Prognostic value of coronary anatomy and myocardial innervation imaging in cardiac disease

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Issue Date: 2016-03-10

Chapter 5

Variation in coronary anatomy in adult patients late after arterial switch operation: a computed tomography coronary angiography study.

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Annals of Thoracic Surgery 2013; 96(4): 1390-7.

ABSTRACT

Background:

The arterial switch operation is the current treatment for transposition of the great arteries. Long-term outcome mainly depends on the patency of the transferred coronary arteries. This study assessed the presence of abnormal coronary findings and neoaortic root dilation late after arterial switch operation.

Methods:

In 30 adult patients after arterial switch operation (22 men, 22 ± 3 years), computed tomography angiography was performed to assess the coronary anatomy and abnormal coronary findings, defined as significant stenosis, interarterial coronary course, and acute angled coronary origins. Neoaortic root dimensions and coronary takeoff height were also assessed.

Results:

The most common coronary anatomy pattern was found in 24 of 30 patients. Variant anatomy patterns were seen in 6 patients (5 with aberrant circumflex artery, 1 with a single ostium). The prevalence of abnormal coronary findings was higher in patients with variant coronary pattern as compared with patients with common coronary pattern (100% and 29%, respectively; $p = 0.003$). In particular, an acute angle of the coronary origin was frequently observed. In patients with an acute angle, larger dimensions of the aortic annulus ($p = 0.016$) and the sinus of Valsalva ($p = 0.002$) were observed. Moreover, a higher takeoff of the right ($p = 0.030$) and left ($p = 0.002$) coronary ostium was noted in patients with acute angles.

Conclusions:

Abnormal coronary findings were frequently observed in adult patients after arterial switch operation, especially in patients with a variant coronary anatomy pattern. Neoaortic root dilation and a higher coronary takeoff may explain part of the pathophysiology. Long-term follow-up is needed to determine the clinical significance of these findings.

INTRODUCTION

Transposition of the great arteries (TGA) is a common form of cyanotic heart disease comprising 3% of all congenital heart defects[1]. Currently, the arterial switch operation (ASO) is the preferred surgical approach for patients with TGA[2,3], with low operative mortality and excellent childhood survival[4]. However, late cardiac complications have been reported in children and young adults, including dilation of the neo-aortic root with subsequent aortic regurgitation[5,6], and coronary obstructions[7-10]. Therefore, lifelong follow-up is recommended after ASO and a one-time evaluation of the patency of the coronary arteries has to be considered according to the current guidelines.[2,3] An advantage of computed tomography coronary angiography (CTA) for the evaluation of the coronary arteries is the ability to visualize the course of the coronary arteries in relation to the great vessels.[11] Indeed, previous studies showed that CTA is valuable for the detection of coronary complications after the ASO[12-15]. However, in the majority of these previous studies the studied patient population is relatively young with a mainly of pediatric patients. The present study evaluated the coronary anatomy and patency at long-term follow-up in adult patients late after ASO with specific attention for the relation between abnormal coronary findings, coronary take-off from the neo-aorta and neo-aortic root dimensions.

PATIENTS AND METHODS

The study population consisted of consecutive patients with TGA corrected by ASO clinically referred for a one-time evaluation of the coronary anatomy by CTA[2,3] in our center between 2008 and 2012. Clinical data were collected from the departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center) and all and CTA images were retrospectively analyzed. The Medical Ethics Committee of the Leiden University Medical Center approved this retrospective evaluation of clinically acquired data and waived the need for written informed consent.

Clinical evaluation

Peri-operative medical and surgical reports were retrospectively reviewed for the description of the pre-operative coronary anatomy pattern using the previously described Leiden classification (Figure 1)[16]. Furthermore, clinical follow-up data were retrieved from the regular visits at the out-patient clinic and were used to assess the presence of chest pain and New York Heart Association (NYHA) class at the time of referral for CTA. In addition, echocardiography was performed, calculating the left ventricular dimensions and ejection fraction from standard apical (4- and 2-chamber) 2D-echocardiography views using the biplane Simpsons' rule[17].

