Therapeutic Utilities of Pediatric Cardiac Catheterization

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Abstract: In an era when less invasive techniques are favored, therapeutic cardiac catheterization constantly evolves and widens its spectrum of usage in the pediatric population. The advent of sophisticated devices and well-designed equipment has made the management of many congenital cardiac lesions more efficient and safer, while providing more comfort to the patient. Nowadays, a large variety of heart diseases are managed with transcatheter techniques, such as patent foramen ovale, atrial and ventricular septal defects, valve stenosis, patent ductus arteriosus, aortic coarctation, pulmonary artery and vein stenosis and arteriovenous malformations. Moreover, hybrid procedures and catheter ablation have opened new paths in the treatment of complex cardiac lesions and arrhythmias, respectively. In this article, the main therapeutic utilities of cardiac catheterization in children are discussed.

Keywords: Cardiac, catheterization, children, heart, interventions, pediatric, therapeutic.

INTRODUCTION

Cardiac surgery has played a fundamental role in the management of congenital heart disease (CHD). However, during the last decades, the advance of transcatheter techniques has led to the substitution of many traditional surgical procedures, due to favorable outcomes, better safety and more comfort for the patient, offered by the former. In addition, the development of special devices and equipment gave the opportunity for more interventions and, in many cases, established therapeutic catheterization as the gold standard of treatment. Nowadays, many CHDs are effectively managed with transcatheter techniques. Patent foramen ovale, atrial and ventricular septal defects, valve stenosis, patent ductus arteriosus, aortic coarctation, pulmonary artery and vein stenosis and arteriovenous malformations are some examples, routinely treated with catheterization in the pediatric population. Purpose of this review is to highlight the main utilities of cardiac catheterization as a therapeutic tool in the pediatric patient, including a brief report on the novel procedures of transcatheter valve replacement and hybrid interventions. A referral to the whole technique’s complications is also made at the end of the article.

PATIENT FORAMEN OVALE (PFO)

Under conditions that increase right atrial pressure, the septum primum flap is pushed away from the septum secundum, allowing blood to flow from the right to the left atrium and PFO generates pathology.

"Cryptogenic stroke" (CS) is linked to PFO, [1-4] which is seen in 20-25% of the general population, but approximately 50% of CS patients. Closure or anticoagulation therapy in PFO patients who experienced stroke or transient ischemic attack (TIA) contributes to secondary stroke prevention, compared to no treatment, but there is controversy on whether closure offers better results for post-CS patients, compared to medical treatment. Nonrandomized studies showed annual recurrence rate of 0-5% for stroke or TIA in patients after device closure [5-7], and 3.8-12% for those under anticoagulants [8-11]. However, randomized controlled trials (RCTs) failed to highlight substantial benefit of percutaneous closure. CLOSURE-I [12] compared recurrence rates of stroke or TIA with device closure (STARFlex device - NMT Medical, Inc.) and medical treatment, showing no superiority of the former. Yet, the STARFlex is not the best choice [13] and CLOSURE-I was criticized regarding patient selection. PC trial compared the Amplatzer PFO Occluder (St. Jude Medical, Inc.) with antithrombotic therapy showing similar results [14]. RESPECT [15] did not demonstrate device closure superiority in the primary intention-to-treat analysis, but emerged positive results in the prespecified secondary per-protocol and as-treated analyses. RE-
DUCE (NCT00738894), examining the efficacy of the Helex Septal Occluder (W.L. Gore & Associates), is ongoing.

Migraine is also associated with PFO [16]. Observational data suggest some improvement with PFO closure [16-19], while from RCTs, MIST [20] failed to yield positive results and PRIMA (NCT00505570) and PREMIUM (NCT00355056), are ongoing.

PFO closure is considered a safe procedure and is performed off-label, depending on the therapist's experience and the institution's policy. Major complication rate has been estimated to be 0.2%-1.5% for hemorrhage requiring transfusion, cardiac tamponade, fatal pulmonary emboli, and death [21]. Minor complication risks, i.e., atrial arrhythmias, device arm fractures, device embolization and thrombosis, and femoral hematomas occur at 7.9%-11.5% of patients [21]. Atrial fibrillation occurs more frequently in patients who received larger devices [22].

High-risk for stroke, frequent right-to-left shunting and cyanosis episodes in the context of a noncompliant right ventricle and orthodeoxia-platypnea syndrome are reasonable indications for PFO closure [21].

