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"PERSISTENT TRUNCUS ARTERIOSUS" - EMBRYOLOGICAL BASIS AND ITS CLINICAL IMPORTANCE

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ABSTRACT

The Truncus Arteriosus (TA) is a vast developmental structure which is present during fetal life and normally divides off to form two separate arteries, the Aorta and the Pulmonary artery. In Persistent Truncus Arteriosus (PTA), the Truncus Arteriosus doesn't divide, giving rise to a single, large trunk, with a correlation between the Aorta and Pulmonary artery, thereby allowing the mixture of oxygenated and deoxygenated blood in the Fetus. This article aims to discuss in the detail, the origin of this congenital heart anomaly and how it affects the population with focus on related clinical studies and possible remedies.

Introduction

As the fetal arterial system develops, it usually undergoes complex stages which transform it into the adult arterial pattern. One of these stages is the division of the Truncus Arteriosus [1]. Naturally, the embryonic heart at its developmental stage devises a means to separately regulate oxygenated blood and deoxygenated blood in the system.

This occurs when a barrier is created between the Bulbous Cordis and the Truncus Arteriosus (TA) by the Aortico-pulmonary septum, thereby apportioning the flow of blood into two separate passages. These passages which originate from the Truncus Arteriosus (the distal end of the Bulbous Cordis) are the Aortic trunk (arising from the left ventricle) and the Pulmonary trunk, (arising from the right ventricle) [4]. The cranial end of the Bulbous Cordis, known as the Conus Cordis, also joins the Truncus Arteriosus in giving rise to the Aortic trunk and the pulmonary trunk.

A Persistent Truncus Arteriosus (PTA) or Common Arterial Trunk, emerges when the primitive Truncus Arteriosus fails to partition into the Aorta and Pulmonary Artery [6], due to this failure in septation, a single arterial vessel arises from the normally formed right and left ventricles, by means of a Semilunar valve (Truncal Valve) [9], before splitting off into the Aorta and Pulmonary Artery. This single arterial trunk overlies a large skewed perimembranous ventricular septal defect [8]. The outcome of this congenital cardiac anomaly would be the mixture of oxygenated and deoxygenated blood (as a demarcation between the two trunks no longer exists) which enters into the systemic, pulmonary and coronary circulation.

PTA is known as one of the rarer congenital cardiac anomalies [5] frequently associated with interventricular septal defect (VSDs) [10] in which affected infants usually present with mild cyanosis as well as signs of heart failure such as tachypnea (abnormal rapid breathing) and excessive perspiration (abnormal sweating) [8]. Clinically on physical examination, a hyper dynamic precordium, increased pulse pressure, a single loud heart S_2sound with a large ejection systolic murmur may be detected due to increased blood flow through the truncal valve [8, 12], a high pitched diastolic mitral flow murmur which may suggest truncal valve insufficiency is distinct along the apex of the heart when pulmonary blood flow increases [8, 12]. Notwithstanding the fact that PTA occurs alongside VSDs, PTA has been found to have variants one of which is PTA with intact Ventricular Septum. Other variants of PTA are classified according to their anatomical occurrences, namely, the Collet and Edwards's classification system (being the most popular) and the Van Praaghs classification system. It can be said that the cause of PTA is idiopathic [1], nonetheless, studies have found PTA to be dominant in minority of patients with Digeorge Sequence/Syndrome, characterized by hypocalcaemia and reduced levels of T-Lymphocytes [12, 3]. Surgical repair is the most common remedy for PTA [9].

This article through an in-depth discussion of variants of Persistent Truncus Arteriosus and accompanying cardiac anomalies, their embryological basis and its clinical significance, possible causes, clinical presentations and remedies, aims to provide more understanding about this sporadic congenital cardiac anomaly.

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Incidence

The incidence of Congenital Heart Disease (CHD) differs from study to study with varied incidence rates from about 4/1000 (for the rare CHDs) to 50/1000 live births for the more common CHDs [13].Falling under the category of a rare CHD, PTA is reported to occur in about 6 to 10 per 100,000 live births, for the more common CHDs [13].Falling under the category of a rare CHD, PTA is reported to occur in about 6 to 10 per 100,000 live births, accounting for only 4% of all critical cases of CHDs in the total population with no racial predilection being apparent [14, 9].In still born births and abortuses, PTA accounts for about 5% of total CHDs. In a study conducted by Keith et al [15], PTA was cited to be < 1% of their congenital heart patients [5], while of the total United States population, PTA represents only 1-2% of CHD in live born infants. Another report conducted between the years 2004-2006 suggests that there are about 300 to 301 cases of PTA in the United States per year [10, 20]. There isn't any significant difference in the number of PTA cases found in the population of other countries. Although very few studies show PTA to be predominant in male infants, there is no substantial evidence to make this ostensible [9].

