Advances in paediatric interventional cardiology since 2000

Nouveautés en cathétérisme cardiaque interventionnel pédiatrique depuis 2000

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Congenital heart defects; Interventional paediatric cardiology; Recent advances

Summary Interventional paediatric and congenital cardiology is expanding at a rapid pace. Validated techniques (such as aortic or pulmonary valve dilatations and occlusion of persistent ductus arteriosus and atrial septal defects) are improving thanks to the use of smaller introducers and sheaths, low-profile balloons and novel devices. Moreover, catheter-based interventions have emerged as an attractive alternative to surgery in other fields: pulmonary valve replacement, balloon and stent implantation for native and recurrent coarctation, and percutaneous closure of ventricular septal defects. On the other hand, percutaneous interventions in the paediatric population may be limited by patient size or the anatomy of the defect. Hybrid approaches involving both cardiac interventionists and surgeons are being developed to overcome these limitations. Based on a better understanding of cardiac development, fetal cardiac interventions are being attempted in order to alter the history of severe obstructive lesions. Finally, some interventional procedures still carry a low success rate—for example, pulmonary vein stenosis, even with the use of conventional stents. Biodegradable stents and devices are being developed and may find an application in this setting as well as in others. The purpose of this review is to highlight the advances in paediatric interventional cardiology since the beginning of the third millennium.

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Résumé La cardiologie interventionnelle pédiatrique et congénitale avance à grands pas. Les techniques percutanées déjà validées (comme la dilatation valvulaire aortique ou pulmonaire, la fermeture de canal artériel persistant ou de communication interauriculaire) s'améliorent encore, de part l'utilisation d'introduceurs et de gaines plus petits, de ballonnets plus minces et de nouvelles prothèses. Par ailleurs, les techniques percutanées commencent à être considérées comme une alternative valable à la chirurgie dans de nombreux domaines : le remplacement valvulaire pulmonaire, la dilatation et l'implantation de stent dans le traitement de coarctations natives ou récurrentes, la fermeture de communication interventriculaire. Toutefois, dans la population pédiatrique, ces techniques se heurtent aux limites de poids du patient ainsi qu'à l'anatomie de la malformation. Les techniques hybrides, impliquant à la fois les chirurgiens et cardiologues Interventionnels, se développent dans le but d'y remédier.

Basé sur une meilleure compréhension du développement cardiaque, le cathétérisme cardiaque fœtal tente de se développer dans le but de modifier le cours naturel des lésions obstruantes sévères. Enfin, les résultats de certaines interventions percutanées restent insatisfaisants, par exemple le traitement des sténoses veinues pulmonaires, malgré l'utilisation de stents conventionnels. Le développement de stents biodégradables et de nouvelles prothèses pourrait être utile dans ce contexte et dans d'autres situations. Le but de cette revue de la littérature est de souligner les nouveautés en cathétérisme cardiaque pédiatrique depuis le début du IIIe millénaire.

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Abbreviations

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<tr>
<th>Abbreviation</th>
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<tr>
<td>ADO</td>
<td>Amplatzer duct occlude</td>
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<td>ASD</td>
<td>atrial septal defect</td>
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<td>ASO</td>
<td>Amplatzer septal occlude</td>
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<td>HLHS</td>
<td>hypoplastic left heart syndrome</td>
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<td>mVSD</td>
<td>muscular ventricular septal defect</td>
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<td>OS</td>
<td>ostium secundum</td>
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<td>PDA</td>
<td>persistent ductus arteriosus</td>
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<td>PFO</td>
<td>patent foramen ovale</td>
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<td>pmVSD</td>
<td>perimembranous ventricular septal defect</td>
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<td>PVS</td>
<td>pulmonary vein stenosis</td>
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<td>RVOT</td>
<td>right ventricular outflow tract</td>
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Vascular occlusion: PDA

State of the literature in 2000

Surgical closure of PDA has been performed for more than 60 years. PDA transcatheter closure was introduced in 1967 and has become the treatment of choice for most PDAs, after the neonatal period. Coils are used to occlude small PDAs. Many devices designed to occlude large PDAs have been developed but most are associated with major drawbacks, including a high incidence of residual shunt and/or embolization, complex delivery systems and the need for a large delivery sheath. The ADO (AGA Medical Corporation, MN, USA) was introduced in 1998 and was adopted quickly by most interventionists for the occlusion of moderate and large PDAs.

Landmark study

In 2004, Pass et al. reported the immediate and short-term results of the multicentre USA Amplatzer PDA occlusion device trial [1]. Four hundred and thirty-nine patients with moderate to large PDAs were treated at a median age of 1.8 years (range: 0.2–70.7) and weight of 11 kg (4.5–164.5). ADO implantation was successful in 435 out of 439 patients. The overall morbidity was 9.4% and no deaths occurred. The median follow-up was 12 months and the 1-year occlusion rate was 99.7%.

Recent advances

Concern has been raised regarding PDA closure using the ADO in infants with large symptomatic ducts because of the risk of aortic and/or pulmonary obstruction [2–4]. An angled ADO was designed to avoid protrusion of the occluder into the descending aorta but yet was never marketed [5].
In February 2008, the ADO II received European CE mark approval; this is also a self-expanding nitinol mesh device, fabric-free, shaped into a cylindrical waist with articulated retention discs on both ends, and can be delivered through 4–5 French catheters. Preliminary results presented by DeGiovanni at the 2008 meeting of the Association for European Paediatric Cardiology showed that it can close almost any type of PDA anatomy [6]. Although limited currently by the manufacturer to patients weighing above 6 kg, further studies will be needed to assess the safety and effectiveness of the ADO II in younger patients. In patients weighing at least 4 kg, we feel comfortable closing PDAs less than 5.5 mm using coils (PDAs less than 2.5 mm) or the ADO II (PDAs above 2.5 mm). In larger patients (> 10 kg), we feel that any size and anatomy of PDA can be addressed with coils, the ADO I or II, or a mVSD device [7].

