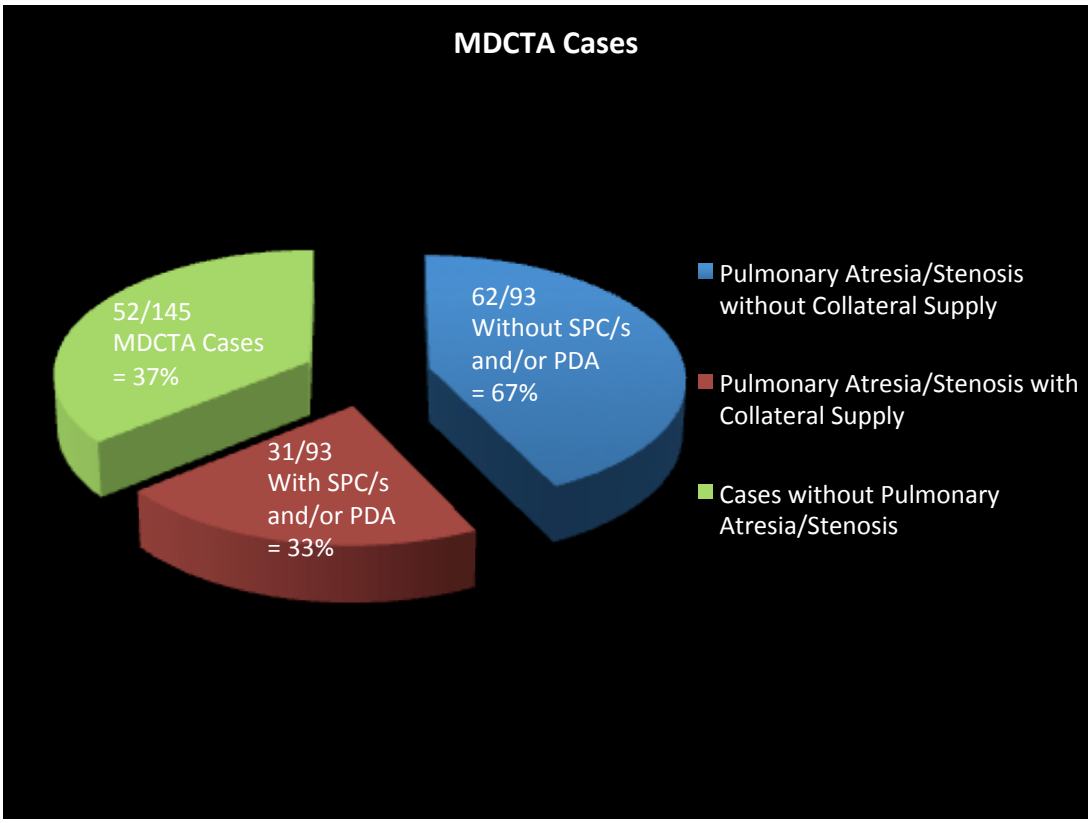
Figure 2. MDCTA Cases With and Without Pulmonary Atresia/Stenosis



Of the eligible thoracic cardiovascular multi-detector computed tomography angiography (MDCTA) cases:

93/145 (63%) were found to have pulmonary atresia (PA) or pulmonary stenosis (PS).

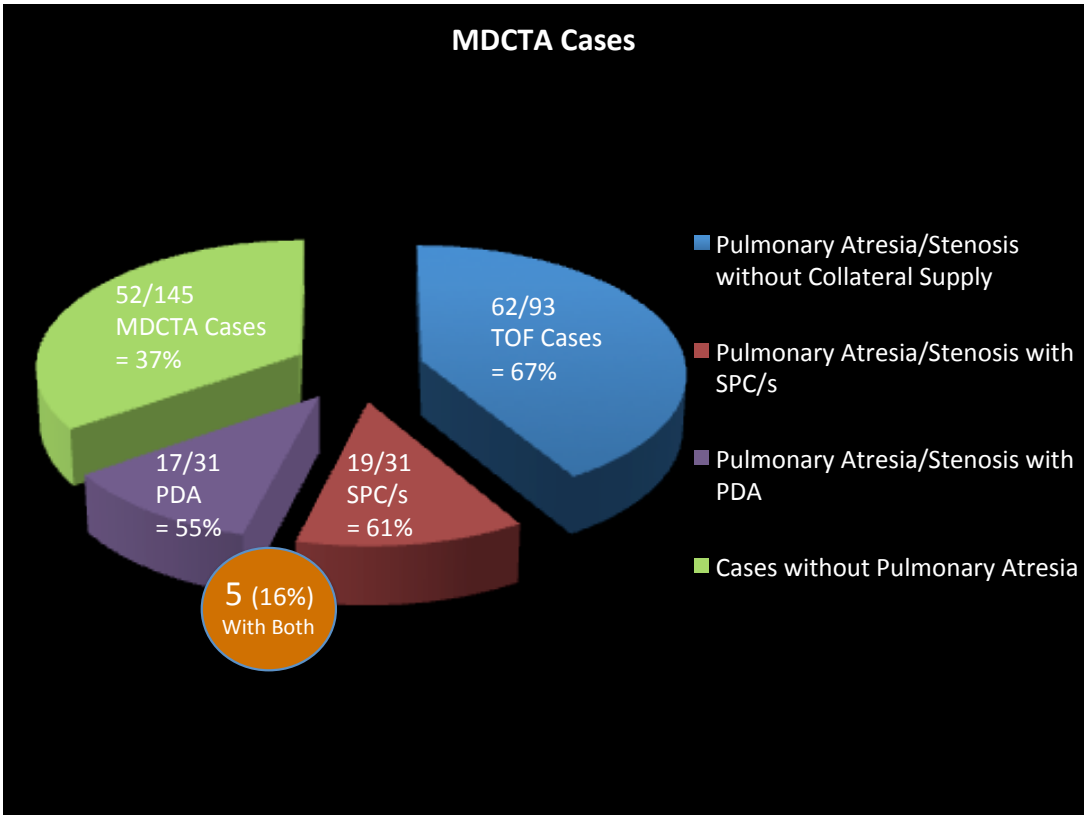
Figure 3. MDCTA Cases With and Without Collateral Supply



