Current treatment of the persistent arterial duct

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INTRODUCTION

To consider possible methods of occluding persistently patent arterial ducts, derived from the Latin term *Ductus arteriosus* a brief introduction of this anatomic structure is necessary.

This is an anatomic structure with vitally important functions in pre-natal life that also has an important participation in circulation modifications in the post-natal period.

Pre-natal aspects

The arterial duct is a vital structure in the life of the fetus, a phase in which the lungs are collapsed and, thus, there is no effective establishment of the pulmonary circulation. Hence, the blood ejected by the right ventricle, with the impossibility of reaching the pulmonary circulation, shunts through the arterial duct to the aorta, arriving at the placental circulation where oxygenation of the fetal blood is achieved [1]. Therefore, the arterial duct must be patent during the pre-natal life, and because of this it is totally formed at the sixth week of embryonic life [2].

Also the location of the arterial duct is important. Originating in the dorsal portions of the sixth pair of arterial arches that unite the central aorta to the dorsal aorta during the embryonic life. At the moment in which the anatomy of the circulation system is developed, the arterial duct establishes a connection between the aorta and the pulmonary artery.

Its aortic end is located a little below the left subclavian artery and its pulmonary end next to the root of the ipsilateral pulmonary artery. In rare cases with the aortic arch to the right, the arterial duct has the same position in respect to the aorta and the pulmonary artery, but to the right of the thorax [3]. Studies in the pre-natal period demonstrate that the histological characteristics of the arterial duct differ greatly to those of the aorta and pulmonary artery to which it is connected.

Whilst the aorta and the pulmonary artery present walls that are rich in elastic fibers arranged in a circumferential form, the arterial duct presents with a dense tunic media, rich in smooth muscle fibers arranged in a spiral format in both directions (left-right and right-left).

This histological characteristic of its tunic media enables the arterial duct on contracting, not only to reduce its diameter, but also to shorten, that is, a reduction in length. This becomes important during modifications in the circulation soon after birth.

Additionally, the arterial duct has a tunic intima that has a thickness four or five times greater than the tunic intima of the aorta or the pulmonary artery [1].
Post-natal modifications

Soon after birth, important modifications occur in the circulation. With the immediate expansion of the lungs, the pulmonary circulation initiates, at the same time at which the placental circulation is eliminated. Establishing the pulmonary circulation, the newborn baby starts with a classical serial circulation, normal to adults [1].

This serial circulation is characteristic by the fact that the blood ejected by the right ventricle passes through the pulmonary circulation and arrives at the left atrium. Then it passes to the left ventricle that ejects to the aorta and, after nourishing the systemic territory, returns to the right atrium with the same initial quantity ejected by the right ventricle, perpetuating this circuit in series.

Thus, in the absence of abnormalities of the heart and the systemic or pulmonary vessels, all the heart chambers present with the same blood flow.

Owing to the expansion of the lungs and the establishing of the pulmonary circulation, an immediate increase in oxygen saturation occurs, which causes a vigorous contraction of the arterial duct. Its tunica media, rich in smooth muscle cells, presents with a great reactivity to increases in the oxygen saturation and to the rises in oxygen tension. Thus, it contracts and, as has been mentioned earlier, by the arrangement of its fibers this causes a significant reduction in its diameter and also its length [1]. From this initial contraction, it closes within two to three weeks due to endothelial invagination, proliferation and ruptures of the sub-intima tunica and also due to formation of connective tissue [3]. Humoral factors seem to interfere in the evolution to complete occlusion too [1,2].

In cases in which closure of the arterial duct does not occur, an abnormal connection between the systemic and pulmonary circulation systems, called a persistently patent arterial duct, remains. Its prevalence is 1:2,000 live births, representing around 10% of all congenital heart defects [2,3].

The clinical manifestations of this congenital abnormality depend on the diameter of the malformation. If the diameter is large, physiopathologic alterations appear that define the pulmonary venous capillary hypertension, with classical congestive phenomenon such as dyspnea, repeated interruptions of breast feeding, profound sudoresis and repetitive bronchitic phenomenon. Also at this initial stage, pulmonary arterial hypertension occurs, initially reversible, from this infection in these patients.

For this all persistently patent arterial ducts, with the exception of the hyper-resistant ones, should be occluded, whether because of their clinical manifestations or because of the risk of evolving infectious endocarditis [4,5]. Their occlusion may be by surgical or percutaneous treatment.

Every time that percutaneous closure of the arterial duct is considered or indicated, a cost-benefit study should be made between the percutaneous and surgical options. It is important to know that the operation to occlude the arterial duct is the safest and more efficient of all surgeries for the treatment of congenital heart diseases [5]. Even with non-congenital heart disease operations, it is still the safest and most effective surgery in the area of heart surgery.

