Retrospektive Analyse und Vergleich zwischen interventionellem Ductus arteriosus Stenting und des chirurgischen aortopulmonalen Shunts als erste Palliation bei Patienten mit pulmonaler Atresie und ventrikulärem Septumdefekt

Inauguraldissertation
zur Erlangung des Grades eines Doktors der Medizin des Fachbereichs Medizin
der Justus-Liebig-Universität Gießen

vorgelegt von Tsianakas, Nikolaos
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Aus dem Fachbereich Medizin der Justus-Liebig-Universität Gießen

Klinik für Kinderherzchirurgie

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1 INTRODUCTION

Definition:

Pulmonary atresia with ventricular septal defect (PA-VSD), alternatively termed Tetralogy of Fallot with Pulmonary atresia (TOF-PA), encompasses a spectrum of congenital cardiac anomalies characterized by an absence of luminal continuity and the interruption of blood flow between either ventricle and the pulmonary artery. This condition can occur in uni- and biventricular hearts presenting with a defect in the interventricular septum. In its most severe manifestations, the native pulmonary arteries may be partially or entirely absent.

Nomenclature:

Despite concerted efforts, an expert consensus regarding the nomenclature of this condition remains elusive. While some authors favour the term PA-VSD, others advocate for TOF-PA. Broadly, pulmonary atresia with ventricular septal defect is recognized as representing the severe end of the Tetralogy of Fallot (TOF) spectrum. For the purposes of this study, the acronym PA-VSD will be adopted to describe the condition.

Epidemiology:

TOF is the most prevalent cyanotic congenital heart disease, with an incidence of 3.26 in 10.000 live births in the United States[1]. Current estimates indicate that PA-VSD accounts for 2.5-3.4% of all congenital heart defects, corresponding to a prevalence of 0.07 in 1000 live births[2,3]. Furthermore, 1.4% of children diagnosed with congenital heart disease as well as 20.3% of children in the TOF spectrum, are affected by PA-VSD. The risk is notably elevated among siblings (2.5-3%) and in children born to parents with TOF (1.2-8.3%)[4]

Genetics:

So far, various genetic mutations have been associated with and/or identified in PA-VSD.

The 22q11.2 deletions syndrome (22q11.2 DS) is the most common chromosomal deletion syndrome, with a prevalence of approximately 1 in 4000-6000 live births[5]. This syndrome encompasses conditions such as DiGeorge-Syndrome, velocardiofacial syndrome and the conotruncal anomaly face syndrome. All patients with these syndromes share a common genetic aetiology, specifically a microdeletion on chromosome 22q11.2. This deletion spans approximately 3 megabases (Mb) and affects around 30 genes[6–11].

Numerous studies have highlighted the significant prevalence of 22q.11.2 DS among patients with congenital heart disease. In particular, patients with TOF exhibit a reported prevalence of 10-30%[12–14]. Additionally, a multivariable regression analysis has identified pulmonary atresia as an independent predictor of this chromosomal deletion[12]. Moreover, 22q11.2 DS is associated with higher mortality[15,16] and morbidity[17] as well as with an increased risk of schizophrenia[18].

The clinical presentation of these syndromes is particularly important for potential complications in the perioperative period, such as hypocalcemia or transfusion-associated graft versus host disease, future learning difficulties and heredity of the disease.

Moreover, VATER syndrome (vertebrae, anus, trachea, esophagus and renal dysfinction) as well as Alagille syndrome are commonly observed. Alagille syndrome, in particular, is consistently regarded as a poor prognostic factor, primarily due to its association with liver dysfunction[19].

Other abnormalities frequently identified in these patients include bronchus suis and enlarged aorta that can lead to tracheobronchial compression, atrial septal defects, multiple VSDs, coronary anomalies, left superior vena cava and retroaortic innominate vein[20].

Embryology/Anatomy:

The anatomical characteristics of PA-VSD are similar to the classic anatomy of TOF. These are:

1. Pulmonary atresia
2. VSD
3. Overriding aorta
4. right ventricular hypertrophy

These defects arise from the anterior displacement of the right ventricular infundibular septum during the embryological phase of development. Normally, the infundibular septum occupies a posteroinferior and rightward orientation. However, in this condition, it shifts to an anterosuperior and leftward position. Consequently, the infundibular septum becomes displaced anteriorly, rather than its normal position between the anterior and posterior limbs. This aberrant displacement results in the fusion of the infundibular septum with the anterior limb, producing the characteristic VSD. Simultaneously, this structural anomaly leads to a narrowing of the infundibulum and pulmonary valve, culminating in pulmonary atresia.
Pulmonary atresia occurs when there is complete obstruction or absence of the connection between the ventricle and the pulmonary arteries. This can be caused by a non-perforated pulmonary valve or by a blockage of muscle tissue at the portal or at the distal end of the subpulmonary infindibulum. Of course, the connection fails in the complete absence of the pulmonary trunk[21].

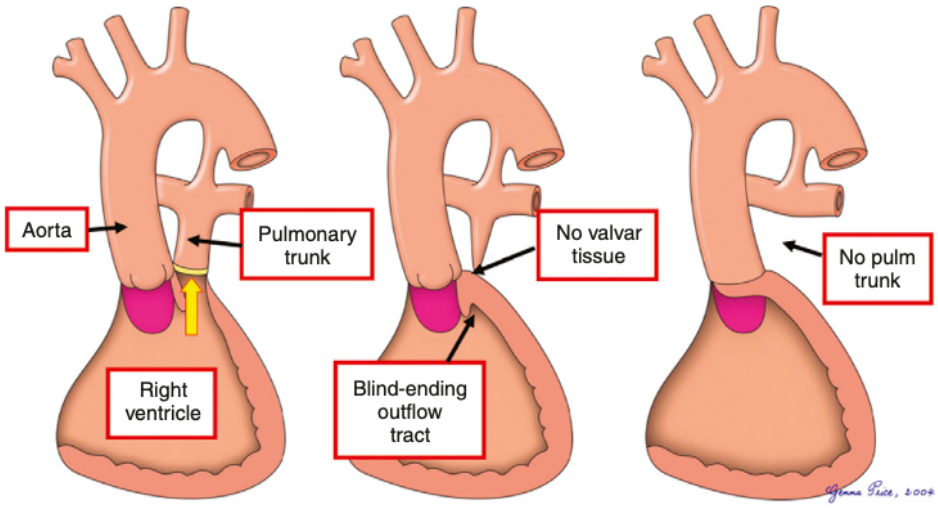

Figure 1 Varying arrangements at the pulmonary ventriculoarterial junction that underscore cardiac variants in TOF/PA. Source: Anderson's Pediatitric Cardiology, 4th Edition

Pathophysiology:

In PA-VSD, the development and anatomical characteristics of the pulmonary artery play a crucial role in determining the clinical presentation and influence the surgical interventions. The atresia of the pulmonary artery can either be confined to a local area, involving the pulmonary valve and the proximal part of the pulmonary trunk, or it can affect a more extensive segment. Communication between the right and left pulmonary arteries may either exist freely (known as confluence) or be absent (referred to as nonconfluence). Pulmonary blood circulation may be maintained through various mechanisms, including a patent ductus arteriosus (PDA), systemic-to-pulmonary collateral vessels, or networks of bronchial and pleural arteries.

The condition of the intrapulmonary arteries is directly impacted by the volume of blood flowing through the pulmonary circulation and the patency of the ductus arteriosus. When a sufficiently large ductus is present and supplies confluent pulmonary arteries, blood flow and the development of intrapulmonary arteries in both lungs are typically normal. Conversely, in cases where numerous collateral vessels exist and the ductus is absent, abnormal intrapulmonary artery branching occurs frequently, resulting in stenosis of certain arteries and the development of pulmonary hypertension.

Systemic-to-pulmonary collateral arteries predominantly originate from the thoracic aorta, although less frequently may arise from the subclavian arteries, internal mammary arteries, intercostal arteries, or even the abdominal aorta. In rare instances, collateral arteries may emerge from the coronary arteries. Approximately 60% of patients exhibit stenosis of collateral arteries either at their origin from the aorta or within the intrapulmonary region, with the severity of the stenosis typically progressing over time.

The VSD associated with this condition is usually membranous or infundibular, often large in size and rarely obstructed by membranous tissue. Additionally, approximately half of patients may also have a secundum-type atrial septal defect (ASD) or a patent foramen ovale (PFO).

The right ventricle (RV) and, to a lesser extent, the right atrium often demonstrate moderate to marked hypertrophy and dilation, while the left atrium and left ventricle (LV) typically appear normal. Although coronary artery anomalies are uncommon, reported abnormalities include a high origin of the coronary ostia or coronary artery-to-pulmonary artery fistulae.

Additionally, PA-VSD is occasionally associated with other cardiac anomalies. These include tricuspid atresia or stenosis, complete atrioventricular (AV) canal defect, complete of the great arteries, left superior vena cava, anomalies of the coronary sinus, dextrocardia, and asplenia or polysplenia syndromes[22].

Patent Ductus Arteriosus

The ductus arteriosus (DA) is a vital vascular structure which connects the proximal descending aorta (distal to the origin of the left subclavian artery) to the roof of the main pulmonary artery close to the left pulmonary artery. Thereby, it forms a vital outflow conduit for right ventricular output to circumvent the high resistance pulmonary-arterial circulation. Physiologically, the DA undergoes functional closure within 12 to 18 hours after birth, with complete anatomical closure typically occurring within 2 to 3 weeks. If the DA remains patent beyond three months in full-term infants or more than one year in premature births, it is named **Patent Ductus Arteriosus**

(PDA), due to the fact that the likelihood of spontaneous closure beyond this threshold, sinks dramatically[23,24].

PDA can manifest in various sizes and structures. Typically, the aortic ending of the PDA tends to be larger than its pulmonary counterpart, leading to a somewhat cone-shaped arrangement. The size, configuration, and relationship to adjacent structures are clinically significant with respect to determining resistance to blood flow and also have important implications with regard to interventional and/or operational procedures[24]. In the context of PA-VSD, the flow in utero, is directed from aorta to the pulmonary artery due to severe right-sided obstructive lesions and the PDA may form an arch with concavity upwards with an inferior angle less than 90°. The PDA is then called "reverse-oriented" PDA[25] If a reverse-oriented PDA is manifested in utero, it is a strong indication to maintain pulmonary blood flow in the early postnatal period[26].

The most widely used PDA-classification is the Krichenko-Classification[27], which introduced 5 different types of PDA:

Type A: Conical duct with well defined aortic ampulla and narrowest portion near the pulmonary artery end.

Type B: Large duct with window-like structure, characterised by a very short length at the aortic insertion.

Type C: Tubular duct without any constriction.

Type D: Complex duct with multiple constrictions.

Type E: Elongated duct with multiple conical constrictions, situated remotely from the edge of the trachea (as viewed on lateral angiography).

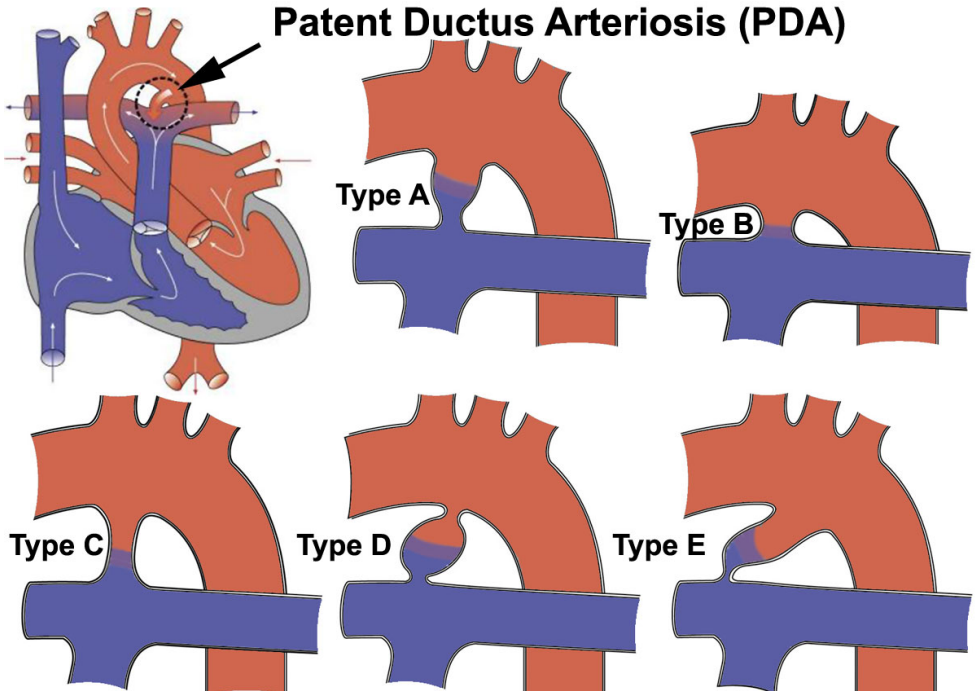

Figure 2 Graphical illustration of the angiographic PDA classification by Kirchenko et al (1989). Source: Elsheikh et al, PMID: 25278722

Major Aorto-Pulmonary Collateral Arteries (MAPCAs)

Major aortopulmonary collateral arteries (MAPCAs) are congenital vascular anomalies consisting of nonregressed systemic-to-pulmonary embryological connections from the aorta or its branches supplying the pulmonary arterial vasculature. These vessels provide an alterntive source of pulmonary blood flow in the setting of cardiac lesions with compromised antegrade flow through the native pulmonary arteries, as in the case of PA-VSD. In this condition, pulmonary lood flow is primarily derived from either a PDA or MAPCAs.

Embryologically, MAPCAs develop as segmental arteries that initially ensure blood supply to the lungs in parallel with the sixth branchial arch-derived branches, which later develop into the pulmonary arteries. In physiological development, blood supply is (50^{th} day of gestation and on) exclusively conducted by the PAs, whereas in case such as PA-VSD, where PAs are in total or partially not well developed, the DA and the segmental arteries continue to compensate the pulmonary blood flow[28,29]

MAPCAS vary substantially in number, origin and branching course. They may form can anastomoses with PAs and are also prone to stenosis at multiple points across their course. They are classified in several ways, primarily according to vessel of origin, communications with other PAs and impact of stenosis[30]

In the context of PA-VSD, the presence of MAPCAs significantly influences both the clinical implications as well as the therapeutic strategy. This is particularly critical given the wide variability in the development of native pulmonary arteries, which can range from normal to complete absence. The coexistence of MAPCAs and abnormal pulmonary arteries can lead to complex interconnections among vessels, which exacerbate the condition and can provoke overflow, heart failure, pulmonary hypertension as well as oligemia in under-supplied lung segments, if the segment is undersupplied, even within the same patient.

Classification of PA-VSD:

Based on the anatomical characteristics of the native pulmonary arteries as well as the collateral ones, patients with PA-VSD can be classified into three different categories (Barbero-Marcial classification[31])

Type A: All bronchopulmonary segments are connected to the central pulmonary arteries. The primary surgical goal in this category is to ensure the presence of pulmonary arteries that have adequate size, distribution and peripheral resistance, thereby facilitating total surgical correction. Patients with Type A PA-VSD can be categorized in 2 distinct subgroups:

- subgroup A1: Patients with normal or underdeveloped pulmonary arteries
- subgroup A2: Patients with stenotic pulmonary arteries.

Type B: Bronchopulmonary segments are supplied partially by branches of the central pulmonary arteries and partially by aortopulmonary collateral arteries (MAPCAs).

In this group, the simultaneous presence of native pulmonary arteries and MAPCAS, necessitates a surgical approach aimed at unifocalising the pulmonary circulation. This is typically achieved by anastomosing the MAPCAs to the native pulmonary arteries, supporting enlargement and normal development. Once sufficient unifocalisation is achieved, complete surgical correction can be planned for a later stage.

Type C: There are no central pulmonary arteries and all bronchopulmonary segments are supplied exclusively by MAPCAS.

In this category, surgical intervention involves anastomosing the MAPCAS and lobar arteries to the pulmonary hilum in order to create an intermediate pulmonary arterial segment. This segment is subsequently supplied via an APS
and can be accessed via a median sternotomy in future corrective operations.

Clinical Presentation

The clinical presentation of PA-VSD depends on the specific anatomical variant, the patency of the ductus arteriosus and the presence and distribution of MAPCAS.

Cyanosis is a frequent, though not universal, finding. More than half of newborns with PA-VSD will be cyanotic in the neonatal stage[32] . The severity of cyanosis is directly proportional to the degree of collateralization. Patients with isolated ductus-dependent pulmonary blood flow, with few or no MAPCAS, will rapidly become cyanotic shortly after birth, once the ductus begins to close. Conversely, when MAPCAS are present, the clinical spectrum is highly variable. Patients may exhibit mild or no cyanosis, or they may present with pulmonary overflow, leading to symptoms and signs of congestive heart failure such as tachypnoea[33] . In exceptionally rare cases, oligosymptomatic patients may experience prolonged life without any treatment if an optimal volume of pulmonary blood flow is achieved, referred to as "natural palliation"[34].

On auscultation, PA-VSD is manifested by the absence of the typical systolic murmur from the right ventricular outflow tract. Instead, continuous heart murmurs are much more common, typically auscultated on the thorax, with increased clarity on the back.

Localized murmurs are more suggestive of a PDA, whereas more widespread murmurs are characteristic of MAPCAS[1].

Diagnostic Evaluation

EKG:

The 12-lead-EKG in neonates with PA-VSD may appear normal at birth, but usually reveals signs of right atrial enlargement and, more prominently, right ventricular hypertrophy as the condition progresses. This finding distinctly differentiates patients with PA-VSD to those without VSD. The axis is usually deviated inferiorly and to the right, usually between +100 and +180 degrees[35,36]

Chest X-Ray:

The signs of PA-VSD are indirect and depend directly on pulmonary blood flow. In the case of pulmonary overflow, there are signs of decompensated heart failure with congested pulmonary segments and an enlarged cardiac silhouette. Conversely, with inadequate pulmonary blood flow, the lungs are darker and oligemic and the cardiac silhouette is normal or smaller than normal. In the presence of MAPCAs, pulmonary segments may demonstrate variable sizes depending on the degree of perfusion, with some segments appearing larger due to overperfusion, while others are reduced in size as a result of underperfusio[21,36]. In addition, in PA-VSD, a right-sided aortic arch is observed in nearly half of the patients.