Of the cases with PA/PS:

31/93 (33%) were found to have collateral supply.

Figure 4. MDCTA Cases With SPC/s and/or PDA



Of the cases with collateral supply:

19/31 (61%) of cases were found to have systemic to pulmonary collateral arteries (SPC/s), equating to 19/93 (20%) of cases with PA/PS and 19/145 (13%) of the MDCTAs;

17/31 (55%) cases were found to have a PDA, equating to 17/93 (18%) of cases with PA/PS and 17/145 (12%) of the MDCTAs;

5/31 (16%) were found to have both a PDA and SPC/s, equating to 5/17 (29%) of cases with PDA, 5/19 (26%) of cases with SPC/s, 5/93 (5%) of cases with PA/PS and (5/145) 3% of the MDCTAs;

14/31 (45%) were found to have (SPC/s) alone, equating to 14/93 (15%) of cases with PA/PS and 14/145 (10%) of the MDCTAs;

12/31 (39%) of cases were found to have a patent ductus arteriosus alone, equating to 12/93 (13%) of cases with PA/PS and 12/145 (8%) of the MDCTAs.

Of the cases with SPC/s:

5/19 (26%) were found to have a single SPC, equating to 5/31 (16%) of cases with collateral supply, 5/93 (5%) of cases with PA/PS and 5/145 (3%) of the MDCTAs;

14/19 (74%) were found to have multiple SPC/s, equating to 14/31 (45%) of cases with collateral supply, 14/93 (15%) of cases with PA/PS and 14/145 (10%) of the MDCTAs.

Table 3. Additional information

Additional Information	No. of Cases	Breakdown of Named Abn. Cases	% of Total MDCTAs	% of Total Cases with PA/PS	% of Total Cases with Collateral Supply	% of Total Cases with PDA	% of Total Cases with SPC/s	% of Total Cases with both SPC/s and PDA
TOF	61		42%	66%				
		16 with Collateral Supply = 26% of TOF			52%			
		9 with PDA = 15% of TOF			29%	53%		
		10 with SPC/s = 16% of TOF			32%		53%	
		3 with both PDA and SPC/s = 5% of TOF			10%			60%
PA + VSD	10		7%	11%				
		5 with Collateral Supply = 50% of PA + VSD			16%			
		1 with PDA = 10% of PA			3%	6%		

		+ VSD						
		4 with SPC/s = 40% of PA + VSD			13%		21%	
		0 with both PDA and SPC/s			0%			0%
Truncus Arteriosus (TA)	8		6%	9%				
		2 with Collateral Supply = 25% of TA			6%			
		2 with PDA = 25 % of TA			6%	12%		
		0 with SPC/s					0%	
		0 with both PDA and SPC/s						0%
Congenital Rubella (CR)	2		1%	2%				
		2 with Collateral Supply = 100% of CR			6%			
		2 with PDA = 100% of CR			6%	12%		
		0 with SPC/s					0%	
		0 with both PDA and SPC/s						0%
Di George (DG)	1		1%	1%				
		1 with Collateral Supply = 100% of DG			3%			
		1 with PDA =			3%	6%		

		100% of DG						
		1 with SPC/s = 100% of DG			3%		5%	
		1 with both PDA and SPC/s = 100% of DG			3%			20%
Dextrocardia with Right-Sided Isomerism (DwRSI)	1		1%	1%				
		1 with Collateral Supply = 100% of DwRSI			3%			
		1 with PDA = 100% of DwRSI			3%	6%		
		0 with SPC/s					0%	
		0 with both PDA and SPC/s						0%
Absent Pulmonary Valve Syndrome (APVS)	1		1%	1%				
		1 with Collateral Supply = 100% of APVS			3%			
		0 with PDA				0%		
		1 with SPC/s = 100% of APVS			3%		5%	
		0 with both PDA and SPC/s						0%

Of the MDCTAs:

61/145 (42%) were found to have tetralogy of Fallot (TOF), equating to 61/93 (66%) of cases with PA/PS.

10/145 (7%) were found to have pulmonary atresia and ventricular septal defect (PA + VSD) equating to 10/93 (11%) of cases with PA/PS.

8/145 (6%) were found to have truncus arteriosus (TA), equating to 8/93 (9%) of cases with PA/PS.

2/145 (1%) were found to have congenital rubella (CR), equating to 2/93 (2%) of cases with PA/PS.

1/145 (1%) was found to have Di George (DG), equating to 1/93 (1%) of cases with PA/PS.

1/145 (1%) was found to have dextrocardia with right-sided isomerism (DwRSI), equating to 1/93 (1%) of cases with PA/PS.

