# Chapter 75

## Transposition of the great arteries: the importance of new strategies for rapid diagnosis

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### 1 INTRODUCTION

Transposition of the Great Arteries (TGA) is considered the predominant cyanotic congenital heart disease (CHD) of the neonatal period, accounting for 5-9% of cardiac malformations. In TGA, the ventriculo-arterial connection is considered discordant, as the ascending aorta arises abnormally from the morphological right ventricle and the pulmonary artery arises abnormally from the morphological left ventricle, connected to the pulmonary trunk (YELBUZ et al., 2018). Therefore, the systemic and pulmonary circulations are in parallel rather than in series, causing oxygen-poor blood to circulate through the body and oxygenated blood to circulate through the lungs (SÉGUÉLA et al., 2016).

In physiological situations, the heart consists of two muscle pumps that act in series, dividing the circulation into pulmonary and/or systemic. The right ventricle receives oxygen-poor blood from the systemic circulation and sends it to the lungs through the pulmonary arteries so that the carbon dioxide can be exchanged for oxygen in the pulmonary capillaries and then returned by the pulmonary veins to the left atrium, thus characterizing the pulmonary circulation. The left ventricle, on the other hand, receives the oxygen-rich blood coming from the pulmonary circulation through the systemic arteries (aorta and its branches). This blood offers nutrients and oxygen to the tissues, making it less oxygenated and thus, returns to the right atrium through the systemic veins (tributaries of the superior and inferior vena cava), characterizing the systemic circulation (MOORE, 2011).

During cardiac development, the conotruncal septum bends in a spiral shape toward the aortic sac, which divides the truncus arteriosus into the pulmonary and aortic ducts. Thus, these become respectively the pulmonary and aortic arteries. In TGA, there is a failure of this spiralization process. Instead, the septum follows a linear orientation, i.e. the aorta originates from the right ventricle and the pulmonary trunk

originates from the left ventricle. Thus, the deoxygenated blood from the systemic circulation returns to the right atrium and, through the contraction of the right ventricle, follows the abnormally developed aorta and returns to the systemic circulation. As for the oxygenated blood, it follows to the left atrium and returns to the pulmonary arteries from the contraction of the left ventricle. So, the cardiac pumping of blood and, consequently, the transport of nutrients, oxygen, and waste entering and leaving the cells happens inefficiently. Thus newborns with TGA are at risk of rapid hemodynamic compromise and usually present cyanosis in the first 30 days of life.(SZYMANSKI et al, 2022)

Unless mixing of oxygenated and deoxygenated blood occurs, the existence of parallel circuits is incompatible with life. This mixing can be due to an atrial or ventricular septal defect, patent ductus arteriosus, or through bronchopulmonary collateral circulation. In addition, interventional cardiologists may also use balloon atrial septostomy (BAS) to facilitate mixing between the atria. (SZYMANSKI et al, 2022).

Generally, NB's with intact ventricular septum (IVS) become cyanotic upon closure of the ductus arteriosus, i.e., within the first few days of life, inevitably leading to progressive hypoxia and acidosis. TGA mortality rates estimate 2.6-4%, and optimizing preoperative management is of paramount importance. Immediate specialized intervention, resuscitative care and/or balloon atrial septostomy (BAS) may be critical. Since the widespread use of BAS and prostaglandin E1 (PGE1), no major new technique other than cardiopulmonary bypass has improved the postnatal condition of these newborns.(YELBUZ et al., 2018).

Although it is the second most common cyanogenic heart disease, the etiology of TGA and its morphogenesis remain unknown. However, it is presumed to be multifactorial. Currently, there are two theories considered to be the main ones on the embryological mechanisms of TGA development: the first theory proposed by De la Cruz; and the second by Goor and Edwards. The first suggested that the aortopulmonary septum fails to spiral at the level of the infundibulum, which causes a linear development of the septum; providing transposition of the great vessels. The second theory proposed that TGA is caused by abnormal resorption or underdevelopment of the subpulmonary cone, with persistence of the subaortic cone. (SZYMANSKI et al, 2022; (SÉGUÉLA et al, 2016).