2-D Transthoracic Echocardiography

PA-VSD can nowadays be diagnosed with relatively high precision in utero. However, the detailed morphology of the pulmonary arteries and the source of pulmonary blood flow cannot be clearly identified and evaluated[37] (Figure 2). The absence of a visualized PDA on prenatal echocardiography, increases the likelihood of the presence of MAPCAs. If the diagnosis is not established in utero, it is confirmed after birth, in almost all cases, by transthoracic echocardiography. An important point of transthoracic echocardiography is its great sensitivity in identifying multiple VSDs, coronary anomalies or atrial septal defects (ASD).

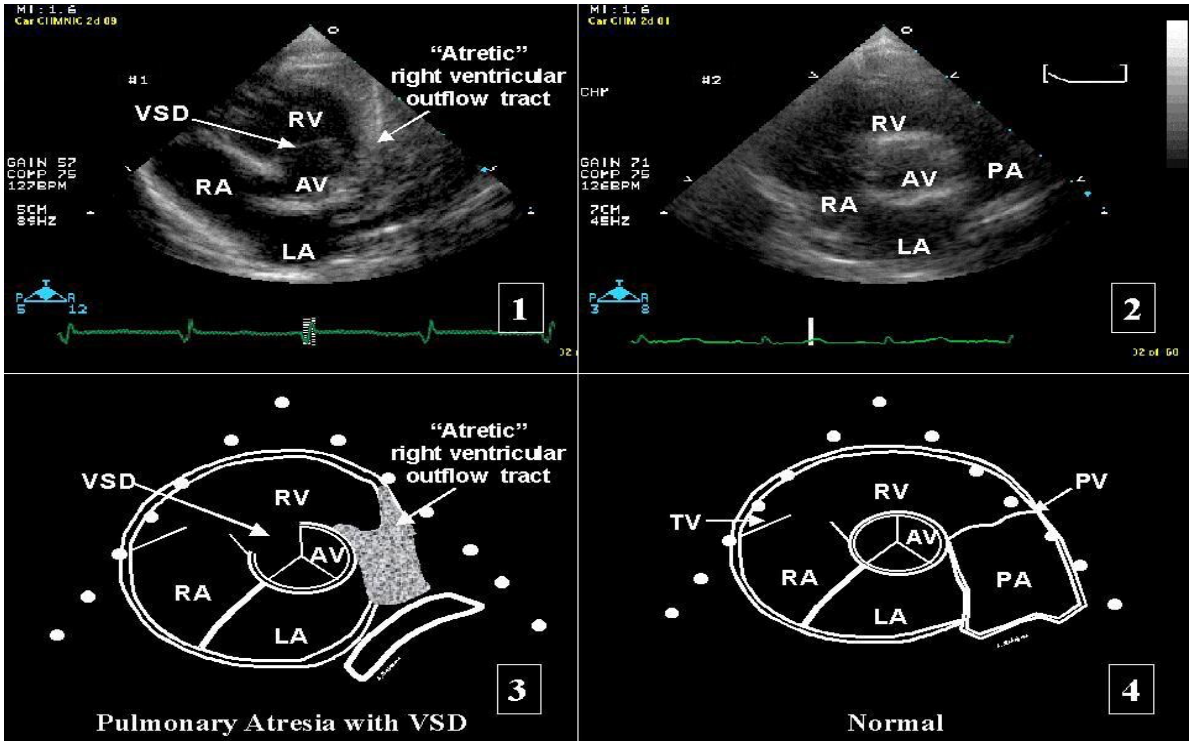

Figure 3 Pulmonary atresia with VSD. Short axis in parasternal view (1) and diagram (3) in a patient with PA-VSD. Short axis in parasternal view (2) and diagram (4) in a patient with normal anatomy, Source: Medscape.com, accessed Apirl 29th 2023)

Cardiac-MRI and Cardiac-CT:

Cardiac magnetic resonance imaging (cMRI), cardiac computed tomography (cCT) and 3D reconstruction of the anatomical structures are extremely helpful and belong to the most important elements in the diagnosis and treatment of PA-VSD. These imaging modalities can offer detailed visualization of the central pulmonary vessels and MAPCAs, albeit exact distribution may be lacking. In the collateral vessels characteristics such as stenosis and existence of dual supply may be missing[38]

Heart catheterization and angiography

After the manifestation of PA-VSD, cardiac catheterization is necessary in virtually all patients. Its primary purpose is to define the precise anatomical features of the pulmonary vasculature, enabling a comprehensive assessment of pulmonary blood flow. Additionally cardiac catheterization facilitates interventional procedures, such as

dilation or stent implantation in the PDA or MAPCAS. In some patients with membranous pulmonary atresia, it is possible to perforate the atresia using a guiding catheter or a radiofrequency current ablation catheter to establish antegrade flow[39,40] The most important piece of information in the context of the catheterization is the evaluation of the native pulmonary arteries (NPA), when present. In approximately 10-30% of patients, NPAs are complete and their size, extent as well as the supplying pulmonary segments can be quantified[41]. To determine the size of the NPAs, the McGoon ratio and the Nakata index are commonly utilised[42] The latter is calculated as the sum of the areas of both NPAs (right and left) in relation to the body surface area (BSA).

Extracardiac Evaluation

Adequate extracardiac evaluation is a critical component of the preparatory strategy for managing PA-VSD, as it significantly influences both therapeutic planning and outcomes.

As previously mentioned, (see Genetics), patients with 22q11.2 DS have an increased risk of mortality, morbidity and perioperative complications as well as a poorer long-term prognosis. Screening for this syndrome is thus essential.

Furthermore, screening should also be performed for Alagille syndrome, which is caused by a mutation in the JAG1 gene. Information regarding relevant anatomical differences between patients with Alagille phenotype and patients with 22q11. DS or no genetic abnormality is limited. However, there are reports of greater hypoplastic tendency in Alagille patients. In addition, Alagille patients are less likely to receive a single-stage total correction and have worse long-term outcomes[21,43].

In addition, extensive pulmonological screening and nutritional evaluation is performed in some centers, particularly in patients with confirmed 22q11 deletion. These patients frequently present with higher morbidity as they are more likely to suffer from airway and oropharyngeal abnormalities[44,45] , necessitating bronchoscopy in many cases[46]. Furthermore, achieving good nutritional status prior to corrective surgery is paramount,

as it significantly enhances recovery from prolonged ventilation. As a result, targeted nutritional interventions and weight optimization are often necessary.

2 THEORETICAL BACKGROUND

Palliation Procedures: PDA-Stent vs. Aortopulmonary Shunt (APS)

The definitive treatment for PA-VSD is total corrective surgery. However, to optimize outcomes, palliative therapy is usually required as an initial step. Currently, two primary palliative procedures are employed: stent implantation in the PDA or surgical creation of an aortopulmonary shunt (APS). These palliative interventions usually aim to modulate pulmonary blood flow, either by increasing or, in rarer cases, by reducing it. Furthermore, they serve a dual purpose: firstly, to relieve acute clinical symptoms and secondly, to bridge the period until the patient is in a more favorable anatomical and physiological condition for definitive corrective surgery.

2.1 PDA-Stenting Procedure

Planning of heart catheterization and pre-interventional management

Following the diagnosis of ductus-dependent pulmonary blood flow, a continuous infusion of PGE-1 is typically initiated immediately to maintain patency of the PDA. TTE is performed if ductus-dependent pulmonary blood flow (PBF) is clinically suspected, usually before the initial cardiac catheterization. This provides valuable information regarding anatomical conditions. If the TTE does not provide sufficient information, further imaging procedures such as MRI or CT angiography are used. These imaging techniques provide a clearer visualization of the systemic arterial origin and its connection to the pulmonary arteries, facilitating the identification of the most appropriate access point for PDA stenting. In PA-VSD there tends to be greater ductal

tortuosity, making CT imaging valuable in evaluating a patient's eligibility for PDA stenting. Especially the morphology of the aortic arch, the PDA (including its origin and confluence), the native pulmonary arteries (if present) and their course, and the pulmonary trunk are analyzed. Furthermore, the existence and course of MAPCAS can be determined and best evaluated by CT or MRI angiography[47]

Stent implantation in the PDA

The procedure begins with the insertion of a flexible guide wire, which is passed across the PDA. For more complex PDA morphologies, e.g. type C[48], microcatheters can also be utilized in addition to the conventional guidewire. The use of a stiff guidewire is not recommended as the risk of perforation of the PDA can be catastrophic. Prior to stent placement, it is crucial to confirm adequate constriction of the PDA in order to ensure proper anchoring of the stent. Accurate measurement must also be obtained to determine the optimal stent(s) length. Once these preparatory steps are complete, the stent is implanted. The size of the stent used is multifactorial and is an individualized decision for each patient. In general, stents with a diameter of 3, 3.5 and 4 mm are most commonly employed. Nowadays, drug-eluting stents (DES) are used in most centers. Compared to the older metal stents (BMS), these have a smaller lumen loss and an advantage due to the lower sirolimus elimination rates[49], which contribute to improved long-term outcomes. Following stent placement, the anatomy is being reassessed in order to decide whether or not further stenting is necessary. It is imperative that the guidewire remains in place until the final decision is made, as subsequent stenting after withdrawal of the wire can be significantly challenging.

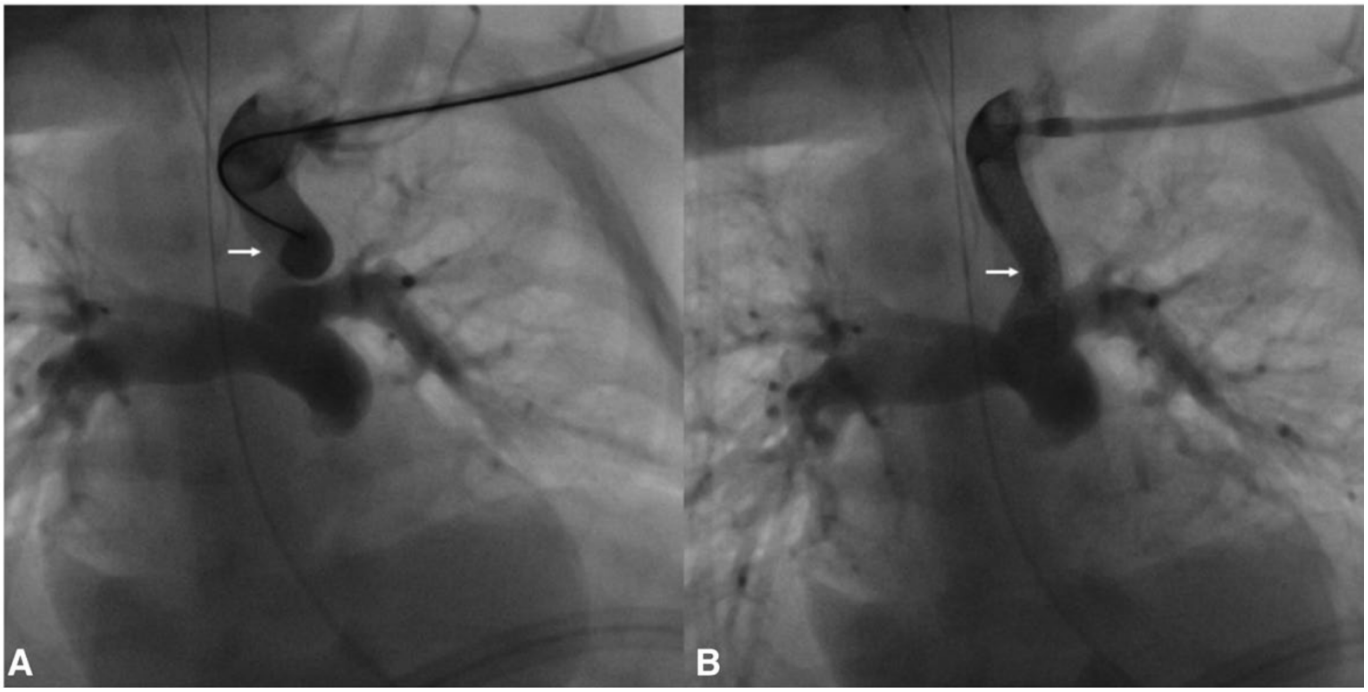

Figure 4 Pre (A)- and post (B)-PDA stent placement images from a percutaneous axillary artery approach in an infant with PA/VSD. Arrows point to the PDA and PDA stent in the respective figures. Source: Aggarwal et al, PMID 30811792

Complications:

PDA stenting is in general regarded as a safe and feasible procedure[47], although it remains an alternative to the gold-standard APS. A recent meta-analysis argued that PDA-Stenting is at least noninferior, and potentially superior, to APS [50]. However, major life-threatening complications include acute thrombosis, PDA spasm and stent-migration.

Acute Complications

Acute thrombosis is a relatively rare complication, occurring approximately in 2-3% of the cases. It should be suspected when there is a sudden decline in oxygen saturation after stent implantation and expansion. Usually, if recognized in time, the complications can be treated by several balloon-inflation maneuvers, thereby breaking up the thrombus mechanically. In some cases, a “stiff-wire” technique- mainly utilized in chronic total occlusion-may be needed to disrupt the thrombus[47,51]. Thrombolytic therapy with streptokinase or recombinant plasminogen tissue activator can also be

used. However, this approach carries a significant risk of bleeding, especially if an emergency operation is needed.[51,52]

PDA spasm is an extremely rare complication (<1%), usually triggered by guidewire manipulation within the ductus. If not managed promptly, it can be life-threatening. If the guidewire is correctly positioned at the time of spasm, immediate stent implantation usually resolves the problem [47,51,52] and PBF is restored. In cases where rapid PDA stenting is not feasible, PGE1 infusion should be resumed and the procedure reattempted after stabilization of the patient[47,52]. In cases of reoccurring PDA spasm, emergency surgical procedure with extracorporeal membrane oxygenation (ECMO) should be performed[51–53].

Stent misplacement or migration is also a potential complication. It can complicate the procedure, especially in cases where the pulmonary end of the PDA exceeds 2.5 mm in diameter. In this case, the stent may either be repositioned or secured with implantation of a second stent. Alternatively, the stent can be advanced in a peripheral branch and expanded there or be left at place, for it to be removed at a future surgical procedure. If none of the above is possible, surgical retrieval and APS needs to be performed.[47,51,54,55]

Late complications

Neointimal proliferation is a common late complication, which can lead to stent stenosis. The endothelization process typically begins within 1 month after implantation[56] and a significant portion of patients undergoing PDA Stenting will require reinterventions within the first 4 months after the procedure [57,58].

Pulmonary overflow leading to mild heart failure is another relatively frequent complication. In some cases, it could provoke pulmonary hypertension and thereby compromising systemic circulation. Adequate treatment with diuretics usually enables effective management of this complication. In cases where the stent diameter is deemed too large, additional stent implantation can be utilized to reduce the lumen size and, consequently, the effective PBF.[51,52,59]

2.2 Aortopulmonary Shunt (APS)

The aortopulmonary (AP) shunt is a surgical technique used to establish of creating a systemic-to-pulmonary artery (PA) connection, providing initial palliation in patients with PA-VSD. The primary objectives of this procedure are to ensure an adequate pulmonary blood flow to the pulmonary arteries, alleviate hypoxia and cyanosis and in general to facilitate the unproblematic somatic growth in affected patients.

History of the Aortopulmonary Shunt

The first APS was developed by Alfred Blalock and Helen Taussig, after observing increased cyanosis after PDA closure in patients with cyanotic disease. Their technique involved connecting the subclavian artery to the pulmonary artery as a way to enhance pulmonary blood flow, a procedure that became known as the Blalock-Thomas-Taussig (BTT) shunt[60].

Subsequent advancements led to various modifications such as the Dubost and Oeconomos graft between subclavian and pulmonary artery utilizing lyophilized human vessels[61], the modified Blalock-Taussig-Shunt (mBTS or mBTTs) in which a nylon, teflon or dacron prosthesis, the free left subclavian artery or interposed azygos vein were used in cases where end-to-side anastomosis between subclavian and pulmonary arteries was not feasible[62] . By the 1970s, the use of interposed expandable polytetrafluoroethylene (PTFE) graft became standard practice, significantly improving surgical outcomes. In the following decades, more techniques developed, namely the Waterson-Cooley-, Sano- or Melbourne- shunt etc.

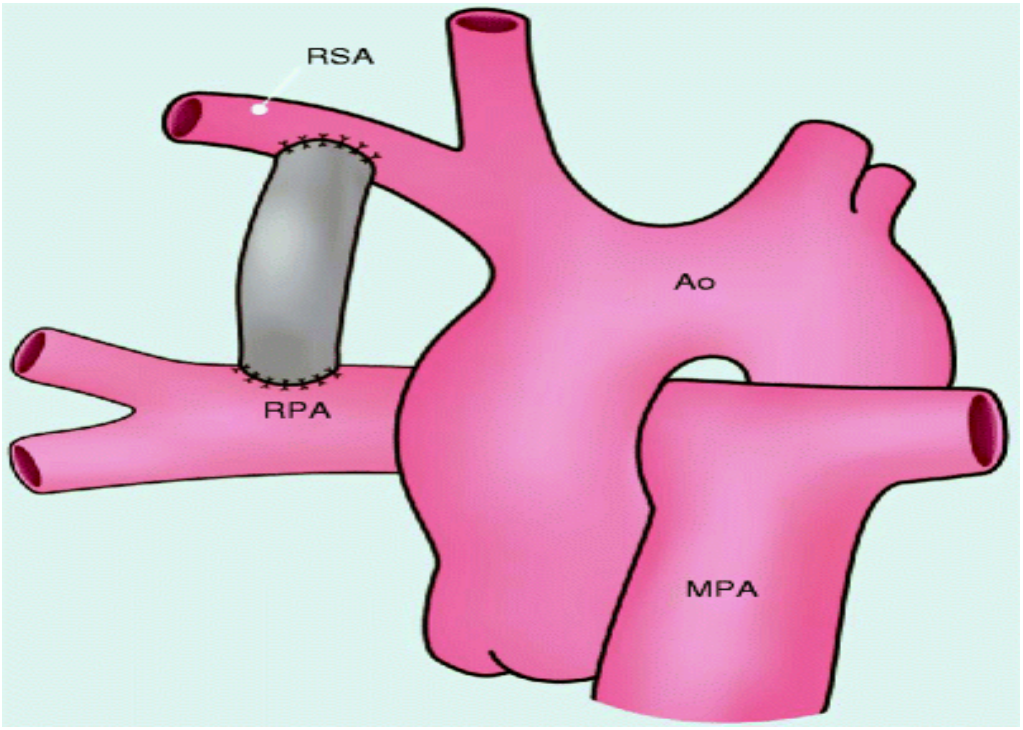

Figure 5: Modified Blalock-Taussig's shunt. AO: aorta; MPA: mainpulmonary artery; RPA: right pulmonary artery; RSA: right subclavian artery, (Source: thoracickey.com, April 29th 2023)

Central Aorto-Pulmonary Shunt

Nowadays, the most widely used variation in patients with PA-VSD is the central APS (CAPS). In CAPS, an anastomosis between the ascending aorta and the main pulmonary artery is created, using a PTFE conduit. Particularly in the setting of very small central pulmonary vessels, this technique seems to be the most reliable, as it minimizes the risk of vessel distortion.