For patients with PDA and pulmonary hypertension, closure can be attempted if the pulmonary/systemic flow ratio is above 2/1 or if the PDA occlusion test shows a decrease in pulmonary pressure [8]. Few studies have reported on the use of the Nit-Occlud Device for the closure of small-to-moderate PDAs [9].

**Vascular occlusion: collaterals and fistulas**

**State of the literature in 2000**

Transcatheter embolization has become the treatment of choice for aortopulmonary collaterals, pulmonary arteriovenous fistulas, venous collaterals and coronary artery fistulas, replacing surgical intervention in most cases. Intravascular coils and detachable balloons were used first and proved to be successful for interventional occlusions of small- or medium-sized vessels. However, they are not ideal in larger fistulas because of the risk of embolization to the systemic circulation. Other devices have also been used (Rashkind-Cardioseal, ADO or Gianturco Grifka, Amplatzer mVSD and atrial VSD occluders) but have major drawbacks, including complex delivery systems and large delivery sheaths.

**Landmark studies since 2000**

In 2001, Qureshi and Tynan reported their experience of using mainly controlled-release coils [10]. Forty patients underwent coronary artery fistula percutaneous occlusion; the procedure was successful in 39 of 40 patients. One 4-month-old infant died 6 h postprocedure. Embolization of the device (coil or detachable balloon) was the main complication and occurred in six patients. All coils were retrieved successfully. At follow-up, complete occlusion of the fistula was noted in 37 out of 39 (97%) patients.

**Recent advances**

The Amplatzer vascular plug was developed to obviate most of the difficulties described previously. This nitinol, fabric-free device, currently in its third generation, is available in sizes that range from 4–16 mm, and can be delivered through low-profile sheaths or guiding catheters (4–7 French). In a multicentre study, Hill et al. reported their initial experience of using the Amplatzer vascular plug (first generation) for embolization of peripheral vascular malformations associated with congenital heart disease [11]. Eighty-nine devices were implanted to treat 84 vessels, in a total of 52 patients. Only one implantation failed, due to non-progression of the device along the sheath through a tight curve. Collateral vessels (45/89; 51%) and fistulas (29/89; 33%) were the lesions occluded most frequently. No deaths or significant procedural complications occurred. One patient underwent surgical ligation of PDA type C after removal of a 14 mm first-generation plug implanted 5 weeks previously, because of significant residual shunt. The second-generation plug has a multisegmented and multilayered design of nitinol to allow more efficient occlusion, as well as extended rims to improve wall apposition and reduce the risk of device embolization. Fig. 1 shows its implantation to occlude a pulmonary arteriovenous fistula. The latest generation, with its lobe shape, is designed specifically for paravalvular leaks.

In the particular setting of coronary fistulas, our experience is to attempt percutaneous closure of all significant malformations (associated with a typical murmur, chamber dilatation or evidence of coronary ischaemia), when the anatomy allows placement of a device distal to the last side branch without compromising coronary blood flow. Most, if not all, fistula anatomies can be approached in this way. Nevertheless, because of reduction in blood flow, side branches proximal to the device are at risk of thrombosis in the long term. The significance of such long-term thrombosis needs to be addressed individually and preventive measures (antiplatelets and/or anticoagulation) adjusted accordingly.

**Figure 1.** Percutaneous closure of an arteriovenous pulmonary fistula using the Amplatzer vascular plug II.
Valvular dilatation: aortic

State of the literature in 2000

Aortic valvuloplasty is an established procedure that is regarded as a valid alternative to the surgical management of congenital aortic valve stenosis in paediatric patients. However, the choice of technique remains highly institution-dependent. A consensus seems to emerge in favour of percutaneous dilatation in patients aged less than 18 years with no valvular calcifications and favourable valvular anatomy (specifically excluding true unicuspid valves).

Landmark studies since 2000

In a neonatal series of 110 patients aged less than 1 month, McCrindle et al. reported the results of surgical versus transcatheter balloon valvuloplasty in neonatal critical aortic stenosis [12]. Early mortality was 11% and 18%, respectively, with no significant difference, even after adjustment for differences in patient characteristics. Likewise, major complication rates were not significantly different. Freedom from aortic reintervention was similar for both groups (91%, 68%, 58% and 48% at 1 month, 6 months, 1 year and 5 years, respectively). The rate of significant aortic regurgitation was higher after balloon valvuloplasty than after surgery, although not significantly so. The same team reported in another study that the only independent predictor of time-related mortality was the presence of moderate or severe left ventricular endocardial fibroelastosis [13]. In a series of 188 patients including neonates and older children, Fraitz et al. reported 10-year rates of freedom from aortic valve surgery after balloon aortic valvuloplasty of 59% in patients aged less than 1 month and of 70% in those aged at least 1 month [14]. Clearly, these studies have increased the popularity of this technique, although the debate is far from settled within the surgical community.