Ontogenesis for the normal development of the Truncus Arteriosus and Conus Cordis

During the fourth week of embryonic development, the essentials required by the embryo (oxygen and nutrients), which diffuse through the placenta and are supplied to the embryo are no longer sufficient, hence, the formation of the heart begins and it becomes the first organ to function within the embryo [2]. The developing embryo has a cranial (towards the head) and a caudal (towards the tail) end. The formation of the heart tubes, occurs consensually, that is, on either sides of the embryo, within the cranial region. Circa 18 days after the removal of the amnion, the longitudinal blood vessels, the dorsal aorta, are formed by the assembling of 'blood islands' on either side of the cranial head. 'Progenitor heart cells' (resident cardiac stem cells) adjacent to the cranial end of the primitive streak, drift into the lateral mesoderm (splanchnic layer), where some of them form the 'primary heart fields (PHFs). From these PHFs, the atria, the left ventricle and part of the right ventricle are formed. Other parts of the right ventricle, consisting of the cranial end of the Bulbous Cordis (Conus Cordis) and the Truncus Arteriosus (the distal end of the Bulbous Cordis) are formed by cells residing in the splanchnic mesoderm known as 'secondary heart fields' (SHFs). Collectively, the Conus Cordis and the Truncus Arteriosus are referred to as the outflow tract [3].

In the fifth week, Cardiac Neural Crest Mesenchymal Cells which are a distinctive subpopulation of cranial neural crest cells [22] and are originally from edges of the neural fold in the hindbrain and are regulated by the SHF via the NOTCH signaling, delaminate and journey over the 3rd, 4th and 6th pharyngeal arteries [16, 3], through the primitive pharynx to reach the outflow tract. Here, they actively proliferate to create pairs of opposing bulbar or truncoconal ridges in the Truncus [17]. These ridges, referred to as cushions or truncus swellings are located on the right superiorly (right truncus swelling) and on the left inferiorly (left truncus swelling). In the sixth week, the ridges grow in a distal-proximal direction towards each other and towards the aortic sac, developing the myocardium in this process [16], as they grow, they spiral around each other at 180 degrees, perchance due to the streaming of blood from the ventricles [17].

As they spiral, they fuse with the atrioventricular endocardial cushions and the interventricular septum, thereby giving rise to a helically shaped Aortico-pulmonary Septum which divides the Truncus Arteriosus into the Aorta and Pulmonary Artery channels [3, 16]. The septation of the TA is completed when the embryo is about 10mm [25].

Due to the spiral alignment of this newly formed septum, the Aorta and the Pulmonary Artery curl around each other [17]. On the ventral and dorsal walls of the Conus Cordis, similar swellings to those of the truncus appear [3]. These equally grow towards each other distally and fuse with the truncus septum. This fusion divides the Conus Cordis into the outflow tract of the right ventricle (anterolateral part) as well as the outflow tract of the left ventricle (posteromedial part) [3]. With this normal development, blood from the Aorta flows into the 3rd and 4th parts of the pharyngeal arches, while blood from the Pulmonary Artery flows into the sixth pair of pharyngeal arches. Deoxygenated blood from the body flows into the lungs through the heart via the Pulmonary Artery while oxygenated blood from the lungs flows from the heart to the body through the Aorta, with no mixture between the two.

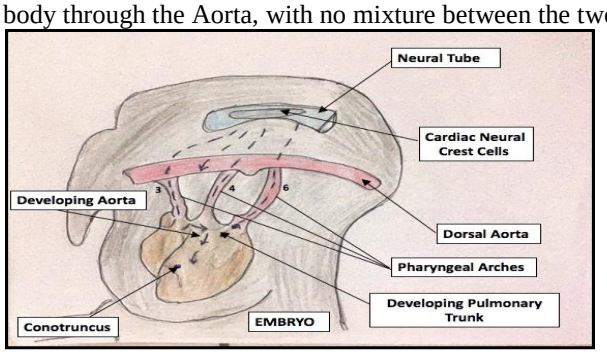
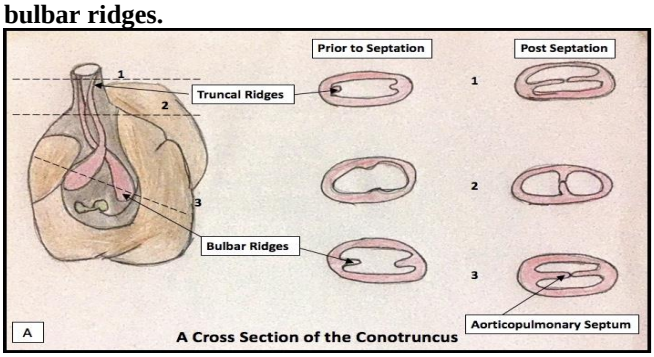


Fig 1. Development of the Truncus Arteriosus. A schematic illustrating the migration of Cardiac Neural Crest Mesenchymal Cells over the 3rd, 4th and 6th Pharyngeal arches towards the outflow tract to form bulbar ridges.