1/195 (1%) was found to have absent pulmonary valve syndrome (APVS), equating to 1/93 (1%) of cases with PA/PS.

Of the cases with TOF:

16/61 (26%) were found to have collateral supply, equating to 16/31 (52%) of the total number of cases with collateral supply;

9/61 (15%) were found to have a PDA, equating to 9/31 (29%) of the total number of cases with collateral supply, 9/17 (53%) of the total number of cases with PDA;

10/61 (16%) were found to have SPC/s, equating to 10/31 (32%) of the total number of cases with collateral supply, 10/19 (53%) of the total number of cases with SPC/s;

3/61 (5%) were found to have both a PDA and SPC/s, equating to 3/31 (10%) of the total number of cases with collateral supply, 3/5 (60%) of cases with both PDA and SPC/s.

Of the cases with PA + VSD:

5/10 (50%) were found to have collateral supply, equating to 5/31 (16%) of the total number of cases with collateral supply;

1/10 (1%) was found to have a PDA, equating to 1/31 (3%) of the total number of cases with collateral supply, 1/17 (6%) of the total number of cases with PDA and 1/19 (10%) of cases with PA + VSD;

4/10 (40%) were found to have SPC/s, equating to 4/31 (13%) of the total number of cases with collateral supply, 4/19 (21%) of the total number of cases with SPC/s;

0/10 (0%) were found to have both a PDA and SPC/s, equating to 0/31 (0%) of the total number of cases with collateral supply and 0/5 (0%) of cases with both PDA and SPC/s.

Of the cases with TA:

2/8 (25%) were found to have collateral supply, equating to 2/31 (6%) of the total number of cases with collateral supply;

2/8 (25%) were found to have a PDA, equating to 2/31 (6%) of the total number of cases with collateral supply, 2/17 (12%) of the total number of cases with PDA;

0/8 were found to have SPC/s, equating to 0/31 (0%) of the total number of cases with collateral supply, 0/19 (0%) of the total number of cases with SPC/s;

0/8 were found to have both a PDA and SPC/s, equating to 0/31 (0%) of the total number of cases with collateral supply, 0/5 (0%) of cases with both PDA and SPC/s.

Of the cases with CR:

2/2 (100%) were found to have collateral supply, equating to 2/31 (6%) of the total number of cases with collateral supply;

2/2 (100%) were found to have a PDA, equating to 2/31 (6%) of the total number of cases with collateral supply and 2/17 (12%) of the total number of cases with PDA;

0/2 (0%) were found to have SPC/s, equating to 0/31 (0%) of the total number of cases with collateral supply, 0/19 (0%) of the total number of cases with SPC/s;

0/2 (0%) were found to have both a PDA and SPC/s, equating to 0/31 (0%) of the total number of cases with collateral supply, 0/5 (0%) of cases with both PDA and SPC/s.

Of the cases with DG:

1/1 (100%) was found to have collateral supply, equating to 1/31 (3%) of the total number of cases with collateral supply;

1/1 was found to have a PDA, equating to 1/31 (3%) of the total number of cases with collateral supply, 1/17 (6%) of the total number of cases with PDA and 1/1 (100%) of cases with DG;

1/1 was found to have SPC/s, equating to 1/31 (3%) of the total number of cases with collateral supply and 1/19 (5%) of the total number of cases with SPC/s;

1/1 (100%) was found to have both a PDA and SPC/s, equating to 1/31 (3%) of the total number of cases with collateral supply, 1/5 (20%) of cases with both PDA and SPC/s.

Of the cases with DwRSI:

1/1 (100%) was found to have collateral supply, equating to 1/31 (3%) of the total number of cases with collateral supply;