All indicated percutaneous treatments should offer to the patient the same safety and efficiency as surgical treatment, at the same or at a lower cost.

Surgical treatment

The surgery to occlude the persistently patent arterial duct presents with very low morbidity and mortality rates. Mortality ranges from 0.2 to 0.5% have been reported [2]. MAVROUDIS et al. [6] published a series of more than one thousand patients operated on during 46 years without any mortality. The extensive and classical left lateral thoracotomy has been reduced over the years [5,6]. This reduction in the
length of the thoracotomy has significantly reduced morbidity, which reached 10% mainly with the involvement, to some degree, of scoliosis, weakening of the joint of the left shoulder, recurrent pain, breast deformation or alterations of the left rib cage owing to the thoracotomies [5].

Ligature of the arterial duct was first performed in 1939 and over the years the techniques have been improved and, principally in small children, where closure of the duct can be achieved by an extra-pleural approach, the thoracotomy is a few centimeters in length.

Another important aspect is that the surgical occlusion of the arterial duct does not require a cardiopulmonary bypass, which reduces the risk and significantly diminishes the cost of the operation. Also there is no necessity for a median sternotomy, which reduces the risk of post-operative infections and eliminates esthetic problems that are relevant in the case of persistently patent arterial ducts, as it is a heart disease that predominantly affects girls with a proportion of 2 to 3:1 [2,3].

Several alternative techniques can be used for the surgical occlusion of this congenital anomaly. Conventional surgery is performed by left lateral thoracotomy and a simple ligature can be made. This is the oldest and least effective of the operative techniques, as it can present with a reappearance of the flow through the arterial duct over the long term in around 22% of the cases [7].

Another option is to perform multiple ligatures, which reduce the incidence of the reappearance of flows through the arterial duct to 3 to 6% [8,9].

Without doubt the most effective technique is by sectioning and ligation the arterial duct, which totally eliminates any possibility of the reappearance of the flow [6]. With this, the risk of infectious endocarditis is also reduced, which can occur after the re-establishing of a flow that is not diagnosed at an early stage. Hence, sectioning and sutures remains the technique of choice for the occlusion of a persistently patent arterial duct [5] (Figure 1).

The operation by video-assisted thoracoscopic surgery using titanium vascular clips to occlude the arterial duct is performed using four incisions with a maximum of seven centimeters each, in the third and fourth intercostal spaces, along the medium and anterior axillary lines (Figure 2). However, this technique has not been widely utilized with few published works [12-15]. LABORDE et al. [12] using two titanium clips had a 2.1% rate of residual reflux in 230 cases. They also reported an incidence of 2.6% recurrent laryngeal nerve injury, although involvement was permanent in only one case. In their first series of 38 patients using this technique, there was a necessity of repeat operations in two cases owing to the inadequate positioning of the clips.
of the ducts, without complications related to the procedure. According to the authors, a clip should be placed as far from the aorta as possible and the second clip at the aortic end of the duct. They emphasize that there were no cases of mortality [12]. BURKE et al. [14] report the occurrence of residual refluxes in the immediate post-operative period in 3.3% of 30 patients submitted to this technique using a single clip, but during the follow up this rate increased to 12%. CHU et al. [15] reported a rate of 8.7%.

Nevertheless, there are no works that demonstrate benefits equal to or better than or lower risks than those experienced with conventional surgery. Also video-assisted thoracoscopic surgery is not indicated on ducts with diameters > 9 mm, calcified arterial ducts or in patients previously submitted to thoracotomy [5,12]. In children the technique is contraindicated in the presence of pleural adherence [12]. The technical modification made by CHU et al. [15], performing ligatures using 2-0 threads on Teflon pledgets placed anteriorly and posteriorly to the duct, enables occlusion by video-assisted thoracoscopic surgery in adult patients or those who previously underwent thoracotomy, in which the incisions are increased slightly.

Premature or newborn babies at full term constitute a separate group. In the case of premature babies with persistently patent arterial ducts and significant symptoms, Indomethacin can be used, with an arterial duct closure rate of up to 70% [2], due to its blocking action on cyclooxygenase, an enzyme that determines the release of prostaglandins. However, if a rapid and significant clinical improvement is not obtained, or in cases where there is a contraindication for the use of Indomethacin, surgery should be indicated immediately.

