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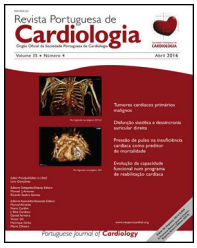

ORIGINAL ARTICLE

Acquired anomalies of the coronary arteries after arterial switch operation. Usefulness of coronary computed tomography angiography and impact on follow-up

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Computed tomography coronary angiography;
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Abstract
Introduction: Mortality and morbidity in patients with transposition of the great arteries after an arterial switch operation depends mainly on the status of coronary perfusion. Coronary computed tomography angiography (CCTA) provides accurate information on coronary morphology, however its use in these patients is not yet routine procedure.
Objective: We sought to assess its accuracy to identify acquired coronary anomalies in this population, compared to conventional angiography in a subset of patients, and assess its impact on postoperative management.
Methods: Retrospective analysis of clinical data on transposition of the great arteries in patients who underwent CCTA between January 2013 and September 2017.
Results: Between January 2013 and September 2017, 18 patients underwent CCTA. Seven patients (39%) disclosed iatrogenic coronary lesions (stenosis 1; kinking 2, occlusion 1; filiform coronary 3). The exam was performed in 78% of patients due to suggestion of myocardial ischemia (symptoms or altered exams). Only 16% needed to undergo additional exams, and in four patients the CCTA result modified therapeutic management.

Conventional coronary angiography was also performed in 10 patients (55%), and in three cases, the results were discordant with underestimation or non-identification of coronary lesions on conventional angiography.

The medium radiation dose used was 2.4 mSv and no complications after CT were reported.
Conclusion: CCTA accurately identified iatrogenic postoperative coronary lesions and it has proven to be superior to conventional angiography in this population. It should be performed routinely in this group of patients, even in the absence of symptoms.

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PALAVRAS-CHAVE
Angiografia coronária por tomografia computorizada;
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Angiografia coronária convencional;
Lesão coronária adquirida;
Anomalia coronária

Anomalias coronárias adquiridas após cirurgia de *switch* arterial. O uso da angiografia coronária por tomografia computorizada e o seu impacto

Resumo
Introdução: A morbilidade e mortalidade em doentes com transposição das grandes artérias (TGA) submetidos a cirurgia de *switch* arterial depende maioritariamente da perfusão coronária. Apesar de a angiografia coronária por tomografia computorizada (Angio-TC) providenciar informação precisa acerca da morfologia coronária, esta ainda não é utilizada de forma rotineira nesta população.
Objetivo: Avaliar a capacidade de identificação de lesões coronárias adquiridas por Angio-TC e avaliar o seu impacto no manejo e seguimento de doentes com TGA, e quando possível comparar os resultados com a angiografia convencional.
Métodos: Análise descritiva e retrospetiva de doentes com TGA submetidos a Angio-TC entre Janeiro de 2013 e Setembro de 2017.
Resultados: Entre Janeiro de 2013 e Setembro de 2017, 18 pacientes foram submetidos ao CCTA. Sete pacientes (39%) revelaram lesões coronárias iatrogénicas (estenose 1; dobra 2, oclusão 1; fili forma coronária 3). O exame foi realizado em 78% dos pacientes devido a sugestão de isquemia miocárdica (sintomas ou exames alterados). Apenas 16% precisaram de ser submetidos a exames adicionais, e em quatro pacientes o resultado do CCTA modified gestão terapêutica.
Conclusão: A Angio-TC consegue identificar com precisão lesões coronárias adquiridas nesta população e nesta amostra mostrou ser superior à angiografia convencional. A Angio-TC deve ser realizada de forma rotineira nesta população, mesmo na ausência de sintomas.

Introduction

An arterial switch operation (ASO) is the surgical treatment of choice for D-transposition of the great arteries (TGA).[1] This surgery has been shown to have an excellent outcome with less than 3% early postoperative mortality in experienced centers.[2,3] Among possible complications associated with ASO, those related to coronary perfusion are the most feared. ASO involves coronary manipulation and reimplantation in the neoaorta, the native pulmonary artery. Most coronary events occur in the early postoperative period and are associated with early morbidity and mortality.[3–5] These coronary events are mainly related to coronary anatomy variation and/or surgical technique difficulties.[4]

Long-term follow-up has shown that 5-7% of TGA patients who undergo ASO may have coronary obstructions in the long-term,[6–8] which is the most common cause of morbidity and mortality in these patients.