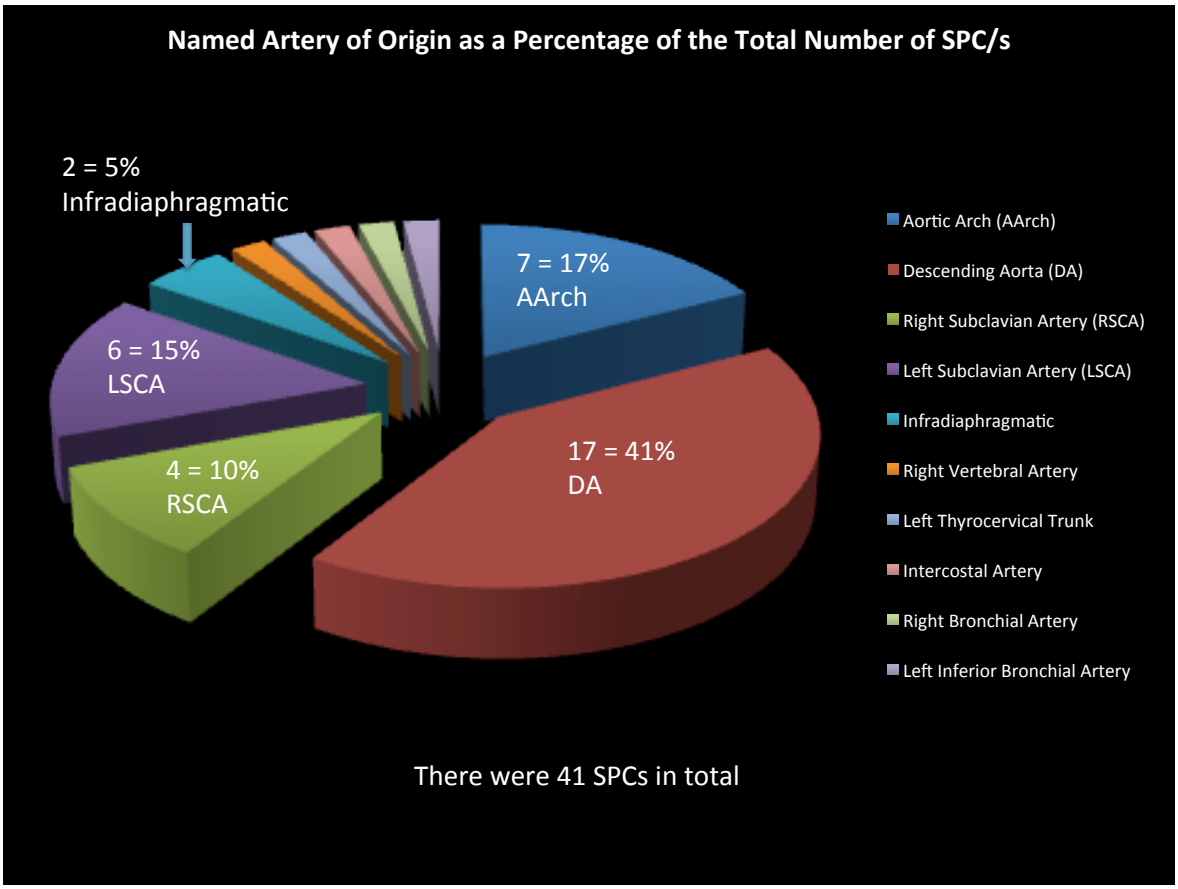
1/1 (100%) was found to have a PDA, equating to 1/31 (3%) of the total number of cases with collateral supply and 1/17 (6%) of the total number of cases with PDA;
0/1 (0%) were found to have SPC/s, equating to 0/31 (0%) of the total number of cases with collateral supply, 0/19 (0%) of the total number of cases with SPC/s;
0/1 (0%) were found to have both a PDA and SPC/s, equating to 0/31 (0%) of the total number of cases with collateral supply and (0/5) 0% of cases with both PDA and SPC/s.

Of the cases with APVS:
1/1 (100%) was found to have collateral supply, equating to 1/31 (3%) of the total number of cases with collateral supply;
0/1 (0%) were found to have a PDA, equating to 0/31 (0%) of the total number of cases with collateral supply, 0/17 (0%) of the total number of cases with;
1/1 (100%) was found to have SPC/s, equating to 1/31 (3%) of the total number of cases with collateral supply and 1/19 (5%) of the total number of cases with SPC/s;
0/1 (0%) were found to have both a PDA and SPC/s, equating to 0/31 (0%) of the total number of cases with collateral supply, 0/5 (0%) of cases with both PDA and SPC/s.

Table 4. Named Artery of Origin

Named Artery of Origin	Total number of Cases with SPC/s originating from the Named Artery of Origin	Total number of SPC/s originating from the Named Artery of Origin	% of the Total Number of SPC/s	Number of Cases with Multiple SPC/s originating from the same Named Artery of Origin	% of Named Artery of Origin with multiple SPC/s
Ascending Aorta (AA)	0	0	0%	0	0%
Aortic Arch (AArch)	6	7	17%	1	17%
Descending Aorta (DA)	9	17	41%	6	67%
Right Subclavian Artery (RSCA)	4	4	10%	0	0%
Left Subclavian Artery (LSCA)	6	6	15%	0	0%
Right Vertebral Artery (RVA)	1	1	2%	0	0%
Left Thyrocervical Trunk (LTCT)	1	1	2%	0	0%
Intercostal Artery	1	1	2%	0	0%
Right Bronchial Artery (RBA)	1	1	2%	0	0%
Left Inferior Bronchial Artery (LIBA)	1	1	2%	0	0%
Infradiaphragmatic Artery	2	2	5%	0	0%
Total Number		41		7	

Figure 5. Named Artery of Origin as a Percentage of the Total Number of SPC/s



A total of 41 SPC/s were found.

Of the cases with SPC/s:

7/41 (17%) were found to have multiple SPC/s originating from the same named artery of origin.

6/19 (32%) of cases were found to have SPC/s originating from the aortic arch (AArch), of which 1/19 (5%) of cases were found to have multiple SPC/s originating from the AArch, equating to 1/6 (17%) of cases with AArch origin SPC/s.

The total number of AArch origin SPC/s was found to be 7/41 (17%) of the total number of SPC/s.

9/19 (47%) of cases were found to have SPC/s originating from the descending aorta (DA), of which 6/19 (32%) of cases were found to have multiple SPC/s originating from the DA, equating to 6/9 (67%) of cases with DA origin SPC/s.

The total number of DA origin SPC/s was found to be 17/41 (41%) of the total number of SPC/s.

4/19 (21%) of cases were found to have SPC/s originating from the right subclavian artery (RSCA), of which 0/19 (0%) of cases were found to have multiple SPC/s originating from the RSCA, equating to 0/4 (0%) of cases with RSCA origin SPC/s.

The total number of RSCA origin SPC/s was found to be 4/41 (10%) of the total number of SPC/s.

6/19 (32%) of cases were found to have SPC/s originating from the left subclavian artery (LSCA), of which 0/19 (0%) of cases were found to have multiple SPC/s originating from the LSCA, equating to 0/6 (0%) of cases with RSCA origin SPC/s.

