

Ductus Arteriosus: Ecographic anatomy and closure mechanisms

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DA: ductus arteriosus

PG: prostaglandins

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ABSTRACT

Ductus arteriosus is an essential anatomical structure in the life of the fetus, which can be treated pharmacologically; and, if its functional and anatomic closure is not completed in the newborn stage, it is considered a congenital heart defect. Its importance motivated us to conduct this review, which deals with aspects related to the embryology, anatomy and function of this structure. It is illustrated with echocardiographic images of fetuses, which were studied at the Fetal Cardiology Department of the William Soler Pediatric Cardiology Hospital, showing the classical views used in its study, and examples of diagnosed anomalies, with the aim of providing summarized information together with our experience in the assessment of ductus and the diagnosis of some of its anomalies.

Key words: Ductus arteriosus, Fetal echocardiography, Prenatal diagnosis, Congenital heart disease

Ductus arterioso: Ecoanatomía y mecanismos de cierre

RESUMEN

El *ductus* arterioso es una estructura anatómica esencial en la vida del feto, que permite ser manipulado farmacológicamente y, de no completarse su cierre funcional y anatómico en la etapa de recién nacido, se considera una cardiopatía congénita. Su importancia fue motivo para efectuar la presente revisión, donde se tratan aspectos relacionados con la embriología, anatomía y función de esta estructura, ilustrados con imágenes ecocardiográficas de fetos estudiados en el Servicio de Cardiología Fetal del Cardiocentro Pediátrico William Soler, en las que se observan las vistas clásicas utilizadas en su estudio, y ejemplos de anomalías diagnosticadas, con el objetivo de ofrecer información resumida acompañada de nuestra experiencia en la evaluación del *ductus*, así como el diagnóstico de algunas de sus anomalías.

Palabras clave: Ductus arterioso, Ecocardiografía fetal, Diagnóstico prenatal, Cardiopatías congénitas

INTRODUCTION

The ductus arteriosus (DA) is a vascular structure connecting the proximal descending aorta to the roof of the main pulmonary artery, near the origin of the left pulmonary artery¹. It was first described in the fetus by Galen (129-200), who even spoke of its postnatal closure in the second century²⁻³. The first mention of the term ductus arteriosus appeared in a book by Arantii Iulii Caesaris, *De humano foetu libellus*, published in 1595. There, he mentions the ductus venosus and the ductus arteriosus⁴. Later, in 1628, William Harvey described the orientation of blood flow through it in fetal life⁵, and Virchow suggested that ductal closure was secondary to the contraction of smooth muscle in its wall. According Marquis⁶, it was recognized as isolated disease with the description of Rokitansky in 1844 and 1852.

The importance of this structure in fetal life and the fundamental aspects that have been published about its embryology, echographic anatomy and closure mechanisms were the reason for this review, which is illustrated with images of studies conducted at the Department of Fetal Cardiology of the William Soler Pediatric Cardiology Hospital, National Reference Center for the diagnosis of congenital heart disease in the fetus and cardiovascular surgery in patients less than

one year of age in Cuba.

EMBRYONIC ANATOMY

In the cephalic portion of the embryo, along the ventral and lateral pharyngeal gut wall, the pharyngeal arches appear with a cephalocaudal sequence. Such pharyngeal arches are bars of mesenchymal tissue that are separated, outside, by the pharyngeal clefts. Similarly, the pharyngeal pouches, which are also in the side walls of the pharyngeal gut, separate the pharyngeal arches. Along the rear wall of the embryo, on both sides of this gut, there are two arteries: the right and left dorsal aortae. And in front of the ventral wall of the gut, there is the aortic sac, which is continuous with the truncus. As each pharyngeal arch appears, the aortic sac contributes with right and left arterial branches, and six pairs of arteries called aortic arches are formed. These arcs join the aortic sac with the right and left dorsal aortae, respectively. The ascending aorta originates from the aortic sac, the transverse portion of the fourth left aortic arch and descending portion on the left dorsal aorta. When the aortic sac is divided by the aortic-pulmonary septum into ascending aorta and pulmonary trunk, the sixth arc loses connection with the aorta and is connected to the pulmonary trunk. On the right side, the ventral