CAPS Procedure

The procedure can be performed without the utilization of cardiopulmonary bypass. After mobilization and snaring of the branch PAs, a central, longitudinal incision is made in the main PA. Ensuring that the incision is centrally positioned is critical to prevent preferential flow to one of the branch PAs. After that, the largest feasible Gore-Tex (Gore-Tex vascular graft, W.L. Gore assoc. Inc, Elkton, MD) conduit is implanted in an end-to-side fashion. After completion of this anastomosis, the appropriate length of the graft is being ascertained. At this step, a subtle curve of the graft is important.

Then, the aorta is clamped with a side-biting clamp and a hole- usually 2.8 to 3.5 mm- is created using an aortic punch instrument. The graft is then being anastomosed to the aortic hole (side end), the graft is de-aired and the proximal end is being closed with clips.

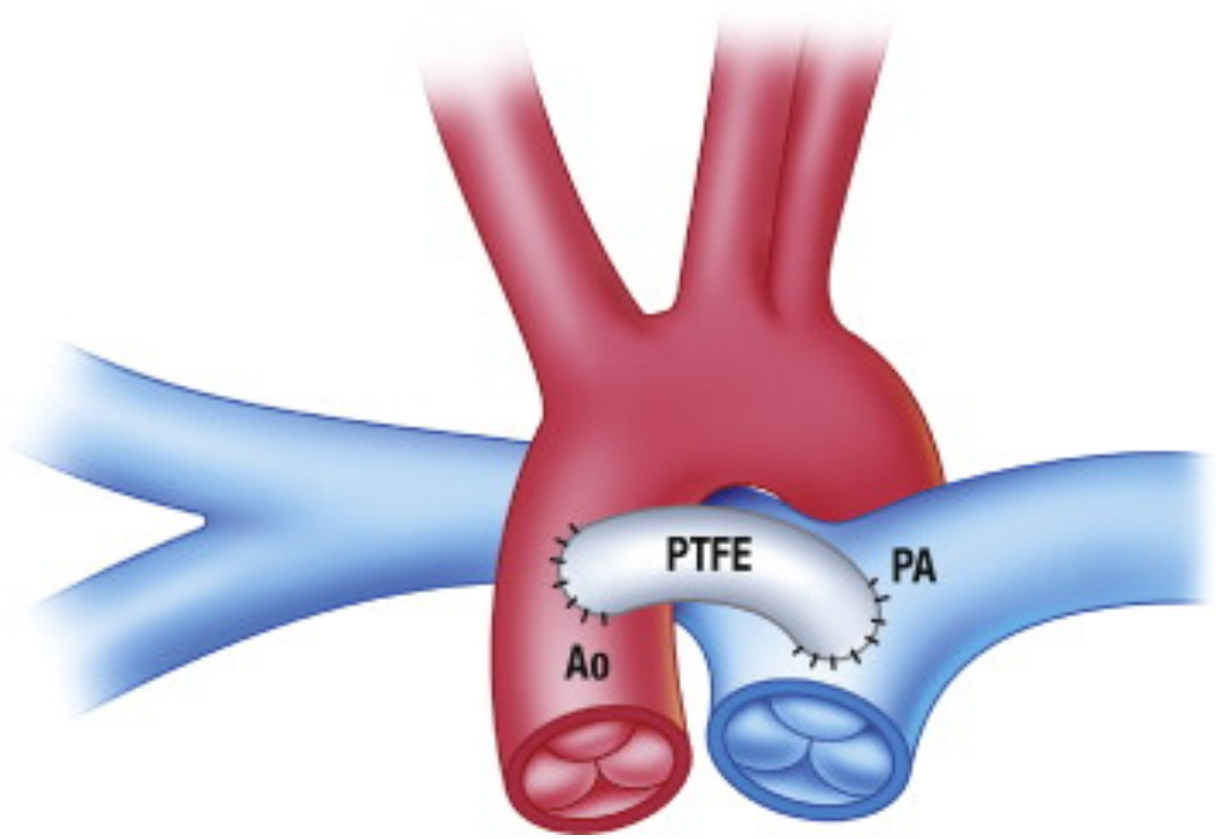

Figure 6: Central shunt. AO: aorta; PA: pulmonary artery; PTFE: polytetrafluoroethene. Source: Yuan et al, PMID: 19664575

Peri- and postoperative Complications

While CAPS have significantly improved survival in cyanotic patients, complications can still occur.

Perioperative complications primarily include the risks of bleeding and shunt thrombosis. The placement of the shunt can lead to hemorrhage due to the anastomosis

between the systemic and pulmonary circulation. Moreover, shunt thrombosis remains a critical early risk, which can cause acute hypoxia and may require immediate surgical intervention. Surgical manipulation during shunt placement also carries a risk of injuring surrounding structures like the phrenic nerve, which can further complicate the recovery process.[63]

Postoperative complications often relate to issues with shunt patency. Shunt thrombosis is one of the most serious concerns in the early postoperative period, and antithrombotic therapy is frequently used to mitigate this risk. Pulmonary overcirculation can lead to heart failure if not carefully monitored. Additionally, infection at the surgical site and fluid imbalance are other complications that can affect recovery.[64] Furthermore, pulmonary artery distortion due to the shunt can complicate future corrective surgeries.

Long-term complications

Long-term complications are largely related to the fact that these shunts are palliative rather than curative. Over time, shunts may become stenotic, which leads to reduced pulmonary blood flow and the recurrence of cyanosis. Prolonged shunting can also cause pulmonary hypertension and right ventricular failure due to increased pulmonary blood flow.[65]

2.3 Complete Surgical Repair

The complete surgical repair in patients with PA-VSD primarily consists of two components, namely the connection between RVOT and PA (+/- LPA or RPA plastic, +/- MAPCA unifocalization) and VSD closure.

The procedure prerequisites adequate growth of both PAs.

Perioperative anesthetic considerations:

Anesthetic induction is of vital importance as certain agents can exacerbate right-to-left shunting and vasodilation, thereby increasing the risk of hemodynamic deterioration. Usually, narcotics and ketamine are used [66,67]. Additionally, special care has to be taken in order to avoid air bubbles in the venous lines as these could reach the systemic circulation and provoke air embolism affecting e.g. myocardial infarction or stroke.

Right Ventricle-To-Pulmonary-Artery (RV-PA) Connection

The procedure begins with a median sternotomy. Thymus size should be taken into account before excision due to the association between PA-VSD and DiGeorge syndrome. After systematic heparinization, aortic and bicaval canulation is being performed.
In case of a pre-existing APS it is being isolated and cardiopulmonary bypass with moderate hypothermia is being performed. The shunt is then ligated proximally and distally. In cases of PA hypoplasia or stenosis at the anastomosis site, the shunt is being removed and replaced by autologous pericardium patch with simultaneous augmentation of the artery. After that, the aorta is clamped and antegrade cardioplegia is being administered. Right ventriculotomy is then performed and the VSD may be closed and an infundibular myectomy is being performed. Muscles band near the infundibular incision may be resected. Thereby, an unobstructed subpulmonary region is being created and the exposure is better aided.

VSD Closure:

Firstly, one of the most important factors about VSD is the timing of the closure as the pulmonary arteries should gave the capacity to receive the systemic venous return from the RV. In case of inadequate cross-sectional area of the PAs, acute right heart failure and low cardiac output will take place. Additionally, one of the most important factors regarding the decision for closure of the VSD is the development of left-to-right shunting through the VSD.

For the VSD closure a series of interrupted horizontal mattress sutures is being used, covering the circumference of the defect. Care should be taken into avoiding injury of the AV-ode and/or the His-Bundle.

Postoperative management:

Patients with PA-VSD undergoing complete surgical repair require the same postoperative management as any patient undergoing complex cardiac surgery with cardiopulmonary bypass. Complications such as pulmonary reperfusion injury, parenchymal hemorrhage and bronchospasm require multidisciplinary management and can severely influence perioperative mortality and prolong hospital and/or ICU stay. Pulmonary reperfusion injury affects the lobes which were underperfused before the surgical repair and requires special permissive hypercarbia and high positive end expsiratory pressure (PEEP) values. In certain cases, venovenous extracorporal membrane oxygenation (VV-ECMO) may be needed until full recovery of the lungs. Pulmonary parenchymal hemorrhage usually is self-resolving, however pre-existing coagulopathy could exacerbate such a situation. Hemmorhage in the bronchial tree is not rarely seen. In most cases, utilization of bronchoscopy and pulmonary toilet is necessary. Bronchospasm is frequently observed in the early postoperative period, particularly in younger infants. This may be attributed to extensive dissection around the tracheobronchial tree during surgery. Typically, the condition resolves within the first few days, although bronchodilatory agents may be necessary to manage symptoms during this time. Bleeding can pose a significant challenge the perioperative period. Usually, bleeding complications can be effectively minimized by utilizing small needles with 7/0 or 8/0 polypropylene sutures and the routine administration of epsilon-aminocaproic acid. In cases where bleeding remains a concern at the conclusion of the operation, the sternum may be left open, and the mediastinum packed with thrombin-soaked Gelfoam and gauze. This approach helps mitigate the risks of tamponade and the need for re-exploration due to postoperative bleeding.

3 METHODS

3.1 Study Hypothesis:

The study aimed to analyse and compare two different palliation strategies in patients with PA-VSD. All data were derived from a single center, namely the Pediatric Heart Center of the University Hospital Giessen.

The question this study aims to answer is whether there are any statistically significant differences between the two procedures in regards with various pre-, peri- as well as post-procedural (e.g. Follow-Up) variables. The variables assessed encompass early or late mortality, baseline characteristics, premature birth, chromosome anomalies, presence of PFO, presence of MAPCAs, PDA-stent and APS characteristics such as size, hospitalization duration and complications, interstage re-interventions and complications, peri-operative characteristics of the total corrective operation such as need of LPA and/or RPA stenosis/hypoplasia, need of re-intervention, complications as well as re-hospitalization, re-intervention conducted, complications and NYHA Class during follow-up.

3.2 Study design:

This study was a retrospective analysis of patient data, undergoing PDA-Closure or APS operation in our center from 1992 to 2019. Initially, 109 patients could be identified. After exclusion of patients with univentricular hearts, 64 patients were identified and were included in the analysis. 30 of them underwent PDA-Closure and 34 of them APS operation as first palliation. The patients were grouped depending on whether they received PDA-Stent or APS. The study examines differences between the two groups in several characteristics at different time points. After follow-up, 63 of the 64 patients had undergone total corrective surgery.

In total, 4 different time points were pre-set (Stages 1-4): Stage 1 refers to the first palliation procedure which was either PDA-Stent-Closure or APS operation. Stage 2 is the period between hospital discharge after Stage 1 up until the correctional operation.

Stage 3 refers to the hospitalization for the correctional operation. Stage 4 refers to the period after Stage 3 discharge until current follow up.

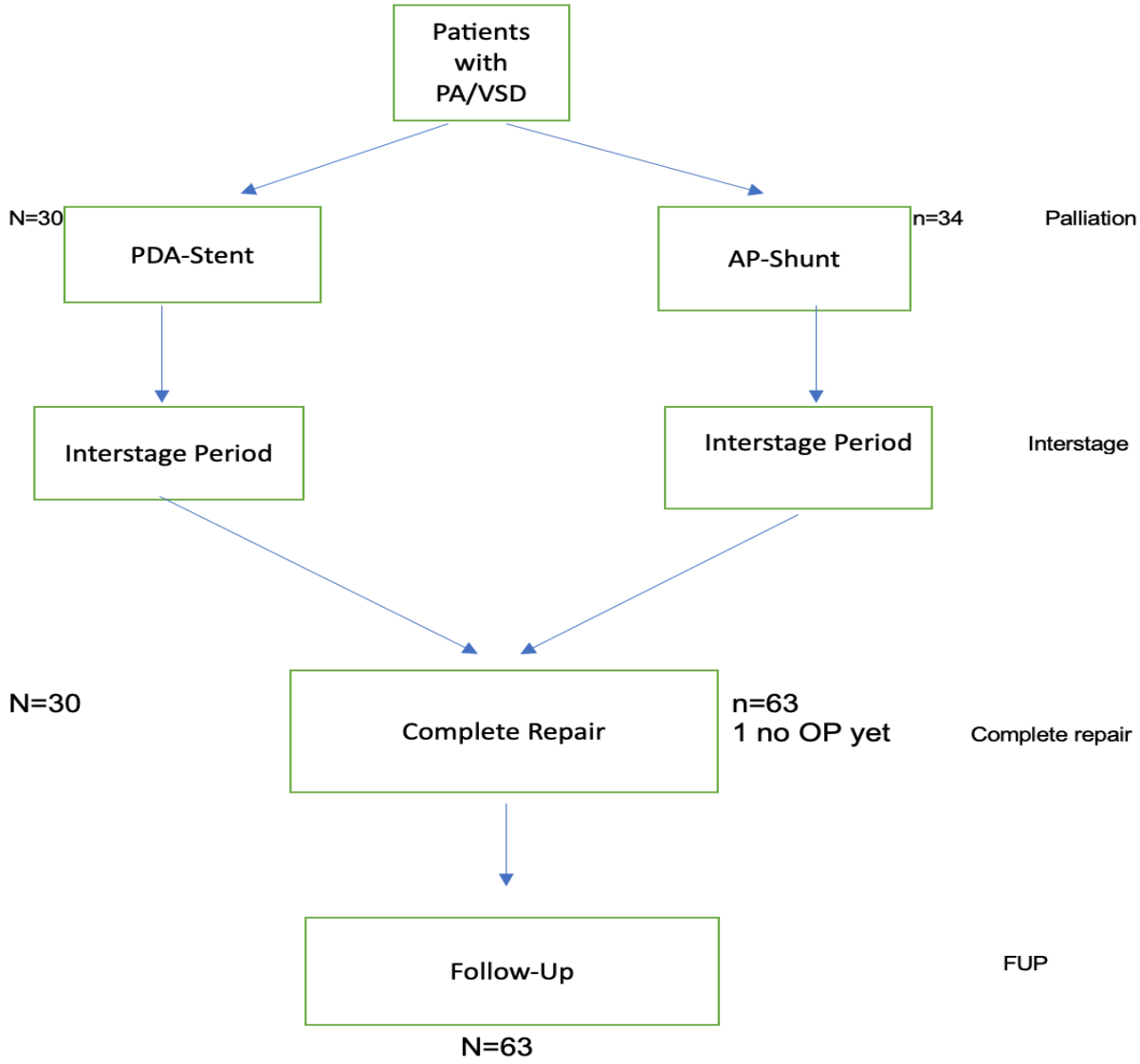

Figure 7: Schematic representation of methedology

3.3 Statistical analysis:

- All categorical measurements were presented as frequencies and percentages, while scale measures were expressed as means and standard deviations or medians followed by the IQR, depending on the results of the Shapiro Wilk test of normality and the visual inspection of the QQ plots. The Pearson's Chi square test was examined to assess the association between categorical variables and the Fisher's exact test was used when assumptions of the Chi Square were not met. The Independent samples t test was used to assess differences in normally distributed scale measurements between the two groups and the Mann Whitney test for skewed outcomes. The analysis was carried out using the SPSS v28.0 and significance was set at 0.05 in all cases. It important to clarify that regarding complications during each stage, analysis included ***patients with complications*** in order to avoid bias that could arise from patients with multiple complications, thereby disproportionately affecting the results.

4 RESULTS

4.1 Stage 1: Palliation

Table 1a. Comparison of birth characteristics

Table 1a compares birth characteristics, including weight, length, and week of birth, between patients in the Stent and Shunt groups. There are no statistically significant differences in any of the measured variables, as indicated by the p-values greater than 0.05. The average birth weight was 2.71 kg for the Stent group and 2.81 kg for the Shunt group (p = 0.659). Similarly, the average birth length was 46.72 cm for the Stent group and 48.08 cm for the Shunt group (p = 0.364). The average week of birth was 36.96 weeks for the Stent group and 37.82 weeks for the Shunt group (p = 0.347). These findings suggest no significant differences in birth characteristics between the two groups.

		N	Mean	Standard Deviation	Median	Range	*t*	*p*
Weight at birth (kgr)	Stent	30	2.71	.85	2.84	4.06	-0.444	0.659
	Shunt	34	2.81	.82	3.06	2.94		
Length at birth (cm)	Stent	30	46.72	6.27	48.00	27.50	-0.916	0.364
	Shunt	34	48.08	4.39	48.50	15.00		
Week of birth	Stent	30	36.96	3.94	38.00	18.71	-0.947	0.347
	Shunt	34	37.82	2.85	38.07	12.57		

Table 1b. Comparison of demographic and clinical characteristics

Table 1b presents a comparison of the demographic and clinical characteristics between the two groups. The variables analyzed include gender, premature birth, chromosome anomalies, specific chromosomal disorders, presence of ASD/PFO, and presence of MAPCAs. Across most categories, there were no statistically significant differences between the groups, as indicated by p-values greater than 0.05. However, a statistically significant difference was observed in the presence of MAPCA (p = 0.020), where it was

more prevalent in the Shunt group (48.4%) compared to the Stent group (20.0%). Overall, these findings suggest similar clinical profiles between the two treatment groups, with the exception of MAPCAs.