The total number of LSCA origin SPC/s was found to be 6/41 (15%) of the total number of SPC/s.

1/19 (5%) of case were found to have SPC/s originating from the right vertebral artery (RVA), of which 0/19 (0%) of cases were found to have multiple SPC/s originating from the RVA, equating to 0/1 (0%) of cases with RVA origin SPC/s.

The total number of RVA origin SPC/s was found to be 1/41 (2%) of the total number of SPC/s.

1/19 (5%) of cases were found to have SPC/s originating from the left thyrocervical trunk (LTCT), of which 0/19 (0%) of cases were found to have multiple SPC/s originating from the LTCT, equating to 0/1 (0%) of cases with LTCT origin SPC/s.

The total number of LTCT origin SPC/s was found to be 1/41 (2%) of the total number of SPC/s.

1/19 (5%) of cases were found to have SPC/s originating from the intercostal artery (IA), of which 0/19 (0%) of cases were found to have multiple SPC/s originating from the IA, equating to 0/1 (0%) of cases with IA origin SPC/s.

The total number of IA origin SPC/s was found to be 1/41 (2%) of the total number of SPC/s.

1/19 (5%) case was found to have SPC/s originating from the right bronchial artery (RBA), of which 0/19 (0%) of cases were found to have multiple SPC/s originating from the RBA, equating to 0/1 (0%) of cases with RBA origin SPC/s.

The total number of RBA origin SPC/s was found to be 1/41 (2%) of the total number of SPC/s.

1/19 (5%) of cases were found to have SPC/s originating from the left inferior bronchial artery (LIBA), of which 0/19 (0%) of cases were found to have multiple SPC/s originating from the LIBA, equating to 0/1 (0%) of cases with LIBA origin SPC/s.

The total number of LIBA origin SPC/s was found to be 1/41 (2%) of the total number of SPC/s.

2/19 (11%) of cases were found to have SPC/s originating from an infradiaphragmatic origin, of which 0/19 (0%) of cases were found to have multiple SPC/s originating from infradiaphragmatic origins, equating to 0/2 (0%) of cases with infradiaphragmatic origin SPC/s.

The total number of infradiaphragmatic origin SPC/s was found to be 2/41 (5%) of the total number of SPC/s.

8. Discussion

8.1. Results in context

As discussed, accurate and comprehensive knowledge of the prevailing vascular network supplying the lungs, including the native pulmonary vasculature and the presence and pattern of systemic to pulmonary collateral supply, is critical to the management of pulmonary atresia (PA) and pulmonary stenosis (PS). The timing and approach to surgical repair is dependent on this information.

In this study, 33% of the cases found to have PA/PS were also found to have systemic to pulmonary collateral supply in the form of a patent ductus arteriosus (PDA), systemic to pulmonary collateral artery/s (SPC/s) or both. Such a high prevalence of systemic to pulmonary collateral supply in PA/PS emphasises the importance of having a diligent and systematic method of search for such vessels.

The prevalence of SPC/s at 20% of cases with PA/PS, and at 61% of cases with systemic to pulmonary collateral supply, is greater than the prevalence of a PDA at 18% and 55% respectively. The relatively high rate of occurrence and known variability in origin and destination of SPC/s also emphasises the importance of having a diligent and systematic method of search.

However, if a PDA is considered to be a specific SPC/s, then the case prevalence of a PDA at 17 cases is nearly double that of any other specific SPC/s prevalence, the next being descending aorta originated SPC/s at 9 cases. In terms of systemic to pulmonary

collateral vessel prevalence, the number of PDAs is equitable to SPC/s originating from the descending aorta at 17 cases each. In other words a PDA is first amongst SPC/s.

Furthermore, in this study, 16% of cases with systemic to pulmonary collateral supply were found to have both a PDA and SPC/s and 74% of cases with SPC/s were found to have multiple SPC/s, again emphasising the importance of having a diligent and systematic method of search for such vessels.

Key to developing a systematic method of search is knowledge of which systemic arteries give origin to systemic to pulmonary collateral vessels and with what frequency.

By definition a PDA arises from the aortic arch (AArch) and communicates with the pulmonary trunk (PT) superiorly at the origin of the left main pulmonary artery (LMPA). This is not surprising given that the ductus arteriosus and LMPA share a common embryological origin from the left 6^{th} primitive aortic arch. Therefore, any persistent communication between the AArch and the PT may be regarded as a PDA. In right-sided isomerism, however, the PDA originates from the right-sided aortic arch and communicates with the PT superiorly at the origin of the right main pulmonary artery (RMPA). One such case is documented in this study. Rarely, bilateral PDAs are known to occur. A PDA may have many morphological appearances for which there have been several proposed classification systems.

The search for SPC/s is challenging due to their variability in origin and destination. In this study, the greatest number of SPC/s originated from the descending aorta (DA) at 41% of

the total number of SPC/s identified, followed by the aortic arch (AArch) at 17%, the left subclavian artery (LSCA) at 15%, the right subclavian artery (RSCA) at 10%, infradiaphragmatic arteries at 5% and the right vertebral artery, left thyrocervical trunk, an intercostal artery, right bronchial artery and left inferior bronchial artery at 2% a piece.

Of note, no SPC/s originated from the ascending aorta (AA) and the pulmonary trunk (PT) received no SPC/s (apart from PDA). Again, embryological development makes this an unsurprising result as both arise from the truncus arteriosus and not the primitive aortic arches.