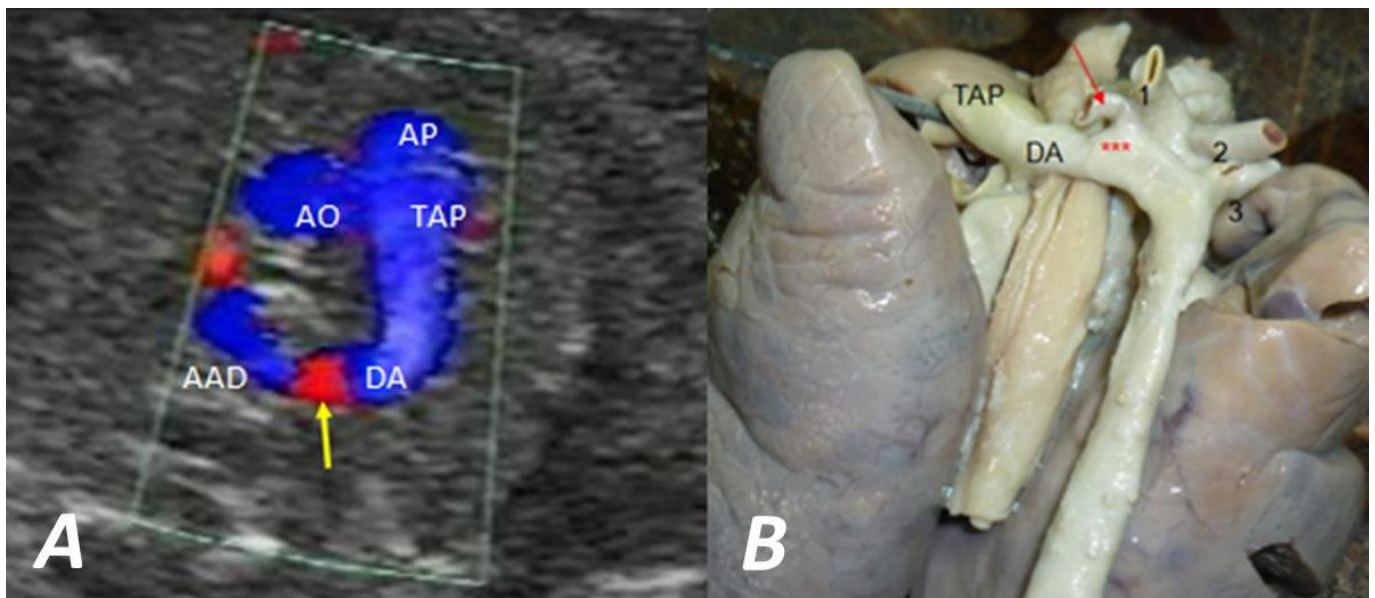


Figure 1. A. Echocardiographic image and **B.** Anatomical specimen where a right aortic arch with left ductus is seen, the latter joins the proximal portion of the left pulmonary artery to the proximal portion of the aberrant left subclavian artery and runs behind the trachea. RAA: right aortic arch, AO: aorta, PA: pulmonary artery, DA: ductus arteriosus, PT: pulmonary trunk, 1: left brachiocephalic trunk, 2: right carotid artery, 3: right subclavian artery, ***: Diverticulum of Kommerell. The arrow points to the aberrant left carotid artery.