		Group				*Pearson Chi-square*	*p*
		Stent		Shunt			
		N	%	N	%		
Gender	Male	20	66.7%	22	64.7%	0.027	0.869
	Female	10	33.3%	12	35.3%		
Premature birth	Yes	9	30.0%	9	31.0%	0.007	.931
	No	21	70.0%	20	69.0%		
Chromosome anomaly	Yes	10	33.3%	14	42.4%	0.551	0.458
	No	20	66.7%	19	57.6%		
If yes, specify which anomaly	CHARGE	2	20.0%	0	0.0%	12.069	0.098
	CATCH 22	3	30.0%	12	85.7%		
	Trisomie 21	1	10.0%	1	7.1%		
	10q26.3	1	10.0%	0	0.0%		
	Rubinstein-Taybi	0	0.0%	1	7.1%		
	2q32.2 und 10p12.31	1	10.0%	0	0.0%		
	LEOPARD-Syndrom	1	10.0%	0	0.0%		
	Smith-Magenis	1	10.0%	0	0.0%		
ASD/PFO	Yes	24	80.0%	21	67.7%	1.184	0.277
	No	6	20.0%	10	32.3%		
MAPCA	Yes	6	20.0%	15	48.4%	5.442	0.020
	No	24	80.0%	16	51.6%		

Table 1c. Baseline characteristics for both groups at the point of palliation procedure

Table 1c shows the differences in Age, Weight and Length between the two groups at the point of the initial palliation procedure. The analysis showed that there is no statistically significant difference regarding Age (t = -1.692; p=0.096) but showed also that the groups differ significantly regarding Weight and Length. Specifically, stent patients appear to have less weight (M=2.95, SD=0.76) comparing to shunt patients (M=4.36, SD=3.31) and the difference is statistically significant with t = -2.241; p=0.029. Similarly, stent patients appear to have smaller length (M=48.96, SD=3.80) comparing to shunt patients (M=55.67, SD=14.63) and the difference is statistically significant with t = -2.235; p=0.022. If a non-parametric Mann-Whitney U test is performed instead of a t-test, there is also a statistically significant difference, also with respect to the values concerning age,

with U=576.000 and p=0.007. The differences appear in the comparative boxplots of Figures 8 and 9.

	N	Mean	Standard Deviation	Median	Range	t	p
Age at stent (days)	30	15.43	20.53	6.50	97.00	-1.692	0.096
Age at shunt (days)	34	253.24	768.67	34.00	3760.00		
Weight at stent (kgr)	30	2.95	.76	2.90	3.50	-2.241	0.029
Weight at shunt (kgr)	34	4.36	3.31	3.45	18.80		
Length at stent (cm)	30	48.96	3.80	49.50	19.00	-2.235	0.022
Length at shunt (cm)	34	55.67	14.63	53.00	81.00		

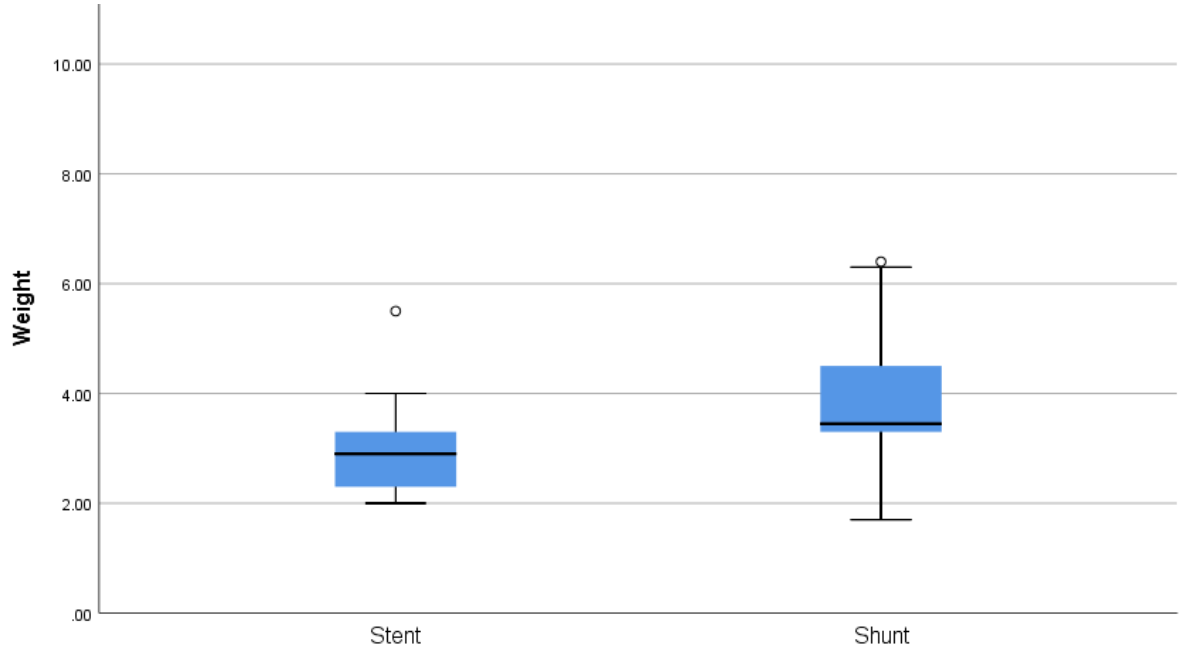

Figure 8: Boxplot highlighting the weight difference at palliation.

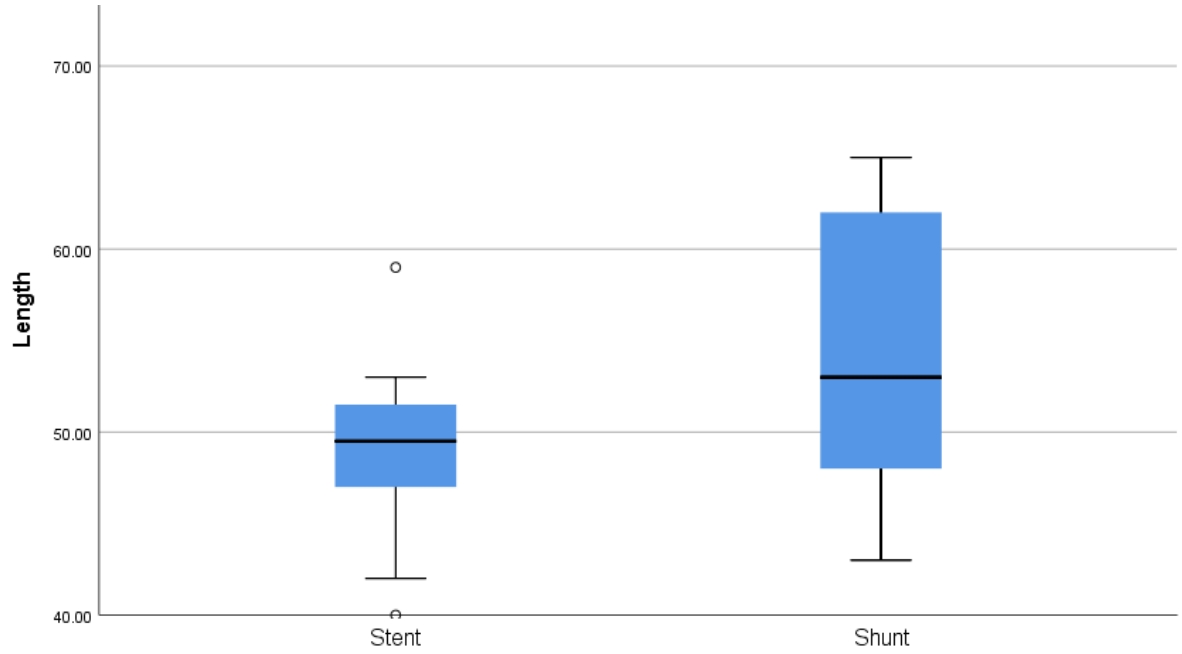

Figure 9: Boxplot highlighting the lentgh difference at palliation procedure

Table 2. Stent characteristics

Table 2 shows the characteristics of the stents of the 30 patients of the study. Eighteen patients (62.1% of them) had 1 stent implanted while 11 had 2 stents. Several types of stents were used, while the most common was “Integrity” (60.7%) and “Driver” (17.9%) and the rest were met in less than two patients each

		N	%
No of stents implantated	1	18	62.1%
	2	11	37.9%
Type of stent	Integrity	17	60.7%
	Driver	5	17.9%
	JO	1	3.6%
	NIR	2	7.1%
	Tsunami	1	3.6%
	BodyVision	1	3.6%
	Rebel	1	3.6%

Table 3. Shunt characteristics

Table 3 shows the characteristics of the shunts of 33 patients of the study. Twenty-eight patients (84.8% of them) had "central APS" while 4 mBTS and 1 had a Waterston-Cooley shunt. The average size of the 31 patients, where it was recorded, was 3.81mm with a standard deviation equal to 0.56mm. According to Table 3, PDA Ligation was recorded in 13 patients (44.8%) and cardiopulmonary bypass (CBP) in 5 only (18.5%). The mean CBP time of these 5 patients was 114.60 min with a standard deviation equal to 50.92 min.

		N	%
Type of Shunt	BT	0	0.0%
	mBTS	4	12.1%
	central APS	28	84.8%
	Waterston - Cooley	1	3.0%
PDA-Ligation	Yes	13	44.8%
	No	16	55.2%
CBP	Yes	5	18.5%
	No	22	81.5%

Table 4. Hospital- and ICU- Length-of-Stay (LOS) comparison between groups

Table 4 shows a comparison of the two groups regarding the Hospital and ICU Time. The Independent Samples t- test that was applied showed no statistically significant differences between the stent group and the shunt group regarding hospital stay time with t = -0.779; p=0.440 and no statistically significant differences regarding ICU time with t = 0.605; p=0.548.

	M	SD	N	*t*	*p*
Stent Hospital Stay time (days)	25.83	43.63	30	-0.779	0.440
Shunt Hospital Stay Time (days)	34.70	42.19	27		
Stent ICU time (days)	18.46	42.23	26	0.605	0.548
Shunt ICU_Time (days)	13.29	15.77	28		

Tables 5a-5f. Complications after initial palliation procedure

Tables 5a-5f presents the number of complications that were recorded in each group and provides also a detailed description of the specific complications encountered. The presence of complications slightly differs between the two groups, as it appears based on the Pearson's Chi Square test with X_1^2 = 0.600; p=0.438. It should be noted that in the Shunt group data on perioperative complications from 4 patients were lost to follow-up.

5a. Prevalence of complications in the Stent-group

		Frequency	Percent	Valid Percent	Cumulative Percent
	Yes	13	43.3	43.3	43.3
	No	17	56.7	56.7	100.0
	Total	30	100.0	100.0	

5b. Complications distribution in the Stent-group

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Resuscitation	1	5.9	5.9	5.9
	Pulmonary overflow	2	11.8	11.8	17.6
	PDA injury	1	5.9	5.9	23.5
	Stent malfunction	2	11.8	11.8	35.3
	Stent migration	3	17.6	17.6	52.9
	Stenosis	1	5.9	5.9	58.8
	Vascular, access site	3	17.6	17.6	76.5

	Arrhythmias	2	11.8	11.8	88.2
	PDA Spasm	2	11.8	11.8	100.0
	Total	17	100.0	100.0	

5c. Prevalence of complications in the Shunt-group

		Frequency	Percent	Valid Percent	Cumulative Percent
	Yes	16	47.1	53.3	53.3
	No	14	41.2	46.7	100.0
	Total	30	88.2	100.0	
Missing	System	4	11.8		
Total		34	100.0		

5d. Complications distribution in the Shunt-group

		Frequency	Percent	Valid Percent	Cumulative Percent
	Resuscitation	6	21.4	21.4	21.4
	Serome	1	3.6	3.6	25.0
	Chylothorax	1	3.6	3.6	28.6
	Bleeding	1	3.6	3.6	32.1
	Acute Shunt thrombosis	4	14.3	14.3	46.4

	Pericardial effusion/Tamponade	6	21.4	21.4	67.9
	Pulmonary Overflow	2	7.1	7.1	75.0
	Kidney failure	1	3.6	3.6	78.6
	Arrhythmias	5	17.9	17.9	96.4
	Wound infection	1	3.6	3.6	100.0
	Total	28	100.0	100.0	

5e. Resuscitation Crosstabulation

			Resuscitation		
			1	2	Total
Stent=1,Shunt=2	Stent group	Count	1	29	30
		% within total number of patients	3.3%	96.7%	100.0%
	Shunt group	Count	6	28	34
		% within total number of patients	17.6%	82.4%	100.0%
Total		Count	7	57	64
		% within total number of patients	10.9%	89.1%	100.0%

5f. Chi-Square Tests for comparison between resuscitation risk

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.352[a]	1	.067		
Continuity Correction[b]	2.044	1	.153		
Likelihood Ratio	3.730	1	.053		

Fisher's Exact Test				.109	.074
Linear-by-Linear Association	3.300	1	.069		
N of Valid Cases	64				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 3.28.

b. Computed only for a 2x2 table

Tables 6 and 7 concern re-interventions during hospitalization for initial palliation. The difference in the rate observed is not statistically significant, 7 in the Stent group and 10 in the Shunt group, based on the Pearson's Chi Square test with X_1^2 = 0.488; p=0.485. The tables also contain information about the type of the interventions, defined as "Cath" or "OP". In the end, the sum of interventions is estimated in each group. The ratio of "Cath" to "OP" does not either differ between the two groups based on the Pearson's Chi Square test with X_1^2 = 1.005; p=0.316.

Table 6. In hospital Re-interventions in the Stent group

Stent		N	%
In Hospital Reinterventions	Yes	7	23.3%
	No	23	76.7%
No of In-Hospital	1	4	57.1%
Reiinterventions	3	2	28.6%
	4	1	14.3%
Type of 1st. In-Hospital	Cath	1	
Reiintervention	OP	6	
Type of 2nd. In-Hospital	Cath	0	
Reiintervention	OP	3	
Type of 3rd. In-Hospital	Cath	0	
Reiintervention	OP	2	
Type of 4th. In-Hospital	Cath	1	
Reiintervention	OP	0	
Type of 5th. In-Hospital	Cath	0	
Reiintervention	OP	1	
Type of Intervenion TOTAL	Cath	2	14,3%
	OP	12	85,7%

Table 7. In hospital Re-interventions in the Shunt group

Shunt		N	%
In Hospital Reinterventions	Yes	10	31.3%
	No	22	68.8%
No of In-Hospital	1	5	50.0%
Reiinterventions	2	4	40.0%
	4	1	10.0%
Type of 1st. In-Hospital	Cath	4	
Reiintervention	OP	6	
Type of 2nd. In-Hospital	Cath	1	
Reiintervention	OP	6	
Type of 3rd. In-Hospital	Cath	0	
Reiintervention	OP	1	
Type of 4th. In-Hospital	Cath	0	
Reiintervention	OP	1	
Type of ReIntervenion TOTAL	Cath	5	29,4%
	OP	12	70,6%

4.2 Stage 2: Interstage Period

Table 8. Interstage period time comparison by group

Table 8 describes the Interstage Period time, compared in the two groups as median and IQR. The Mann Whitney U test that is applied indicates a statistically significant difference between the two groups (M-W = 723;p=0.002). Specifically higher times are expected in the shunt group as shown on the comparative boxplot of Figure 3.

	N	Median	IQR	p
Stent	29	161.00	303.5	0,002
Shunt	34	387.00	677.25	

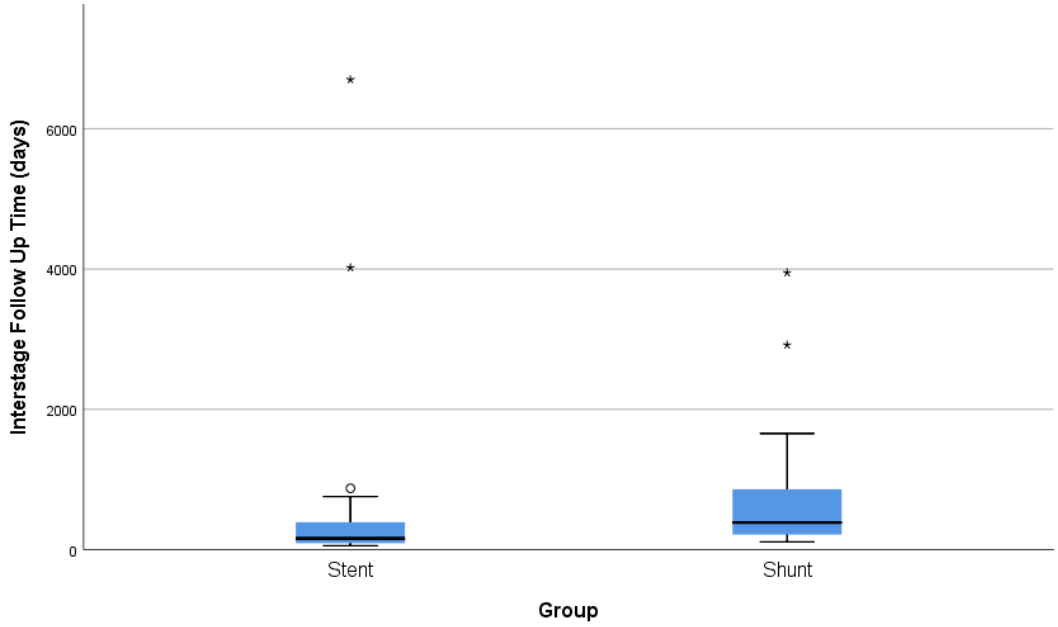

Figure 10 : Boxplot highlighting the longer interstage-period in the APS group

Tables 9a-9c. Complications and complications distribution in the interstage period.

Interstage mortality was not observed in either of the two groups but complications were observed and are attributed in Tables 9a-9c. The total number of complications was not significantly different in the two groups based on the Pearson's Chi Square test with $X_1^2 = 1.647$; p=0.199. PDA stent stenosis was the most frequently met complication in the Stent group (71,4%) while the Shunt thrombosis was the most frequently met complication in the Shunt group (50%).