8.2. Pitfalls

Variability in bronchial artery morphology is well described and the Cauldwell classification system is commonly sited. Up to 80% of bronchial arteries arise from the descending aorta at the T5-T6 level. In this study, several cases with pulmonary atresia or pulmonary stenosis were found to have dilated, ectatic bronchial arteries augmenting pulmonary blood supply. These bronchial arteries might easily be misinterpreted to be SPC/s and caution must be exercised to not label SPC/s in this region unless definite communication with the pulmonary arterial circulation is identified. It is also important to distinguish SPC/s from the artery of Adamkiewicz as ligation or “unifocalization” of this artery would likely have catastrophic neurological consequences.

Specific infradiaphragmatic vessels of SPC/s origins were not visualised due to predetermined setting of the inferior scan limit to reduce radiation burden. The accurate

depiction of the infradiaphragmatic origin SPC/s may therefore justify the dose penalty incurred by increasing the field of view.

8.3. Limitations of the current study

This study's sensitivity and specificity are dependent on the acquisition, display and interpretation of images. Whilst the hardware, software, acquisition technique and image display fall comfortably within international standards, improvements such as a more advanced, higher slice capability CT scanner, more advanced software and the use of prospective ECG-synchronised MDCTA acquisition methods to diminish cardiac motion artefact may further positively influence the quality of results.

Streak artefact generated by contrast within the subclavian vein on the side of contrast administration from upper limb cannulation may have obscured undiagnosed SPC/s. Exclusive use of foot veins for the administration of contrast would alleviate this limitation.

In addition, whilst the reading of this study's MDCTAs was done by both a diagnostic radiology consultant and a senior diagnostic radiology registrar, on two different occasions with temporal separation of at least 3 months, and routine co-interpretation of the images with the involved cardiologist was performed, involvement of further readers might positively influence the quality of results.

The data collection period spanned 4 years at RCWMCH, the largest dedicated paediatric hospital in Southern Africa, however a longer time period of collection and the inclusion of other paediatric imaging centres might increase the size of the data set and positively influence the quality of results.

8.4. Future applications

Information from this study could be utilised to aid the investigation of whether specific sites and degrees of PA/PS correlate with specific patterns of systemic to pulmonary circulation collateral supply.

9. Conclusion

In light of this study's results, any MDCTA performed that demonstrates pulmonary atresia or pulmonary stenosis should be closely evaluated for a patent ductus arteriosus (PDA) and systemic to pulmonary collateral arteries (SPC/s). The results indicate that the recommended pattern of search should be for a PDA first, then for SPC/s originating from the descending aorta (DA), aortic arch (AArch), left subclavian artery (LSCA) and right subclavian artery (RSCA). Given, in this study and published literature, that SPC/s have been found to arise from a variety of smaller vessels such as vertebral, bronchial and intercostal arteries as well as infradiaphragmatic sources and hence no systemic artery can be neglected. The frequency of infradiaphragmatic origin SPC/s may justify the dose penalty incurred by increasing the field of view.

Knowing that comprehensive knowledge of the alternative vascular network supplying the lungs is critical to the management of pulmonary atresia and pulmonary stenosis advocates the development of an accurate, informative and standardised nomenclature system for systemic to pulmonary collateral arteries. In this study, 40% of SPC/s were found to originate from arteries other than the aorta, which strongly supports using the term systemic to pulmonary collateral artery/s (SPC/s) and not major aortopulmonary collateral artery/s (MAPCA/s) as a general term. The large variability in location of SPC/s makes a classification system impractical and encourages descriptive characterization, the fundamental integrals of which are origin and destination. For example, descending aorta to left main pulmonary artery (DA to LMPA), or right subclavian artery to right upper lobe pulmonary artery (RSCA to RUL-PA), or, in slightly more complex situations, aortic arch with a branch to the right main pulmonary artery and a branch to the right lower lobe (AArch to RMPA and RLL). Whilst descriptive, this format fulfils the requirements of being accurate, informative and standardised.

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11. Appendices

Appendix 1 - see 5.3.1.1. Multi-detector Computed Tomography Scanner

PHILIPS

Brilliance CT: NCTB422

Key for system no. 10173

System Details

Date of Creation	27/10/2009 21:38:08
Created By	Carole Bucco
System Serial Number	10173
Job Number	4502719191
System Identifier	0023AE701170
Service Tag	F1CT74J
Subsidiary	South Africa
Site	The Red Cross War Memorial Children's Hospital
Software Version	2.4.5
Slices	64

Configurations

Packages		
Description	**Part Number**	**Philips P.N.**
CT Fluoroscopy Pkg - Cart/Ceiling Mount		MCU1201/MCU1191
Rate Responsive CV Toolkit	455011203161	MCU1042/NCTB870

Basic Options		
Description	**Part Number**	**Philips P.N.**
2*0.6, 4*4.5mm Slice Modes		
DVD-Archive	455011602441/455011702251	MCU2111/NCTB210
Head Centering		
MRC X-ray tube, 8.0 MHU		
Scan Tools		
ScanTools Pro		MCU0651
Split Study	455011204211	MCU1241

Options		
Description	**Part Number**	**Philips P.N.**
0.4 sec Rotation	455011201211	MCU0111
Calcium Scoring	455011202721	MCT6331/NCTA920
Cardiac Viewer(Cardiac Review)	455011205631	MCT9061/MCU1611/MCU1831
Continuous CT Ceiling/Cart		MCT5611
CT Fluoroscopy	455011204201	MCU1211
CT Reporting	455011205261	MCU1111/MCU1481/NCTA690/NCTA840
Jog Scan Option	455011204191	MCU1031
Prospective Gating	455011201511	MCT6181
Retrospective tagging	455011201051	MCT6191