In the 21st century, medicine has had much evolution with the advent of technology, new strategies and tests to diagnose diseases that were previously unknown. However, prenatal ultrasound detection is difficult, its rates ranging from 15%-53%, due to the essentially normal vision of the four chambers and the lack of crossing of the exit tracts being missed. However, current non-invasive technologies allow us to closely monitor these patients and identify those who are likely to benefit from early surgery. (BRAVO-VALENZUELA et al, 2020; WOODS et al, 2012).

Despite the increased survival of patients with TGA (current survival rates of over 95% after corrective surgery), several complications can arise from corrective operations, such as arrhythmias, baffle

obstruction or leakage, pulmonary artery stenosis, coronary artery stenosis, aortic root dilatation, and aortic regurgitation.(SZYMANSKI et al, 2022).

The diagnosis of CHD has improved with the assessment of outflow tracts in the four-chamber view during cardiac screening and with the use of advanced ultrasound technologies, such as three-dimensional (3D) and four-dimensional (4D) ultrasound/echocardiography. In most prenatal series, the reported detection rate of TGA is less than 50%. (BRAVO-VALENZUELA et al, 2020). The aim of this work is to understand possible consequences of the slow treatment of TGA, as well as, the importance of its prompt diagnosis.

## 2 METHODOLOGY

The study is an integrative literature review, carried out from the analysis of data present in the Pubmed platform, via MEDLINE. In all, 1005 articles were found, which were later submitted to the evaluation criteria. The descriptors used were "Trasposition" and "Great" and "Arteries", connected by the Boolean operator "AND", according to the Medical Subject Headings (MeSH).

The inclusion criteria were articles that addressed the themes proposed for this research, published in the last 10 years and only free full texts. In addition, we excluded articles that were not related to the theme, duplicates and/or that were only in abstract format, and articles that did not meet the aforementioned inclusion criteria. The authors had no conflicts of interest.

After the selection, 16 remained for the elaboration of the work, these were submitted to a thorough reading for data collection.

## Signs that help diagnose TGA in the prenatal period

Transposition of the great arteries (TGA) is characterized as the most common cyanotic congenital heart defect (CHD) in the neonatal period, with a correspondence of 5 to 9% of cardiac malformations.In this pathology the pulmonary and systemic circulations are in parallel, so deoxygenated blood is recirculated through the body (right ventricle-aorta connection). Two of three possible communications between the pulmonary and systemic circulations are required to support early survival: a patent ductus arteriosus, an atrial septal defect (always present during pregnancy) or a ventricular septal defect (VSD) (SÉGUÉLA et al,2017).

Little is known about the etiology and pathogenesis of TGA. Studies have been done about its origin, however, it remains a "mysterious" heart defect (YELBUZ et al, 2018). It has been added to the group of conotruncal heart defects, which includes abnormally positioned malformations of the great vessels, such as double right ventricular outflow tract and Tetralogy of Fallot. It is suspected to originate from malformations in the development of the embryonic heart outflow tract, these, which are linked to genetic defects affecting the development of the cardiac neural crystal or the development of the secondary cardiac

field (YELBUZ et al, 2018). TGA is rarely found with other malformations in the ventricular outflow tract. When it does occur, it is most associated with heterotaxy syndrome; which is etiologically linked to genetic defects that affect the normal establishment of the left-right axis of the body. Another striking observation in the literature is that about 50% of cases of TGA and atrioventricular septal defect is related to right isomerism, and it is important to pay attention if the patient has epidemiology compatible with suspected TGA (YELBUZ et al, 2018).

With the evaluation of the outflow tracts of the heart in the four-chamber view during cardiac screening and the use of advanced ultrasound technology, such as three- and four-dimensional ultrasound, the diagnosis of various congenital heart diseases has become more frequent (BRAVO-VALENZUELA et al, 2020). As one of the most frequent congenital heart diseases (CHD), it comprises about 5% to 9% of cardiac malformations (SÉGUÉLA et al, 2017). TGA continues to have a high level of underreporting in utero, having a diagnosis rate of less than 50% (BRAVO-VALENZUELA et al, 2020).