**Atrial Septal Defect (ASD)**

ASD accounts for about 8.5% of all CHDs. Although small defects (<8mm) are commonly found soon after birth, the majority closes spontaneously within the first year. Approximately 90% of ASDs are secundum ASDs, while the 10% includes primum, sinus venosus and unroofed coronary sinus defects. The first attempt for percutaneous ASD closure was in 1976 [23], but FDA approved the Amplatzer Septal Occluder (ASO, St. Jude Medical, Inc.) only in 2001 (Fig. 1). ASO is a double-disc, self-expandable device composed of a Nitinol wire mesh. The discs are connected with a waist and polyester fabric inserts are sewn into the discs and the waist to facilitate closure. Before release of the delivery cable, the device can be easily repositioned. The Helex Septal Occluder (HSO) and the Amplatzer Multi-fenestrated Septal Occluder (AMFSO - St. Jude Medical, Inc.) or “Cribriform” Occluder, followed (Fig. 1). The HSO consists of a single nitinol strand connected to a piece of an expanded polytetrafluoroethylene membrane, while the AMFSO resembles the ASO. ASO is most widely used and can close ASDs up to 38mm. HSO is mostly used for small- to moderate-sized defects (<2cm), and AMFSO for multifenestrated ASDs. Catheter-based closure is routinely performed under intracardiac or transesophageal ultrasound. Percutaneous ASD closure seems to be equally successful to surgical repair with 98% success, and lower complications rates, shorter operative and hospitalization time and faster recovery [24-26]. Very large ASDs (>38mm), troublesome cases with insufficient defect rims and non-secundum types of ASD are amenable to surgical repair. Dyspnea, fatigue, paradoxical embolism, tachyarrhythmias and right heart failure are possible manifestations of untreated ASDs. Complications of percutaneous ASD repair include device migration and malposition, cardiac perforation resulting in tamponade, and ativoventricular block. A multicenter study of 442 children showed 7.2% overall complication rate with 1.6% considered to be major, due to device embolism, cardiac arrhythmia requiring major treatment, marker band embolization, and cerebral embolism with extremity numbness [24].

**Ventricular Septal Defect (VSD)**

VSD is the commonest CHD of childhood, but its spontaneous closure decreases its prevalence in adults. VSD's subtype are: perimembranous (pmVSD-80%), muscular (mVSD-10%), inlet (5%), supractristal (<5% in non-Asians).
and rarely multiple VSDs (“Swiss-cheese”). Currently, percutaneous VSD closure is performed only on mVSD. Usually, small VSDs are asymptomatic with excellent prognosis needing no treatment. Although percutaneous approach has been successfully tested on pmVSD [27], most studies show increased postoperative AV-block incidence [28, 29] and surgical closure is the treatment of choice in moderate or large pmVSD. According to the American Heart Association Indications for Cardiac Catheterization and Intervention in Pediatric Cardiac Disease, percutaneous VSD device closure is indicated only for infants >5kg and children and adolescents with hemodynamically significant defect (left heart chambers overload or pulmonary-blood-flow:systemic-blood-flow >2:1) [30]. The first labelled device was the Amplatzer Muscular VSD Occluder (St. Jude Medical, Inc.) (Fig. 2), approved by the FDA in 2007, after successful use in transcatheter mVSD closure [31]. It consists of a self-expandable, double-disc implant made of wire mesh and Dacron polyester fabric and a delivery system, which facilitates transport of the implant to the defect. In the prospective study of Hozler et al. following patients with mVSDs after device closure, 45% of patients suffered at least one procedure-related complication, with conduction anomalies, hypertension/cardiac arrest, hematoma/pseudoaneurysm, cerebrovascular accident, and device embolization being the most common [31]. Neonates and smaller infants with hemodynamically significant mVSD are amenable to surgical or better hybrid procedure [30], with which cardiopulmonary bypass is avoided and may also be helpful in multiple VSDs [32].