Computed tomography angiography: data acquisition

Patients were scanned using a 320-row CTA scanner (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan). Patients with a heart rate exceeding 65/min received 50-100mg metoprolol orally 1h before data acquisition, unless contraindicated. Scan acquisition was performed using prospective triggering at 70-80% of the RR-interval and using a mean dose of 60-80mL contrast media (Iomeron400; Bracco, Milan, Italy) intravenously. The mean radiation dose was 3.2±1.0mSv.

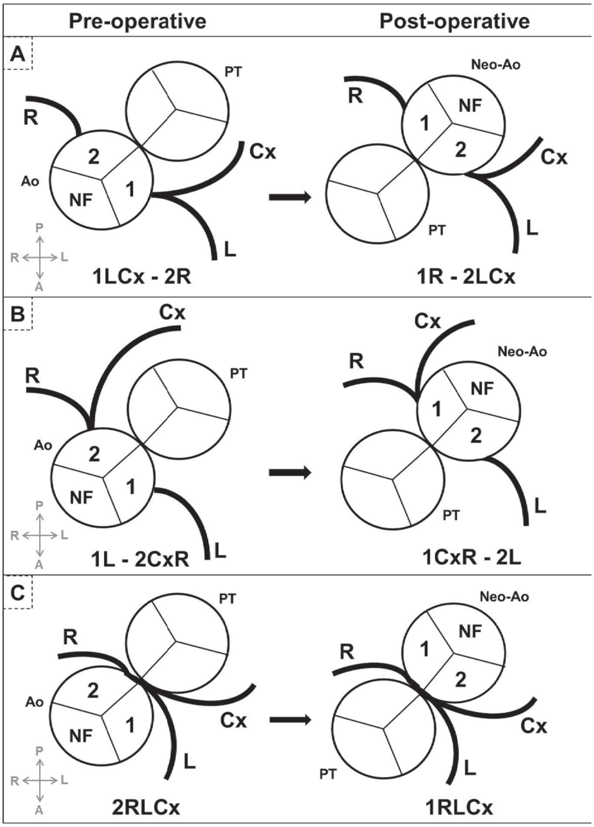

Figure 1. Leiden classification for the pre- and post-operative coronary anatomy pattern.
The coronary arteries arise from the facing sinuses and the non-coronary sinus is called the non-facing(NF) sinus. The observer is positioned in the NF cusp, looking towards the pulmonary trunk(PT), and the sinus on his/her right hand sinus is designated "sinus 1" and the left hand sinus "sinus 2". The coronary arteries are considered separately. The most common coronary artery pattern is depicted in box A. Box B shows the most frequently observed variant coronary artery pattern in patients with TGA, with an aberrant Cx artery arising from the RCA artery. A single ostium coronary anatomy, where the RCA, LAD and Cx artery all arise from the same sinus is depicted in box C.
Ao=Aorta ; Cx=Circumflex artery; L= left anterior descending artery; Neo-Ao=neo-aorta; NF=non-facing; PT=pulmonary trunk; R= right coronary artery. Direction arrows in figure: *A=anterior; L=left; P=posterior; R=right.*

Computed tomography angiography: image analysis

Image analysis was performed by 2 experienced observers in consensus on a dedicated workstation (Vitrea FX 1.0, Vital Images, Minnetonka, MN, USA). The Leiden classification (Figure 1) was used now to describe the post-operative coronary anatomy pattern on CTA and the following abnormal coronary findings were noted: significant coronary stenosis (≥50% luminal narrowing), an inter-arterial coronary course and an acute angle of the coronary origin causing non-significant ostial luminal narrowing of approximately 30%. For measurement of the coronary angle, the angle between the neo-aortic wall and the midline of the proximal coronary segment was measured on the axial slices (Figure 2). A sharp take-off of the coronary artery was defined as an acute angle, when the angle measured was ≤30 degrees and this could be confirmed visually on 3D-reconstructions.