In the neonatal department, surgery on premature babies has been performed within the nursery, in the baby’s cot, without the necessity of taking the patient to the surgical center. For the arterial duct occlusion in these patients, vascular clips are used, thereby significantly reducing the operative time. Even in this group of newborns, with very low weights, the surgery has a low morbidity-mortality rate. Closure by video-assisted thoracoscopic surgery in premature babies was initiated by LABORDE et al. [13] in 1993. FÖRSTER [16], in 1993, reported his first three cases of arterial duct occlusion by video-assisted surgery in premature babies employing single clips. The surgeries were performed in the neonatology unit within the incubator of the babies using minimal thoracotomies, with a total incision of 15 mm. The success of these procedures was confirmed by echocardiography, which demonstrated total occlusion of the ducts, without complications related to the procedure.

Closure using this technique was also successfully achieved by BURKE et al. [14] in five premature babies.

Transaxillary surgery in premature babies, without drainage of the thorax and with an incision, on average, of two centimeters in the third left intercostal space, occluding the arterial duct using a clip was performed by MILES et al. [17]. It was demonstrated that not using drainage material, the reduction of nursing care and the significant reduction in the number of control radiographs, as well as early hospital release, significantly reduced the hospital costs. There were no mortalities related to the surgical technique, but three deaths occurred due to the extreme prematurity.

With full-term newborn babies, if clinical improvement is not obtained with anti-congestive therapy, surgical treatment should be promptly indicated. In these patients the use of Indomethacin is not indicated. Also in these patients the surgery presented with the same low mortality rate already mentioned and an extra-pleural access allows minimal thoracotomies, which reduces the long-term morbidity rate [6,12,14].

It is important to emphasize that with full-term newborn and premature babies percutaneous treatment is not indicated [13,16].

Percutaneous occlusion

Percutaneous occlusion is neither a novelty nor a recently introduced procedure for the treatment of persistently patent arterial ducts. In 1971, PORSTMANN et al. [18] reported their successful initial experience with the occlusion of arterial ducts utilizing an Ivalon plug, a conical-shaped device made of plastic foam. However, to deliver this device large caliber catheters were necessary, which made the technique impossible to use on small children, thus making its use restrictive.

In 1978, RASHKIND [19] utilized a single-disk prosthesis invented by himself, to close this congenital anomaly, but with unsatisfactory results, which were published in 1983, when he demonstrated his initial experience. He was successful, on the other hand, with the use of his double-disk system for the occlusion of persistently patent arterial ducts. From this initial experience, the Rashkind double-disk system widely dominated the percutaneous occlusion field of the arterial duct and it was the most commonly utilized device during the rest of the 1980s and during part of the 1990s [20-25].

This system consisted of metallic legs that supported two disks that were lined with polyurethane foam. However, in 1999, the Rashkind double-disk system stopped being used owing to a high percentage of up to 35% of residual flows over the long-term [24,26,27] and also owing to its high cost of about 2,500 dollars just for the device.

During this long period in which the Rashkind system...
was widely used, some other prostheses were tested for percutaneous closure of the arterial duct.

In 1989, BRIDGES et al. [28] successfully utilized Clamshell’s prosthesis, designed for the percutaneous occlusion of interatrial connections, to close small-caliber arterial ducts of up to 14 mm. However, the utilization of this prosthesis did not spread.

The same happened with the prosthesis of Sideris, whose results of occlusion in children were published in 1991 by RAO et al. [29]. This prosthesis was used a little more in Europe, but owing to the great preference for the Rashkind double-disk system, its repercussion was limited and few works were published.

In 1992, CAMBIER et al. [30] reported for the first time the results of occlusion of small-caliber arterial ducts (≤ 2.5 mm) using unassisted delivery of Gianturco coils (Cook Inc., Bloomington, IN, USA). Due to the good results and the low cost of these devices (35 dollars per pair in the USA and around 215 dollars per pair in Brazil), the unassisted coil deployment soon became widely used worldwide.

HIJAZI et al. [31] in 1994, published the results of occlusion of moderate-caliber arterial ducts using multiple unassisted coil deployment which, consequently, started to be used in adults [32]. Hence, this device became progressively more utilized and some comparative studies demonstrated its superiority over the Rashkind double-disk system [33-35], which also decisively corroborated to the abandon of the Rashkind system for the occlusion of arterial ducts.

In 1996, preliminary results of assisted coil deployment were published [33,36], whose delivery systems were being developed, including the current systems of thread that are extremely safe. However, these devices have a cost several times greater than a pair of unassisted coils.

Additionally, assisted coil devices did not completely eliminate the risk of embolization of the coils to the pulmonary arteries and not even the persistence of the residual flows [32-35].

In 1996, apart from the Cook disposable coils (Cook Inc., Bloomington, IN, USA) a new device called the “Duct Occlud pm” (PRM, Cologne, Germany) was also employed especially in Europe, with its assisted deployment it was a variation to coils. The device formed a large number of loops and presented after delivery the aspect of a sand-glass [5]. These characteristics should have made it very efficient to close chronic ducts but this was not confirmed in publications, with divergent data [37-39].