Recent advances

Right ventricular pacing during balloon inflation has been reported and widely accepted, in order to decrease left ventricular stroke volume and pressure, thus increasing balloon stability during inflation [15]. Furthermore, thanks to the use of small arterial introducers (3 French), along with smaller balloons such as the Tyshak-Mini balloon dilatation catheter (B. Braun Medicals, Melsungen, Germany), balloon aortic valvuloplasty can be performed safely and efficiently in neonates, as reported in a series of 20 patients with a mean age of 26 days and a mean weight of 3.6 kg [16]. Mean transvalvular gradient decreased from 76 to 26 mmHg, changes in aortic insufficiency were grade one or less in 19 out of 22 procedures, while no significant vascular complications were reported.

Valvular dilatation: pulmonary

State of the literature in 2000

Pulmonary valvuloplasty is an effective and safe treatment for pulmonary valve stenosis, and is considered as the treatment of choice for non-dysplastic valves. Classic balloon dilatation is often ineffective for dysplastic valves. RVOT palliative dilatation in patients with tetralogy of Fallot is advocated by many teams but remains controversial.

Landmark studies since 2000

The Valvuloplasty and Angioplasty of Congenital Anomalies Registry relates to 533 patients aged 1 day to 55 years (median: 3.7 years) [17]. After a median follow-up of 33 months, freedom from reintervention was 84%. Predictors of a suboptimal long-term outcome included a small annular size (characteristic of patients with dysplastic valves), a higher immediate residual gradient and a smaller balloon/valve ratio than in those with typical pulmonary valve stenosis. The optimal suggested balloon/valve ratio was between 1.2 and 1.4.

Balloon dilatation of RVOT in a symptomatic infant with tetralogy of Fallot has been reported as a palliative step before corrective surgery [18–20].

Recent advances

Whereas the use of cutting balloons has been reported for branch pulmonary artery stenosis (see later section) there are no reports on their use in pulmonary valvular stenosis. In an unpublished case, our team has used a cutting balloon (slightly smaller than the annulus diameter, followed by a larger regular balloon) successfully in a case of dysplastic pulmonary valve, after unsuccessful traditional balloon dilatation.

Implantation of stent in RVOT is quite recent [21]. In this report, nine symptomatic children (mean age: 23 days, range: 3–119) with tetralogy of Fallot and unsalvageable pulmonary valves underwent RVOT stenting. Arterial oxygen saturation increased from a median of 73 to 94% and the median Nakata index increased significantly from 56 mm²/m² (range: 21–77) to 150 mm²/m² (range: 123–231) over a median time of 76 days (range: 42–267) (p = 0.008). There were no deaths and no procedural severe complications. Two patients developed significant cyanosis due to progressive muscular narrowing below the stent and underwent successful additional RVOT stent placement. After a median time of 125 days (range: 40–315), six out of nine patients underwent successful repair; three are still awaiting surgical correction. Further publications are needed to validate these initial results and sort out indications for this promising procedure in a multidisciplinary discussion with our surgical colleagues.

Valvular dilatation: mitral

State of the literature in 2000

Percutaneous mitral commissurotomy (using the Inoue technique) is the treatment of choice for postrheumatic mitral stenosis, where fusion of commissure is a predominant mechanism, but the procedure remains controversial in patients with congenital mitral stenosis.
Landmark studies since 2000

McElhinney et al. from Boston have reported their experience of transcatheter and surgical (valvuloplasty and replacement) therapy for severe congenital mitral stenosis in 108 infants and children with a median age of 18 months [22]. Balloon mitral valvuloplasty was the preferred mode of treatment in most cases, especially in those with typical congenital mitral stenosis (thickened leaflets, short or absent chordae tendineae and two separate, but often closely spaced, papillary muscles) and double orifice mitral valve. Surgery was favoured when mitral stenosis was due to a supravalvular ring, or when significant mitral regurgitation or important associated anomalies requiring cardiomyotomy were present. Overall survival was 77% at 5 years. After percutaneous treatment, significant mitral regurgitation occurred in 28% of cases, and freedom from failure of biventricular repair or mitral valve reintervention was 55% at 1 year compared with 69% after surgical valvuloplasty. However, these results reflect the experience of only one large referral centre, and surgery is the usual approach in most other institutions.

Balloon dilatation and stenting of vessels: pulmonary arteries

State of the literature in 2000

Percutaneous intervention has become the treatment of choice for stenotic pulmonary arteries, most frequently after surgery. The inclusion of high pressure balloons and stents in the interventionist’s armamentarium at the beginning of the 1990s has improved results considerably. However, placement of stents in growing patients inevitably leads to restenosis and is used more cautiously. As most stents can be redilated, we feel comfortable implanting them in patients who have reached two-thirds of their anticipated adult size (which corresponds to an age of 6 or 7 years). In younger patients, this alternative is also reasonable if further surgery is anticipated, or in unstable patients.

Landmark studies since 2000

McMahon et al. reported their series of 664 Palmaz stent implantations in 338 patients with a mean age of 12.2 years [23]. Right ventricular to aortic pressure ratio decreased from 0.66 before stenting to 0.45 immediately after stenting, and was 0.50 at a mean follow-up of 5.6 years. Five deaths were reported, including one fulminant pulmonary oedema and one massive haemoptysis. The rate of restenosis was 2%. Patients with a diagnosis of isolated congenital pulmonary artery stenosis had a less optimal outcome and a higher complication rate.