Table 9a. Interstage complications by group

		Group					
		Stent		Shunt			
		N	%	N	%	X^2	*p*
nterstage	Yes	7	23.3%	13	38.2%	1.647	0,199
Complications	No	23	76.7%	21	61.8%		

Table 9b. Complications during interstage period in the Stent-Group

	Frequency	Percent	Valid Percent	Cumulative Percent
Stent-Stenosis/-Thrombosis	5	71.4	71.4	71.4
Stent migration	1	14.3	14.3	85.7
Aborted corrective surgery (intraoperatively)	1	14.3	14.3	100.0
Total	7	100.0	100.0	

Table 9c. Complications during interstage period in the Shunt-Group

	Frequency	Percent	Valid Percent	Cumulative Percent
Shunt-Stenosis/-Thrombosis	7	50.0	50.0	50.0
Pulmonary Overflow	2	14.3	14.3	64.3
Resuscitation	1	7.1	7.1	71.4

	Seroma	1	7.1	7.1	78.6
	LPA-Stenosis	1	7.1	7.1	85.7
	MAPCA-Stenosis	1	7.1	7.1	92.9
	Stroke	1	7.1	7.1	100.0
	Total	14	100.0	100.0	

Table 10. Interstage interventions by group

Table 10 describes the number of interventions in each group, as well as the total number of interstage interventions and the type of each intervention. At the bottom line of the table, the total number of interventions appears along with the percentage and the comparison in the two groups. The table indicates that the total number of interventions was not significantly different in the two groups based on the Pearson's Chi Square test with X_1^2 = 0.166; p=0.683. It is also evident that the distribution of the number of interstage interventions is almost identical in the two groups. The total number of reinterventions was 11 "Cath" and 6 "OP" for the stent group and 14 "Cath" and 10 "OP" for the shunt group. This difference was not statistically significant based on the Pearson's Chi Square test with X_1^2 = 0.169; p=0.680

		Group					
		Stent		Shunt			
		N	%	N	%	X^2	*p*
Intervention during interstage period	Yes	10	33.3%	13	38.2%	0.166	0.683
	No	20	66.7%	21	61.8%		
No of Interstage Interventions	1	5	50.0%	6	46.2%		
	2	4	40.0%	6	46.2%		
	4	1	10.0%	0	0.0%		
	6	0	0.0%	1	7.7%		
Type of 1st. Interstage Intervention	Cath	7		7			
	OP	3		6			
Type of 2nd. Interstage Intervention	Cath	3		4			
	OP	2		3			
Type of 3rd. Interstage Intervention	Cath	1		0			
	OP	0		1			
Type of 4th. Interstage Intervention	Cath	0		1			
	OP	1		0			
	Cath	0		1			

Type of 5th. Interstage Intervention	OP	0		0			
Type of 6th. Interstage Intervention	Cath	0		1			
	OP	0		0			
Type of Re-Intervention TOTAL	Cath	11	64,7%	14	58,3%	0.169	0.680
	OP	6	35,3%	10	41,7%		

4.3 Stage 3: Complete Repair

Table 11. Patients with complete repair by group

Table 11 shows the patients with complete repair by group. There was only one patient, specifically in the stent group, with no complete repair. As expected, the difference was not statistically significant comparing to the total of complete repair patients of the Shunt group. Fisher's exact test that was equal to 1.151; p=0.283.

			Group			
			Stent	Shunt	*Fisher's test*	*p*
Complete Repair	Yes	N	29	34	1.151	0.283
		%	96.7%	100.0%		
	No	N	1	0		
		%	3.3%	0.0%		

Table 12. Patients' characteristics at complete repair.

Table 12 shows the Age, Weight and Length in each group of patients. The Independent samples t test that was applied showed statistically significant differences in all three parameters. Regarding Age, higher values were observed in the Shunt group (M=960.79, SD= 1504.86) comparing to the Stent group (M=258.17, SD= 232.57) with t = -2.685; p=0.011. Regarding Weight, higher values were observed in the Shunt group (M=12.09, SD= 9.21) comparing to the Stent group (M=6.76, SD= 2.54) with t = -3.145; p=0.003. Finally, regarding Length, higher values were observed in the Shunt group (M=82.27, SD= 27.23) comparing to the Stent group (M=66.12, SD= 10.48) with t = -3.109; p=0.003. The differences are attributed by the comparative boxplots of Figures 4, 5 and 6.

	Group	N	M	SD	*t*	*p*
Age at OP (days)	Stent	29	258.17	232.57	-2.685	0.011
	Shunt	34	960.79	1504.86		
Weight at OP (days)	Stent	29	6.76	2.54	-3.145	0.003

	Shunt	32	12.09	9.21		
Length at OP (days)	Stent	29	66.12	10.48	-3.109	0.003
	Shunt	32	82.27	27.23		

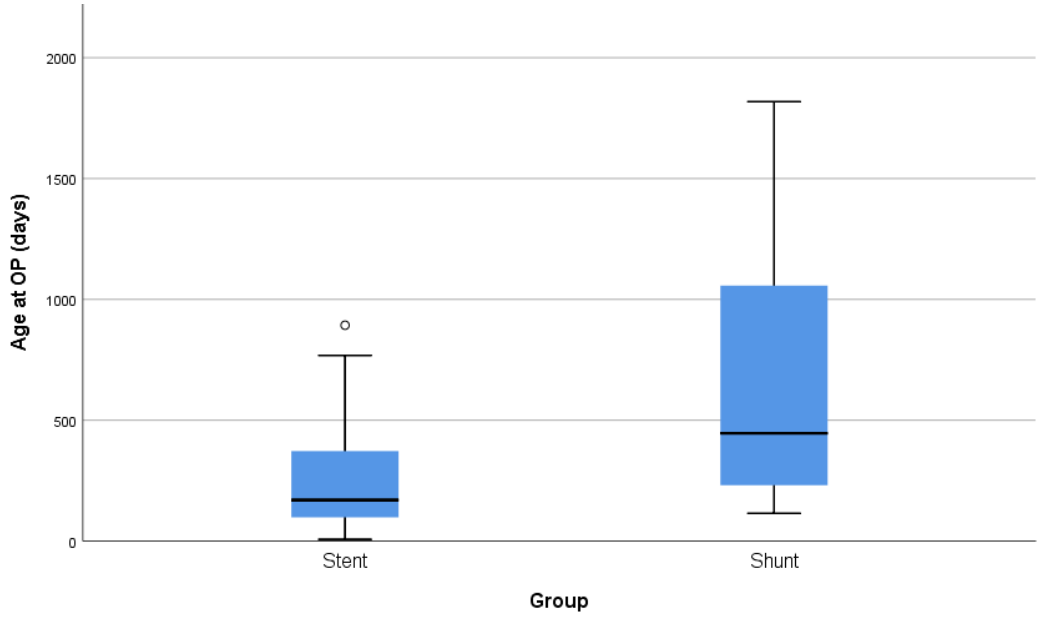

Figure 11 Boxplot highlighting the age difference at the point of corrective surgery

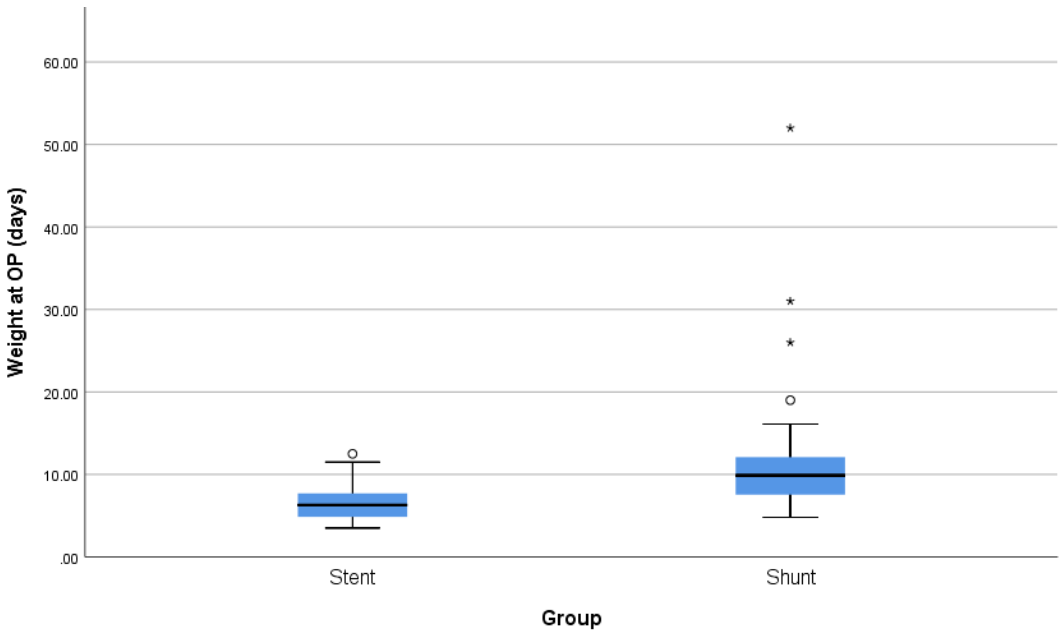

Figure 12 Boxplot highlighting the weight difference at the point of corrective surgery

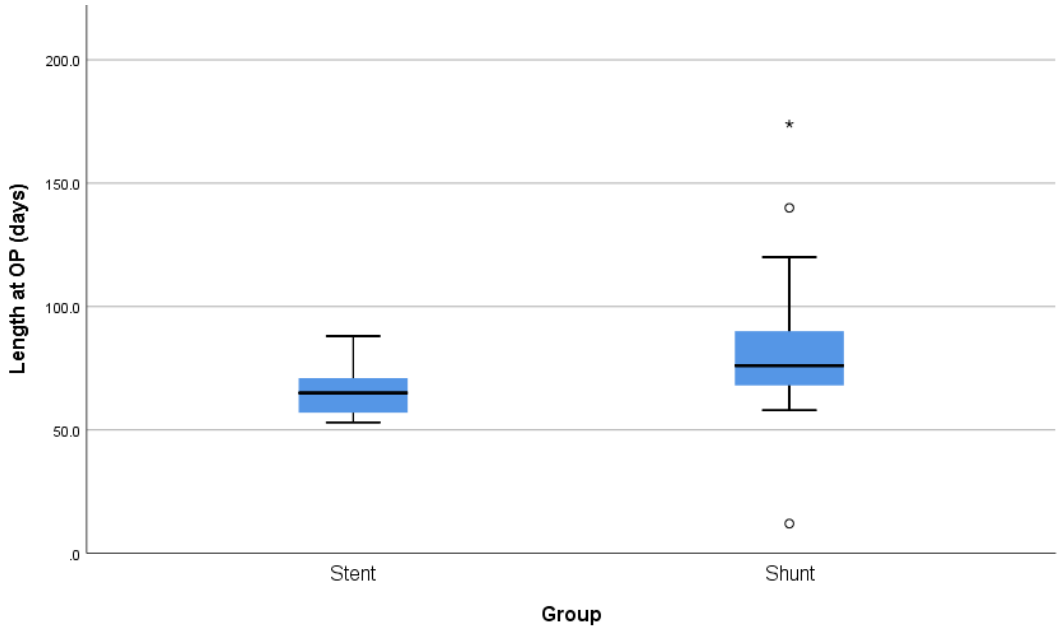

Figure 13 Boxplot hightlighting the length difference at the point of corrective surgery

Table 13. RV-PA connections in each group

Table 13 presents the type of RV-PA connections that were recorded in each group. The types of connections differ between the two groups, but not statistically significant as it appears, based on the Pearson's Chi Square test with $X_4^2 = 5.979$; p=0.141. The most common types in both groups were Contegra Conduit (Medtronic, Inc, Minneapolis, Minn) and "Autolog, Xenoperikard, Dacron".

			Stent	Shunt	X^2	*p*
RV-PA Connection	Contegra Conduit	N	11	20	5.979	0.141
		%	37.9%	58.8%		
	Autolog, Xenoperikard, Dacron	N	10	4		
		%	34.5%	11.8%		
	Corematrix	N	1	1		
		%	3.4%	2.9%		
	Homograft	N	0	1		
		%	0.0%	2.9%		
	Other	N	7	8		

	%	24.1%	23.5%	

Table 14. LPA and RPA Enlargement in each group

Table 14 presents the LPA Enlargement, the RPA Enlargement and either of them, that were recorded in each group. Regarding LPA Enlargement the percentage differs statistically significant between the two groups, based on the Pearson's Chi Square test with X_1^2 = 8.213; p=0.004. Specifically, LPA enlargement was observed in 65.5% of the Stent group and in 29.4% in the Shunt group. The difference was smaller in the RPA enlargement and not statistically significant, X_1^2 = 1.605; p=0.205. When considering either RPA or LPA, the percentage differs statistically significant between the two groups, based on the Pearson's Chi Square test with X_1^2 = 6.513; p=0.011 with a higher percentage in the Stent group again. The differences are attributed by the comparative bar charts of Figures 7 and 8.

		Group					
		Stent		Shunt			
		N	%	N	%	X^2	*p*
LPA Enlargement	Yes	19	65.5%	10	29.4%	8.213	0.004
	No	10	34.5%	24	70.6%		
RPA Enlargement	Yes	13	44.8%	10	29.4%	1.605	0.205
	No	16	55.2%	24	70.6%		
LPA or RPA Enlargement	No	9	32.1%	22	64.7%	6.513	0.011
	Yes	19	67.9%	12	35.3%		

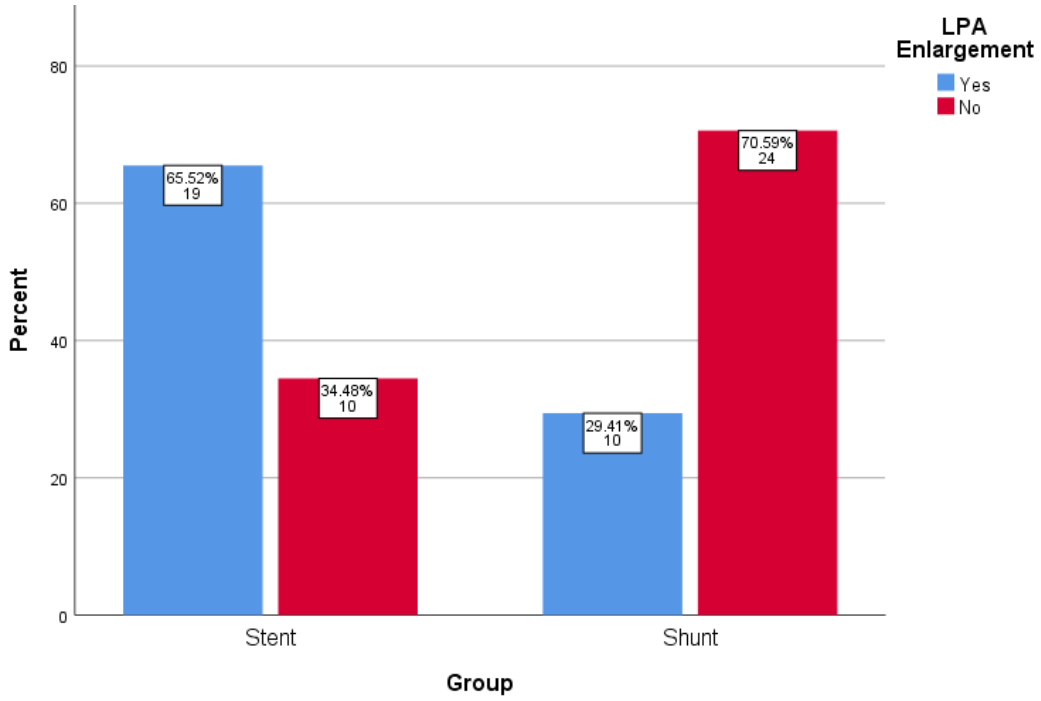

Figure 14 Bar chart highlighting the difference in need for LPA enlargement between the two groups

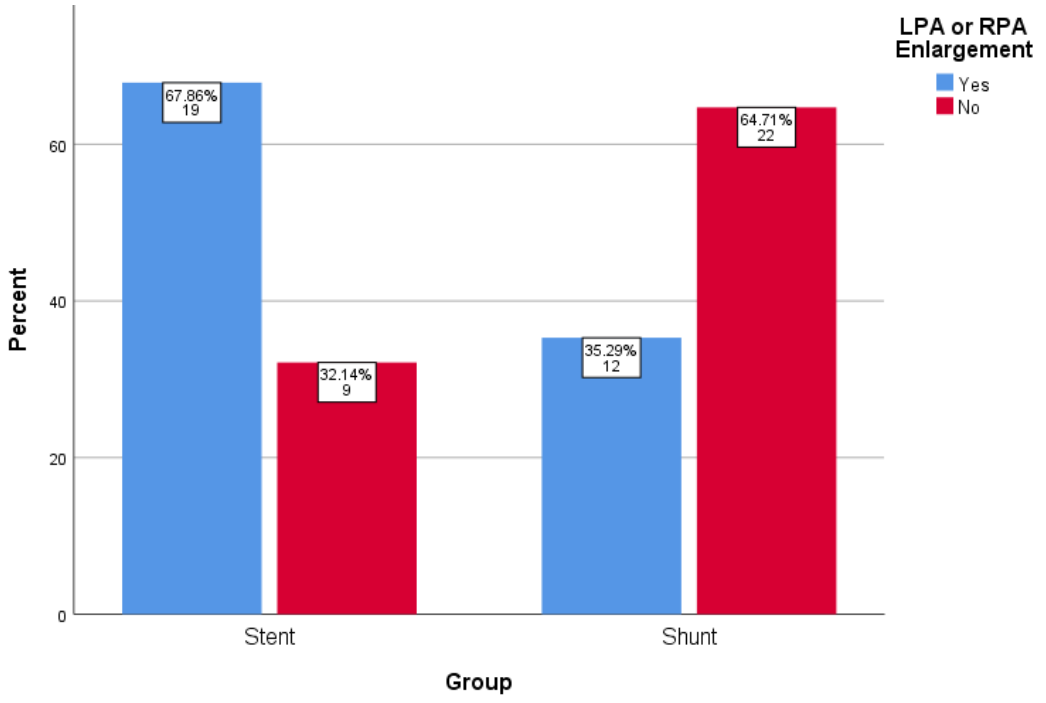

Figure 15 Bar chart highlighting the difference in need for either LPA or RPA enlargement between the two groups

Table 15. MAPCA Unifocalization in each group

Table 15 presents data on MAPCA unifocalization outcomes. While unifocalization was utilized in 3.4% of patients in the Stent group compared to 18.2% in the Shunt group, the difference was not statistically significant ($X^2 = 3.272$, $p = 0.109$).