ATRIAL SEPTOSTOMY AND TRANSSEPTAL APPROACH

Balloon atrial septostomy (BAS) was the first interventional cardiac transcatheter technique performed [33]. Through femoral or umbilical vein a balloon is guided to the left atrium via the right atrium and the foramen ovale. After confirming the position by fluoroscopy or echocardiography, an abrupt pull tears the septum magnifying the interatrial communication. Pressure gradient is checked across the defect and the procedure is ongoing until atrial pressures are equalize. Mostly used catheters are the Miller (Edwards Lifesciences) and the NuMed (NuMed, Inc.). In children >1 month and adults the septum is thick, and the foramen ovale closed, thus BAS cannot be performed and atrial septostomy (BIAS) is the gold standard, creating a defect via a blade, which is then enlarge by a static balloon septostomy or BAS. Alternatively, a Brockenbrough needle (Medtronic, Inc.) or radiofrequency may be used to puncture the septum [30, 34]. Stents can, ultimately, be deployed for more solid results. Primary indication for BAS is newborns and infants with transposition of the great arteries and PFO in order to ensure a few days of survival, since PFO’s enlargement offers hemodynamic stabilization and prolonging survival until the surgery. Hypoplastic left heart syndrome with intact interatrial septum is another indication, again as a life-saving procedure, relieving left atrial hypertension and increasing oxygen content in the systemic circulation. Other indications are patients with right-heart obstructive lesions (e.g. tricuspid atresia, pulmonary valve stenosis/atroresia) with intact interatrial septum and patients with severe pulmonary hyper-tension as a last resort therapeutic option [35, 36]. Finally, many left-heart interventions are routinely managed with the transseptal technique when the specialist deems it favorable or when retrograde left-heart access is contraindicated [30]. BAS and the other transseptal techniques are not entirely safe; cardiac perforation, arrhythmias, air embolization and valve injury are some of the complications.

AORTIC STENOSIS

Congenital aortic stenosis is characterized by thickening of the valve leaflets and variable degree of commissural fusion, that hinders blood ejection to the aorta, causing left-heart obstruction. Transcatheter techniques have a palliative nature, aiming to reserve the valve and delay surgery or replacement until after adolescence. Results are not permanent, since restenosis occurs often [37]. Aortic balloon valvuloplasty is a percutaneous procedure, involving the inflation of a balloon at the aortic annulus with intention to rip the commissural fusions and fix the obstruction. Concomitant right ventricular pacing stabilizes the balloon by decreasing left ventricular systolic pressure [38]. Before the procedure a diagnostic catheterization is necessary to collect useful data (pressure gradient across the valve, annular diameter, coexisting regurgitation). Indications include neonates with critical stenosis without regurgitation, irrespective of the pressure gradient, infants and children with stenosis without regurgitation, with resting peak-to-peak systolic gradient >50mmHg and infants and children with stenosis and no regurgitation with resting peak-to-peak systolic gradient >40mmHg and concurrent signs of ischemia (angina, ST changes) or syncope [30]. Annular diameter is important for determining the balloon size (ideally 90-100%) [39]. Smaller sizes lead to suboptimal results with residual obstruction and higher restenosis risk, whereas larger predispose to postprocedural regurgitation [37, 39, 40]. Vascular injury at the injection site, thromboembolic stroke, mitral valve injury, and myocardial perforation in newborns are other potential adverse events [30]. Gradient reduction at least 50% with no induced regurgitation achieves optimal results. Aortic balloon valvuloplasty can be performed by retrograde arterial or antegrade venous access through the interatrial septum. Fratz et al. followed 188 pediatric patients (group <1 and group ≥1 month of age) that had undergone aortic balloon valvuloplasty to show that 10-year survival free from surgical therapy was 59% for group <1 month and 70% for group ≥1 month [41]. Concordant were the results of Pedra et al. who followed 87 children ≥6 months of age at the time of the dilatation (median age 6.9 years) and found that freedom from reintervention was 86%, 67% and 46% after 1, 5 and 12 years respectively, [37] while for neonates, it was 48% at a 5-year period in the study of McElhinney et al. [42] and McElhinney et al. [43] showing that necessity for reintervention is earlier when balloon dilatation is performed in neonatal age.

A double-balloon percutaneous technique has been used sporadically over the last years. The smaller catheters and balloons, allow for less vascular damage during insertion, manipulation and withdrawal, something particularly useful in cases where the annular diameter is large compared to the femoral vessels [44-47].
In the last years, fetal aortic valvuloplasty has gained popularity. This promising intervention enables avoidance of left ventricular fibrosis, normal left ventricle development and prevention of hypoplastic left heart syndrome [48-51].