Recent advances

Cutting balloons have been used successfully in the setting of small-vessel pulmonary artery stenoses resistant to high pressure balloon angioplasty [24]. In this study, 12 patients diagnosed with tetralogy of Fallot and a total of 38 pulmonary vessels were treated with the cutting balloon technique, alone or associated with high pressure balloon dilatation and/or stent implantation. The procedural success rate was 92% (> 50% diameter increase). The diameter of these vessels increased from 1.3 ± 0.7 to 2.8 ± 0.9 mm (p < 0.001). There were no deaths, but one case of unconfined tear needing resuscitation was reported among a total of seven major complications. Follow-up was not available for all patients, and revealed a 50% rate of occlusion (three out of six vessels) at 6 months, predominantly in those vessels treated with stent implantation. Further technological advances, such as biodegradable stents, may further expand the indications for pulmonary artery stent implantation to all age groups [25].

Balloon dilatation and stenting of vessels: coarctation

State of the literature in 2000

Although widely accepted in the treatment of recoarctation (because of the increased difficulty and morbidity of repeated surgery), consensus still has not been reached on balloon angioplasty of native coarctation, due to its somehow higher rate of recurrent stenosis and aneurysm formation, and, ultimately, reintervention, compared with surgery. It is an accepted alternative to surgery for children (aged: 1–7 years) but remains highly controversial in neonates and infants because of a very high incidence (> 50% in most series) of recoarctation. For patients near adult size (aged: 7 years or above 35 kg), primary stenting is used increasingly; these patients will usually need planned elective redilation after complete growth.

Landmark studies since 2000

A multi-institutional study reported an immediate success rate of 97.9% (563 out of 565 procedures) after stenting native and recurrent aortic coarctation in patients aged above 4 years, and an acute complication rate of 14.3% (81 out of 565), including two deaths, six aneurysms and nine aortic dissections [26]. The risk of aortic dissection after implantation of bare stent is higher in cases of nearly atretic coarctation or if coarctation is associated with a hypoplastic aortic arch. The incidence of aneurysm formation has been found to increase with a larger percentage increase in coarctation diameter poststent implantation, a balloon/coarctation ratio above 3.5 and balloon predilatation of the lesion.

Recent advances

Several series report the growing use of covered stents and balloon-in-balloon in the setting mentioned above, with an almost 100% immediate success rate and good midterm results [27,28]. Covered stents can also isolate aortic aneurysms [29] or bail out from acute rupture [30]. The Cheatham platinum-covered stent (NuMED Inc, Hopkinton, NY, USA), made of platinum–iridium alloy and covered with expandable polytetrafluoroethylene, is used most widely. Fig. 2 shows its implantation in an acquired atresia, after radiofrequency perforation [31].
Figure 2. Recanalization of a complete coarctation with isthmus occlusion in a 16-year-old patient using radiofrequency and covered stent implantation. A, B. Simultaneous angiograms after gaining femoral and brachial arterial accesses, in frontal and lateral planes. C. Perforation of the occluded segment using a 0.035 radiofrequency wire (Powerwire, Baylis Medicals, Montreal, Canada). D. Predilatation using a coronary balloon. E. Implantation of a Cheatham platinum-covered stent crimped on a balloon-in-balloon. F. Final lateral aortic angiogram.

The use of biodegradable metal stents for the treatment of aortic recoarctation in a 3-week-old neonate has been reported [32]. This balloon expandable stent consists of an absorbable magnesium alloy and seems promising, along with other types of resorbable stents, for the treatment of severe vascular stenoses in newborns and infants. Further studies are needed, however, to validate the indications and long-term results.

Balloon dilatation and stenting of vessels: pulmonary veins

State of the literature in 2000

Congenital PVS is a relatively rare condition, usually with a guarded prognosis. Neither surgery nor percutaneous intervention (balloon dilatation or stenting) achieves freedom from reintervention or death at midterm follow-up. After surgical repair, overall freedom from death or reoperation at 5 years is around 50% [33]. Balloon dilatation and/or stenting are seldom associated with mid- or long-term success.

Landmark studies since 2000

In 2006, Devaney et al. reported their experience of surgical repair of PVS over almost 15 years [34]. Among 36 patients, 14 had congenital PVS, four of whom underwent intraoperative stent placement. Only one out of four was reported as being alive 10 years after the procedure. Among the 22 patients with acquired PVS after correction of total anomalous pulmonary venous connection, 11 underwent sutureless pericardial marsupialization. This technique was found to be associated significantly with better survival without restenosis. Median follow-up was 30 months (1 month to 14 years) and 14 out of 36 (38.9%) patients died during follow-up. Only small studies reporting percutaneous balloon dilatation and/or stent placement for congenital PVS have been reported. In a non-randomized study, Prieto et al. compared the results of balloon angioplasty versus stent implantation for the treatment of acquired PVS after pulmonary vein isolation for atrial fibrillation ablation in 44 patients [35]. A total of 80 pulmonary veins were affected, but intervention was impossible in 12 occluded vessels; 55 of the 68 pulmonary veins treated initially were available for follow-up. Balloon dilatation was performed in 39 out of 55 lesions and primary stenting in 16 out of 55 lesions; immediate success (residual stenosis at most 30%) rates were 42% and 95%, respectively (p = 0.001). There were no deaths. Three significant complications occurred: one transient neurological event and two tamponades requiring drainage. There were 24 additional lesions treated with stent implantation during a mean follow-up of 25 months. At 4 years, freedom from restenosis was 20% and 40% after balloon dilatation and stent implantation, respectively, and reached 80% for implanted stents at least 10 mm.