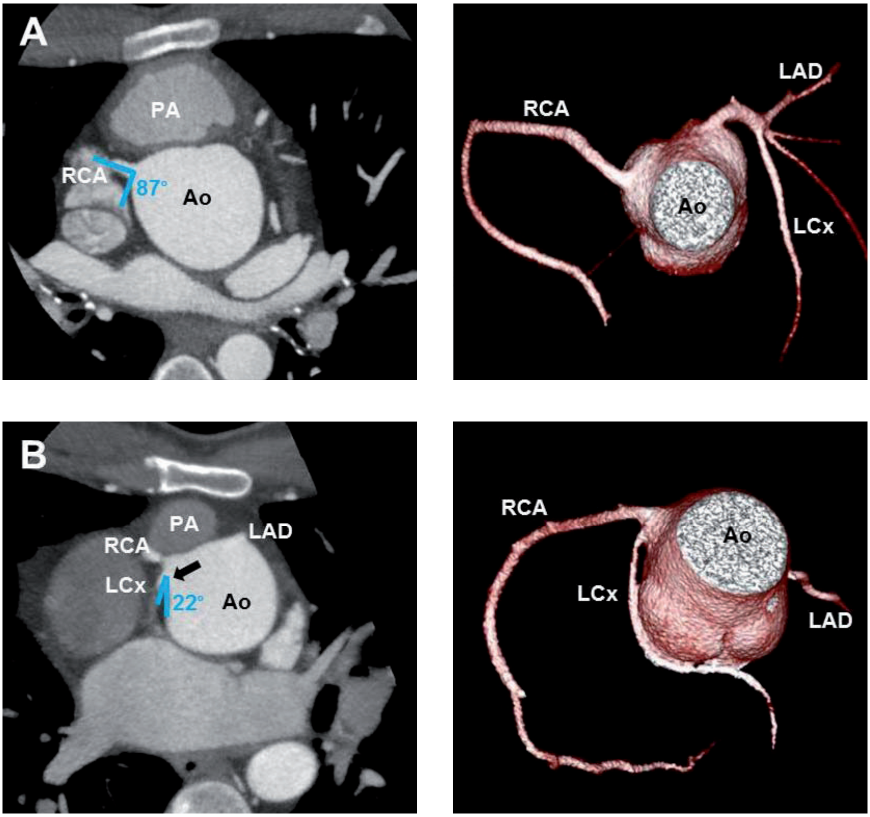

Figure 2. Example of the coronary angle measurement on CTA.
Panel 2A shows an example of the measurement of a normal angle of the RCA origin(left panel, axial slice) as was confirmed on the three-dimensional view(right panel). Panel 2B shows an example of a patient with an acute angle of the Cx origin (22 degrees, left panel, axial slice), as confirmed on the three-dimensional view(right panel).
Ao=neo-Aorta; LAD=left anterior descending coronary artery; Cx=Circumflex coronary artery ; PT=pulmonary trunk; RCA=right coronary artery.

Neo-aortic root dimensions were measured as previously described[18], excluding patients with a previous Bentall procedure. In brief, the cross-sectional diameters were measured at the level of the aortic valve annulus (directly beneath the lowest insertion points of the aortic cusps) and at the level of the sinus of Valsalva after alignment of the axial, sagittal and coronal planes. The coronary take-off height was defined as the distance between the aortic valve annulus and the coronary ostium on coronal and sagittal planes.

Statistical analysis

Statistical analysis was performed using SPSS (version 18.0, SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviations (SD) and categorical variables as numbers and percentages. Differences were tested using a 2-sided Fisher's exact-test or one-way analysis of variance (ANOVA) as appropriate. For comparison purposes patients were divided into 2 groups: 1) patients with the common coronary pattern (1R-2LCx) and 2) patients with variant coronary artery pattern. In addition, the neo-aortic root dimensions between patients with and without an acute angle of the coronary origin were compared. P value ≤ 0.05 was considered statistically significant.