**PULMONARY VALVE STENOSIS**

Pulmonary stenosis is characterized by a dome-shaped pulmonary valve with diffuse leaflet thickening and commissural fusion, blocking the blood flow to the pulmonary artery. Pulmonary valvuloplasty has replaced surgical valvotomy and constitutes the treatment of choice for all ages [52-54]. The major indications are symptomatic pulmonary stenosis and pulmonary stenosis with peak-to-peak valve gradient ≥40mmHg determined by catheterization or echocardiography [30], although Rao suggests ≥50mmHg [55]. Newborns with pulmonary atresia are also candidates, and so are patients with tetralogy of Fallot, mostly for palliative reasons before surgery [56-59]. Dysplastic valves, subvalvular and supravalvular stenosis have lower success rate than typical stenosis [60, 61], though some teams yielded favorable results with dysplastic valves [62, 63]. Widely recommended balloon size has 120-140% the annular diameter [64], although Rao [55] suggests the lowest size range (120-125%), since it ensures lower chances for postoperative pulmonary regurgitation. Balloon inflations are undertaken until a peak-to-peak gradient <30mmHg is achieved. In the end, contrast is injected in the right ventricle, to delineate the leaflets’ motion and confirm blood flow across the valve.

Postprocedural pulmonary regurgitation and restenosis are the most significant complications. Outcomes of pulmonary balloon dilatation are good as the Valvuloplasty and Angioplasty of Congenital Anomalies Registry pointed out in a study of 533 patients aged between 1 day and 55 years (median 3.7 years). At a median 33-month follow-up freedom from reintervention was 84%, and 23% judged to be suboptimally treated [64]. Rao et al. [65] observed 85 patients <20 years (mean 7.0±6.4 years) having undergone pulmonary balloon valvuloplasty to find that 10-year freedom from reintervention was 84%. Transcatheter treatment is superior to surgery, with lower incidence of regurgitation and lower morbidity and mortality rates but relatively higher restenosis rates.

Simultaneous double-balloon dilation has been trialed in several studies with excellent results, yet not superior to the single-balloon technique. Use in older patients with annular diameter >20mm is suggested by most researchers [66-68].

**MITRAL STENOSIS**

Mitral stenosis (MS) is divided into rheumatic and congenital, with the latter further divided into several subtypes. Percutaneous mitral valvuloplasty has excellent outcome in selected adult patients, while in children it is mostly used for isolated rheumatic MS with excellent results, comparable to surgery [69-73]. A single-balloon (Inoue balloon - Toray Medical Co., Ltd.) and a double-balloon approach have been introduced with the former most commonly implemented [74]. Few trials that compare these techniques have been conducted, showing similar results [75-79]; however, Inoue is considered the gold standard for rheumatic MS, due to ease of use and more established experience [74]. In acquired MS, fusions are easy to tear-off and complications, such as postprocedural regurgitation, are less likely to occur compared to congenital, where valve morphology often makes percutaneous approach tricky. This is why only carefully selected patients with congenital MS and favorable valve morphology (e.g. commissural fusion) are candidates for balloon valvuloplasty, while for other forms surgical intervention is preferable [80, 81]. The most complete series of pediatric patients treated for congenital MS is the McElhinney et al. [80] from Boston Children’s Hospital, where 108 children (median age 18 months) with severe congenital MS were managed with percutaneous balloon valvuloplasty, surgical valvuloplasty or mitral valve replacement. Percutaneous approach was the most used option and yielded positive results in children with favorable mitral anatomy by improving left ventricular inflow, reducing left atrial pressure and delaying ultimate mitral valve replacement, while surgical treatment was preferable for supravalvular ring, concomitant mitral regurgitation and coexistent cardiac anomalies that required cardiotomy. Mitral regurgitation followed 28% of percutaneous valvuloplasties. Freedom from failure of biventricular repair or mitral valve reintervention within 1 year was 55% for mitral balloon dilatation, and 69% for surgical treatment.

**TRANSINTER PULMONARY VALVE REPLACEMENT**

The lifespan of right ventricular outflow tract (RVOT) conduits for the management of complex CHD (most commonly tetralogy of Fallot) is limited as calcification and myocardial remodeling progressively lead to obstruction and/or regurgitation. Endovascular bare stent deployment was used in order to prolong conduit longevity with good results in view of conduit stenosis, but worse in terms of regurgitation. With the study of Bonhoeffer et al. [82] on animal models the novel practice of percutaneous pulmonary valve placement was introduced. Melody (Medtronic, Inc.) is the valve currently approved by the FDA, which is a bovine jugular venous valve sutured inside a NuMED Cheatham Platinum stent (NuMed, Inc.) and mounted on a 22-Fr delivering catheter guided with fluoroscopy. A coverage sheath protects the valve during delivery and a balloon-in-balloon system secures exact positioning of the valve. Due to limited available size, RVOT 16-22mm in size is compatible with bioprosthetic valve implantation, although limited new data show potential success beyond this range [83]. Major complications of this practice are stent fracture and endocarditis [84-86]. This novel technique has minimized the need for repeat heart surgery in patients with right ventricle to pulmonary artery conduits and, consequently, improved their quality of life. The US Melody valve trial showed encouraging success rates and uncommon incidence of adverse effects in experienced hands [87, 88]. At the same time, it holds promises for further innovations as it has been used off-label in alternative positions, such as the aortic, mitral, tricuspid valve and the pulmonary artery, with encouraging early results [89-92].