Key Parameters

Key (108 bytes long)

1: DD6C 2: 762D 3: 0146 4: E371
5: 34B5 6: 37D9 7: 5817 8: 1CBA
9: 4A99 10: 48C7 11: 5885 12: AFDA
13: A294 14: 5922 15: A0F5 16: 935A
17: 2312 18: 7582 19: 6E25 20: 73D9
21: F337 22: 4777 23: 9DE4 24: 9C8D
25: 9A4F 26: 34CF 27: 2C36

Key Full String

Appendix 2 - see 5.3.1.2. Workspace

Extended Brilliance Workspace: NCTA440

Key for system no. 12743

System Details

Date of Creation	27/10/2009 21:40:16
Created By	Carole Bucco
System Serial Number	12743
Job Number	4502719191
System Identifier	0023AE83BCE8
Service Tag	5M3LB4J
Subsidiary	South Africa
Site	The Red Cross War Memorial Children's Hospital
Software Version	4.0.0

Configurations

Packages

Description	Part Number	Philips P.N.
Advanced Brain Perfusion	455011702161	NCTA520/NCTA720
CV Pro Analysis	455011702181	NCTA592

Basic Options

Description	Part Number	Philips P.N.
CD/DVD writer	455011202641	MCT5691
CT Viewer		

Options

Description	Part Number	Philips P.N.
Advanced Brain Perfusion with Summary Maps	455011602881	NCTA510
Advanced Brain Perfusion without Summary images	455011702011	TBD
AVA Stenosis	455011202261	MCT5921/MCT5941/NCTA560/NCTA740
AVA Stent Planning	455012901331	MCT9732/MCU0351/NCTA570/NCTA750
Calcium Scoring	455012901251	MCT6532/MCU1411/NCTA920/NCTA930
CCA Coronaries Analysis	455011602891	NCTA620/NCTA800
CCA Viewer	455011602901	NCTB190/NCTB200
COMPREHENSIVE CARDIAC ANALYSIS	455011702091/455011702241	NCTA850/NCTA880
CT Reporting	455011205261	MCU1111/MCU1481/NCTA690/NCTA840
Dual Monitor	455012902391/455011205311/455011205321	MCU0291/NCTC520/NCTC523/NRTE015
Functional - CT	455011702021	NCTA940

Appendix 3 - see 5.3.1.3. CT Injection System

Appendix 4 – see 5.3.1.4. Reporting Station

Diagnostic Workstation

Hardware

Diagnostic monitors : Two 3 megapixel monitors
Navigation monitor: One MDRC-1119 (1 megapixel)
Graphics card: MXTR 5250
Tower: Requirements specified below

Software

Specs for XIRIS and XRE

Product	Supported Client Operating Systems
Xiris Release 8.2.15	Windows 7
XRE Release 2.1.11	Windows 7

Specs for iSite

- **iSite Enterprise Desktop and System**
- **Requirements**
- **Minimum**
- CPU 1 Intel® Pentium® 4 processor
- RAM 2 1 GB (Windows XP)
- Operating System 3 Windows® XP Home & Professional SP3
- Internet Browser 3 Microsoft Internet Explorer 7.0
- Monitor 4 1024 x 768 resolution, 24-bit color
- **Recommended**
- CPU 1 Intel® Core™ 2 Duo processor or higher
- RAM 2 2 GB
- Operating System 3 Windows® XP Home & Professional SP3
- Internet Browser 3 Microsoft Internet Explorer 7.0
- Monitor 4 1280 x 1024 resolution, 24-bit color

- **iSite Radiology Desktop and System**
- **Requirements**
- **Minimum**
- CPU 1 Intel® Pentium® 4 processor 1.0 GHz
- RAM 2 1 GB
- Operating System 3 Windows® XP Professional SP3
- Navigation Monitor 1024 x 768 resolution, 24-bit color
- Diagnostic Monitors 5 Optional: 1, 2, or 4 diagnostic displays (2, 3, or 5 megapixels)
- **Recommended**
- CPU 1 Intel® Core™ 2 Duo processor or higher
- RAM 2 4 GB
- Operating System 3 Windows® XP Professional SP3
- Navigation Monitor 1280 x 1024 resolution, 24-bit color
- Diagnostic Monitors 5 2 or 4 diagnostic displays (2, 3, or 5 megapixels)

Specs for IntelliSpace Portal

Philips IntelliSpace Portal
Version: 4.0.3.10012

Supported operating systems:
Windows XP SP2 and above
Windows Vista
Windows 7

File Size: 76 MB

Appendix 5 – see 5.4 Data Collection

Cardiac CTA Inclusion Cases

Case	Recognisable Pattern of Congenital Heart Disease (Type or No)	Pulmonary Arterial System Atresia (Yes or No)	Patent Ductus Arteriosus (Yes or No)	Systemic to Pulmonary Collateral Artery (Origin/s or No)
1	?	?	?	?
2	?	?	?	?
3	?	?	?	?
4	?	?	?	?
5	?	?	?	?
Etc.	Etc.	Etc.	Etc.	Etc.