RESULTS

Patient population

The study population comprised 30 consecutive patients (22 male, 22±3 years) referred for CTA after ASO. In 27 patients (90%) there was no associated congenital heart disease. Arterial switch operation was performed at a median age of 5 days [25–75th percentile: 3-13 days]. During clinical follow-up (Table 1), 8 (27%) patients were re-operated: in 6 patients a severe supravalvular pulmonary stenosis was treated and in 2 patients a Bentall was performed because of neo-aortic root dilation and severe aortic regurgitation. Furthermore, 2 patients received an implantable cardiac defibrillator because of ventricular arrhythmias. At the time of referral for CTA, atypical chest pain was noted in 7 patients (23%), all patients were in NYHA class I or II and left ventricular ejection fraction was 57±8%, mean left ventricular end-diastolic volume was 144±34ml and mean end-systolic volume 63±19ml (Table 1).

Computed tomography coronary angiography results

The pre-operative coronary anatomy reported during the ASO corresponded with the post-operative coronary anatomy pattern observed on CTA in all patients: 1R-2LCx in 24 patients (80%), 1CxR-2L in 5 patients (17%) and 2RLCx in 1 patient (3%). The latter 2 patterns were designated as variant coronary anatomy pattern and 1R-2LCx as common coronary anatomy pattern.

Table 1. Patient characteristics – at time of CTA

	Total n=30
Gender (male)	22 (73%)
Age (years) [range]	22±3 [18-28]
Clinical characteristics	
BMI (kg/m^2) [range]	23±3 [17-32]
Resting blood pressure (mmHg)	
Systolic	123±12
Diastolic	74±8
Cardiovascular Risk Factors	
Hypertension*	1 (3%)
Family history of premature CAD†	7 (23%)
Smoking	4 (13%)
Cardiac clinical history	
Patients requiring re-operation during follow-up	8 (27%)
Correction of supravalvular pulmonary stenosis	6 (20%)
Aortic valve and ascending aorta replacement	2 (7%)
Other severe adverse cardiac events	
Peri-operative myocardial infarction	1 (3%)
Arrhythmias needing ICD implantation	2 (7%)
Cardiovascular medication	
Beta-blocker	2 (10%)
ACE-inhibitor	2 (7%)
Anticoagulants	3 (10%)
Chest pain (atypical)	7 (23%)
NYHA function Class	
NYHA class I	24 (80%)
NYHA class II	6 (20%)
NYHA class III or IV	0 (0%)
Echocardiography	
LV-EF (%)	57±8
LV-EDV (mL) [range]	144±34 [97-220]
LV-ESV (mL) [range]	63±19 [39-110]

*Defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or the use of antihypertensive medication. †Defined as presence of coronary artery disease in first degree family members at <55 years in men and <65 years in women.

ACE-inhibitor=angiotensin-converting-enzyme inhibitor; BMI=body mass index; CAD=coronary artery disease; EDV= end diastolic volume; EF=ejection fraction; ESV= end systolic volume; ICD=Implantable Cardioverter Defibrillator; NYHA=New York heart association; LV=left ventricle.

Abnormal coronary findings were observed in 13 patients (43%). In particular, 1 patient had significant coronary luminal narrowing in the proximal LAD (Figure 3A). The CTA of this patient showed that the stenosis was due to a fibrotic lesion rather than to atherosclerotic plaque formation. Conventional coronary angiography confirmed the significant stenosis and subsequently stent implantation was performed. An inter-arterial coronary course was observed in 5 patients (17%), including 1 patient with a single ostium coronary anatomy, in whom the inter-arterial course was also present pre-operatively (Figure 3B: Case example). Inherent to the course of the coronary arteries when running between the neo-aorta and the pulmonary artery, the coronaries had an acute angle of the coronary origin in all 5 patients with an inter-arterial course. An acute angle of the coronary origin, as solitary abnormal coronary finding, was noted in 7 patients (23%) (Figure 3C: Case example). Notably, in 4 out of 7 patients with an acute angle both the left and the right coronary ostia were affected. There was no significant association between the presence of chest pain symptoms and the abnormal coronary findings (P=0.427).

The mean diameter of the aortic valve annulus was 27±3mm and the mean diameter of the sinus of Valsalva was 38±4mm (Table 2). Both diameters were relatively large as compared to normal values[19]. The take-off height of the right and left coronary ostia was 28±5mm and 26±6mm, respectively, exceeding the normal values of 15±3mm and 20±3mm for the right and left coronary ostium, respectively (Table 2).