			Group		X^2	p
			Stent	Shunt		
MAPCA unifocalization	Yes	N	1	6	3.272	0.109
		%	3.4%	18.2%		
	No	N	28	27		
		%	96.6%	81.8%		

Here insert short text explaining finding on MAPCA unifocal

Table 16. Hospital, ICU, CBP and ischemia time by group

Table 16 presents the Hospital, ICU, CBP and ischemia times that were recorded in each group. The means and standard deviations appear and the results of the statistical comparisons between the two groups based on the independent samples t test also appear. None of the aforementioned times differ significantly between the two groups and the reported p values were in all cases above 0.18

	Group	N	M	SD	t	p
Hospital Time (days)	Stent	29	30.97	45.406	1.365	0.183
	Shunt	33	19.30	7.927		
ICU_time (days)	Stent	29	13.10	19.229	0.732	0.467
	Shunt	32	10.38	8.288		
CBP time (min)	Stent	29	210.21	42.125	-1.173	0.246
	Shunt	30	226.27	61.581		
Ischemia time (min)	Stent	29	106.48	31.407	-0.647	0.520
	Shunt	30	112.93	43.936		

Tables 17a-17c presents the complications at this stage and the specific types of them on the two groups. Based on the Pearson's Chi Square test with $X_1^2 = 0.037$; p=0.847 it is clear that the percentage of complications does not differ statistically significant in the two groups. Moreover, in the distribution analysis, there is a consistency in the type of complications with Arrhythmias and Bleeding complications being the most commonly observed ones in both groups.

Table 17a. Complications by group

		Group			
		Stent		Shunt	
		N	%	N	%
Complications	Yes	20	69.0%	22	66.7%
	No	9	31.0%	11	33.3%

17b. Perioperative complications during corrective surgery in the Stent-Group

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Resuscitation	3	9.7	9.7	9.7
	Pulmonary Overflow	1	3.2	3.2	12.9
	Bleeding	7	22.6	22.6	35.5
	Dry tamponade	2	6.5	6.5	41.9
	Low Cardiac Output	2	6.5	6.5	48.4
	Pericardial effusion/Tamponade	2	6.5	6.5	54.8
	SIRS	1	3.2	3.2	58.1
	Arrhythmia	10	32.3	32.3	90.3
	Renal failure	2	6.5	6.5	96.8
	Pulmonary hypertensive crisis	1	3.2	3.2	100.0
	Total	31	100.0	100.0	

17c. Perioperative complications during corrective surgery in the Shunt-Group

	Frequency	Percent	Valid Percent	Cumulative Percent
Resuscitation	1	3.2	3.2	3.2
Pulmonary overflow	1	3.2	3.2	6.5
ECMO	1	3.2	3.2	9.7
Bleeding	9	29.0	29.0	38.7
Dry tamponade	1	3.2	3.2	41.9
Low cardiac output syndrome	2	6.5	6.5	48.4
Pericardial effusion/Tamponade	2	6.5	6.5	54.8
SIRS	1	3.2	3.2	58.1
Arrhythmia	11	35.5	35.5	93.5
Renal failure	1	3.2	3.2	96.8
Pneumothorax	1	3.2	3.2	100.0
Total	31	100.0	100.0	

Table 18. Postoperative reinterventions by group

Table 18 describes the number of interventions in each group, as well as the total number of Re-interventions and the type of each intervention. At the bottom rows of the table, the total number of interventions appears along with the percentage and the comparison in the two groups. The table indicates that the total number of interventions was not significantly different in the two groups based on the Pearson's Chi Square test with X_1^2 = 0.201; p=0.654. It is also evident that the distribution of the number of interventions is rather similar in the two groups. The total number of reinterventions was 5 "Cath" and 10 "OP" for the stent group and 6 "Cath" and 9 "OP" for the shunt group. This difference was not statistically significant based on the Pearson's Chi Square test with X_1^2 = 0.144; p=0.705

		Stent		Shunt			
		N	%	N	%	X^2	*p*
Reinterventions	Yes	10	35.7%	10	30.3%	0.201	0.654
	No	18	64.3%	23	69.7%		
No of Reiinterventions	1	7	70.0%	6	60.0%		
	2	1	10.0%	3	30.0%		
	3	2	20.0%	1	10.0%		
Type of 1st Reintervention	Cath	4		5			
	OP	6		5			
Type of 2nd Reintervention	Cath	0		0			
	OP	3		4			
Type of 3rd Reintervention	Cath	1		1			
	OP	1		0			
Reinterventions total	Cath	5	33,3%	6	40,0%	0.144	0.705
	OP	10	66,7%	9	60,0%		

4.4 Stage 4: Follow-Up

Table 19. Follow-up days in the two groups

Table 19 presents the number of follow up in days that were recorded in each group. The means and standard deviations appear and the results of the statistical comparisons between the two groups are based on the independent samples t test. There is a significantly larger follow up in the Shunt group (Median = 4991, IQR = 5148.5) comparing to the follow up of the Stent group (Median =1541, IQR = 2815) with M-W =642.5 ;p=0.039. The difference is attributed by the comparative boxplot of Figure 9 that follows.

FUP_Days					
	N	Median	IQR	MW	p
Stent	29	1541	2815		0.039
Shunt	34	4991	5148.5		

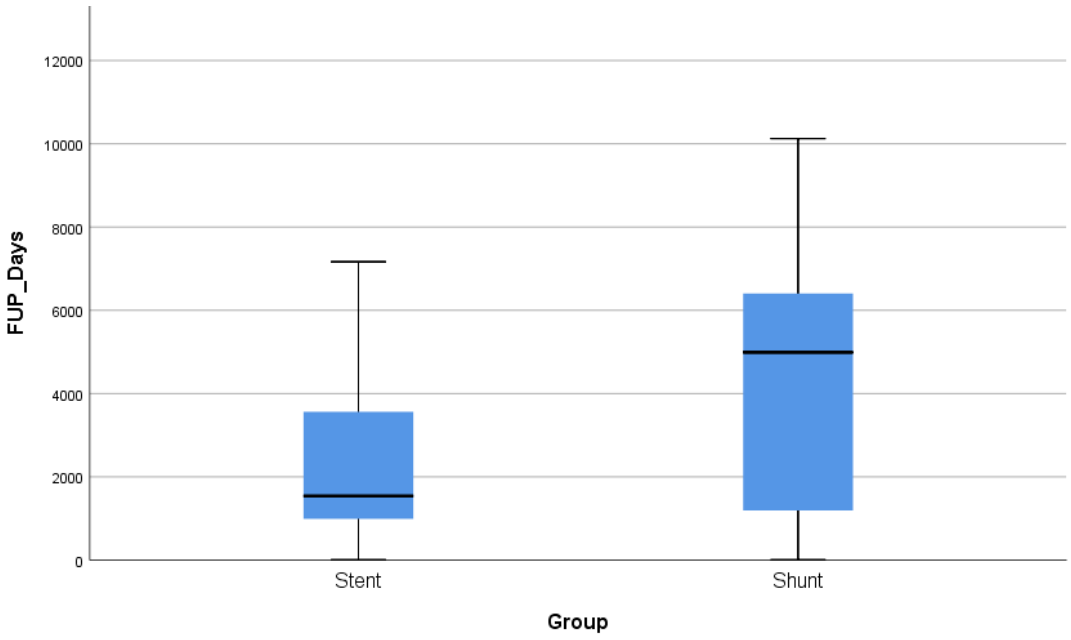

Figure 16 Boxplot highlighting the difference in follow-up duration between the two groups.

Table 20. Early and Late Mortality by group

Table 20 shows that early mortality was observed in only 1 patient in the Shunt group which is a non-significant difference to the Stent-group of patients based on the Pearson's Chi Square test with X_1^2 = 0.867; p=0.352. No late mortality was observed in either group.

		Group					
		Stent		Shunt			
		N	%	N	%	X^2	*p*
Early_mortality	Yes	0	0.0%	1	2.9%	0.867	0.352
	No	29	100.0%	33	97.1%		
Late_Mortality	Yes	0	0.0%	0	0.0%	-	-
	No	29	100.0%	34	100.0%		

Table 21. Reinterventions during Follow-Up

Table 21 describes the number of interventions in each group during Follow up, as well as the type of each intervention. At the bottom line of the table, the total number of interventions appears along with the percentage and the comparison in the two groups. The table indicates that the total number of interventions was not significantly different in the two groups based on the Pearson's Chi Square test with X_1^2 = 3.082; p=0.082, although this difference is close to statistical significance. The distribution of the number of Re interventions at the follow up is rather similar in the two groups although more 3-fold reinterventions were observed in the Shunt group (7) comparing to the Stent group (1). The total number of reinterventions was 29 "Cath" and 18 "OP" for the stent group and 38 "Cath" and 36 "OP" for the shunt group. This difference was not statistically significant based on the Pearson's Chi Square test with X_1^2 = 1.246; p=0.246.

		Stent		Shunt			
		N	%	N	%	X^2	*p*
Re Interventions during FUP	Yes	18	62.1%	27	81.8%	3.025	0.082
	No	11	37.9%	6	18.2%		
No of Re-Interventions	1	8	44.4%	7	25.9%		
	2	3	16.7%	7	25.9%		
	3	1	5.6%	7	25.9%		
	4	4	22.2%	2	7.4%		
	5	0	0.0%	1	3.7%		
	6	0	0.0%	2	7.4%		
	7	2	11.1%	1	3.7%		
Type of 1st. Re-Intervention	Cath	10		18			
	OP	8		9			
Type of 2nd. Re-Intervention	Cath	9		10			
	OP	1		10			
Type of 3rd. Re-Intervention	Cath	3		1			
	OP	4		12			
Type of 4th. Re-Intervention	Cath	4		4			
	OP	2		2			
Type of 5th. Re-Intervention	Cath	0		3			
	OP	2		1			
Type of 6th. Re-Intervention	Cath	1		1			
	OP	1		2			
Type of 7th. Re-Intervention	Cath	2		1			
Follow up Reinterventions total	Cath	29	78.4%	38	51.4%	1.246	0.264
	OP	18	21.6%	36	48.6%		

Table 22. Number of PA/LPA/RPA reinterventions by stage and group.

Table 22 presents a comparison of the number of PA/LPA/RPA interventions observed in the two groups. Most of them appear in the Follow up stage in both groups. In both groups, the total number or reinterventions is n=24, thus no further statistical test were performed regarding the cumulative burden of reinterventions.

Group	No. Of PA/LPA/RPA Interventions	N	Minimum	Maximum	Mean	Std. Deviation
Stent	In hospital	0				

	Interstage	4	1	2	1.50	.577
	Complete Repair	3	1	1	1.00	.000
	Follow-Up	17	1	7	2.24	1.786
Shunt	In hospital	1	1	1	1.00	.
	Interstage	2	1	1	1.00	.000
	Complete Repair	6	1	1	1.00	.000
	Follow-Up	15	1	5	2.20	1.207

5 DISCUSSION

This study compares the outcomes of two palliative approaches, PDA stenting and aortopulmonary (AP) shunt, in neonates with pulmonary atresia (PA) and ventricular septal defect (VSD) with biventricular heart physiology. The goal of these interventions is to provide pulmonary blood flow and allow these patients to survive until a complete surgical repair is possible. This study analysed a comprehensive range of clinical parameters, including patient demographics, perioperative outcomes, complication rates, reinterventions, stent and shunt characteristics as well as long-term outcomes, to shed light on the relative advantages and limitations of these two widely used approaches.

5.1 Stage 1 – Initial Palliation Procedure

Patient Demographics and Baseline Characteristics at birth and at palliation procedure.

As it can be demonstrated in Table 1a there was no statistically significant differences in birth characteristics, including weight, length, and gestational age, between the two groups. These findings suggest that the cohorts were comparable in terms of their baseline physical attributes at birth ($p > 0.05$ across all variables). This parity in baseline characteristics ensures that subsequent analyses of outcomes can be interpreted without bias arising from physical disparities between the groups.

Similarly, Table 1b highlights homogeneity in most demographic and clinical variables, including gender, premature birth rates, chromosomal anomalies, and the presence of atrial septal defects (ASD) or patent foramen ovale (PFO). Notably, there were no statistically significant differences in these categories, indicating that the groups were well-matched across most clinical characteristics. However, the presence of major aortopulmonary collateral arteries (MAPCAs) showed a significant difference ($p = 0.020$), being more common in the Shunt group (48.4%) compared to the Stent group (20.0%). The higher prevalence of MAPCAs in the Shunt group may reflect a clinical

preference for employing shunt procedures in cases with complex pulmonary vasculature requiring augmented blood flow, as MAPCAs often indicate more intricate anatomical challenges and often the need for unifocalization in the initial palliation procedure[68].

Furthermore, our data regarding baseline characteristics at the initial palliation procedure, highlight significant differences between the two groups in terms of weight and length. While no statistically significant difference in age was found between the Stent and Shunt groups ($t = -1.692$; $p = 0.096$), significant differences were observed for both weight and length. Patients in the Stent group had a lower mean weight ($M = 2.95$ kg, $SD = 0.76$) compared to those in the Shunt group ($M = 4.36$ kg, $SD = 3.31$), with the difference being statistically significant ($t = -2.241$; $p = 0.029$). In a similar study, comparing PDA-Stent with APS, patients included had a weight at intervention of 4.6 and 5.5 kg, respectively[69] while another study reported weight at intervention of 3.2 and 3.1 kg respectively[54]. This heterogeneity highlights the differences in patient population included in reported studies as well as the various preferences of each centre. Similarly, patients in the Stent group were shorter ($M = 48.96$ cm, $SD = 3.80$) than those in the Shunt group ($M = 55.67$ cm, $SD = 14.63$), and this difference was also statistically significant ($t = -2.235$; $p = 0.022$). These findings were further supported by a non-parametric Mann-Whitney U test, which revealed statistically significant differences in age as well ($U = 576.000$; $p = 0.007$).

The observed differences in weight and length may indicate that patients undergoing stent procedures are typically smaller and possibly less developed than those receiving shunts. This difference likely reflects clinical decision-making practices, as stents may be preferred in smaller patients due to their minimally invasive nature and lower surgical burden compared to shunts. The significant difference in age observed through non-parametric testing suggests that patients receiving shunts may also be older at the time of palliation, likely due to differences in the timing and progression of their clinical conditions. It is important to note that in these categories, variables were calculated using mean values and standard deviations rather than medians. The results were likely influenced by four outliers in the Shunt group, who underwent initial palliation at a late age. Two of these patients had ages of 3,764 days and 2,665 days at the time of their initial palliation.

Overall, these findings underline the importance of considering patient-specific characteristics, such as size and age, when selecting the most appropriate initial palliation strategy. The lack of significant differences in other clinical and demographic parameters supports the comparability of the two groups, strengthening the validity of subsequent evaluations of procedural outcomes. However, the observed disparity in MAPCA prevalence highlights the need for careful consideration of anatomical factors when selecting between stent and shunt procedures. Finally, it is important to note that the literature search yielded a relatively limited number of results, and not all of them are directly applicable to the discussion presented in this section.

PDA-Stent Characteristics

The choice and characteristics of the stents used in the PDA-Stent group provide insight into the variability in interventional cardiology approaches. In this study, **62.1%** of patients received one stent, while **37.9%** required two stents. Among the stents used, the **Integrity** stent was the most common (60.7%), followed by the **Driver** stent (17.9%). Less commonly used stents included the **NIR**, **JO**, and **Tsunami** stents, which were used in only a few cases ($N < 2$ for each).
The choice of stent type is influenced by the anatomy of the PDA and the specific physiological needs of the patient. The **Integrity** stent, for instance, is a flexible, low-profile device that can be deployed in tortuous anatomies and is thus favoured in smaller infants. The **Driver** stent, being more rigid, is preferred in cases where more structural support is needed. The need for multiple stents (37.9% of patients) may reflect either technical challenges during the initial procedure or the progression of stenosis requiring additional stenting. Stent-related complications such as migration or malfunction, which occurred in **15.4%** of patients respectively, highlight the technical difficulties associated with stenting small, fragile vessels.

While no direct comparison was made between stent types in terms of outcomes in this study, the differences in material, design, and flexibility of stents can influence long-term durability and the risk of complications such as restenosis or stent fracture. These factors are critical when considering the suitability of stenting versus shunting, as the need for future catheter-based reinterventions is often tied to the initial choice of stent.

Interestingly, to our knowledge there are currently no studies directly comparing different stent models. Most studies provide data on stent size, type of stent (bare metal vs. drug-coated)[70–72] and/or access site (femoral vs. carotid/axillaris)[73,74].

AP-Shunt Characteristics

In the AP-Shunt group, **84.8%** of patients received a central APS, while a smaller subset (12.1%) underwent a modified Blalock-Taussig shunt (mBTS). One patient received a Waterston-Cooley shunt. The average shunt size was **3.81 mm** (SD = 0.56 mm).

Shunt size and type are critical determinants of the success of the procedure. Central shunts are preferred when the anatomy allows, as they are thought to provide more reliable, uniform pulmonary blood flow. The **mBTS**, a variation of the classic Blalock-Taussig shunt, is more commonly used when a smaller, less disruptive approach is required, particularly in cases where anatomy or patient size limits the feasibility of a central shunt. The larger number of central shunts in this study may reflect the tendency to use this approach in patients with relatively favourable anatomy, while the use of mBTS may indicate more complex or restrictive anatomies. Interestingly, **44.8%** of patients in the AP Shunt group required patent ductus arteriosus (PDA) ligation, which could indicate a pre-existing PDA or an effort to control blood flow more effectively during the procedure. Only a small percentage of patients (**18.5%**) required cardiopulmonary bypass (CPB), with an average bypass time of **114.60 minutes** (SD = 50.92 minutes). The relatively low usage of bypass may reflect the avoidance of this technique in most AP Shunt procedures due to its association with increased post-operative morbidity and mortality.