**PATENT DUCTUS ARTERIOSUS (PDA)**

Ductus arteriosus is of vital significance for the fetus securing blood flow from the pulmonary artery to the aorta
bypassing the lungs. After birth, it normally closes within hours, but it can remain open (patent ductus arteriosus - PDA) with increased risk for pulmonary hypertension, myocardial hypertrophy and heart failure; PDA accounts for 5-10% of all CHD, and its closure can be interventional or surgical. Surgical ligation was the first technique [93] with high success and low complication rates. In 1992, Cambier et al. [94] reported successful transcatheter closure of small PDA using Gianturco coils delivered by a small-sized (5 Fr) catheter. Today, coils offer high closure rates and low morbidity in PDAs <4-5mm. Amplatzer Duct Occluder (ADO - St. Jude Medical, Inc.) was introduced and approved by the FDA in the late 1990s. This is a self-expandable, nitinol wire mesh device with a single retention disc and a cylindrical stem, into which polyester fabric is sewn, and which is set- tled into the PDA. The delivery system involves a delivery cable, a delivery sheath, a loader, a dilator and a pin vise. The device is usually deployed via venous approach. The outcomes in multiple patient series were excellent. In 2004, Pass et al. [95] demonstrated the results of a multicenter USA study examining immediate and 1-year results with ADO closure. 439 children (1.8 years median age, 11kg median weight) with moderate-to-large PDAs had an ADO implanted. The 1-year occlusion rate was 99.7% with no deaths and morbidity at 9.4%. Yet, closure is usually seen immedi- ately after device implantation. Today, ADO is used with excellent results and safety in infants and children ≥3kg (manufacturer recommends ≥6kg) and can easily close PDAs up to 16mm. Complications, such as aortic or pulmonary device protrusion with subsequent obstruction (mostly in small infants) and late device embolization, are rare. Al- though the angled ADO seemed a promising device for the prevention of those complications, it never entered the market [96]. Device embolization risk reduces with correct de- vice size and avoidance of disc intrusion into the PDA. The new Amplatzer Duct Occluder II (ADO II - St. Jude Medi- cal, Inc.) has gained CE mark approval for use in Europe for all PDA types [97]. Its symmetrical double-disc design of- fers the choice of arterial or venous approach, while the fab- ric-free technology allows for mounting on a low-profile catheter. Immediate and short-term outcomes have also been examined with the Nit-Occlud PDA-R (pfm medical, Inc.) with favorable results, needing further follow-up [98]. Can- didates for percutaneous PDA closure are symptomatic chil- dren, asymptomatic children with moderate or large PDA and left-to-right shunt that leads to pulmonary overflow or enlarged left heart chambers and some rare cases of small PDAs. Established pulmonary hypertension with no response to oxygen or nitric oxide and no improvement with tempo- rary balloon occlusion test, as well as fixed right-to-left shunts, are contraindications for PDA closure.

**COCARTION OF THE AORTA (COA)**

CoA is a narrowing of the descending aorta right after the origin of the left subclavian artery, that poses an obstruction to the blood flowing to the lower torso and limbs, causing elevated blood pressure in the upper limbs and low blood pressure in the lower limbs, but can also present at a later time, with heart failure. CoA accounts for 5-8% of all CHD. Treatment can be surgical or interventional. Surgical tech- niques, such as resection of the narrowed segment and end- to-end anastomosis, are preferred in neonates and infants, in which incidence of recoarctation is high with interventional methods [99, 100]. Yet, percutaneous balloon angioplasty can be performed in those patients for palliative reasons and stabilization, bridging them for surgery [101]. Surgical repair is widely used, since symptoms usually present early in life. Existing data also advocate balloon dilatation in neonates and infants with favorable results and some practitioners manage these patients less invasively [102, 103]. Still there is controversy on whether balloon angioplasty should be preferred to surgery for native coarctation. Although short-term outcomes of balloon angioplasty are comparable with those of surgery, in long-term follow-up incidence of restenosis and aneurysm is higher [104], but repeat surgery - usually required after surgical repair - is avoided. The cur- rent trend is to perform transcatheter balloon dilatation in children >1 year of age and repeat in restenosis. Discrete coarctation and a resting systolic pressure gradient >20mmHg obtained by catheterization, or less in the pres- ence of collateral vessels or left ventricular dysfunction, are necessary, according to the American Heart Association Indica- tions for Cardiac Catheterization and Intervention in Pediatric Cardiac Disease [30]. Balloon dilatation is also indicated in postsurgical coarctation recurrence [105]. Elong- gate narrowing or CoA associated with arch hypoplasia may require stent deployment. Stents are mostly implanted in older children and adolescents, who resemble sufficiently to adult corpus, to ensure more durable results, and decrease incidence of aortic aneurysm caused by balloon dilatation [106-108] (Fig. 3). Repeat dilation is necessary with grow- ing, in order the stent to suit perfectly to the aorta. Newer stent technologies, introduced in the last decade, include balloon-expanding and self-expandable stents and covered stents that diminish complications triggered by bare metal