Table 2. Neo-aortic root dimensions on CTA in patients after ASO and normal references values.

	Patients after ASO (n=28)*	Normal references†
Aortic Annulus (mm) [range]	27±3 [22-33]	23±3 [16-30]
Sinus of Valsalva (mm) [range]	38±4 [29-47]	34±4 [26-44]
Right coronary ostium height (mm) [range]	28±5 [16-37]	15±3 [8-26]
Left coronary ostium height (mm) [range]	26±6 [16-39]	20±3 [13-28]

*Two patients with previous Bentall-procedure in the cardiac history were excluded from this analysis.
†Normal references are adapted from the control population in the study of Stolzmann et al.[19].

Computed tomography findings in common versus variant coronary anatomy pattern

The observed abnormal coronary findings on CTA were noted in 7/24 patients (29%) with a common post-operative coronary anatomy pattern and in all 6 patients (100%) with a variant coronary anatomy pattern (P=0.003, Table 3). In addition, a high occurrence of an acute angle of the coronary origin was noted, with a higher prevalence in patients with variant coronary anatomy (13% vs. 67% for common and variant coronary pattern, respectively, P=0.016). Furthermore, the take-off of the left coronary ostium was higher in patients with variant coronary pattern (24±5 vs. 31±6mm for common and variant anatomy, respectively, P=0.016). No differences in the aortic root dimensions were observed between patients with common and variant coronary pattern.

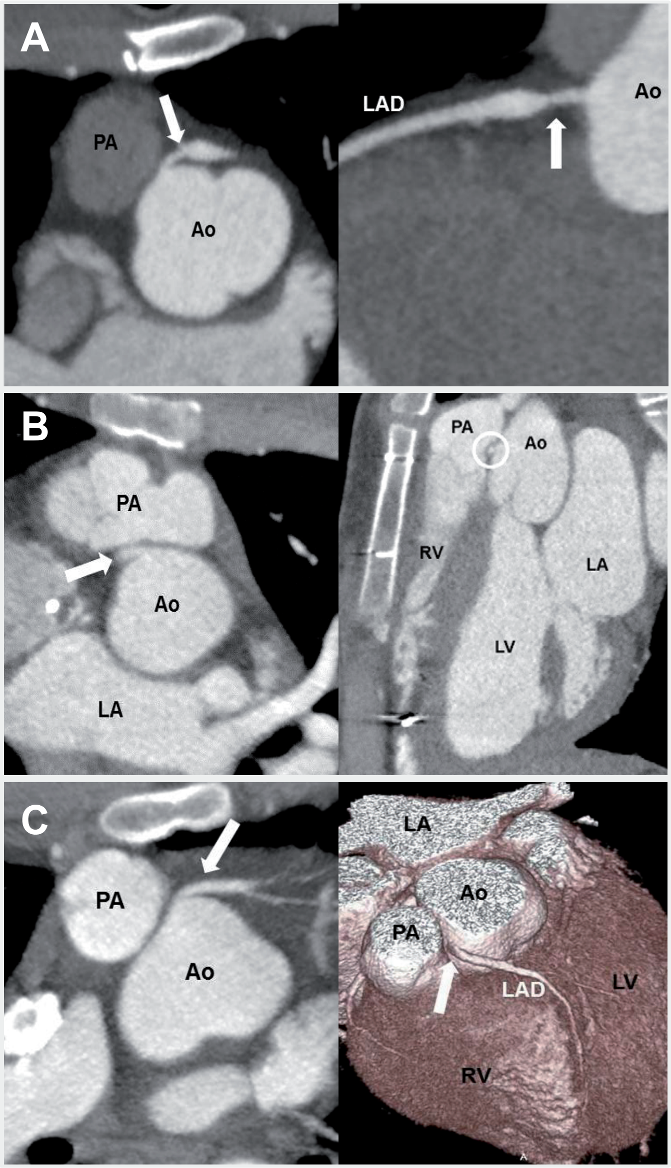

Figure 3. Case examples of patients with abnormal coronary findings on CTA.