Recent advances

Further catheter-based interventions have been attempted: balloon dilatation using high pressure balloons [36] and cutting balloons to treat native lesions [37] or in-stent stenosis [38]. Again, immediate improvement is usually seen angiographically, but recurrent stenosis occurs in a large majority of patients. There is still no reported experience to date with the use of sirolimus or paclitaxel drug-eluting stents in this situation, although unreported cases may exist. In our institution, a covered stent has been implanted in
Advances in paediatric interventional cardiology since 2000

Figure 3. Recanalization of an occluded left superior pulmonary vein (A, B, C) followed by the implantation of a covered stent (D, E), with perfect angiographic and haemodynamic results (F). The left lower pulmonary vein was completely occluded (C) and not recanalizable.

a 26-year-old girl with congenital left upper and lower pulmonary vein occlusion with venovenous collaterals (unreported case; Fig. 3). The occluded left superior pulmonary vein was reopened using a terumo guide, and a covered stent (Jostent, Abbott Vascular, Abbott Park, IL, USA) was then implanted. Although no residual gradient was present at the end of the procedure, restenosis developed over the next few years and redilatation was required.

PFO closure

State of the literature in 2000

PFO closure in patients with previous cerebral embolic events remains controversial. When indicated, however, percutaneous closure is replacing surgery progressively.

Landmark studies since 2000

Results of percutaneous PFO closure in a large cohort of 307 patients with previous thromboembolic events using three well-established occlusion devices (PFO-STAR, Amplatz PFO occluder and CardioSEAL/STARFlex) were reported [39]. Implantation was successful in all patients. Three major peri-interventional complications occurred: one dislodgment and two transient ischaemic attacks. Complete closure rates were 56%, 69%, 94% and 96% immediately after the procedure, at 1 month, 1 year and 2 years of follow-up, respectively. Freedom from recurrence for the combined endpoint of transient ischaemic attack, stroke or peripheral embolism was 99% at 6 months. There was a trend towards a lower rate of complications and a higher percentage of complete PFO closures using the Amplatz PFO occluder.

Recent advances

A host of new devices has been introduced [40]. The BioSTAR (Organogenesis, Canton, MA, USA)—a bioabsorbable device—consists of an acellular porcine intestinal collagen layer matrix mounted on the STARFlex framework, and has been used in a phase I clinical trial [41]. Other devices include the Premere occluder (St Jude Medicals, Inc., Maple Grove, MN, USA), the Solysafe septal occluder (Swissimplant AG, Solothurn, Switzerland) and the Inrasert PFO occluder (CARDIA, Inc., Burnsville, MN, USA), which is a new version of the PFO-STAR occluder. Relative advantages of each device need to be determined.

While some indications (recurrence of neurological embolic event and platypnea–orthodeoxia syndrome) have been validated, others (migraine and initial neurological embolic event) are still controversial. The results of the MIST I trial (a prospective, randomized, double-blind study aiming to evaluate the effectiveness of PFO percutaneous closure, using the STARFlex device, in eliminating migraine headache) were published earlier this year [42]. No significant difference was observed in the primary endpoint between implanted and sham groups. Many ongoing randomized trials (PC-trial, CLOSURE I and RESPECT for cerebrovascular events and PREMIUM, PRIMA and MIST II for migraine headaches) aim to compare different strategies (percutaneous versus medical treatment) and different devices (mainly the Amplatz and STARFlex devices), in order to clarify the optimal management of PFO.

ASD closure

State of the literature in 2000

Percutaneous closure of OS ASD has become the treatment of choice, except for very large defects and/or insufficient rims, where surgery may still be preferred. Several devices have been used, including the CardioSEAL/STARFlex devices, the Sideris buttoned device, the HELEX device and the ASO. The ASO has become the most widely used because of its
high closure rates, safety of use, ease of deployment and eventual retrieval, and ability to close large defects.

**Landmark studies since 2000**

From January 1997 to May 2008, 359 mostly paediatric patients (median weight: 18.7 kg [range: 5.2–135] and median height: 109.5 cm [range: 63–178]) underwent 360 OS ASD closure attempts using the ASO device at our institution (unreported results). Systematic transcatheter closure has been performed since 2000 (N=280), regardless of size. Successful implantation was achieved in 358 out of 360 (99.4%) cases, with no failure since 2000. Significant complications occurred in 27 out of 360 (7.5%) cases, including one respiratory arrest with successful resuscitation, transient high-degree atioventricular block in 16 cases [43], one aortic erosion and one catheter-related tamponade (treated by surgical repair and percutaneous drainage, respectively, with neither requiring device excision), one device embolization (recaptured and repositioned) and one cerebral embolism (with full recovery). No procedure-related death or surgical excision of a device occurred. Median ASD size was 12 mm (range: 4–33) at transthoracic echocardiography and 14 mm (range: 2.5–33) at transoesophageal echocardiography. Median implanted device size was 19 mm (range: 4–38). Complete occlusion was achieved in 86.5% and 96% of all cases, at 24 h and at 1 year, respectively. Indications for closure of a small ASD (< 10 mm) were right-to-left shunt or poor left ventricle compliance and consequent low cardiac output state.

**Recent advances**

Long-term follow-up is now available after implantation of the ASO device, confirming the initial excellent results. Yet concern has been raised regarding the occurrence of cardiac erosion after OS ASD occlusion using the ASO device [44]. A total of 24 cardiac events were reported in a retrospective study, and were conclusive for device-related cardiac perforation. About one-fifth occurred before hospital discharge and were amenable to intervention. About two-thirds occurred after hospital discharge and were thought to be device-related cardiac perforation [44]. A recent review suggested that device oversizing and deficient anterosuperior rim are risk factors for cardiac perforation [45], which has led most implanters to modify their guidelines and technique. Erosions have also been reported with other devices (CardioSEAL-STARFlex, Sideris buttoned, Cardia, etc), but their true incidence is less well known. Interestingly, this complication has not been reported with the HELEX device.