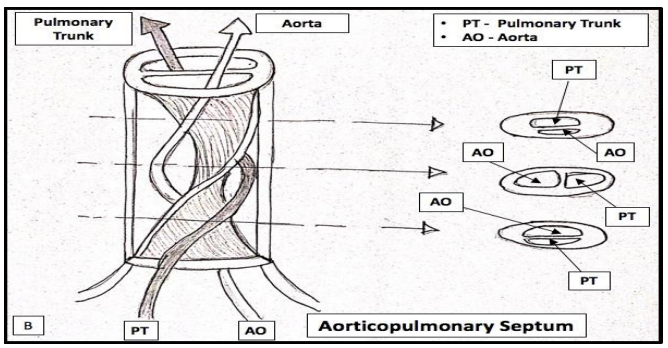


Fig2.Outflow tract division and septation, A. Illustration depicting the shape and state of truncal and bulbar ridges pre and post septum formation, B. Schematic of bulbar ridge spiral fusion (180°) with AV cushion, to form the Aorta and PA with complete AP septum.

Ontogenesis for normal development of Interventricular Septum

The expansion of the primitive ventricles at the end of the fourth week is achieved by the continuous growth of the myocardium outside, as well as the continuous diverticulation and trabeculae formation on the inside. The medial walls of these primitive ventricles appose and merge to form the Muscular Interventricular Septum. The two ventricles communicate via a crescentric interventricular foramen [17] which is located between the fused endocardial cushions and the rim of the muscular interventricular septum, created as a result of the incomplete merging of the medial walls of the ventricles [3]. As further development occurs, the complete closure of the interventricular foramen, located above the muscular portion of the interventricular septum forms the Membranous part of the interventricular septum by the end of week 7, this tissue fuses with the Aortico-pulmonary septum and the muscular portion of the interventricular septum, thereby enabling the pulmonary trunk to communicate with the right ventricle and the Aorta with the left ventricle. Thus, septum formation in the ventricles is completed [17].

Embryological basis for the Persistent Truncus Arteriosus

Neural crest cells migrate throughout a developing embryo, contributing to the formation of various tissues and miscellaneous cell types [19]. Thus, failure of these cells to migrate and proliferate correctly gives rise to a number of abnormalities and malformation in the developing embryo. In the case of Persistent Truncus Arteriosus, the Cardiac Neural Crest Mesenchymal Cells which differentiate to create the truncoconal ridges migrate abnormally in such a way that bulbar ridges fail to form [17,3]. Hence, there is incomplete or failed partitioning of the Truncus Arteriosus [6]. This means that there is no formation of the Aortico-pulmonary septum and consequently, no division of the outflow tract. The outcome of this malformation is a single large trunk which is derived from both ventricles, overrides both ventricle sand receives mixed blood from both ventricles [18, 3], there is also the absence of truncal spiraling and ventricular looping [21]. Due to the fact that these truncoconal ridges contribute in the formation of the interventricular septum, PTA majority of the time is complemented by a VSD, with the membranous VSD being the most common [18]. There is also impairment in the creation of separate aortic and pulmonary valves due to the non-development of Aortico-pulmonary septum, giving rise to the single truncal valve linked with PTA [14].

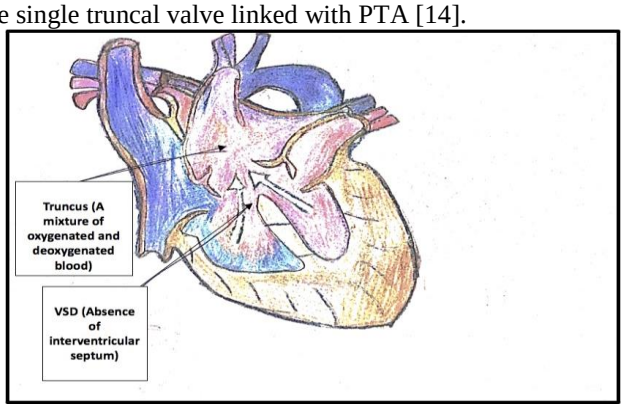


Fig 3.Schematic of the heart, illustrating PTA. Lack of AP Septum with VSD due to failure of proper migration and proliferation of Cardiac Neural Crest Cells. There is a connection between the Aorta and Pulmonary Artery, causing the mixture of oxygenated and deoxygenated blood.