A. A significant proximal LAD stenosis caused by fibrocellular intimal thickening. The stenosis is located close to the ostium(arrow) and a post-stenotic dilation can be observed. Axial slice(Left panel); multi-planar reconstruction of the LAD artery(right panel).

B. Inter-arterial course of the RCA, coursing between the neo-aorta and the pulmonary artery(arrow: left panel), as is also visible on the sagittal axis image(white circle: right panel).

C. Acute angle of the LAD artery(white arrows), possibly causing coronary ostium compression. Axial slice(Left panel); 3D-reconstruction(right panel).

Ao=neo-Aorta ; LA=left atrium; LAD=left anterior descending coronary artery; LV=left ventricle; PT=pulmonary trunk; RCA=right coronary artery; RV=right ventricle.

Table 3. Coronary findings on CTA according to the post-operative coronary anatomy pattern.

	Total n=30	Common coronary anatomy (1R-2LCx) n=24	Variant coronary anatomy n=6	p-value
Patients with abnormal CTA	13 (43%)	7 (29%)	6 (100%)	0.003
Significant coronary stenosis (>50%)	1 (3%)	0 (0%)	1 (17%)	0.200
Inter-arterial coronary course	5 (17%)	4 (17%)	1 (17%)	0.746
Acute angled coronary origin	7 (23%)	3 (13%)	4 (67%)	0.016
Height of the coronary ostia (mm)*				
Right coronary ostium [range]	28±5 [16-37]	27±5 [16-35]	30±6 [20-37]	0.306
Left coronary ostium [range]	26±6 [16-39]	25±5 [16-38]	31±6 [22-39]	0.021

*Two patients with previous Bentall-procedure in the cardiac history were excluded from this analysis.

Acute angle versus neo-aortic root dimensions

In the patients with an acute angle of the coronary origin the diameters of the aortic valve annulus and the sinus of Valsalva were significantly larger than in patients without an acute angle (P=0.016 and P=0.002 respectively, Table 4). In addition, higher coronary take-off was observed in patients with an acute angle as compared to patients without an acute angle (P=0.030 and P=0.002 for the right and left coronary artery, respectively, Table 4).

Table 4. Neo-aortic root dimensions and coronary ostial height in patients with and without an acute angle of the coronary origin on CTA.

	Normal angle (n=21)	Acute angle (n=7)	p-value
Aortic Annulus (mm) [range]	27±3 [22-33]	30±2 [28-33]	0.016
Sinus of Valsalva (mm) [range]	36±4 [29-43]	42±3 [39-47]	0.002
Right coronary ostium height (mm) [range]	26±5 [16-32]	31±5 [24-37]	0.030
Left coronary ostium height (mm) [range]	24±5 [16-31]	32±6 [25-39]	0.002

COMMENT

The current study evaluated the coronary anatomy in adult patients with a TGA corrected by ASO. The main observations were: 1) a high prevalence of abnormal coronary findings, 2) a higher occurrence of these coronary abnormalities in patients with a variant coronary anatomy pattern, and 3) larger neo-aortic root dimensions and higher coronary take-off in patients with an acute angle of the coronary origin. These observations may partly explain the pathophysiology of coronary ostial lesions in patients after ASO.

Coronary artery anatomy pattern and the occurrence of coronary obstructions

In patients with TGA a large variability in coronary anatomy is encountered and the pre-operative coronary anatomy pattern is known to influence the prognosis of patients after ASO[5-8]. A high prevalence of coronary stenosis has been reported after ASO, ranging from 7% to 12%, even in asymptomatic patients.[5,20] In our study a significant coronary stenosis of the proximal LAD with post-stenotic dilation was found in 1 patient. Of interest, this patient did not experience chest pain and had excellent exercise capacity. Lack of symptoms in patients after ASO could be attributable to per-operative sympathetic denervation[21]. Furthermore, an inter-arterial course was observed in 5 patients. Three of these patients underwent subsequent myocardial perfusion SPECT, showing persistent perfusion defects, but no signs of ischemia. Perfusion defects on myocardial scintigraphy in patients after ASO are usually related to the insult of open heart surgery rather than to coronary artery lesions, hampering the interpretation of myocardial scintigraphy results in patients after ASO[22]. An inter-arterial coronary course is often seen in coronary arteries where the coronary artery origin is located close to the commissure[23], as was observed in this study in the patient with the single ostium. Furthermore, post-operative inter-arterial coronary course could reflect technical problems during the operation, such as insufficient length of the coronary artery to allow coronary transfer to a more lateral position by the surgeon[24]. On the other hand, the inter-arterial course may become more pronounced in adult patients due to growth of the neo-aorta.