![Image](image.png)
PULMONARY ARTERY STENOSIS (PAS)

PAS is a narrowing of the pulmonary artery or its peripheral branches and accounts for 2-3% of all CHD. This stenosis hinders the ejection of blood to the pulmonary circulation with only the severe constriction to be associated with clinical manifestations like fatigue, shortness of breath and peripheral edema. The therapeutic modalities implicated in the management of PAS are surgical and percutaneous. Surgery may be chosen in proximal PAS but in most other cases balloon angioplasty is preferred, being the only option for distal PAS. Balloon angioplasty is the treatment of choice for the withdrawal of severe PAS and achieves satisfying immediate relief rates (50-60%). Yet, at follow-up, >15% of patients present with restenosis and require recatheterization [111, 112]. Recurrence is most prevalent in patients <6 years old due to somatic growth. Endovascular stent implantation is used, in order to sustain the newly-opened circulation and achieve long-term results, although redilation may still be needed to overcome restenosis and fit with somatic growth [113, 114]. The most widely used stents are the balloon-expandable Palmaz stents (Cordis, Inc.). Stents are deployed in patients large enough to bear a stent and in selected small-sized patients for transient palliation. The novel technology of cutting balloons has been a notable adjunct for the management of PAS resistant to standard angioplasty and offers better results than high-pressure balloon therapy, yet it is equally safe [115]. They consist of blades or microtomes along the balloon length, which cause micro-incisions to the arterial wall for greater luminal expansion, also maintained at follow-up [116]. Complications of cutting balloon angioplasty are similar to those of the simple balloon angioplasty and include vascular trauma, wall rupture, stent embolization, hemodynamic instability and arrhythmia, among others [117].

PULMONARY VEIN STENOSIS (PVS)

PVS is a rare condition with guarded prognosis characterized by narrowing of the pulmonary veins. It can be acquired (after RF ablation for atrial tachycardia or repair of anomalous pulmonary venous connections) or, most commonly in childhood, congenital. Today, no ideal therapy exists and treatment depends on specialist’s experience and center’s strategy. The options include balloon angioplasty (simple, high-pressure or cutting), with or without stent, and surgery (sutureless marsupialization). However, none of these achieves sustained results and repeat intervention is frequently required. Surgical treatment may result in satisfying mid-term outcomes, although freedom from reoperation is still low (49% after 5 years) [118, 119]. As for transcatheter techniques, better follow-up results are achieved with stent dilatation. In a study of Prieto et al. [120], stent angioplasty was found to be superior to standard balloon angioplasty in adult PVS complicating previous pulmonary vein isolation with immediate success rates 95% and 42% and restenosis rates 33% and 72%, respectively. Restenosis was settled later when a stent had been deployed and was even less frequent if the stent diameter surpassed 10mm. Stents placed in children should have adult-size potential capability for future redilation. Cutting balloons offer immediate relief, but future redilation is usually needed [121]. Some children end up needing lung transplantation [122]; a management considered first-choice only for critically ill patients with poor prognosis [123]. The long-term outcomes of this therapeutic step have not been studied.