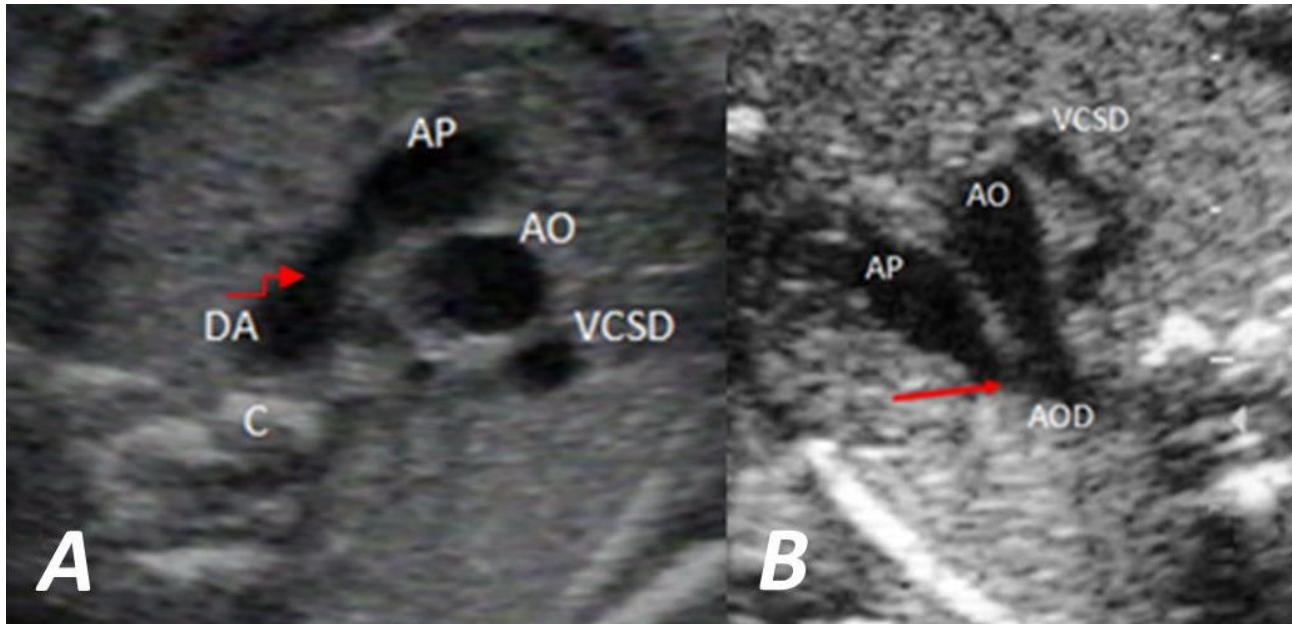


Figure 2. A. Extended echocardiographic view of the three vessels (three vessels and ductus) showing the ductus arteriosus as a straight continuation of the pulmonary trunk that joins to the descending aorta in front of the vertebral column. **B.** A slight angulation of the transducer allows us to see the ductus arteriosus and the transverse arch together forming a V in the posterior region of the thorax, with the pulmonary trunk and the DA as the long branch, and the transverse aortic arch as the short branch. PA: pulmonary artery, AO: aorta, DAO: descending aorta, DA: ductus arteriosus, VC: vertebral column, RSVC: right superior vena cava. The arrows indicate the ductus arteriosus.

portion of the sixth aortic arch finally turns into the proximal portion of the right pulmonary artery, while the dorsal portion disappears. On the left side, the ventral portion is absorbed into the pulmonary trunk and the dorsal segment becomes the DA. This is why the ductus connects the pulmonary trunk, on its roof, near the origin of the pulmonary arteries, with the proximal portion of the descending aorta^{7,8}.

When the aortic arch is on the right and the ductus is on the left, it will join the pulmonary trunk with the aberrant left subclavian artery; this means it can go in front of or behind the trachea, in which case a vascular ring is formed⁹ (**Figure 1**). There may also be a double DA in cases with severe obstruction to pulmonary flow, and in some cases of double aortic arch^{10,11}.

ECHOCARDIOGRAPHY

The visual display of DA can be assessed performing different echocardiographic cuts of the fetus through several views¹⁰⁻¹⁵:

1. Cross-sectional cut of the fetus: specifically in the extended echocardiographic view of the three vessels (three vessels and ductus), where it is shown as a straight continuation of the pulmonary trunk that

joins the path of the descending aorta in front of the vertebral column (**Figure 2A**). A slight angulation of the transducer allows us to observe the DA and the transverse arch together, forming a V in the posterior region of the thorax, with the pulmonary trunk and the DA as the long branch, and the transverse aortic arch as the short branch (**Figure 2B**).

2. Angled cut: the view of the long axis of the right ventricle is seen, where the pulmonary artery coming from the right ventricle and its continuation with the DA that ends in the descending aorta can be seen (**Figure 3**).
3. Longitudinal cut: it will show the so-called ductal arch, where the pulmonary artery coming from the right ventricle and its continuation with the descending aorta is seen (**Figure 4**).

FETAL HEMODYNAMICS AND ANATOMY

Under normal conditions, the flow of DA is always directed towards the vertebral column.

There are several references to disturbances of the DA; for example, the absence of pulmonary valve agenesis, or the presence of a small and tortuous DA

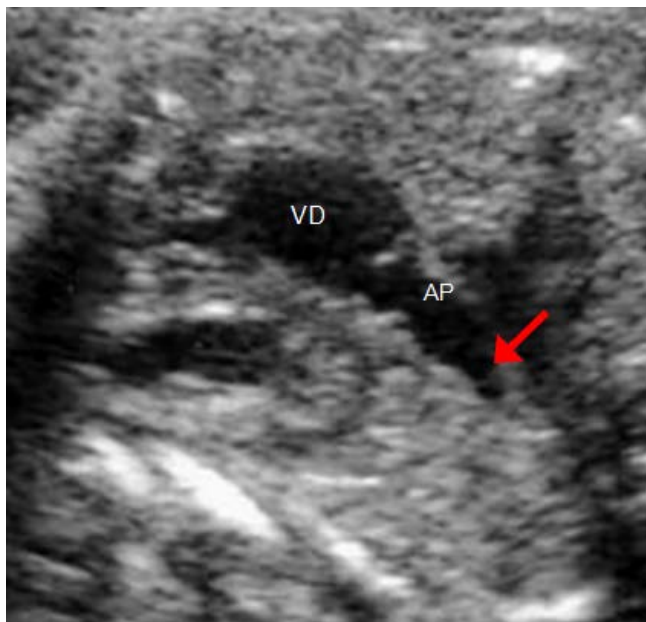


Figure 3. Echocardiographic view of the right ventricular long axis where the pulmonary artery coming from the right ventricle is seen; and the ductus arteriosus (arrow), which ends in the descending aorta, is noticeable. RV, right ventricle PA: pulmonary artery.