Late coronary obstruction requiring reintervention has an incidence of 3–10%.[4,7,9] These iatrogenic anomalies are mainly mechanical acquired defects related to compression, kinking, or stretching of the coronary arteries during surgical manipulation and reimplantation of the coronary arteries, ostial fibrosis at the suture lines and spatial rearrangement of the great arteries distorting coronary circulation during growth in children.[8,10–12] On the other hand, stretching and kinking of coronary arteries could prompt flow abnormalities, resulting in intimal thickening with cellular proliferation.[6,13,14] As these patients reach adulthood, these abnormalities will undoubtedly increase risk factors for atherosclerotic and ischemic disease. Follow-up of these patients should then be targeted to identify coronary lesions and screen myocardial perfusion defects.

At a pediatric age, routine diagnostic tools to assess myocardial ischemia are the level of serum myocardial enzymes, electrocardiogram (ECG), and echocardiogram, besides clinical evaluation. When patients are old enough to cooperate, exercise testing is routinely used. When obstructive coronary lesions are suspected, conventional coronary angiography remains the gold standard.[15] However, in recent years, coronary computed tomography angiography (CCTA) has demonstrated its essential role in this area. It is a secure and safe procedure at a pediatric age and provides accurate, detailed information of coronary morphology, function, and its relationship with adjacent structures.[16,17]

Characterization of coronary morphology and iatrogenic anomalies after ASO surgery seems to be of paramount importance because some of these patients have atypical clinical manifestations of myocardial ischemia or even remain asymptomatic.[18–20] Szymeczyk et al. recently demonstrated that 24% of TGA patients who underwent ASO had significant coronary obstruction and were asymptomatic.[20]

There is still no consensus regarding routine coronary evaluation in TGA operated patients during long-term follow-up. Also, consensual management of post-ASO coronary lesions remains a subject of debate.[6,21] In our experience, studies performed during follow-up using conventional angiography, exercise testing and myocardial scintigraphy have revealed perfusion anomalies in asymptomatic patients but unclear morphologic lesions.[22] Nevertheless, the lack of evidence of long-term

consequences and prophylactic therapeutic intervention in these patients leads us to question the need for these tests.

Recently, we introduced CCTA to screen for postoperative coronary lesions even in asymptomatic patients.

The authors aimed to describe the accuracy of CCTA in diagnosing coronary anomalies compared to conventional coronary angiography in post-ASO patients and assess their implications on postoperative management in these patients.

Materials and method

This is a descriptive, retrospective, single center, cohort study of D-TGA patients who underwent ASO (the trap-door technique was used in all patients) and CCTA at our institution between January 2013 and September 2017.

An analysis of clinical records was performed to assess demographics, clinical symptoms and signs of ischemia suggested by standard examinations, CCTA results concerning coronary morphology and its relationship to the surrounding structures, and conventional standard coronary angiography, when available. We compared CCTA and conventional angiography results and aimed to identify their impact on management. The results are summarized using frequencies and percentages for categorical variables and medians for continuous variables.

Computed tomography angiography

All CT scans were performed with a 64-slice CT machine (LightSpeed; GE Medical Systems, Milwaukee, Wisconsin).

Patients were in sinus rhythm and, if not contraindicated, older children and young adults received oral beta-blocker medication (propranolol 1 mg/kg up to 40 mg total) one hour before the scan to obtain optimal heart rate during the image acquisition for the proper assessment of the coronary arteries.

Short-term sedation was performed using chloral hydrate in small infants (concentration: 10%, 50 mg/kg up to 1000 mg total) or an intravenous injection of ketamine (1 mg/kg) in children between two and six years of age. Older patients (>6 years) were able to comply with breath-hold commands during the acquisition.

Most CT examinations used a prospective ECG-triggering protocol to reduce the dose of radiation. Acquisition parameters were adapted to the patient's age/weight to further reduce the radiation dose. Patients were scanned in a craniocaudal direction, extended from the pulmonary trunk to just below the base of the heart. A region of interest was placed on the descending aorta.

Iodine contrast agent (iomeprol 350 mg/mL) was injected via peripheral veins at a rate of 1.5–3 ml/s, followed by 20 ml of saline solution. The injected volume was calculated according to the bodyweight (1–1.5 ml/kg).

Data were processed on a workstation. Multiplanar reformatting, maximum intensity projection, and three dimension reconstruction (volume rendering) were used to visualize the great vessels and assess the pattern of the coronary arteries and their relationship with the surrounding structures. Coronary lesions were stated as significant if >30% obstruction. The results of these examinations were compared with those obtained in conventional coronary angiography.

Conventional coronary angiography

Conventional coronary angiography was performed with oral sedation (hydroxyzine, 1 mg/kg, one hour before the exam) and general anesthesia in all cases according to the center's routine protocol. In smaller patients, aortography was routinely performed and only followed by selective coronary angiography in cases where coronary anatomy was considered unclear. Older patients always underwent selective coronary angiography.