New devices have been introduced: the Intrasept in 2003 and more recently the Occlutech Figulla device (Occlutech GmbH., Jena, Germany). As with PFO closure, the relative advantages of each device need to be determined in comparative studies.

Closure of a large OS ASD can be challenging, even when using the ASO. Different deployment strategies are described (use of specially-shaped sheaths [Hausdorf], deployment of ASO in the left or right pulmonary vein, etc). In our experience, the use of the balloon technique [46] (deployment of the device using the support of a spherical balloon inflated across the defect) has always been successful, even in cases where all other techniques failed (Fig. 4).

Hybrid procedures have been performed to close OS ASD through a peratrial approach, especially in infants [47].

**mVSD occlusion**

**State of the literature in 2000**

The surgical closure of an mVSD can be a challenge for the surgeon. It also involves a significant risk of mortality,
reoperation and ventricular dysfunction due to right or left ventriculotomy [48]. Percutaneous closure was attempted in the late 1980s using various devices designed for other malformations, notably the Rashkind and Clamshell devices, and since 1998, using the specific Amplatzer mVSD occluder. This self-expandable device consists of two retention disks linked via a central connecting waist, which is 7 mm long. Both retention disks are 5 mm larger than the connecting waist. Device size (4—18 mm) is usually chosen equal to or 1—2 mm greater than the size of the VSD. The device can be deployed in very small patients, as demonstrated on Fig. 5. Various approaches can be used, according to the anatomy of the mVSD: femoral vein for anterior defects, jugular vein for midmuscular and apical defects, trans-septal, retrograde aortic or periventricular (hybrid procedure).

**Landmark studies since 2000**

Immediate and midterm results of mVSD closure using the Amplatzer mVSD occluder have been reported by Holzer et al. [49]. In this USA registry, closure was attempted in 83 procedures involving 75 patients (mean age: 1.4 years, range: 0.1—54.1), with a successful implantation rate of 86.7%. In five out of 75 patients, implantation was performed through a periventricular approach. Ten major complications occurred, including two deaths (cardiac perforation and haemorrhagic shock). At 12 months, complete closure (or any residual shunt less than 2 mm) was 100%. Results of the European registry concerning transcatheter closure of congenital ventricular septal defects were reported by Carminati et al. [50]. Of the 430 patients, 119 had mVSDs. The Amplatzer mVSD occluder was the device used most frequently. One death was reported after attempted closure of a residual VSD in a 6-year-old boy with corrected transposition of the great arteries and multiple VSDs.

**Recent advances**

Hybrid procedures using a periventricular approach for the implantation of an Amplatzer mVSD occluder have been reported, with encouraging results [51,52]. As discussed later, hybrid procedures have the advantage of avoiding cardiopulmonary bypass, while overcoming vascular access limitations and haemodynamic instability in small patients.

The use of Nit-Occlud coils has been reported as an alternative to the Amplatzer devices for closure of mVSDs and pmVSDs of small to moderate size (≤ 7 mm). In 2006, results of the international experience were presented by Lê TP at the Pediatric Interventional Cardiac Symposium. Forty-five patients underwent percutaneous closure of both pmVSDs (N = 36) and mVSDs (N = 9) at a mean age of 14.7 years. Mean VSD size was 4.5 mm (range: 3—8). Successful implantation was achieved in 41 out of 45 cases. Coil displacement necessitating surgical removal occurred in one case. Complete occlusion rate at 6-month follow-up was 82%.

**pmVSD occlusion**

**State of the literature in 2000**

Until the beginning of this century, surgery was the gold standard for pmVSD closure. Percutaneous attempts to close pmVSDs with Rashkind and buttoned devices (non-specific to pmVSD) were reported in the late 1990s, but with a high incidence of residual shunt and complications.
Landmark studies since 2000 and recent advances

The Amplatzer pmVSD occluder was introduced in 2002 as the first device designed specifically for pmVSD occlusion. This self-expandable device is made of nitinol wire with Dacron fabric incorporated. It consists of two flat disks linked via a central connecting waist that is 0.5 mm long. Its diameter corresponds to the size of the device (ranging from 4 to 18 mm). The left disk is asymmetric with almost no (0.5 mm) superior (aortic) rim and a longer 5 mm inferior rim. The right disk is symmetrical and 4 mm larger than the waist. Contraindications to percutaneous closure are extension of the defect to the subpulmonary area (so-called the waist. Contraindications to percutaneous closure are extension of the defect to the subpulmonary area (so-called subarterial defects) as well as greater than mild aortic prolapse and/or insufficiency.

Initial and midterm results have been reported by Holzer et al. in an international registry involving 100 patients [53]. Successful implantation of the Amplatzer pmVSD occluder was achieved in 93 out of 100 patients. Median VSD size by transthoracic echocardiogram was 7 mm (range: 1.5–13) while median device size was 10 mm (range: 4–16). No procedure-related deaths occurred. Complications were reported in 29 out of 100 patients including two complete atrioventricular blocks requiring permanent pacemaker implantation and nine new or increased aortic insufficiency (none progressing or requiring surgery). At 6-month follow-up, complete closure rate was 83.6%.