Appendix 6 – see 5.4 Data Collection

Totals and Percentages

	No. of Cases	% of total CTAs	% of cases with PA	% of cases with Collateral Supply	% of cases with PDA	% of cases with SPCs
Total Cardiac CTAs	?					
Total without PA	?	?%				
Total with PA	?	?%				
PA without Collateral Supply	?	?%	?%			
PA with Collateral Supply	?	?%	?%			
PDA cases Total	?	?%	?%	?%		
SPC cases Total	?	?%	?%	?%		
PDA only cases	?	?%	?%	?%		
SPCs only cases	?	?%	?%	?%		
Both SPCs and PDA cases	?	?%	?%	?%	?%	?%
Number of Cases with single SPC	?	?%	?%	?%		?%
Number of Cases with Multiple SPCs	?	?%	?%	?%		?%

Appendix 7 – see 5.4 Data Collection

Recognisable Pattern of Congenital Cardiac Disease (CHD)

Recognisable Pattern of CHD	**No. of Cases**	**Breakdown of Named Abnormality Cases**	**% of total CTAs**	**% of Total Cases with PA**	**% of Total Cases with Collateral Supply**	**% of Total Cases with PDA**	**% of total cases with SPC/s**	**% of Total Cases with both SPC/s and PDAs**
?	?		?%	?%				
		? with Collateral Supply = ? of TOF			?%			
		? with PDA = ?% of TOF			?%	?%		
		? with SPC/s = ?% of TOF			?%		?%	
		? with both PDA and SPC/s = ?% of TOF			?%			?%
?	?		?%	?%				
		? with Collateral Supply = ? of TOF			?%			
		? with PDA = ?% of TOF			?%	?%		
		? with SPC/s = ?% of TOF			?%		?%	
		? with both PDA and SPC/s = ?% of TOF			?%			?%
Etc.		Etc.	Etc.	Etc.	Etc.	Etc.	Etc.	Etc.

Appendix 8 – see 5.4 Data Collection

Named Artery of Origin

Named Artery of Origin	**Total number of Cases with SPCs originating from the Named Artery of Origin**	**Total number of SPC/s originating from the Named Artery of Origin**	**% of the Total Number of SPC/s**	**Number of Cases with Multiple SPCs originating from the same Named Artery of Origin**	**% of Named Artery of Origin with multiple SPC/s**
?	?	?	?	?	?
?	?	?	?	?	?
?	?	?	?	?	?
?	?	?	?	?	?
?	?	?	?	?	?
Etc.	Etc.	Etc.	Etc.	Etc.	Etc.
Total Number		?		?	

Appendix 9 – Departmental Research Committee Approval

UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

8. Declarations and Signatures

This application will not be processed unless all the required declarations and signatures are completed according to the Committee's Standard Operating Procedures. (see: SOP)

8.1 Head of Department or Division

My signature confirms that:

i. The researcher(s)/student(s)/supervisor(s) have the skills, training (including research ethics training), experience and time to undertake this research.
ii. There are adequate resources (e.g. equipment, space, support services) to perform this research.

Signature of Head		Date	1/12/2017
Print name	Prof. Steve Beningfield		

Note: Where the PI is also Head of Department, confirmation must be obtained from an authorised designee. PIs may not approve their own research.

8.2 Chairperson of the Departmental Research Committee (DRC)

My signature confirms that:

i. This research protocol has undergone peer review by a person(s) experienced in the field of study.
ii. This research is well-designed and scientifically sound.
iii. Where relevant, all methodological issues have been resolved to the satisfaction of the peer reviewer(s).
iv. If conducted according to the protocol, this research is expected to yield valid and useful findings.

Signature of Chairperson		Date	6/12/17
Print name	A.J. Hunter		

Note: Where the PI is also the Chairperson of the DRC, confirmation must be obtained from an authorised designee. PIs may not approve their own research.

8.3 Principal Investigator

My signature confirms that:

i. Information in this application is true and accurate.
ii. I will begin the research only after written HREC approval is obtained.
iii. I accept full responsibility for the conduct of this research and the protection of participants' rights and welfare.
iv. I will conduct the research according to all ethical, regulatory and legal requirements stipulated in the HREC's Standard Operating Procedures.
v. I will provide progress reports to the HREC as requested, including a final closing report at the end of the research.
vi. I will notify the HREC in writing if any change to the research is proposed and await approval before proceeding with the proposed change except when urgently necessary to protect participants' safety.
vii. I will notify the HREC in writing immediately if any adverse event or unanticipated problem occurs during the research.
viii. I will allow an audit of my research if requested by the HREC.
ix. I have the time, training, experience and resources to oversee this research.
x. I will endeavour to publish and disseminate the findings of the study.

Signature of Principal Investigator		Date	04/12/17
Print name	Dr. Ebrahim Banderker		

Appendix 9 – Human Research Ethics Committee Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

08 December 2017

HREC REF: 855/2017

Dr E Banderker
Radiology
Red Cross War Memorial Children's Hospital

Dear Dr Banderker

PROJECT TITLE: FREQUENCY OF ORIGINS OF SYSTEMIC TO PULMONARY COLLATERAL ARTERIES IN PATIENTS WITH PULMONARY ARTERY ASTRESIA OR STENOSIS AS DETERMINED USING MULTIDETECTOR COMPUTED TOMOGRAPHY ANGIOGRAPHY (MMED CANDIDATE - DR M SMITH)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 December 2018.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

The HREC acknowledge that the student, Dr Mark Smith will also be involved in this study.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 855/2017