Classification of Persistent Truncus Arteriosus and Its Variants

Subtypes of PTA have been discovered and classified so as to be identified. Several classification systems exist, however, the most common classifications for PTA are the Colette and Edwards classification and Van Praaghs classification. Being the earliest to emerge, precisely in 1949 [9], the Colette and Edwards system is the most popularly used PTA classification system. It distinguishes variants of PTA into Types I to IV, based on the degree of the main Pulmonary Artery development and the origin of Pulmonary Arteries [23, 24]. The other recognized classification of PTA was proposed by Van Praagh in 1965. This system is rather complex as it divides PTA variants into Types A and B, with A consisting of PTA variants accompanied with VSD and Type B being without VSD. However, there are very rare reports of Type B PTA in literature, hence, it is said to be non-existent [24]. The Van Praaghs classification system subdivides Type A PTA into four subtypes, namely, A1, A2, A3 and A4 [8, 9, 24].These variants are sometimes accompanied by other cardiac anomalies based on the way they develop. In the case of Type IV PTA, the 4^{th} pharyngeal arch poorly develops, while the 6^{th} pharyngeal arch develops well, leading to hypoplasia, coarctation, or disruption at the level of the aortic neck and a large Patent Ductus Arteriosus (PDA) [24]. In Types A1 – A3, the branchial 4^{th} arch develops well and the branchial 6^{th} arch poorly develops, as a result, there is an absent PDA [9].

Colette and Edwards Type I Persistent Truncus Arteriosus

This is depicted by the origin of a single short main Pulmonary Artery arising from the left lateral aspect of the Truncus Arteriosus [9] which divides and branches off into the left and right pulmonary arteries. In this subtype of PTA, the spiral septum is formed incompletely, thus, a partial separation between the Aorta and the main Pulmonary Artery occurs. Distal to the origin of the Aorta and the main pulmonary artery, the Aorta and the main Pulmonary Artery are discernible [8, 23, 24]. Type I is the most common variant as it accounts for about 48%-68% cases of PTA [23, 24].

Colette and Edwards Type II Persistent Truncus Arteriosus

This variant of PTA presents as separate origins of the left and right Pulmonary Arteries branching from the posterolateral aspect of the TA very close to each other in the absence of the main Pulmonary Artery. About 29% - 48% of cases of PTA are Type II [23, 9, 24].

Colette and Edwards Type III Persistent Truncus Arteriosus

In Type III PTA, the branching Pulmonary Arteries arise independently from the TA or pharyngeal arch [9], reasonably distant from one another, mostly from the left and right lateral aspects of the TA. Occasionally, one Pulmonary Artery originates from the underside of the pharyngeal arch, usually from a ductus arteriosus (a vessel which connects the Pulmonary Artery to the proximal descending Aorta) [8, 9], nonetheless, in majority of cases there is no main Pulmonary Artery present. Reports state that Type III accounts for 6% - 10% of PTA cases and is the least common of all PTA variants [23, 24].

Colette and Edwards Type IV Persistent Truncus Arteriosus

Type IV PTA is referred to as 'Pseudotruncus.' Most studies have characterized it as a Type of PTA in which there is a complete absence of the main and branch Pulmonary

Arteries. Contrariwise, a comprehensive text on CHD by Vijayalakshmi et al states that there are branch Pulmonary Arteries arising from different parts of the Aorta in addition to the absence of the main Pulmonary Artery [23]. In this case, the lungs are supplied by collateral vessels (Aortico-pulmonary collaterals) from the descending Aorta. Type IV PTA which was originally proposed in 1949 by Colette and Edwards as a form of lesion is no longer seen within the spectrum of PTA but is now thought to represent a variation of Pulmonary Atresia with VSD and also seen to be a more precise extreme form of Tetralogy of Fallot [8, 9, 23, 24, 26].

Van Praaghs Type A1 Persistent Truncus Arteriosus

This is seen to be identical to Type I PTA of the Colette and Edwards classification system [8, 24]. There is a presence of the main Pulmonary Artery which arises from the Truncus Arteriosus and biruficates into branch pulmonary arteries [24], with a partially formed Aortico-pulmonary septum [26].

Van Praaghs Type A2 Persistent Truncus Arteriosus

Type A2 can be seen as a combination of both Type II and Type III of the Colette and Edwards's classification in which there is an absent main Pulmonary Artery and Aortico-Pulmonary septum with separate branch Pulmonary Arteries originating from the right and left posterolateral sides of the Truncus Arteriosus [8, 9, 24, 26].

Van Praaghs Type A3 Persistent Truncus Arteriosus

In this subtype, one lung is supplied by the right Pulmonary Artery which originates directly from the Truncus Arteriosus while the left Pulmonary Artery connected to the pharyngeal arch (a subtype of Colette and Edwards Type III) [9] via a stenotic ductus or ductus like vessel [27], supplies the other lung.

Van Praaghs Type A4 Persistent Truncus Arteriosus

This subtype is not classified according to the pattern in which the Pulmonary Arteries originate but by the co-occurrence of an interrupted pharyngeal arch.