The major concern is the occurrence of complete atrioventricular block during the procedure, shortly after or even several months later, and requiring pacemaker implantation (ranging from 2 to 5.7% in multicentre studies [50,53,54]). Although no risk factor has been linked statistically to this complication in these studies, most investigators agree that oversizing of the device, large size of defect, patient weight below 10 kg and extension of the defect posteriorly (inlet septum) or inferiorly (high muscular septum) are plausible associations, and have modified their inclusion guidelines and technique accordingly. No consensus exists regarding the management of complete atrioventricular block. In cases of periprocedural complete atrioventricular block, if the device has not been released, the interventional cardiologist usually chooses to retrieve it [54,55]. Medical treatment using corticosteroids is advocated by most teams if complete atrioventricular block develops in the first week(s), with a good recovery rate [54–56]. However, cases appearing later are usually irreversible. Obviously, this complication has cooled the initial enthusiasm for the procedure considerably, and might prompt modifications of the device or its abandonment if the incidence has not decreased significantly in the next published series. Interestingly, complete atrioventricular block has not been described with other devices for pmVSD occlusion, most notably the Nit-Occlud.

The use of robotic-assisted surgery has been reported widely since early 2000, in extracardiac specialties. Cardiac surgeons have also reported its use in performing totally endoscopic coronary artery bypass and mitral valve repair [57–59]. Reports in paediatric patients are infrequent. Robotic-assisted percutaneous closure of pmVSD has been performed by Amin et al. in an animal study, using the Da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) [57]. An Amplatzer pmVSD device was implanted successfully in five out of seven Yucatan pigs, which have a naturally occurring pmVSD. Nevertheless, further investigations and studies are needed before its application in humans.

RVOT obstruction and percutaneous pulmonary valve implantation

State of the literature in 2000

The lifespan of a bioprosthetic right ventricular to pulmonary artery conduit is limited because of progressive obstruction and regurgitation. Endovascular treatment using balloon dilatation and bare stent implantation were increasingly accepted to extend conduit lifespan and reduce the number of open heart surgeries.

Landmark studies since 2000

The team from Boston Children’s Hospital has reported its experience of endovascular stenting of obstructed right ventricular to pulmonary artery conduits [60]. Over a 15-year period, deployment of bare stents was attempted in 242 obstructed conduits in 221 patients. There were no deaths and only one failure of attempted stent placement was reported. Acute complications requiring surgical stent removal occurred in five patients. Median freedom from conduit replacement after stent placement was 2.7 years.

Recent advances

While resolving the problem of conduit obstruction, bare stent placement inescapably leads to creation or deterioration of pulmonary regurgitation. To overcome this problem, Bonhoeffer et al. were the first to report their experience of transcatheter pulmonary valve replacement using a biological valve harvested from a bovine jugular vein (Medtronic, Inc., Minneapolis, MN, USA) and mounted in a balloon expandable vascular Cheatham platinum stent (Numed, Inc., Hopkinton, NY, USA) [61]. This procedure is illustrated and described on Fig. 6. Owing to valve availability and size, as well as the need for a stiff structure to anchor the stent, indications for this valved stent are limited to patients with right ventricular to pulmonary artery conduits of 16–22 mm diameter or presented RVOT. Yet most indications of pulmonary valve replacement are encountered in patients who have dilated RVOT secondary to transannular patch repair for tetralogy of Fallot. To overcome these limitations, Boudjemline et al. have devised and reported in animal studies different ways to reduce the size of the RVOT before implanting the valved stent, such as a hybrid approach with a surgical pulmonary artery banding primarily [62] or implantation of an intravascular stent reducer [63]. Other percutaneous pulmonary valves have been implanted by different teams.

In a recent study, Lurz et al. reported the immediate and long-term results of percutaneous pulmonary valve replacement performed by a single operator in 155 patients since the introduction of the Melody valved stent.
Figure 6. Percutaneous pulmonary valve implantation. A. Before implantation, simultaneous balloon inflation in the RVOT and coronary angiography are performed to document any potential risk of coronary obstruction with the valved stent. B. Deployment of the preloaded valved stent advanced over an extrastiff guide wire, by inflating the inner and outer balloons. C. Final angiogram confirming the correct position of the stent, and showing trivial pulmonary regurgitation.

in 2000 [64]. Successful implantation was achieved in 150 out of 155 patients (five immediate explantations). Major complications included device dislodgement and instability (N=2), homograft rupture (N=3), compression of the left main coronary artery (N=1) and compression of the origin of the right pulmonary artery (N=1). Freedom from reoperation was 86% and 70% at 30 and 70 months, respectively.

Percutaneous aortic valve implantation

Percutaneous aortic valve implantation has been achieved in high-risk (high EuroSCORE) patients with severe aortic stenosis as an alternative to open heart surgery. Several valves have been used, mainly the Cribier-Edwards valve and the CoreValve [65]. This technique, which is used only in compassionate indications, has provided haemodynamic and clinical improvement for up to 2 years in patients with severe symptomatic aortic stenosis [66]. The valves currently available are being evaluated in the setting of North American and European trials. The extremely low mortality rate of surgical management in standard-risk patients, and its favourable long-term follow-up, forbids the use of this technique in this population for now, thus excluding young patients.

Hybrid approach

State of the literature in 2000

The use of complex transcatheter techniques in the management of congenital heart disease can be limited in small patients due to the use of large sheaths and their manipulation within the heart. Open-heart surgery can also lead to significant morbidity and mortality in this population, specifically for interventions such as mVSD closure or stage I Norwood palliation.

Landmark studies since 2000 and recent advances

To overcome these limitations, interventional cardiologists and surgeons have worked hand-in-hand to develop hybrid procedures. These have been attempted in the past 8 years in different fields—mainly VSD closure, HLHS management and perventricular valve implantation.