AORTOPULMONARY COLLATERALS, CORONARY ARTERY FISTULAS, PULMONARY ARTERIOVENOUS MALFORMATIONS

Aortopulmonary collaterals are blood vessels originated from the aorta and/or the periaortic arteries (e.g. subclavian) and drained to the pulmonary circulation causing a left-to-right shunting. They are mostly found in patients with tetralogy of Fallot, pulmonary atresia and, those with surgically palliated single-ventricle physiology (Fontan, Glenn procedures). Coronary artery fistula constitutes a vascular connection between coronary arteries and a heart chamber or another vessel (e.g. pulmonary artery). Pulmonary arteriovenous malformations are direct arteriovenous connections in the lungs bypassing the capillaries and causing a right-to-left shunting, which can result in hypoxia. The main concept behind these vascular malformations’ management is their definitive closure. Today, surgical resection and closure has been limited and transcatheter procedures, i.e. embolization with coils and occlusion via the Amplatzer vascular plugs (AVP - St. Jude Medical, Inc.) are mostly performed. Coils, especially detachable coils, constitute a good choice small to moderate-sized vascular malformations in children, while closure of large vessels is, usually, labored and carries additional risks [124-127]. The Amplatzer vascular plug occluders represent a family of 4 devices (AVP-I, AVP-II, AVP-III, AVP-IV), each with specific indications and advantages [128] (Fig. 4). AVP-I is the most well-tested and has proved its efficacy in the embolization of vascular malformations.
malformations. AVP-II is a 3-segment plug, convenient when rapid occlusion is required, while AVP-III is mostly used in paravalvular leak management. AVP-IV is the latest-generation vascular plug, which, delivered through a 4-Fr catheter, offers the ability for access and device deployment in small and tortuous vascular fields [128, 129]. The AVP devices are considered effective and safe options for closure of moderate-sized to large vascular malformations and continue to unfold further usage capabilities [129-133].

Other devices (e.g. ADO, ASO, CardioSeal) have also been used [134-136], but current literature includes well-documented data only on the use of AVPs. In addition, the long-term efficacy and safety of the AVPs, especially the latest representatives, is not known yet.

ARRHYTHMIAS

Arrhythmias in children can be congenital or acquired, related to a congenital heart defect or not. The majority represents asymptomatic, benign irregularities of the heart rate, which do not require treatment. However, they can sometimes present with constant and worrisome symptoms or pose a life-threatening underlying anomaly, making therapy necessary. During the last two decades, catheter ablation has evolved as a revolutionary therapy in the field of pediatric electrophysiology. Radiofrequency catheter ablation (RFCA), producing low-voltage, high-energy electricity, has been the primordial energy resource used and, soon after, cryoablation (CA), producing excess cold down to -75°C using liquid nitric oxide, emerged. RFCA is a highly effective treatment modality with 95.2% lately reported success rate, according to the Pediatric Radiofrequency Catheter Ablation Registry (90.4% in the initial era of use), with varying complication rate depending on the underlying arrhythmia pathway and age [137]. The corresponding success rate of CA is comparable, but recurrence occurs more frequently [138]. Yet, CA has the advantage of inducing a better-controlled cardiac tissue injury, since with RFCA trauma expands further, even after removal of the catheter tip. Thereby, complications seen with RFCA, like coronary artery occlusion [139] and AV-block [140], become less frequent with CA. Moreover, CA offers the potential of imitation of the post-ablation electric conduction pattern (cryomapping), by chilling cardiac tissue at -30°C to -20°C and causing a temporary electric alteration, before proceeding to definite tissue damage [141-143]. Although CA has been increasingly used during the last decade and has become the treatment of choice for specific arrhythmias [144, 145], a recent retrospective study [146], which included 333 children undergoing RFCA, showed excellent outcomes, with 0.3% major complication rate (one pericardial hemorrhage), no reported AV-block and no deaths, suggesting that proper training and specializing may lead to better outcomes. Further research and RCTs are required, in order to determine credible indications on the use of each technique.

HYBRID PROCEDURES

Hybrid approach is a relatively new innovation, combining surgical and percutaneous techniques. It constitutes a good alternative for children too sick to undergo an open-heart surgery or too small to tolerate typical catheter insertion. These procedures are executed in special operating suites where both surgical and interventional interference is offered [147], alongside with fluoroscopy and transesophageal echocardiography (Fig. 5).

Hybrid techniques are most commonly performed for hypoplastic left heart syndrome (HLHS) and single-ventricle physiology, perventricular closure of mVSD and perventricular valve implantation.