The prenatal diagnosis of TGA is characterized by identifying the bifurcation of the pulmonary artery, which in this malformation originates in the left ventricle (LV) and aided by the parallel path of TGA. In contrast, the branches of the pulmonary artery in the LV outflow view are not easy to visualize, so it may be one of the factors that the identification of TGA in utero is somewhat complex, especially in patients with simple TGA, one in which there are no associated heart defects, in which the four-chamber view appears to be within normal standards (BRAVO-VALENZUELA et al, 2020).

Thanks to the presence of abnormalities in the ventricular outflow tract, many important sonographic markers involving the right ventricular (RV) and LV outflow tracts have been formed, such as the presence of two vessels in the three-vessel tracheal view, a situation that is in parallel with TGA, being one of the main markers for its diagnosis (BRAVO-VALENZUELA et al, 2020).

The aorta (Ao) is usually located anterior and to the right of the pulmonary artery. In some situations on ultrasound we can see signs that help in the diagnosis. When the pulmonary artery is located side by side with the aorta, which resembles the character of the Sanrio frog, characterizing the Big-Eyed Frog Sign, being another important marker to observe (BRAVO-VALENZUELA et al, 2020). Other situations that may enable the diagnosis or suspect the fetus to have TGA is when the fetal echocardiogram of a patient regarding the evaluation of the ventricular outflow tract shows a convex curvature and the first trimester fetal echocardiogram shows a reverse curvature of the right ventricular outflow tract in the form of boomerang.

The LV outflow tract on echocardiography shows that the pulmonary artery arises from the LV. The bifurcation of the pulmonary artery forms the image of a bird's beak (BRAVO-VALENZUELA et al, 2020). This, which is another sign that can suggest the transposition of the great arteries. Thus, it is possible to verify that there are great markers that assist in the diagnosis of TGA and enabling a higher rate of life of children born with this malformation.

**The importance of surgical correction to the patient with TGA and the increase of survival**

With early and well-defined diagnosis, surgical interventions for therapeutic purposes are possible, in particular the arterial switch operation (ASO), as it is a predominant surgical procedure for D-TGA, with a low operative mortality rate of 2-3% and a 10-year survival. If the arterial oxygen saturation is only mildly decreased and the atrial communication is adequate, the infusion of PGE1 is possible and will allow the opening and maintenance of the patency of the ductus arteriosus. However, if the patent foramen ovale has a small opening, PGE1 may increase the blood return to the left atrium and thus close the foramen ovale flap, a factor that leads to *decreased* mixing, with increased left atrial pressure and pulmonary edema (MARINHO-DA-SILVA et al, 2021).

In the case of neonates with severe hypoxemia, who do not show rapid improvement with PGE1 or have very restricted foramen ovale, cardiac catheterization and balloon atrial septostomy (Rashkind technique) may offer improvement in systemic arterial oxygen saturation. Thus, the balloon catheter reaches the left atrium through the open foramen ovale. The balloon will be inflated and diverted into the right atrium in order to enlarge the opening in the atrial septum (KEMPNY et al, 2017).

The definitive surgical correction of D-TGA is performed with arterial cerclage (Jatene's operation), in the first week of life. The technique is characterized by the transplantation of coronary arteries to the root of the pulmonary artery, which will become a neoaortic root. Thus, the aorta will be connected to the left ventricle and the pulmonary artery to the right ventricle (MARINHO-DA-SILVA et al, 2021).

The most frequent post-surgical complications are related to the complexity of the associated anomalies (interventricular communication, aortic coarctation, and valve stenosis), neovessel suture sites, pulmonary branching, and neoaorta dilation (MARINHO-DA-SILVA et al, 2021).

**Factors that increase morbidity and mortality in patients diagnosed with TGA**

Among the main factors of high relevance that can lead to higher mortality rates and poor prognoses in general are late diagnosis and premature birth. In the case of late diagnosis (after birth), due mainly to complications such as delayed hospital admission and the complexity of the TGA condition, which has the capacity to suddenly become acutely life-threatening after birth, the patient has a high chance of presenting a worse prognosis, especially until the first year of life. However, when diagnosed early, the prognosis is usually better, with easier management and faster recovery (NAGATA et al, 2020).