Figure 4. Longitudinal cut of the ductus called ductal arch (in a patient with ventricular septal defect), where the pulmonary artery coming from the right ventricle and its continuation with the descending aorta can be seen. Between them, the ductus arteriosus is indicated. AO: aorta. DAO: descending aorta. PT: pulmonary trunk

in abnormal position, as seen in some cases of tetralogy of Fallot with pulmonary atresia and non-confluent branches. Tortuosity is also seen as gestational age advances, which also becomes less straight.

Some authors as Allan *et al*¹⁰ have noticed a bulbous dilated duct in late pregnancy, with the appearance of a cyst in the lower left part of the chest, but has been seen as a normal structure that regresses after birth.

The reverse flow in the DA confirms a serious obstruction in the outflow tract of the right ventricle¹⁰.

While it is known that there is a balance between vasoconstriction and vasorelaxation and that, therefore, the prevalence of one over the other causes the closure or the persistence of the vessel, currently the factors that keep the duct permeable during pregnancy are better known. As a result, the analysis focuses on the ways of vessel muscle relaxation and its possible flaws.

The persistence of the ductus open during fetal life is due to two main factors:

1. The high pressure in the lumen of the ductus, due to the constriction of the pulmonary bed, due to (among other things) the mechanism of hypoxic vasoconstriction (typical of the pulmonary vessels) resulting from low alveolar oxygen pressure¹⁶.
2. The basal production of vasodilators (prostaglandins [PG] and nitric oxide): The action of vasodilating prostaglandin E₁, I₂, E₂. The most abundant is I₂, but E₂ is the most important to keep the ductus open, as its ductal vasodilating power is 400-1000 times that of E₁ and much more potent than I₂. It seems that it has a placental origin. Normally, the major site of metabolism of prostaglandins is the pulmonary vascular bed. Therefore, because circulation through the pulmonary bed is reduced in the fetus, a physiological imbalance between placental production of PGE₂ and its metabolism occurs, which favors high levels of this molecule. This is important from a practical point of view, as the use of prostaglandin inhibitors is contraindicated, mainly in late pregnancy. Nitric oxide is produced by the ductus itself, and seems to play an important role in early stages of pregnancy¹⁷.

CLOSURE MECHANISMS

The closure of the ductus arteriosus occurs in two phases. The first phase is of functional type, which occurs in the first few hours after birth and is due to vasoconstriction generated by the smooth muscle of the ductus itself. In newborns, the functional closure of the ductus occurs at 24 hours in 50% of them, at 48 hours in 90% and at 72 hours in 100%. These events are favored by different mechanisms^{16,17}:

- Increased blood pressure of O₂: The cytochrome P₄₅₀ (located in the muscle cells of the duct) would act as a trigger of events induced by oxygen, which consist in closing K⁺ channels, which are called oxygen-sensitive channels, generating a depolarization of the cell membrane. The amount of these channels and their sensitivity to oxygen vary between species and even in different times of pregnancy.
- Increased formation of endothelin (a potent vasoconstrictor).
- The decrease in pressure within the lumen, due to the decrease in pulmonary vascular resistance.
- The fall in PGE₂ plasma levels, by placental tissue loss and increased pulmonary circulation (virtually the entire flow ejected by the heart).
- The decreased expression of PGE₂ receptors.
- The expression (by myocytes) of myosin isoform with greater contractile capacity, as pregnancy progresses.

The second phase of the closure is the anatomical one. It occurs after several days, due to hyaluronic acid production by endothelial cells (which, in turn, begin to proliferate), which provides a favorable environment for the migration of muscle cells of the tunica media, all of which produces a progressive thickening of the tunica intima¹⁷⁻²⁰. Furthermore, myocyte contraction generates ischemia in the media due to the occlusion of the vasa vasorum, which induces apoptosis of muscle cells, resulting in a thinning of the tunica media. Once the contraction of the ductus by one or more of these mechanisms begins, there is a stagnation of blood, and it alters the nutrition of the ductus wall (which essentially happens from inside the vessel). This causes ischemic degeneration, necrosis of the wall and cytolytic changes. Subsequently there is a proliferation of fibroblasts, leading the ductus to become ligamentum arteriosum¹⁷.

The DA is a noble and very important structure because of three key elements: it is essential in fetal life, can be treated pharmacologically and may exist as a heart disease; hence the specialists related to this branch of medicine need to deepen their knowledge on the subject.

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