Results

Between January 2013 and September 2017, 18 TGA patients underwent CCTA, with a medium age of 14 years (from 14 months to 22 years); half of the patients were female.

Eleven patients had simple D-TGA and seven had D-TGA with ventricular septum defect. Four of these patients also had abnormal coronary patterns identified during surgery/CCTA (anomalous bifurcation in three patients and bridging of the anterior descending coronary artery in one patient).

All patients, with the exception of one, underwent CCTA after ASO. One patient underwent this exam before ASO surgery because he had previously had palliative surgery (pulmonary artery banding) during which an abnormal coronary pattern was identified but with an incomplete diagnosis.

The main indication for CCTA was suspicion of myocardial ischemia (14/18 – 78%); other causes were diagnosis of coronary anatomy[2] and/or assessment of the relation between coronary arteries and the main pulmonary artery before to percutaneous intervention.[3]

Suspicion of myocardial ischemia was characterized by unspecific symptoms such as fatigue and chest pain (11 patients – 78%) and/or altered previous exercise testing, scintigraphy or cardiac magnetic resonance imaging (MRI) (seven patients – 50%) or visible ventricular dysfunction seen on echocardiography (one patient – 7%). Among the studied population with suspected ischemia,[14] three patients (22%) were completely asymptomatic.

Coronary computed tomography angiography was performed to clarify the mechanism of myocardial ischemia by assessing coronary anatomy abnormalities and the relationship between coronary arteries and surrounding structures (pulmonary artery trunk and right ventricle-to-pulmonary artery conduit). In some patients, it was performed to assess previously identified pulmonary obstruction, and one patient underwent the exam due to an iatrogenic coronary lesion during cardiac surgery related to pulmonary obstruction.

Coronary computed tomography angiography identified a total of seven patients (39%) with acquired coronary lesions. Coronary stenosis was identified in one patient, kinking in two patients, occlusion in one patient, and filiform coronary in three patients. CCTA also identified congenital coronary anomalies in four patients (mentioned previously). Of note, only four of the seven patients with

acquired coronary lesion presented chest pain, with unspecific symptoms such as fatigue being more prevalent.

For four patients with identified acquired coronary lesions, there were therapeutic modifications after CCTA, such as, coronary surgery in three of them and medical therapy modification in one. For the remaining patients, management was conservative due to the absence of symptoms and/or evidence of ischemia.

The acquired coronary lesions related principally to the left coronary system (five out of seven – 71%), either left main coronary artery (three patients) in which the lesions were located at the ostium, anterior descending artery (one patient), or circumflex artery (one patient). Two patients presented with right coronary artery lesions.

The medium age at which symptoms presented and CCTA was performed was 14.4 years for patients with coronary lesions. Only 16% of all patients needed to undergo complementary exams to clarify their clinical status (mainly cardiac MRI to evaluate perfusion) after CCTA. Slightly more than half of the patients (55%) had previously undergone a conventional coronary angiography. Pulmonary obstruction was the indication to conduct the exam in half of these patients. A coronary abnormality (coronary lesion or abnormal bifurcation) was identified in 50% of the patients. Still, all patients required a CCTA to clarify the anatomy or the significance of the abnormalities found.

There were three patients in which CCTA and conventional angiography were discordant. In one patient, the coronary anatomy was different; one patient had an underestimated coronary lesion on conventional angiography, and in one patient a coronary lesion was not identified by conventional angiography.

None of the patients presented complications after CCTA, and only 22% (four) needed sedation (two) or general anesthesia (two). Patients who underwent conventional angiography also did not experience any complications, but all required general anesthesia. The medium dose of radiation in CT angiography was 2.4 mSv.

Discussion

At present, there is no consensus concerning routine coronary evaluation in TGA patients who undergo ASO. Although conventional angiography is still widely used for coronary evaluation, CCTA usage is increasing and is currently the method of choice for coronary assessment in many centers. It has been demonstrated to be a safe exam for pediatric patients and to give accurate and detailed information on coronary anatomy and its relationship with adjacent structures, enabling correct detection and quantification of coronary lesions.[17,23]

Despite being the gold standard, conventional angiography is an invasive procedure prone to vascular complications, but above all, it provides less accurate anatomic information, when compared with CCTA,[24] due to restricted image projections and foreshortening or overlapping of the obtained images.

Coronary computer tomography angiography enables tridimensional evaluation, thus assuring correct evaluation of coronary anatomy (and lesions) and its relations with surrounding structures, which in some cases can be involved in the mechanism of coronary lesion. The vessel's luminal structure, wall thickness, and calcification score can all be assessed using this exam.