Prenatal diagnosis has increased significantly in a recent period, about 51.3%, such an achievement can be explained by improved follow-up of patients in the gestational period (DEBOST-LEGRAND et al, 2015). Two major studies report and follow up the impact and benefits of prenatal diagnosis of TGA over a period of about two decades. In both studies, when the diagnosis of TGA or suspected cardiac malformation is pointed out before birth, the pregnant woman is referred to a joint obstetric unit to a referral cardiac center so that the follow-up of the pregnancy until the birth of the child is done properly, offering

specialized care immediately after birth, resulting in early intervention (ESCOBAR-DIAZ et al, 2015; DEBOST-LEGRAND et al, 2015). In contrast, patients who do not have prenatal diagnosis potentially experience a delay in time of admission to the cardiac care center, which can be nine to twenty-four hours on average.

Patients who have a prenatal diagnosis of TGA are admitted to intensive care units, have early hospital admission and surgical intervention, have less need for mechanical ventilation, fewer cases of postoperative complications, metabolic acidosis and hypoxemia, and have a lower preoperative morbidity. On the other hand, patients with postnatal diagnosis develop a greater number of short- and long-term complications, authors point out as examples: need for preoperative extracorporeal membrane oxygenation (ECMO), higher incidence of metabolic acidosis, complications arising from pulmonary embolism, low oxygen saturations, i.e. severe hypoxemia, which can lead to a greater chance of multi-organ failure and higher mortality rate (ESCOBAR-DIAZ et al, 2015).

Patients diagnosed late commonly need immediate high complexity care, often requiring emergency transport to major centers. This considerably increases the risk of life of these patients during the trip, which can last for many hours; external interventions are often necessary before the corrective surgery. This fact contributes to poor prognosis, besides having the ability to aggravate deleterious conditions related to anatomical change; such as arrhythmias, which are common in infants with D-TGA, making it necessary in many cases the use of various auxiliary therapies for stabilization and management of these newborn patients; which are high risk (CHIRIAC et al, 2022).

In patients with D-TGA, the most used treatment and with better prognosis is surgical, requiring the presence of a specialized team, adequate operating rooms and specific equipment, all this support is usually found in reference centers in large cities. For this factor, the pregnancy planning, especially the number of weeks at the time of delivery is essential, because it allows the anticipation of difficulties in surgery and post-surgery, among the most commonly encountered difficulties can be listed the complementary surgeries performed, such as emergency atrial septostomy, performed in fetuses with closed foramen ovale and also greater need for ventilatory support, attributed to hypoxemia and cyanosis normally present (HU et al, 2022).

Therefore, it is of great importance that the pregnancy last as long as possible in a healthy way, because the maturation of fetal organs and systems is fundamental for a better prognosis in the newborn. In the case of the infant born at term, since the pre-surgical support, during surgery until the post-surgical evolution of the picture is more positive with a lower number of complications, presenting significantly lower mortality, less need for inotropic support, less need for intensive care in general, besides the need for red blood cell transfusions being drastically lower (BOOS et al, 2021).

On the other hand, in the case of premature patients, the difficulties are diverse: greater need for intensive care, more frequent red blood cell transfusions, more inotropic support, the presence of a greater

number of comorbidities in the delivery room, during the perinatal and postoperative period is also perceived (BOOS et al, 2021). Also, several severe postoperative changes are much more commonly perceived in premature patients that may require further interventions, such as venous thrombosis, chylous effusions in the chest, as well as late chest closure and increased need for postoperative ventilatory support. In addition, in general, in-hospital mortality increases significantly in cases of prematurity, even with adequate support and specialized care, reaching more than 15 times higher than conventional term-born infants (BOOS et al, 2021).