Untreated HLHS has high mortality in the first month of life. It is characterized by hypoplasia of the left ventricle and the aorta, while systemic oxygenation is achieved through the PDA. Hybrid intervention is indicated either as a stage 1 palliative procedure or as bridge to transplantation [30]. A small sternotomy is undertaken to secure access and shortly after, the right and left pulmonary arteries are banded with PTFE graft segments, in order to enhance blood flow through the PDA to the systemic circulation and reduce pulmonary and right heart overflow. A purse-string suture is also done on the main pulmonary artery to pass a sheath, through which a catheter will access the PDA and a stent will be implanted to keep PDA open. Eventually, a BAS allows atria blood mixing, offering the left atrium the opportunity to expand. This procedure is performed during the first week of life, being a critical life-saving first step in the management of the newborn. It is a fair alternative of the Norwood palliation, which carries many risks, and it results in a less radical reconstruction, providing a better terrain for im-

Fig. (5). Hybrid operating room in New York-Presbyterian Hospital.
pending bi-directional Glenn shunt, while simultaneously avoids cardiopulmonary bypass.

Hybrid treatment of mVSD is gaining ground in the management of neonates and infants <5kg with hemodynamically significant defect, for which percutaneous intervention alone would bear notable risks. It causes less hemodynamic instability, is safer than transcatheter approach for small patients and less invasive, when compared to surgery, while it eliminates the need for cardiopulmonary bypass [148-151]. First, a purse-string suture is placed on the free right ventricular wall, through which a guidewire is inserted into the right ventricle and, eventually, through the VSD, to the left ventricle. Then, a sheath and dilatator are directed over the guidewire to the left ventricle. An Amplatzer Muscular VSD Occluder can be used to close the defect; first, the left disc is expanded in the left ventricle and then it is gently pushed against the ventricular septal rim, allowing for expansion of the right disc, as well. Deployment is screened with fluoroscopy or echocardiography and the device is released.

Perventricular valve implantation is also an emerging trend, used in access difficulty or increased risk with transcatheter valve implantation or open-heart surgery alone [152-154].

**COMPlications**

Complications seem to be relatively rare in pediatric cardiac catheterization, although they cannot be ignored. Older studies showed a complication incidence of 8.8-11.1% in the pediatric age group, either life-threatening or trivial [155, 156], while recent publications displayed higher incidence (>14.7%) in similar age groups and an increase of major adverse events in the sum of adverse events [157-159]. The more complex heart disease encountered nowadays and the higher frequency of neonates and small children catheterization could partly justify these results. Mortality rates do not seem to have changed over the years. In a cohort of 1037 catheterizations [155], Cassidy et al. reported 2 deaths directly associated to the catheterization and 2 more (totally 0.39%), in which the procedure contributed to the aggravation of their distress, whereas in the study of Vititello et al. [156], 4952 catheterizations were performed, with 7 deaths associated with the procedure (0.14%), the 5 concerning infants. Recently, similar cohorts reported mortality rates around 0.30%, which resembles older results [158, 159]. Young age (<6 months and especially neonates), low body weight (<5kg), interventional catheterization, male gender and inpatient status are universally considered independent risk factors for emergence of adverse events [155-164]. Arrhythmias constitute the majority of considerable adverse events, accounting for >20% [155, 156, 158, 159, 164]. Atrial tachycardia and AV-block are the most common usually reverting spontaneously or with minor interference. Vascular complications are very common. The majority concerns arterial thrombosis in the limb (ameliated with heparin sulfate but rarely needing thrombolytic agents), and topical limb hematoma. Air embolization (usually after repeatedly catheter exchange or large catheter manipulation) and balloon rupture do not usually cause much problem. Device embolization may be prevented with proper heparinization in high-risk cases. Cardiac perforation and cardiac tamponade are severe complications and pericardiocentesis is usually required. Aortic valve dilatation seems to have the highest risk for periprocedural complications [156, 164], while pulmonary atresia, Tetralogy of Fallot RVOT dilatation and aortic coarctation angioplasty, have also considerable complication rates.

**SUMmary**

The progress of cardiac catheterization has been swift in the recent years. Catheter-based interventions have become the mainstay of treatment for many cardiac lesions in the pediatric population, due to favorable outcomes, better safety, less need for general anesthesia, and rapid post-interventional recovery. The development of devices for closure of anatomic lesions, the use of stents for maintaining vessel patency, and catheter innovation have expanded the spectrum of heart disease that can be treated this way, while improving therapeutic techniques. Nowadays, surgical management has been limited in many cases or serves as an adjunct to percutaneous treatment in contemporary hybrid procedures. Considering the constantly evolving techniques and technologic development, we believe that cardiac catheterization will continue playing major role in the future management of pediatric heart disease.

**CONFLICT OF INTEREST**

The authors report no financial relationships or conflicts of interest regarding the content herein.

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