Hospital- and Intensive Care Unit- (ICU) Length-of-Stay (LOS)

The length of hospital- and ICU-LOS, as primary indicators of post-operative recovery, did not reveal a statistically significant difference between the groups. Hospital stay duration was **25.83 days** (SD = 43.63) for the PDA-Stent group and **34.70 days** (SD = 42.19) for the AP Shunt group ($t = -0.779$, $p = 0.440$). However, ICU stay was **18.46 days** (SD = 42.23) for the PDA-Stent group and **13.29 days** (SD = 15.77) for the AP-Shunt group ($t = 0.605$, $p = 0.548$).

These findings are partially consistent with the results reported in current literature. Reduced hospital-LOS for patients undergoing PDA-Stent has consecutively been reported in independent studies[75,76] as well as in a meta-analysis[77]. However, in our study, ICU-LOS was slightly longer in the PDA-Stent group, a finding that is not commonly observed. A possible explanation for this, could be the relatively small sample size as well as ICU capacities of the referring hospitals, which may have contributed to longer stays.

Complications

The study revealed that complications occurred slightly more frequently in patients from the AP Shunt group (53.3%) compared to the PDA-Stent group (43.3%), though this difference was not statistically significant ($X^2 = 0.600$, $p = 0.438$). Higher procedural complications during AP-Shunt procedures have also been reported in a recent meta-analysis[78] as well as in a large retrospective study[79]. However, the both studies are c constrained by the limitation that they did not directly compare PDA stenting and AP shunt in the context of PA-VSD, they instead encompassed patients with various underlying cyanotic diseases with duct-dependent blood flow requiring palliation.

Complications in the PDA-Stent group included stent migration (15.4%) and vascular complications from the access site (17,6%). Interestingly, in the AP-Shunt group, the most prominent complications were resuscitation (21,4%), and pericardial effusion (21,4%). However, an independent analysis on resuscitation risk between the groups, yielded no statistically significant differences (Pearson Chi-Square 3,352, p=0,067).

The types of complications differ based on the nature of the procedure. PDA stenting, though minimally invasive, carries risks related to the physical properties of the stent, such as migration, thrombosis, or restenosis. On the other hand, AP-shunts, being more invasive, are associated with resuscitation and significant surgical risks, including thrombosis and hemodynamic instability Acute shunt thrombosis, in particular, is a life-threatening complication that may necessitate urgent surgical reintervention, adding to the complexity of care for these patients.

Reinterventions rate

When comparing reinterventions, several studies show a favourable outcome for patients undergoing AP-Shunt[79–81]. It is important to note, that these studies from current literature were designed differently and had various outcome measurements. In this study, reintervention rates were calculated separately for each individual Stage. Interestingly, we found comparable reintervention rates between the two groups, both during the initial hospital stay. 23.3% of the patients in the PDA-Stent group and 31.3% in the AP Shunt group required reintervention ($X^2 = 0.488$, $p = 0.485$). Despite the fact that there is no statistically significant difference, our finding is contradictory to those reported in concurrent studies.

AP-Shunt patients often require open surgical reinterventions due to shunt occlusion or failure, which carries higher morbidity and risk. Despite expecting patients with PDA-Stent to require more catheter-based interventions, our study showed that patients from this group require in majority of the cases surgical reintervention. More specifically, 70.6% of reinterventions conducted in the AP Shunt group required surgery, compared to 85,7% in the PDA-Stent group ($p = 0.316$). Whereas there is no statistically significant difference, it underlines the fact the initial PDA-Stent does not necessarily mean complete avoidance of additional surgery. Ultimately, more often than not, the choice between surgical and percutaneous reintervention to address shunt and pulmonary blood flow challenges, is inherently guided by the institutional programmatic philosophy.

5.2 Stage 2 - Interstage Period

The interstage period was defined as the period between hospital discharge after the initial palliation procedure up to the point before admission for corrective surgery. We compared both groups in terms of complications and reinterventions required.

Stage 2 was significantly shorter in the PDA-Stent group compared to the AP Shunt group. The median interstage period for PDA-Stent patients was **161.00 days** (IQR = 303.5), while for AP Shunt patients, it was significantly longer at **387.00 days** (IQR =

677.25; Mann Whitney U = 723, p = 0.002). The shorter interstage period in the PDA-Stent group may be attributed to more favourable pulmonary artery growth, as well as the more controlled and uniform blood flow provided by the stent. This earlier readiness for complete repair could reduce the risk of long-term complications associated with prolonged exposure to abnormal hemodynamic. In contrast, the longer interstage period in the AP Shunt group reflects the increased risk of complications such as thrombosis or insufficient pulmonary artery growth, which can delay the timing of definitive repair.

Complications

Complications during the interstage period were more common in the AP-Shunt group. In total, 38.2% of patients in the AP Shunt group experienced interstage complications, compared to 23.3% in the PDA-Stent group ($X^2 = 1.647$, $p = 0.199$). Although the overall difference was not statistically significant, the nature of the complications is critical to consider.

The most frequent interstage complication in the PDA-Stent group was PDA stent stenosis or thrombosis, occurring in 71.4% of patients who experienced complications. Similarly, the AP-Shunt group, 50 % of interstage complications in the AP-Shunt group were due to shunt thrombosis or stenosis.

These differences reflect the fact that while stents are prone to restenosis, particularly in growing neonates, shunts are also at high risk of thrombosis, especially if flow dynamics are suboptimal or the shunt becomes occluded. It can be hypothesized that patients in both groups exhibit a relatively high incidence of stenosis or thrombosis, suggesting that optimized antiplatelet or anticoagulation protocols may be necessary to mitigate this complication more effectively.

The existing literature does not provide specific analyses of interstage complications. However, indirect inferences can be drawn from available data on reinterventions during this period, under the assumption that the most significant complications would likely necessitate an intervention. Nonetheless, a comprehensive understanding of the full spectrum of interstage complications remains lacking, highlighting the need for

further research to systematically assess morbidity during this critical phase and develop targeted strategies for early identification and management.

Reinterventions

Regarding the burden of reinterventions during the interstage period, no significant difference between the two groups was observed (Chi-square = 0.166, p= 0.683). Specifically, 33.3% of patients in the stent group and 38.2% of those in the AP-Shunt group required interventions. Based on the fact that no significant difference was observed in the complications rate either, as mentioned above, this result is rather expected.

The distribution of the number of interstage interventions was nearly identical, with most patients undergoing one or two procedures (accounting for 90% in both groups). However, one patient in the AP-Shunt group underwent six interventions, highlighting an outlier in the dataset.

Regarding the type of interventions, catheter-based procedures were more common than surgical procedures in both groups. The stent group had 11 catheter-based interventions (64.7%) compared to 14 (58.3%) in the AP-shunt group. Similarly, operative interventions account for 6 (35.3%) in the stent group and 10 (41.7%) in the shunt-group. This difference was also not statistically significant (Chi-square =0.169, p=0.680).

These findings suggest that the burden of interstage interventions is comparable between the two groups, both in frequency and type. The lack of significant different may reflect similarities in post-procedural care need, underlying patient characteristics and/or the unique patient approach and treatment choice of the centre.

The existing body of literature presents inconsistent findings. A study by McMullan et al yielded comparable results to those observed in this research, wherein no significant differences were identified in the number of interval interventions required to sustain adequate pulmonary blood flow[82]. Conversely, another study reported significantly higher reintervention rates within the stent cohort [83.] The latter findings were

subsequently corroborated by a propensity-score analysis which similarly showed no significant differences in reintervention rates, even during extended follow-up periods[79].

5.3 Stage 3 – Definitive surgical repair

Timing of corrective surgery

The ultimate goal of palliative procedures in patients with PA-VSD is to facilitate eventual complete repair, restoring normal cardiac function and anatomy. It must be noted, that
the decision for corrective surgery is a unique, patient-tailored decision, which is being made by several factors.

In this study, **96.7%** of patients in the PDA-Stent group and **100%** of patients in the AP Shunt group progressed to complete repair (Fisher's exact test = 1.151, p = 0.283), indicating that both approaches are effective in facilitating effective palliation until corrective surgery. One patient from the stent group is still did not receive corrective surgery yet. Achievement of complete repair is significantly higher than the reported ones, who usually report a rate of around 70%.[84,85]

However, the timing of complete repair was significantly earlier in the PDA-Stent group. The mean age at the time of complete repair was **258.17 days** (SD = 232.57) in the PDA-Stent group, compared to **960.79 days** (SD = 1504.86) in the AP Shunt group (t = -2.685, p = 0.011). As a result, patients in the PDA-Stent group were significantly lighter (M = 6.76 kg, SD = 2.54) and shorter (M=66.12 cm, SD 10.48) compared to the AP Shunt group (M = 12.09 kg, SD = 9.21; t = -3.145, p = 0.003 and M=82.27, SD=27.23, t=-3.109, p=0.003) at the time of complete repair. The earlier timing of complete repair in the PDA-Stent group is a significant clinical finding as the appropriate timing of corrective surgery in patients with PA-VSD is unclear. The presence or absence of MAPCAs is crucial for this decision, as patients with MAPCAs show distinctive features and require far more complex treatment. This becomes apparent when examining the prevalence of MAPCAs in this cohorts. As seen in Table 1b, there is a statistically significant difference between the two groups (Stent-group

20%, Shunt-group 48.4%, Chi-Square=5.442, p=0.02). Therefore, it could be assumed that the higher prevalence of MAPCAs led to a longer waiting period for corrective surgery in order to conduct a patient-tailored unifocalization of the MAPCAs intraoperatively, after having secured an adequate growth of the pulmonary artery vasculature, a strategy which has already been implemented elsewhere[86].

Connection between pulmonary artery (PA) and right ventricle (RV)

The type of RV-PA connection employed during complete repair is critical for ensuring optimal right ventricular function and pulmonary blood flow. According to Table 13, the most commonly used RV-PA connection was the **Contegra® Conduit** (Medtronic,USA) utilized in 37.9% of the PDA-Stent group and 58.8% of the AP Shunt group. The second most common connection type was **Autologous, Xenopericardial, or Dacron conduits**, which were used in 34.5% of the PDA-Stent group and 11.8% of the AP Shunt group.

A valve conduit fulfils a dual function. Firstly, it facilitates an unimpeded extracardiac pathway for blood to travel from the RV to the PA and it prevents regurgitation into the RV during diastole. The selection of inappropriate conduit is influenced by several consideration, notably its availability, ease of implantation, and anticipated durability. In developing countries, the economic burden can be a significant factor in the decision-making process[87].

The choice of conduit reflects the need for durable, flexible connections that can grow with the patient and minimize the risk of obstruction or thrombosis. **Contegra Conduits** are often favoured due to their flexibility and resistance to calcification, making them a common choice for paediatric cardiac repairs and gaining widespread popularity.[88] The higher use of autologous and xenopericardial conduits in the PDA-Stent group suggests that this approach may allow for greater flexibility in conduit selection, potentially leading to more customized repairs based on individual patient anatomy.

Intraoperative left pulmonary artery (LPA) or right pulmonary artery (RPA) enlargement

Insufficient pulmonary artery growth poses a significant barrier to surgical repair in patients with cyanotic congenital heart disease.[89–91] In this cohort, rigorous inspection of the LPA and RPA was performed intraoperatively and appropriate enlargement was conducted, when needed.

Table 14 highlights statistically significant differences between the two groups. We found that **65.5%** of patients in the PDA-Stent group had the need for LPA enlargement, compared to only **29.4%** in the AP Shunt group ($X^2 = 8.213$, $p = 0.004$). When considering either LPA or RPA enlargement, the rate was again, significantly higher in the PDA-Stent group (67.9%) compared to the AP Shunt group (35.3%; $X^2 = 6.513$, $p = 0.011$).

These findings suggest that patients undergoing PDA-stenting as a palliation procedure, develop significantly more often underdeveloped LPAs, which require correction during surgery. Therefore, it could be assumed that AP shunting promotes more balanced pulmonary artery growth compared to PDA-Stenting. This finding stands in contrast to the results of current literature. Santoro et al, who investigated the growth of diminutive pulmonary arteries following PDA-Stenting and showed balanced results[92]. However, it is important to note that their study did not directly compare patients undergoing PDA-Stenting with those receiving AP-Shunt as first palliation. Furthermore, PA-growth was assessed using the Nakata-Index rather than intraoperative examination. Additionally, the same study group found no difference in PA growth when directly comparing PDA-Stenting and surgical palliation, albeit with two major limitations: the patients suffered from cyanotic disease and not PA-VSD only and the number of patients was extremely small (n=27)[93]. Finally, in another study, which researched the short-outcomes after palliation with PDA-stent or surgical shunt, the 6-month follow-up revealed significantly larger RPA diameter in the stent group[94], thereby indirectly confirming our findings.

Unifocalization of MAPCAs

Unifocalization of MAPCAs in PA-VSD is a critical surgical strategy aimed at optimizing PBF and improving overall patient outcomes. It involves surgically combining collateral arteries into a single conduit to improve pulmonary blood flow[95].

The presence of MAPCAs and their management can have significant impact on pulmonary artery growth and the success of complete surgical repair. In this study, MAPCA unifocalization was more commonly performed in the AP Shunt group (18.2%) compared to the PDA-Stent group (3.4%), although this difference was not statistically significant ($X^2 = 3.272$, $p = 0.109$). This difference is expected because the prevalence of MAPCAs was higher in the AP-Shunt group, as mentioned above.

The surgical approach can vary depending on the anatomical configuration of MAPCAs, which may originate from various sources, including the aorta, subclavian artery or even coronary arteries[95]. Studies have shown that unifocalization can lead to favourable outcomes, particularly when performed in a timely manner[95,96]. However, complications such as stenosis of the unifocalized vessels and the need for reinterventions can occur, particularly in patients, with complex anatomical configurations[97]. It should be noted that, to our knowledge, there are no published studies examining the impact of MAPCAs in a direct comparison between PDA-stent or shunt as first palliation.

Hospital- and ICU-Stay, CPB- and Cross-clamp-time

Hospital and ICU stay durations are critical indicators of post-operative recovery. Mean hospital stay was longer in the PDA-Stent group ($M = 30.97$ days, $SD = 45.41$) compared to the AP Shunt group ($M = 19.30$ days, $SD = 7.93$), but this difference was not statistically significant ($t = 1.365$, $p = 0.183$). These findings are relatable

The mean ICU time was also slightly longer in the PDA-Stent group ($M = 13.10$ days, $SD = 19.23$) compared to the AP Shunt group ($M = 10.38$ days, $SD = 8.29$; $t = 0.732$, $p = 0.467$).

In terms of CBP time, the mean cardiopulmonary bypass time in the PDA-Stent group was 210.21 minutes (SD = 42.13), while in the AP Shunt group, it was 226.27 minutes (SD = 61.58; t = -1.173, p = 0.246).

Similarly, ischemia time was 106.48 minutes (SD = 31.41) in the PDA-Stent group compared to 112.93 minutes (SD = 43.94) in the AP Shunt group (t = -0.647, p = 0.520).

Perioperative complications

The overall complication rate was comparable between the two groups, with 69.0% of PDA-Stent patients and 66.7% of AP Shunt patients experiencing at least one complication ($X^2 = 0.037$, p = 0.847).

In the PDA-Stent group, the most common complication was arrhythmias, occurring in 32.3% of patients, followed by bleeding with 22.6% and resuscitation with 9.7%. In the shunt-group, arrhythmias were also the most frequent complication with 35.5%, followed by bleeding with 29%. Resuscitation occurred less than in the stent-group (3.2%), although without a statistically significant difference.

The incidence of arrhythmias and conduction disturbances is significant due to both their prevalence and clinical consequences. In a cohort of patients under 3 months of age undergoing surgery, the prevalence of arrhythmias was 29%[98], which aligns with our findings, although the population in our study was older at the time of surgery. During the early postoperative period, right bundle branch block (RBBB) is the most frequently observed disturbance. In cases involving ventriculotomy, RBBB occurs in over 90% of the patients[99]. Complete atrioventricular block is rare with a reported incidence ranging from 1% to 3%. The most common arrhythmia is junctional ectopic tachycardia (JET) with a prevalence of 48%.[98]

Intraoperative bleeding represented the second most frequently observed complication in both groups. It is important to highlight that the location of haemorrhage plays a pivotal role in clinical outcomes. in these cases, is extremely important. Pulmonary

haemorrhage typically resolves spontaneously over time; however, any underlying coagulopathy should be corrected. In contrast, haemorrhage within the bronchial tree haemorrhage is relatively common and necessitates intervention with bronchoscopy and pulmonary lavage to ensure adequate airway clearance[100]

Resuscitation was documented in both groups, with a higher occurrence in the stent group. Notably, no perioperative mortality was recorded, as evidenced by the collected data. This finding reinforces the procedure's feasibility and safety, even in instances requiring intraoperative or early postoperative resuscitation. This observation is further supported by current data. Recent studies similarly report a low mortality rate, ranging from 0% to 3%, reinforcing the procedure's safety profile[101–103].

Additionally, one major complication among paediatric patients undergoing surgical repair for congenital diseases with VSDs is pulmonary arterial hypertension (PAH). Incidence of PAH ranges from 5% to 15%[104]. In this cohort, only one instance PAH is seen in each group, with a prevalence of 3.2%, which is lower than the minimum average documented in literature.

Postoperative re-interventions

The analysis of reinterventions in the stent and shunt groups, as presented in Table 18, reveals no statistically significant differences between the two treatment modalities. The overall proportion of patients requiring reintervention was comparable (35.7% in the stent group vs. 30.3% in the shunt group), with a Pearson's Chi-Square test result of $X^2 = 0.201$; $p = 0.654$, indicating no significant association between the intervention type and the need for reintervention. Furthermore, the number of reinterventions per patient followed a similar distribution, with most requiring only one additional procedure. The types of reinterventions, whether catheter-based (Cath) or operative (OP), were also proportionally similar between groups, further supporting the lack of a significant difference ($X^2 = 0.144$; $p = 0.705$). These findings suggest that both treatment strategies exhibit comparable mid-term procedural stability in terms of the need for subsequent interventions.

There is a limited amount of data available on the rates of in-hospital reinterventions during the immediate postoperative period. The current literature primarily focuses on

long-term reintervention rates, often overlooking the frequency and impact of early postoperative interventions.