## 3 CONCLUSION

Therefore, it is the technological advances that have been contributing to the early diagnosis of TGA, especially with the use of three-dimensional and/or four-dimensional ultrasound, because they assess the cardiac region with greater accuracy and quality. However, even with the development of technology, there is a high number of underreporting, especially in utero. Associated with this, there is that the prenatal diagnosis is more difficult to be made, because the arterial branches that leave the LV are not easily visualized. Thus, one should pay attention to other possible signs that may appear such as right isomerism, frog sign, bird's beak sign, and even the position of the exit of the aorta from the ventricle. Among the possible therapeutic forms, the main one is surgical intervention, among which we can mention arterial exchange operation, Jatene's operation and atrial septostomy with balloon, and their choices will vary according to the clinical picture presented by the patient. Moreover, the use of PGE1 can be used as therapy when the foramen ovale is patent, improving among other things the arterial oxygen saturation. In this sense, a consistent prenatal follow-up is essential. When TGA is identified, it is essential that a gestational planning with integrated teams of obstetricians, cardiac surgeons, and intensivists be done; since newborns who have this support and organization have a lower mortality rate and post-surgical complications. They may be associated with prematurity and maturation of fetal organs and systems.

## REFERENCES


Bonnet D. Impacts of prenatal diagnosis of congenital heart diseases on outcomes. Transl Pediatr. 2021 Aug;10(8):2241-2249. doi: 10.21037/tp-20-267. PMID: 34584895; PMCID: PMC8429871.

Boos V, Bührer C, Cho MY, Photiadis J, Berger F. The Impact of Prematurity on Morbidity and Mortality in Newborns with Dextro-transposition of the Great Arteries. Pediatr Cardiol. 2022 Feb;43(2):391-400. doi: 10.1007/s00246-021-02734-7. Epub 2021 Sep 24. PMID: 34561724; PMCID: PMC8850285.

BRAVO-VALENZUELA, Nathalie Jeanne; PEIXOTO, Alberto Borges; ARAUJO JÚNIOR, Edward. Prenatal diagnosis of transposition of the great arteries: an updated review. Ultrasonography, [S.L.], v. 39, n. 4, p. 331-339, 1 out. 2020. Korean Society of Ultrasound in Medicine. http://dx.doi.org/10.14366/usg.20055.

Castaneda AR, Norwood WI, Jonas RA, Colon SD, Sanders SP, Lang P. Transposition of the great arteries and intact ventricular septum: anatomical repair in the neonate. Ann Thorac Surg. 1984 Nov;38(5):438-43. doi: 10.1016/s0003-4975(10)64181-1. PMID: 6497474.

Chiriac A, Cheema KP, Giardi D, Espinosa SM, Fitzgerald P, Perez-Downes JC, Umadat G, Hodge DO, Phillips SD, Madhavan M, Asirvatham SJ, McLeod CJ. Atrial Arrhythmia Ablation in Patients With D-Transposition of the Great Arteries and Atrial Switch. Circ Arrhythm Electrophysiol. 2022 Jul;15(7):e010546. doi: 10.1161/CIRCEP.121.010546. Epub 2022 Jun 28. PMID: 35763440.

DEBOST-LEGRAND, Anne; OUCHCHANE, Lemlih; FRANCANNET, Christine; GOUMY, Carole; PERTHUS, Isabelle; BEAUFRÈRE, Anne-Marie; GALLOT, Denis; LEMERY, Didier; LUSSON, Jean-René; LAURICHESSE-DELMAS, Hélène. Impact of prenatal diagnosis on the outcome of patients with a transposition of great arteries: a 24-year population-based study. **Birth Defects Research Part A**: Clinical and Molecular Teratology, [S.L.], v. 106, n. 3, p. 178-184, 21 dez. 2015. Wiley. http://dx.doi.org/10.1002/bdra.23474.

Hu Q, Deng C, Zhu Q, Yang X, Liu H, Liao H, Wang X, Yu H. Dextro-transposition of the great arteries in one twin: case reports and literature review. Transl Pediatr. 2022 Apr;11(4):601-609. doi: 10.21037/tp-21-569. PMID: 35558975; PMCID: PMC9085950.