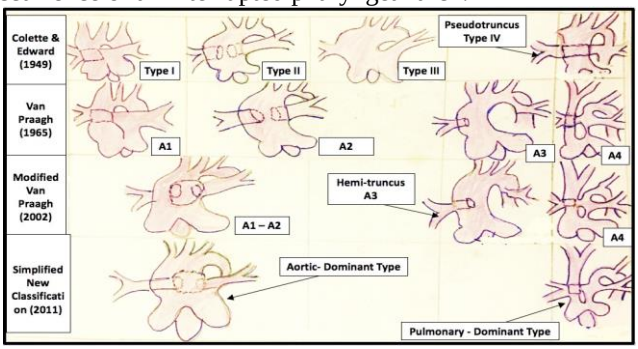


Fig 4.A table elucidating variants of PTA and their various anatomical classification categories from top to bottom in the order of Colette and Edwards (1949), Van Praagh (1965), A newly proposed nomenclature (modified version of Van Praaghs, 2000) and A most recent proposed nomenclature dividing PTA variants into only two categories (2011).

Causes of Persistent Truncus Arteriosus

The main cause of Persistent Truncus Arteriosus is idiopathic. Nevertheless, there is increasing evidence which shows that this cardiac anomaly is strongly impacted by genetics. The most common genetic defect which is associated with PTA is Digeorge Syndrome (DGS). This defect is described by a label known as CATCH, where C = cardiac anomalies involving the outflow tract (PTA), A= abnormal facies, T= thymic hypoplasia, C=cleft palate and H=hypocalcaemia due to parathyroid gland dysfunction [10, 3, 26].

Digeorge syndrome happens to be the most frequent micro-deletion syndrome. It is a primary immunodeficiency disease (PIDD) caused by a hemiazygous deletion of the chromosome 22q11.2 (the Digeorge syndrome region), thus leading to abnormal neural crest cell and tissue development during fetal growth [28, 29]. Due to poor white blood cell (T-cell) production and immune system function, this syndrome is associated with susceptibility to recurrent infections which may decrease later on in childhood and adulthood depending on the severity of the syndrome, as it is a lifelong condition [28].Based on a screening carried out on 251 patients, this micro-deletion has been found incirca 20% - 30% of patients with Persistent Truncus Arteriosus [24] and can be detected using the fluorescent in situ hybridization technique (FISH). PTA patients with DGS seldom have craniofacial anomalies as a result of the neural crest cells playing important roles in the development of the face and the heart [3, 24]. Other factors which may be responsible for PTA are said to be multifactorial, possibly due to utero environmental exposures, i.e. intake of harmful substances during pregnancy and/or excessive use of alcohol [21, 10, 30]. The medical history of the parent equally matters as it has been found that mothers with past history of viral illnesses such as Rubella (German Measles), maternal type 1 diabetes mellitus, maternal hypertension or even a parent who might have had a congenital heart defect will predispose the infant to being diagnosed with PTA [21, 30].

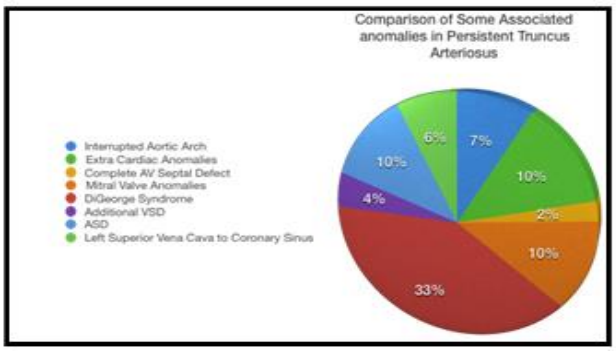


Fig 5. Incidence of associated anomalies in PTA. A pie chart plotted based on a compilation of results from various studies [24], showing a well-defined comparison between various anomalies which may cause PTA. Most cases of PTA are highly associated with Digeorge syndrome (2q11.2). This explains why it has the highest percentage compared to other anomalies.

Clinical Manifestation of Persistent Truncus Arteriosus

An infant with PTA will present with mild cyanosis in the first week of life, this is a typical clinical presentation of PTA, which occurs due to the fact that deoxygenated blood mixes into the systemic circulation [1], hence, infant's oxygen levels are seldom slightly lower than normal. This mixture exudes on the infant's skin, lips and fingertips as a bluish – purple discoloration which increases when infant cries, with this presentation, the infant is said to be cyanotic [10, 30, 18]. Before birth, the fetus doesn't make use of its lungs, thus, it receives oxygenated blood from its mother and sends deoxygenated blood to its mother by sending blood through the Foramen Ovale [1]. This gives rise to a relatively high vascular resistance and pressure in the pulmonary circulation, which is also similar to that in the Systemic circulation. The Pulmonary blood flow is obtained from a combined ventricular output, as outflow from both ventricles are directed towards the TA, the size of the flow depends on the ratio of resistances in the pulmonary and vascular beds [9].