In the same year, sporadic results with the vascular occlusion device of Gianturco-Grifka were published, which consisted of a nylon pouch with a coil inside which inflated on release [40]. It was mainly used for the occlusion of large-diameter arterial ducts with satisfactory results [41]. Nevertheless its use was sporadic and infrequent.

In 1997, the most reliable and efficient of percutaneous arterial duct occlusion systems, the Amplatzer occlusion system, appeared [42-44]. This device presented with a conical format that was made from nitinol and lined with polyester. Its main characteristic is an extremely safe release cable, whose threaded system enables the device to be returned to the sheaf and repositioned several times, until the ideal position for its release is achieved. This manipulation and repositioning can be performed with great safety, with minimum risk of embolization, damage to the prosthesis or vascular injury. The Amplatzer device (AGA Medical, Golden Valley, MN, USA) has created the possibility of occluding small or large-diameter ducts with the same efficiency and safety [43] (Figure 3). However, the use of this device is not viable in poor and developing countries, such as Brazil, due to its high cost of around 4,000 dollars.

Over all the development of percutaneous occlusion of arterial ducts, the coils have been the most used devices in the entire world [45] mainly the unassisted coil devices owing to their low cost. The unassisted coil devices consist of a metallic structure of stainless steel, entirely lined with a dense fringe of Dacron, which gives it high thrombogenicity [46]. They are commercially presented inside of a metallic

Fig. 3 - Example of arterial duct occlusion using the Amplatzer occlusion system. A) Shows the device and its release cable. B) Aortogram showing an extensive arterial duct (arrow). C) Amplatzer prosthesis being manipulated by the release cable to adjust its position (arrow). D) Aortogram showing total occlusion of the duct after release of the device (arrow)
The release of these coils has been made by retrograde or anterograde approaches. The retrograde approach is achieved utilizing one of the femoral arteries and advanced by catheter to the aorta. The arterial duct is crossed in the aortic to the pulmonary artery direction. With the help of the guide wire, the first loop is released at the pulmonary end of the duct and by carefully pulling the catheter back on the guide wire the other loops are released at the aortic end. In cases where release is made via the anterograde approach, one of the femoral veins is used and the catheter is advanced up to the pulmonary artery and the arterial duct is crossed in the pulmonary artery to the aorta direction. The first loop is released in the descending aorta, the entire assemblage is pulled in the direction of the aortic end of the arterial duct where the second loop is released and the third loop is released at the pulmonary artery end.

Therefore, after release, the coils should present with a loop at the pulmonary end and two at the aortic end of the arterial duct. Additionally, the release can be made of a single loop or multiple loops, depending on the diameter of the arterial duct to be occluded and the technical choice made by the surgeon [31,32,47-49] (Figure 5).

Despite of widespread utilization of these coils using unassisted deployment, doubts still remain in respect to the technical aspects of their release in arterial ducts with larger calibers. There is no consensus in respect to safety and efficiency in the utilization of multiple coils for ducts greater than 3 to 4 mm in diameter [31,34,41,50,51].

Some data has suggested satisfactory results with the utilization of balloon catheters, special guides or Bioptomes to anchor the distal loop of the coils during their release, reducing the incidence of embolization of the devices to the pulmonary artery [50,52-54]. Also thicker coils, with a 0.052-inch thick metallic structure, have been employed in an attempt to obtain better results in ducts with greater diameters [52,55]. Coils capable of forming as many as five loops have also been used to avoid the reappearance of flows in previously occluded ducts [56-58].

In small-caliber arterial ducts (up to 2 mm), percutaneous occlusion with unassisted coil deployment has given excellent results [41,47,59-62], with safety and efficiency similar to results of surgical treatment and at a lower cost [63].

In reality, unassisted coil deployment has been demonstrated to be the only percutaneous occlusion device of the arterial duct with a lower cost than surgical treatment [5,63], as long as artificial techniques for its release such as special guides or Bioptromes are not used.

Publications confirm the variety of technical possibilities, surgical or percutaneous, that can be utilized for the occlusion of persistently patent arterial ducts. These data show that use of all techniques depends on three principal factors: a)
the country’s and cardiology department’s economic situations where the procedures are performed b) fundamentally on the diameter of the malformation and c) on the age and weight of the carrier of the anomaly.

In the surveyed literature, the impossibility to attribute an absolute superiority to any single existing technique was evidenced, which justifies the non-systematic utilization of the different options for persistently patent arterial duct occlusion.

**BIBLIOGRAPHIC REFERENCES**