Kempny A, Dimopoulos K, Uebing A, Diller GP, Rosendahl U, Belitsis G, Gatzoulis MA, Wort SJ. Outcome of cardiac surgery in patients with congenital heart disease in England between 1997 and 2015. PLoS One. 2017 Jun 19;12(6):e0178963. doi: 10.1371/journal.pone.0178963. PMID: 28628610; PMCID: PMC5476245.

KORDOPATI-ZILOU, Kalliopi; SERGENTANIS, Theodoros; PERVANIDOU, Panagiota; SOFIANOU-PETRAKI, Danai; PANOULIS, Konstantinos; VLAHOS, Nikolaos; ELEFTHERIADES, Makarios. Dextro-Transposition of Great Arteries and Neurodevelopmental Outcomes: a review of the literature. Children, [S.L.], v. 9, n. 4, p. 502, 2 abr. 2022. MDPI AG. http://dx.doi.org/10.3390/children9040502.

Marinho-da-Silva, Antonio Joaquim. Artérias Coronárias Após a Operação de Jatene para Transposição das Grandes Artérias: O Papel da Angiografia Coronária por Tomografia Computadorizada no Seguimento. Arquivos Brasileiros de Cardiologia [online]. 2021, v. 116, n. 6 [Acessado 16 Janeiro 2023],

pp. 1117-1118. Disponível em: <https://doi.org/10.36660/abc.20210403>. Epub 14 Jun 2021. ISSN 1678-4170. https://doi.org/10.36660/abc.20210403.

NAGATA, Hazumu; GLICK, Lauren; LOUGHEED, Jane; GRATTAN, Michael; MONDAL, Tapas; THAKUR, Varsha; SCHWARTZ, Steven M.; JAEGGI, Edgar. Prenatal Diagnosis of Transposition of the Great Arteries Reduces Postnatal Mortality: a population-based study. **Canadian Journal Of Cardiology**, [S.L.], v. 36, n. 10, p. 1592-1597, out. 2020. Elsevier BV. http://dx.doi.org/10.1016/j.cjca.2020.01.010.

SÉGUÉLA, Pierre-Emmanuel; ROUBERTIE, François; KREITMANN, Bernar; MAURIAT, Philippe; TAFER, Nadir; JALAL, Zakaria; THAMBO, Jean-Benoit. Transposition of the great arteries: rationale for tailored preoperative management. Archives Of Cardiovascular Diseases, [S.L.], v. 110, n. 2, p. 124-134, fev. 2017. Elsevier BV. http://dx.doi.org/10.1016/j.acvd.2016.11.002.

Straub L, Huybrechts KF, Bateman BT, Mogun H, Gray KJ, Holmes LB, Hernandez-Diaz S. The Impact of Technology on the Diagnosis of Congenital Malformations. Am J Epidemiol. 2019 Nov 1;188(11):1892-1901. doi: 10.1093/aje/kwz153. PMID: 31241162; PMCID: PMC6825822.c
SZYMANSKI, Michael W.; MOORE, Sheila M.; KRITZMIRE, Stacy M.; GOYAL, Amandeep. Transposition Of The Great Arteries. Treasure Island: Statpearls Publishing Llc., 2022. 1 v.

XU, Qiteng; DUAN, Shuhua; XING, Pengchao; CHEN, Rui. Primary repair of transposition of the great arteries with an interrupted aortic arch: a case report and literature review. Journal Of Cardiothoracic Surgery, [S.L.], v. 15, n. 1, p. 1-7, 11 jun. 2020. Springer Science and Business Media LLC. http://dx.doi.org/10.1186/s13019-020-01177-0.

YELBUZ, Talatmesud; AL-ZAHRANI, Ranas; ALHARBI, Samaherh; A TUWAIJRI, Rawanm; ALZOMAILI, Bayant; ALTHUBAITI, Alaa. Transposition of the great arteries: a laterality defect in the group of heterotaxy syndromes or an outflow tract malformation?. Annals Of Pediatric Cardiology, [S.L.], v. 11, n. 3, p. 237, 2018. Medknow. http://dx.doi.org/10.4103/apc.apc_24_18.