However, after birth, infant starts making use of its lungs, vascular resistance decreases in the infant, streaming still accounts for some differential flow, where the Pulmonary Artery saturation is normally less (roughly 10% less) than the systemic circulation. None the less due to the mixture of pure and impure blood from both ventricles during systole, there are subnormal levels of systemic oxygen saturation [8, 9, 10, 26]. Due to the fact that the systemic and pulmonary circulations are also parallel, there is a Right – Left shunt of blood as [18] pulmonary blood flow now increases about three times more than the systemic circulation and so the amount of blood flow to the lungs increases significantly [9], giving rise pulmonary over circulation [26] and increased myocardial function which will in turn lead to an increase in demand for resting oxygen and decreases in the Oxygen metabolic reserve [9]. The outcome of this would be a Congestive Heart Failure (CHF), thus, infants with PTA typically present with CHF (due to the excess amount of blood flowing to the lungs) and are usually in distress during their first few weeks of life [26].

Other progressively worsening symptoms which maybe observed in PTA patients include edema of the face, leg and arms due to accumulation of fluid, failure to thrive, recurrent respiratory infections, poor feeding and thus lack of weight gain coupled with growth delays, hypoxia [30], dyspnea, tachypnea, fatigue, tachycardia and extreme sleepiness [21, 26, 10]. On physical examination, cardiomegaly maybe found at varying grades with increased pulmonary vascular markings, prominent ascending aorta via chest x-rays and echo's, which might be suggestive of a right aortic arch. This has been found in about 25% -33% of PTA cases [12, 24]. Feasibly, a gradual development of obstructive lung disease may equally be observed [30], Echocardiogram would show the collective ventricular hypertrophy bearing in mind that the pulmonary overload might indicate left atrial enlargement, while A grade 2 to 4/6 systolic murmur, along the left sternal border and a mid-diastolic mitral flow murmur at the apex of the heart maybe audible on auscultation [9, 12 10]. An MRI of the patient's heart is also aides in detecting cardiac anomalies, which may cause the heart to present in abnormal forms [33].

Remedies for Persistent Truncus Arteriosus

Early complete primary surgical restoration with the goal of repairing the Truncus Arteriosus and closing the VSD [10, 31], to enable separate flow of deoxygenated blood to the lungs via the pulmonary system and oxygenated blood to the body via the systemic system is the most rational form of approach to resolving PTA in this current dispensation [24, 26], depending on the severity of symptoms which the PTA patient clinically presents [12, 10]. Nonetheless, before surgery is considered, the main aim would be to stabilize the patient and manage presenting symptoms such as the Congestive Heart Failure which is common amongst PTA patients [32]. In this aspect, medication such as diuretics, digoxin and ACE inhibitors are administered with the aim of decreasing blood pressure, strengthening the heart muscles and ridding the excess accumulated fluid, advanced pediatric life support is also used to soothe infant [12, 10, 9, 21].A special hypercaloric formula might be also administered via a feeding tube where infant feeds poorly and prior to surgery, prophylaxis is provided for the infant against Infective Endocarditis and Respiratory Syncytial Virus (RVS) [21, 10], In a case where immediate surgical repair can't be carried out, a palliative procedure is instituted in other to limit blood flow to the lungs and further manage the CHF.

Nonetheless this procedure isn't popular in this current age as it involves the banding of the Pulmonary Artery which might be technically difficult due to its length and difficulties faced in attempts to find the exact size band for each pulmonary artery [12, 24, 26].This is why, although the exact timing of surgical repair may vary based on the unambiguous features of each PTA patient, the American Heart Association [31] states that it is essential to carry out surgical repair of PTA at early infancy if not as a newborn, precisely within less than 6 weeks after birth [21]so as to prevent damages to the infant's lungs, compass myocardial function and to prevent pulmonary hypertension due to the high blood pressure in the Pulmonary Arteries [21, 31].

To achieve this, three major steps are involved, the first step being the closure of the hole between the ventricles which causes the VSD using a patch, the separation of the pulmonary arteries from the main truncus [32, 24] and a technique referred to as Rastelli repair. This is a process in which the Pulmonary Artery is disconnected from the TA and a conduit (usually a homograft, xenograph Pulmonary Artery or direct anastomosis)with or without an artificial valve is placed from the right ventricles to the Pulmonary Arteries to decrease blood flow pressure and conduct the flow of deoxygenated blood to the lungs [21, 31,10].The truncal valve ordinarily doesn't require surgical interference except in cases of regurgitation and substantial stenosis [24].Post-surgery, infants may experience episodes of pulmonary hypertensive crisis which may be relieved with postoperative management. This involves sedating infants with analgesics, sedatives and putting in place ventilative strategies to prevent hypoxia and hypercapnia (excess carbon dioxide in blood stream due to inadequate respiration). A follow up on infants well-being by a cardiologist is also necessary in order to monitor progress and avoid further complications [31,10].