Hybrid VSD closure was attempted in animal studies in the late 1990s and shortly afterwards in humans [51,67]. A right perventricular puncture is performed through a mini-sternotomy, without cardiopulmonary bypass, and a guide is advanced through the VSD under transoesophageal guidance. A delivery catheter is advanced over the wire and the device is then deployed as usual. Two of the largest series of mVSD or pmVSD hybrid closures, both using the Amplatzer device, included 13 and 11 patients, with a mean age of 1.3 and 14.6 years, a success rate of 92.3% and 100%, and a complication rate of 23% (3/13) and 0%, respectively [52,68].

Ideally, hybrid interventions for HLHS should take place in a specially designed hybrid suite [69]. The surgeon bands both pulmonary arteries through a median sternotomy, while the interventional cardiologist implants a stent in the arterial duct through a purse string in the main pulmonary artery. In cases of restrictive atrial septal communication, an atrioseptostomy is performed and/or a stent is placed across the septum. Although the hybrid approach reduces the initial mortality of the first procedure, it leads predictably to increased interstage mortality and a more complex second-stage palliation (arch reconstruction, stent excision and bidirectional Glenn procedure). Over a 2-year period, Calderone et al. compared the results of 18 hybrid procedures with those of 25 classic Norwood stage I interventions in the treatment of mainly HLHS [70]. Although not assigned randomly, no difference was found between the two groups in terms of age and weight at the time of the procedure. Survival rate at 1 year was around 70%, with no significant difference between the two groups. Similar conclusions were drawn by Pizarro et al. who compared both approaches in 33 high-risk neonates with HLHS [71]. It can therefore be argued that this procedure still needs to be refined to match the surgical results in high-volume centres. However, it already represents an interesting alternative in centres with suboptimal surgical outcomes.

Although sequential (or pseudohybrid) approaches have been described (initial surgical banding, followed by percutaneous PDA stenting and ASD enlargement), with encouraging results [72], the true hybrid approach submits the patient to only one procedure, under more stable conditions. An exclusively percutaneous approach (with bilateral banding devices) has also been described but leads to more...
complications arising from the procedure itself and the less precise control of the final pulmonary flow, and has now been abandoned in favour of the hybrid procedure.

Experienced teams now prepare the intra-atrial anatomy during the extended second-stage surgery (by performing a patched anastomosis between the right pulmonary artery and the superior vena cava or a lateral fenestrated Fontan tunnel) to allow percutaneous completion of the palliation [73,74]. When indicated, the patch can be perforated percutaneously and a single-covered or multiple-covered stent(s) can direct the inferior vena cava flow to the pulmonary circulation. Alternatively, an intra- or extra-atrial tunnel (with large fenestration) can also be constructed during the extended second-stage palliation. A covered stent can thus be used during the percutaneous completion, with device closure of the fenestration [75]. Such percutaneous Fontan operations, by avoiding mechanical ventilation and cardiopulmonary bypass, permit a much smoother transition to complete cavopulmonary physiology, thus reducing mortality, morbidity and hospital stay predictably.

The hybrid approach (left ventricular apical puncture through thoracotomy) is also used increasingly for aortic valve implantation to overcome the limitations of a percutaneous approach [76].

Fetal interventions

State of the literature in 2000

Fetal cardiac interventions generate a great deal of interest but are still controversial. They are based on the hypothesis that early relief of intracardiac obstacles might improve the development of the affected cardiac chambers. The first fetal dilatation of the aortic valve, through abdominal maternal and thoracic fetal punctures, was accomplished in 1991. A worldwide study of 12 cases, however, showed discouraging results, with a technical success rate of 58% and only one patient still alive at the time of publication [77].

Landmark studies since 2000

Tworetzky et al. from Boston reported their fetal aortic stenosis series [78,79]. Fetal aortic dilatation was attempted in 22 fetuses. Four died in utero (one termination, three dismissions). Among the 18 liveborns, 14 had a successful procedure, but only three ended with biventricular circulation. Overall, technical success was achieved in 16 out of 22 (73%) patients, with a better chance of success if maternal laparotomy was an option. Details of intervention are described elsewhere [78]. The same team identified physiological features predicting the progression of midgestation fetal aortic stenosis to HLHS, aiming at optimizing patient selection for fetal intervention. While availability of fetal balloon valvuloplasty is limited and results still need to demonstrate superiority compared with neonatal surgery, it clearly holds the promise of promoting in utero left ventricle growth and improving function. However, these possible benefits have yet to be clearly demonstrated and ought to be weighed against the definite risks of such interventions. Further series need to be published before these procedures become mainstream.

Recent advances

Fetal pulmonary valvuloplasty has seldom been reported [80]. Atrial septostomy has been attempted in fetuses with HLHS and an intact or restrictive atrial septum [81]. Technical success was achieved in six out of seven fetuses but only one was liveborn.

Finally, the use of high-intensity focused ultrasound has been reported and seems to be a promising tool for fetal cardiac interventions [82]. Using frequencies of 500 kHz to 10 MHz, high-intensity focused ultrasound causes focal tissue lesions at adjustable depths without the need for direct tissue contact and without injuring intervening tissue. This non-invasive technique has been used in urology, neurosurgery and oncology, as well as in some reported cases of cardiac conduction tissue ablation. Its more immediate fetal application would be atrial septostomy in cases of HLHS, and possibly aortic or pulmonary valve stenosis relief. However, it is still in the experimental phase and in vivo human studies are awaited.

Conflict of interests

None.

References

Advances in paediatric interventional cardiology since 2000