The most common indication for early reintervention following repair is residual right ventricular outflow tract (RVOT) obstruction[100]. Residual stenosis may occur at the infundibular level, valvular level, or within the branch pulmonary arteries (PAs). The incidence of reoperation varies significantly depending on the patient population. A study conducted by the group at Texas Children's Hospital reported an early reoperative rate of 3%[105]. Catheterisation, including interventional procedures to treat stenosis or the embolization of MAPCAs, has been demonstrated to be safe, even in the early postoperative period following cardiac surgery[106]. Our analysis does not account for the specific indications for each reintervention. However, the comparable rates observed in both groups, both in terms of percentage and type of reintervention, strongly suggest the consistent utilisation of both procedural approaches. Furthermore, these findings indicate that catheter-based and surgical reinterventions in the immediate postoperative period are not mutually exclusive but rather complementary. The integration of both techniques facilitates the management of adverse events, ultimately contributing to improved patient outcomes

5.4 Stage 4 – Follow-up and long-term outcomes

Follow-Up duration and Mortality

The duration of follow-up was significantly longer in the AP Shunt group (Median = 4991 days/13.7 years, IQR = 5148.5) compared to the PDA-Stent group (Median = 1541 days/4.22 years, IQR = 2815; Mann Whitney U = 642.5, p = 0.039).

The longer follow-up duration for the AP Shunt group likely reflects the more established use of shunting as a palliative approach, whereas PDA stenting is a relatively newer procedure with less long-term data available.

Mortality data revealed that one patient in the AP Shunt-group experienced in the early postoperative period after corrective surgery, while no deaths were recorded in the

PDA-Stent group ($X^2 = 0.867$, $p = 0.352$). Cause of death is unknown due to loss to follow-up.

The absence of late mortality in either group is an encouraging finding, indicating that both approaches are highly effective in facilitating survival to definitive repair and beyond.

Long-term reinterventions

The analysis of reinterventions during follow-up, as presented in Table 21, indicates no statistically significant difference between the two groups in terms of overall intervention rates, despite a trend toward significance ($X^2 = 3.082$; $p = 0.082$). The proportion of patients requiring reintervention was higher in the shunt group (81.8%) compared to the stent group (62.1%), suggesting a possible tendency for increased procedural necessity in the former. This could be attributed to the rather small sample size and the tendency for statistical significance could be unveiled with a larger cohort.

Additionally, although the overall distribution of reinterventions is similar between the two groups, there is a clear difference in the frequency of multiple reinterventions. Notably, cases requiring three reinterventions were significantly more frequent in the shunt group (7 cases) than in the stent group (1 case). This observation suggests that while initial interventions may have been effective in both groups, patients in the shunt group were more likely to require repeated procedures over time.

Regarding the type of reintervention, catheter-based procedures were more frequent in both groups; however, their proportion was significantly higher in the stent group (78.4%) compared to the shunt group (51.4%). Conversely, the shunt group exhibited a higher frequency of surgical reinterventions (48.6% vs. 21.6%). Despite these differences, statistical analysis did not confirm a significant difference in the total number of reinterventions between the groups ($X^2 = 1.246$; $p = 0.246$). This finding suggests that while the distribution of procedural types varied, both treatment strategies necessitated a comparable overall number of follow-up interventions.

To the best of our knowledge, no study has specifically examined long-term reintervention rates following corrective surgery while comparing patients who initially

underwent either patent ductus arteriosus (PDA) stenting or aortopulmonary (AP) shunt as palliation. Kaskinen et al. reported a 61% rate of either reoperation or catheter-based reintervention over a 20-year follow-up period, a finding that aligns with our results for the stent group. However, a separate study investigating long-term outcomes after complete repair in patients with PA-VSD reported an 89% incidence of at least one re-sternotomy for right ventricle-to-pulmonary artery (PA) conduit replacement. Given that the follow-up period for the AP shunt group in our study was significantly longer (13.7 years vs. 4.22 years), the higher reintervention rate observed in this group can be reasonably attributed to the extended duration of follow-up.

Reinterventions in Left- (LPA), Right- (RPA) and Main-Pulmonary-Artery (MPA)

The analysis of pulmonary artery (PA), left pulmonary artery (LPA), and right pulmonary artery (RPA) reinterventions, as presented in Table 22, demonstrates a comparable cumulative burden between the stent and shunt groups, with both groups recording a total of 24 reinterventions each. Given this equal distribution, no further statistical testing was performed to assess total group differences. The majority of reinterventions occurred during the follow-up stage, with 17 cases in the stent group and 15 in the shunt group, suggesting that long-term surveillance and management are critical regardless of the initial palliative approach. Additionally, the interstage and complete repair periods exhibited minimal variation between groups, indicating that the necessity for reintervention is relatively stable across these surgical stages.

This finding is particularly noteworthy when considering that intraoperative observations in this study revealed a significantly higher incidence of left pulmonary artery (LPA) stenosis during complete surgical repair. As previously mentioned, 65.5% of patients in the PDA-stent group required LPA enlargement, compared to only 29.4% in the AP shunt group. When these findings are examined collectively, it can be concluded that, LPA stenosis, when appropriately addressed intraoperatively during surgical repair, does not appear to contribute to an increased burden of reinterventions in the long term. This suggests that timely surgical intervention effectively mitigates the potential adverse effects of LPA stenosis, ensuring comparable long-term outcomes regardless of its initial prevalence. Additionally, this finding further underscores the

critical importance of meticulous assessment and intraoperative management of the pulmonary arteries during corrective surgery.

A potential pathophysiological mechanism underlying the significant LPA stenosis observed in the PDA-stent group is the altered perfusion dynamics caused by the stent placement. The PDA stent is often positioned with a curvature toward the RPA, ensuring sufficient perfusion of the RPA. However, the LPA receives blood flow through the stent struts, which may result in substantially reduced perfusion, eventually becoming hypoplastic and/or stenotic.

6 SUMMARY

6.1 Clinical Implications

The results of this study have significant clinical implications for the management of neonates and infants with PA-VSD. The shorter interstage period, lower rates of life-threatening complications, and earlier timing of complete repair in the PDA-Stent group suggest that this approach may be particularly beneficial for smaller, more fragile infants. The ability to manage most stent-related complications with catheter-based interventions is another important advantage, reducing the overall morbidity associated with the procedure. Additionally, PDA stenting is performed in paediatric catheterization laboratories without the need for anaesthesia support, utilizing conscious sedation and avoiding intubation. In contrast, APS is a fully operative procedure conducted under general anaesthesia, typically involving a sternotomy and, in some cases, the use of a heart-lung machine. Generally, the less invasive nature of PDA stenting is associated with a lower risk of complications, particularly in neonates with a birth weight of less than 3 kg. However, the AP Shunt remains a valuable option for larger infants and those with complex anatomy, where the reliability of shunting may outweigh the risks associated with a more invasive procedure. The longer follow-up duration for shunt patients reflects the more established nature of this approach, and the absence of long-term mortality in either group suggests that both procedures are highly effective in achieving long-term survival.

6.2 Limitations

This study has several limitations that must be acknowledged. First, its retrospective design inherently introduces certain biases, including selection bias and potential inconsistencies in data collection across different time periods. Additionally, the small sample size limits the generalizability of the findings, as statistical power is reduced, making it more challenging to detect subtle but potentially meaningful differences between groups. This limitation is particularly relevant given that the study focuses on a rare disease, further restricting the availability of large patient cohorts for analysis.

Another major limitation is the significant heterogeneity observed both in the disease itself and in its treatment. The pathophysiology of PA-VSD exhibits extensive variability, with anatomical differences in pulmonary artery morphology, collateralization, and associated defects making direct comparisons between patients difficult. Likewise, there is considerable heterogeneity in the surgical and palliative approaches used, with different institutions employing a variety of strategies, including PDA stenting, aortopulmonary shunts, management of MAPCAs and other tailored interventions. This institutional variability complicates direct comparisons and makes it challenging to draw firm conclusions regarding the superiority of one approach over another.

A key limitation of this study is the significantly longer follow-up period in the AP-shunt group compared to the PDA-stent group. This difference in follow-up duration may have influenced the reported reintervention rates, as patients in the shunt group had more time to develop complications or require additional procedures. Consequently, comparisons between groups must be interpreted with caution, as longer follow-up inherently increases the likelihood of detecting reinterventions. Additionally, when analysing reintervention rates, we did not distinguish between planned and unplanned reinterventions. This distinction is crucial because some centres follow structured protocols for planned reinterventions at predefined intervals, while others perform reinterventions only when clinically indicated. The lack of differentiation in our analysis may limit direct comparability with other studies that incorporate planned reinterventions as part of routine management.

Furthermore, the existing literature on this specific topic remains limited, with most published studies focusing either on native Tetralogy of Fallot (ToF) or PA/VSD/MAPCAs, rather than on the broader spectrum of PA-VSD with or without MAPCAs patients. As a result, direct comparisons with previously published data are difficult, and there is a lack of high-quality evidence addressing the specific challenges faced in this patient population.

Additionally, conducting randomized controlled trials (RCTs) in this field is inherently challenging, given the rarity and complexity of the disease, ethical considerations, and the necessity of individualized treatment approaches. The absence of RCTs means that most available evidence, including this study, is based on observational and retrospective analyses, which inherently carry limitations.

An additional limitation is the lack of available literature specifically addressing complications during the interstage period, which represents a crucial timeframe in patient management. Many studies focus on perioperative or long-term outcomes, leaving a gap in knowledge regarding complications and risk factors that may arise between initial palliation and complete repair. This study was also limited by the unavailability of MRI imaging data, which would have provided a more comprehensive assessment of pulmonary artery (PA) growth and remodelling over time. Without advanced imaging techniques, certain aspects of PA development and post-surgical adaptation remain incompletely understood, restricting the ability to draw more precise conclusions regarding vascular changes following different interventions.

Despite these limitations, the findings of this study contribute valuable insights into the management of PA-VSD and highlight important areas for future research. Further multicentre studies with larger sample sizes, standardized treatment protocols, and advanced imaging modalities are necessary to enhance our understanding of long-term outcomes and refine treatment strategies for this complex patient population.

6.3 Conclusion

In conclusion, this study provides a comprehensive comparison between PDA stenting and AP shunting in neonates and infants with PA-VSD. While both procedures are viable options for palliation, PDA stenting appears to offer several advantages,

including shorter interstage periods, fewer life-threatening complications, and the ability to achieve complete repair at an earlier age. However, the AP Shunt remains a valuable alternative for larger infants and those with more complex anatomy. Further prospective studies with larger sample sizes and longer follow-up durations are needed to validate these findings and refine clinical decision-making in this complex patient population**.**

7. Structured Abstract

Background: Pulmonary atresia with ventricular septal defect (PA-VSD) is a complex congenital heart defect that requires staged palliation before definitive repair. Two primary palliative strategies—patent ductus arteriosus (PDA) stenting and aortopulmonary (AP) shunting—are commonly employed to maintain pulmonary blood flow. This study retrospectively compares outcomes between these two approaches.

Methods: A retrospective analysis was conducted on 64 patients who underwent initial palliation with either PDA stenting (n=30) or AP shunting (n=34) between 1999 and 2019 at the Centre for Congenital Heart Disease (Kinderherzzentrum) Giessen. Outcomes were assessed across four stages: initial palliation (Stage 1), interstage period (Stage 2), complete surgical repair (Stage 3), and long-term follow-up (Stage 4). Primary endpoints included procedural success, complication rates, reintervention rates, and long-term survival.

Results: Birth characteristics, including weight, length, and gestational age, were similar between groups. However, MAPCAs were more frequently observed in the AP shunt group (48.4% vs. 20%, p=0.020). At the time of initial palliation, the PDA stent group had significantly lower weight (p=0.029) and length (p=0.022). The hospital stay and ICU length were not significantly different between groups. Perioperative complications occurred in both groups but were slightly more frequent in the AP shunt cohort (53.3% vs. 43.3%, p=0.438).

During the interstage period, complications were observed in 38.2% of the AP shunt group and 23.3% of the PDA stent group (p=0.199), though reintervention rates were comparable (p=0.683). Patients in the PDA stent group underwent complete repair significantly earlier (258.17 vs. 960.79 days, p=0.011). MAPCA unifocalization was more frequent in the AP shunt group (18.2% vs. 3.4%, p=0.109). The need for

intraoperative LPA- or either RPA- or LPA-enlargement was higher in the PDA-Stent (65.5% vs. 29.4%, p=0.004 and 67.9 vs. 35.3, p= 0.011).

Long-term follow-up showed no statistically significant difference in mortality, with one early postoperative death in the AP shunt group (p=0.352). The need for reintervention was slightly higher in the AP shunt group (81.8% vs. 62.1%, p=0.082), though not statistically significant. The type of reintervention differed, with PDA stent patients undergoing more catheter-based procedures and AP shunt patients requiring more surgical reinterventions.

Conclusions: Both PDA stenting and AP shunting are viable palliative options for PA-VSD, with similar long-term survival outcomes. However, PDA stenting appears to facilitate earlier complete repair with fewer interstage complications. AP shunting remains a reliable approach, particularly in patients with MAPCAs. And seems to reduce the burden of PA stenosis requiring enlargement intraoperatively. Future studies with larger cohorts and longer follow-up as well as randomized clinical trials are necessary to refine treatment algorithms further.

Structured Abstract (German Version)

Hintergrund: Pulmonalatresie mit Ventrikelseptumdefekt (PA-VSD) ist ein komplexer angeborener Herzfehler, der eine schrittweise Palliation vor der definitiven Korrektur erfordert. Zwei primäre palliative Strategien—die Stentimplantation des offenen Ductus arteriosus (PDA) und die aortopulmonale (AP) Shunt-Anlage—werden häufig eingesetzt, um den pulmonalen Blutfluss aufrechtzuerhalten. Diese Studie vergleicht retrospektiv die Ergebnisse dieser beiden Ansätze.

Methoden: Eine retrospektive Analyse wurde an 64 Patienten durchgeführt, die zwischen 1999 und 2019 im Zentrum für angeborene Herzfehler (Kinderherzzentrum) Gießen entweder eine PDA-Stentimplantation (n=30) oder eine AP-Shunt-Anlage (n=34) als erste Palliation erhielten. Die Ergebnisse wurden über vier Stadien hinweg bewertet: initiale Palliation (Stadium 1), Interstage-Periode (Stadium 2), vollständige chirurgische Korrektur (Stadium 3) und Langzeit-Follow-up (Stadium 4). Primäre Endpunkte umfassten den Erfolg des Eingriffs, Komplikationsraten, Reinterventionsraten und das Langzeitüberleben.

Ergebnisse: Die Geburtsmerkmale, einschließlich Gewicht, Länge und Gestationsalter, waren zwischen den Gruppen ähnlich. Allerdings wurden MAPCAs in der AP-Shunt-Gruppe häufiger beobachtet (48,4 % vs. 20 %, p=0.020). Zum Zeitpunkt der initialen Palliation hatten die Patienten der PDA-Stent-Gruppe ein signifikant geringeres Gewicht (p=0.029) und eine geringere Körperlänge (p=0.022). Die Dauer des Krankenhausaufenthalts und der Intensivstation (ICU) unterschied sich nicht signifikant zwischen den Gruppen. Perioperative Komplikationen traten in beiden Gruppen auf, waren jedoch in der AP-Shunt-Kohorte leicht häufiger (53,3 % vs. 43,3 %, p=0.438).

Während der Interstage-Periode traten Komplikationen in 38,2 % der AP-Shunt-Gruppe und 23,3 % der PDA-Stent-Gruppe auf (p=0.199), obwohl die Reinterventionsraten vergleichbar waren (p=0.683). Patienten der PDA-Stent-Gruppe erhielten die vollständige Korrektur signifikant früher (258,17 vs. 960,79 Tage, p=0.011). Die MAPCA-Unifokalisierung wurde in der AP-Shunt-Gruppe häufiger durchgeführt (18,2 % vs. 3,4 %, p=0.109). Die Notwendigkeit einer intraoperativen LPA- oder entweder RPA- oder LPA-Erweiterung war in der PDA-Stent-Gruppe signifikant höher (65,5 % vs. 29,4 %, p=0.004 bzw. 67,9 % vs. 35,3 %, p=0.011).

Das Langzeit-Follow-up zeigte keinen statistisch signifikanten Unterschied in der Mortalität, wobei ein früher postoperativer Todesfall in der AP-Shunt-Gruppe auftrat (p=0.352). Die Notwendigkeit für Reinterventionen war in der AP-Shunt-Gruppe leicht erhöht (81,8 % vs. 62,1 %, p=0.082), jedoch nicht statistisch signifikant. Der Typ der Reintervention unterschied sich: Patienten mit PDA-Stent unterzogen sich häufiger kathetergestützten Eingriffen, während Patienten mit AP-Shunt eher chirurgische Reinterventionen benötigten.

Schlussfolgerungen: Sowohl die PDA-Stentimplantation als auch die AP-Shunt-Anlage sind tragfähige palliative Optionen für PA-VSD mit ähnlichen Langzeitüberlebensraten. Allerdings scheint die PDA-Stentimplantation eine frühere vollständige Korrektur mit weniger Interstage-Komplikationen zu ermöglichen. Der AP-Shunt bleibt eine zuverlässige Alternative, insbesondere bei Patienten mit MAPCAs, und scheint die Notwendigkeit für intraoperative PA-Erweiterungen zu verringern. Zukünftige Studien mit größeren Kohorten, längeren Follow-up-Zeiten und randomisierten klinischen Studien sind erforderlich, um die Behandlungsalgorithmen weiter zu verfeinern.

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9 List of Abbreviations

APS Aorto-pulmonary shunt
BTS Blalock-Taussig-Shunt
BMS Bare-Metal-Stent
cCT Cardiac Computer-Tomography
cMRA. sCardiac Magnetic Resonance Angiography
DES Drug-Eluting-Stent
CI Confidence Interval
Mb Megabase
mBTS modified Blalock-Taussig-Shunt
MRT Magnetic Resonance Tomography
NPA Native Pulmonary Arteries
PA Pulmonary Atresia
PA-VSD Pulmonary Atresia with Ventricular Septal Defect
TOF-PA Tetralogy of Fallot with Pulmonary Atresia
PDA Patent Ductus Arteriosus
PBF Pulmonary Blood Flow
PGE-1 Prostaglandin E-1
TOF Tetralogy of Fallot
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