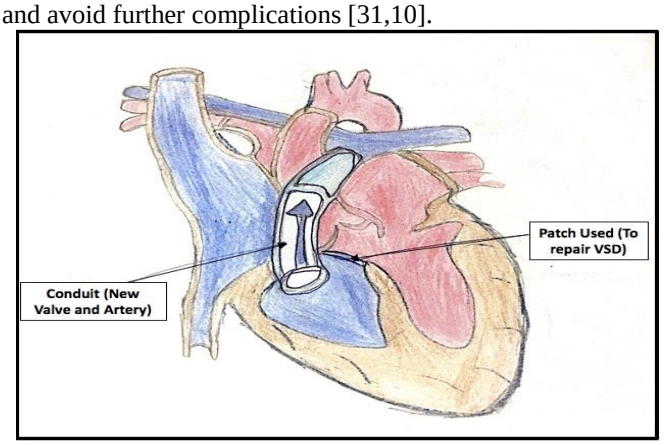


Fig 6. Post-surgical repair, a diagram illustrating one of the surgical interventions used to remedy PTA (Rastelli repair). A conduit with or without a valve is connected from the right ventricle to the Pulmonary Arteries to establish direct anastomosis and decrease pulmonary hypertension. The VSD is rectified by using a patch to seal the hole between both ventricles.

Mortality of Patients with Persistent Truncus Arteriosus

Pre surgical repair, mortality rates of PTA patients are relatively high as untreated cases of PTA usually lead to death during or < 1 year of life, approximately 50% die in 2 and half months while 80% die by 1 year [33, 9, 26] mostly due to cardiac arrest and multiple organ failure as systemic perfusion is incompetent in meeting up metabolic demands, thus, gradual metabolic acidosis and myocardial dysfunction emerge [9].

With the advancement of medicine, intervention of complete surgical repair being administered, early post-surgery mortality for PTA patients has decreased from a whopping 25% circa 20 years ago to <10% in recent times [26, 9, 24] and has led to long term survival for PTA patients, about 80% based on a 10 to 20 years follow up post-surgery. The 20% postoperative mortality mostly results from re-interventions, late surgical repair or recurrent physiological abnormalities [9].

Discussion

Persistent Truncus Arteriosus is a complex and atypical congenital heart defect which accounts for roughly 1.2% of all congenital cardiac malformations [36] of which its embryological origin is as a result of abnormal neural crest cell migration resulting in the malformation of the Aorticopulmonary septum(which divides the Pulmonary Artery from the Aorta and the interventricular septum and also separates the right and left ventricle's, failure of proper truncoconal septum), as a result, PTA is seldom accompanied by VSD with the membranous VSD being the most common to occur. Notwithstanding this fact, studies are still ongoing to further elucidate its embryological origin [18, 36, 3]. Anatomically, PTA features include the origination of a single vessel from a combined right and left ventricular outflow tract which supplies systemic, pulmonary and coronary blood flow [36, 37]. Genetics are seen to be highly related to PTA as an infant born of a parent with a history of CHD is more prone to PTA [21], although PTA is favorably associated with Digeorge Syndrome, a 1997 study by Kazuo, M *et al* suggests that this association hasn't been definitely proven [40]. Colette and Edward, Van Praaghs are the two main classification systems which are used to portray the anatomical dysfunction of PTA based on the presence /absence of the main Pulmonary Artery and the origin of branch Pulmonary Arteries. Although these two historical classification systems are recognized, with the Colette and Edwards classification [23] being the first classification system to come into existence in 1949 [24], the most popular and commonly used system, the Society of Thoracic Surgeons and the Europeans Association of Cardiothoracic surgery sponsored the Congenital heart nomenclature and database project in the year 2000 [24] which has proposed a new unified classification structure for PTA [26, 24]. This new nomenclature is a modified version of VanPraaghs classification system, which he proposed in 1965 and differs from that of Colette and Edwards. The goal of this modification is to standardize the description of PTA and establish an information based database which would be inclusive of important details of PTA e.g. demographics, complications and treatments [24, 26, 27]. This proposed classification suggests the elimination of the vague terms Pseudotruncus (classified by Colette and Edwards and Type IV PTA where blood flow is wholly supplied by collateral atresia). It proposes this to be more associated with extreme Tetralogy of Fallot rather than PTA. Another term is Hemitruncus (where there is an abnormal origin of a single Pulmonary Artery and a normal connection between the right ventricle and the remaining Pulmonary Artery) and Type 1 ½ truncus which was used by Colette and Edwards to classify PTA defect when the anatomy was transitional between Type I and Type II PTA. This new classification system deems it unnecessary to differentiate the quality or the position of the main pulmonary trunk [26, 24].