At our institution, the main indication for performing CCTA was suspicion of ischemia, either due to patient symptoms or due to perfusion defects revealed by altered exercise testing, scintigraphy, or cardiac MRI. The majority of these patients were symptomatic, presenting with fatigue or chest pain. Around 55% of symptomatic patients had a coronary lesion identified on CCTA. Although patients with coronary lesions presented mainly with chest pain in this study, these patients can have atypical forms of presentation of myocardial ischemia.[8,18] This is due to the disruption of the cardiac nerves adjacent to the great arteries during surgery. This means that patients can be asymptomatic or have atypical symptoms (fatigue or palpitations).[25] Another possible explanation is the progressive way in which these late coronary lesions develop, allowing the creation of collaterals, or allowing the patient to adjust to the lesion and adapt their level of effort to remain asymptomatic. Despite being widely used in TGA patient surveillance, exercise testing might not be the most adequate test to evaluate ischemia. Several studies have shown that TGA patients with significant coronary lesions can present with normal exercise test results.[4,8,18,26] Although it is a useful non-invasive diagnostic modality to evaluate exercise capacity, it fails to accurately screen subclinical coronary abnormalities in the pediatric population. This is problematic, especially considering that the first presentation of coronary lesions can be sudden cardiac death.[9,26]

Furthermore, TGA patients who undergo ASO have a high incidence of pulmonary obstruction, which usually manifests itself as fatigue. Patients with fatigue should therefore be thoroughly assessed for myocardial ischemia, even in the presence of pulmonary obstruction, because these patients can have myocardial ischemia even if chest pain is absent.

Concerning the location and type of coronary lesions identified, our series is in line with others, with left coronary artery lesions being more frequent.[16-18,20] In our series, the lesions occurred mainly at the ostia or the proximal section of the coronary. The type of lesions found is also in line with those described in the literature, with kinking and stretching (filiform appearance) being the most frequent. This phenomenon is explained by the growth and change in position of the surrounding structures after surgical manipulation, causing either angulation of the arteries, extrinsic compression, or stretching.

As mentioned before, many coronary lesions are located at the ostia, more specifically at the suture lines, used to implant coronary buttons. Conventional angiography can underestimate these types of lesions because the coronary catheter surpasses the ostial region to perform angiography. Thus, CCTA has a clear advantage in assessing ostial and proximal coronary lesions.

Comparing conventional angiography with CCTA, we report in our series that conventional angiography did not always identify a coronary abnormality, and even when it did, a CCTA was always performed later either to better characterize the lesion found or to assess surrounding structures that could be involved in the mechanism of the

coronary lesion, which was necessary to plan treatment management.

A very small proportion of patients were administered general anesthesia to undergo a CCTA. In contrast, all patients needed general anesthesia for a conventional angiography, which implies an aggravated risk. Moreover, CCTA currently uses low doses of radiation, even lower than that used in conventional angiography.[27,28] This is particularly important in the pediatric population because this group is more sensitive to ionizing radiation than adults and has a greater cumulative possible dose during long-term follow-up.[29]

In the majority of patients, there was no need to perform additional complementary exams after CCTA. Most importantly, CCTA results altered the course of action in four patients, with three undergoing revascularization surgery.

In this retrospective analysis, we found an elevated rate of coronary abnormalities. However, there is some bias to this sample because, at our institution, CCTA is not routinely performed, except when clinical symptoms appear or myocardial perfusion defects are demonstrated by other exams.

Other limitations of this study are its retrospective nature, the size of the sample, and the fact that not all patients underwent both exams, diminishing the strength of comparison between results.

In the studied sample, CCTA was shown to be safe. It seems to be a superior imaging exam compared to conventional angiography, with high accuracy to identify coronary lesions and the underlying mechanisms.

There is a subset of TGA patients who undergo ASO that develop significant coronary lesions, but are asymptomatic. Additionally, conventional screening tests, such as transthoracic echocardiogram and exercise testing, fail to identify patients with coronary perfusion defects accurately. For these reasons, routine CCTA in these patients may be beneficial in the long-term and should be implemented regardless of the absence of symptoms. Despite the limitations previously mentioned, this is, to our knowledge, the first report of on CCTA usage in TGA patients in the Portuguese population.

Conclusion

Coronary computer tomography angiography is safe to be performed in the pediatric population. It is at least as accurate as conventional angiography in identifying coronary lesions in TGA patients after ASO, with the advantage of it being a non-invasive exam with exposure to a smaller radiation dose. It should be performed routinely in TGA patients after ASO, even in symptom-free patients.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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