Furthermore, variations in coronary artery branching patterns are associated with complicated coronary transfer[9,10]. The most frequently observed variant coronary anatomy pattern, with an aberrant Cx artery arising from the RCA artery (1CxR-2L), was observed in 17% of our patient population. In the study by Ou et al.[12] all Cx lesions occurred in patients with this variant coronary pattern. Our study showed a higher occurrence of an acute angled coronary origin in patients with this variant coronary pattern. These observations may be related to a more challenging coronary transfer in patients with this pattern, where the long initially retro-aortic Cx artery is possibly stretched by its new positioning behind the neo-aorta. Yet, the occurrence of an acute angle may also relate to the neo-aortic growth during follow-up.

Coronary take-off in relation with the neo-aortic root dimensions

A frequently observed complication after ASO is neo-aortic root dilation[9,23]. A possible explanation for neo-aortic root dilation could be the structural vascular differences of the aorta and pulmonary artery in patients with TGA[24]. In this study, 2 patients underwent a Bentall procedure for severe neo-aortic root dilation. In the remaining 28 patients, slightly enlarged aortic root dimensions were observed, with even larger dimensions in patients with an acute angle of the coronary origin. Based on these observations, we hypothesize that dilation of the neo-aortic root could contribute to the development of an acute angle of the coronary origin during follow-up after ASO.

Not surprisingly, the height of take-off of the coronary ostia was larger in our patients as compared to healthy subjects[19], related to the technique of ASO where the coronary ostia are always implanted at a higher level than their natural level to avoid coronary kinking. In our center, whenever feasible, the coronary arteries were re-implanted as buttons, keeping the coronary ostial height limited compared to when a trap-door technique is used[25]. In patients with an acute angle of the coronary ostial height was larger, possibly explaining part of the pathophysiology of this coronary abnormality.

Limitations and strengths

The current study has several limitations. First, this is a retrospective study of prospectively gathered data. However, all patients were clinically referred for CTA, regardless of the presence of chest pain symptoms and CTA was performed using the same protocol, making a reliable comparison feasible. Secondly, the present patient population is relatively small. Still, data on coronary anatomy in adult patients after ASO are scarce and as only adult patients after ASO were included in the current study, the mean ages of this patient population was relatively high. Thirdly, although these angled origins may be potential risk locations for the development of future ostial coronary lesions causing limitations in coronary blood flow ,the clinical significance of the described abnormal coronary findings, mainly the presence of an acute angle of the coronary origin, remains uncertain. Importantly, to our best knowledge this is the first study proposing a pathophysiological relation between the observed coronary anatomy and the neo-aorta root dimensions in adult patients late after ASO.

CONCLUSIONS AND CLINICAL IMPLICATIONS

The present study provided detailed information on the coronary anatomy late after the ASO and showed that abnormal coronary findings on CTA are often encountered in adult patients after ASO. Abnormal coronary findings were more frequently observed in patients with a variant coronary anatomy pattern, with a higher occurrence of an acute angle of the coronary origin. Significantly larger neo-aortic root dimensions and higher coronary artery take-off were observed in patients with acute angled coronary origins. Accordingly, these findings could be predictors for the development of an acute angle of the coronary origin during follow-up. The current observations may help explaining the pathophysiology of the ostial coronary lesions that are frequently encountered in patients after ASO. Although the clinical significance of these findings remains uncertain until longer-term follow-up is available, we feel that the lack of symptoms and the potential life-threatening consequences of coronary flow obstruction may justify repeated imaging, especially in patients with a variant coronary anatomy and/or neo-aortic root dilation since these patients seem to be at increased risk for developing coronary abnormalities.

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