Macarteny, Deverall, and Scott (1973), are of the view that Type IV PTA should not be classified as a PTA variant because the 4th and 6th pharyngeal arches are not 'communis' due to the obliteration of the latter in embryonic development [39]. Contrary to this, an anatomical study of Truncus Arteriosus communis conducted by Gaetano T *et al., 1976*states that it is indeed debatable as to whether or not Type IV PTA should be classified as a variant of PTA [38], however, they accept the hypothesis of Type IV PTA being indeed a 'true variant of PTA' based on their study carried out on 12 specimens of PTA with focus on their conal anatomy and cardiac distortions which may give rise to complication post-surgical repair. In their study, there was a complete failure of the truncoconal septation as can be seen in other variants of PTA and thus they concluded that agenesis of the 6th pharyngeal arch can be perceived as a result of developmental deficiency in PTA [38]. In collaboration with Prof. RH Anderson, a surgical group in Chicago, proposed a new and simple (though no yet in clinical use) form of classifying PTA into two subtypes, Aortic-dominant or Pulmonary-dominant [24]. Their argument is based on their study carried out on 28 autopsy specimen, where 20 were found to be Aortic – dominant. Pulmonary – dominance was associated with the presence of a hypoplastic distinct aorta and a PDA which supplied majority of blood flow to the Aorta. [24]. It's established that surgical repair is the most ideal remedy for PTA [24,26], in which transformation of the truncus and truncal valve into the aorta and aortic valves correspondingly, and the correction of the VSD into the left ventricular flow out tract are some of the main steps [41]. Nonetheless, reports still place emphasis on some difficulties faced by surgeons in the process of this surgical repair [38]. These difficulties include the lack of partitioning between the Aorta and Pulmonary Artery, the degree of the pharyngeal arch, the state of the truncal valve and the size of the ventricular septal defect [41, 42, 43]. The presence of a truncal vale with regurgitation worsens the prognosis of the surgical repair outcome significantly and also decreases survival rates, thus, truncal valve replacement or repair haven't produced good results, this is why it is a problem for surgeons and sometimes isn't repaired if there is no stenosis and regurgitation. Conduits used in surgical repair are placed in early infancy and so its size may narrow, it may be blocked or become inadequate as infant grows, thus, it needs to be replaced from time to time and the easiest way of alleviating stenosis in the conduit would be through Cardiac Catheterization, a method of dilating the conduit with the help of a balloon tipped catheter [31,9, 33]. Endocarditis prophylaxis administered to the infant prior to surgical repair is only required for the first 6months' post-surgical repair except in cases of a residual defect close to the surgical patch. A clinical study conducted by Espinola-Zavaleta N *et al., 2008* on 6 adult patients for 4 years (May 2003 to June 2007), purposed to describe factors which allow the survival of PTA patients until adult life, but came after their study, they came to the conclusion that the actual survival time for patients with complex CHD such as PTA is actually unknown, as there are factors such pulmonary branch hyperplasia and pulmonary hypertension which are detrimental in life for some CHD cases but allow for survival of patients in other CHD cases such as PTA.

Conclusion

In order to fully understand Persistent Truncus Arteriosus and its clinical implications, it is vital to grasp the embryology of cardiac development and formation of the Truncus Arteriosus [26].

With this knowledge it is assumed that the origin of this cardiac anomaly is more elucidated. Having thoroughly examined various studies and reports in this article, it can be concluded that amongst known congenital heart defects, PTA accounts for a very small percentage 1-2% thus, it is a rare but intricate CHD with minimal prevalence, as it affects a small number of the total population [13, 14, 9, 15, 5, 10]. It is a cardiac defect in which the main key player leading to its origination (more research is still ongoing in this aspect) is the failure of correct migration of neural crest cells in septation of the Aortico- Pulmonary septum which divides the Truncus Arteriosus into the Pulmonary Artery (supplying deoxygenated blood to lungs) and the Aorta (supplying oxygenated blood to the body). It is frequently accompanied with a VSD and is highly associated with Digeorge syndrome and velocardiofacial syndromes, although its main cause is idiopathic [3, 22, 17, 6, 25, 24]. Its developmental theory, causes and classification into variants are still being challenged, nonetheless, two historical methods of classification are still recognized with Colette and Edwards classification being tops. Cyanosis and severe Congestive Heart Failure are the two major clinical manifestations of PTA patients, however, through the help of ECG chest x-rays, Ultrasonography and other diagnostic strategies, PTA can be detected and identified. It is extremely important to carry out a complete primary surgical repair of diagnosed cases of PTA at the earliest possible stage, so as to decrease mortality and increase survival rates of affected infants because this is the goal of surgical intervention. This method of treatment is the most ideal in remedying PTA compared to the Palliative method of banding the Pulmonary artery, as the latter present's fraught difficulties and might be a waste of time. The goal of surgical intervention in PTA is also to repair the Truncus Arteriosus in which one of the main stages would be the connection of a conduit to reduce pulmonary hypertension and restore normal breathing and oxygen levels to the infant. Nevertheless, prior to surgical repair, it is crucial to manage the severe symptoms which the affected infant presents, such as treatment of the CHF with diuretics and administration of prophylaxis pre and post-surgical repair to prevent Endocarditis. There has been generally a positive outcome post-surgical repair in patients affected with PTA but it is essential for clinicians to follow up patients over the course of years in order to prevent any complications which may arise.

Taking into consideration the in-depth discussion of Persistent Truncus Arteriosus carried out in this study, it is clear that PTA should be treated with every form of severity, taking the right precautive measures at every step to ensure that a higher survival rate greater than 80% is achieved post-surgical repair [9] in the future.

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