

Research Article

Critical Observations on the Dynamic Change in Caliber of Interarterial Segment of Anomalous Coronary Arteries on CT Angiogram with Chest Pain and Treadmill Test Findings-A Potential 'Game changer' Observations in Management

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Abstract

Aims and background

The incidence of coronary artery anomaly is rare in the general population, anomalous origin of right coronary artery being the most common. These anomalies, particularly anomalous coronary arteries with an interarterial course (ACAIAC) are potentially dangerous. Due to their low incidence, meticulous clinical and imaging guidelines have not yet been defined in assessing such patients and guiding management.

Methods and results

CT coronary angiograms of patients who underwent the study for exclusion of coronary artery disease were reviewed. Patients with ACAIAC were recorded. The images were reviewed and reconstructed to measure the

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caliber and area of the narrowest interarterial segment of ACAIAC in systolic and diastolic phases using Philips Intellispace version 12.1 software. Percentage change in area (p value 0.093) and diameter (p value 0.108) of the interarterial segment in systolic and diastolic segments, was statistically significant between anomalous coronaries with high and low interarterial course. Percentage change in area and diameter between patients with positive and negative TMT findings was also statistically significant (p<0.001 in both cases).

Conclusion

Significant positive correlation between change in vessel caliber in the interarterial course of coronary arteries during the cardiac cycle and TMT findings, suggests elevated risk of inducible ischemia in patients with significant vessel compression. Hence the change in vessel caliber demonstrated by CT imaging can be used as a potential criterion for risk assessment and management of patients with ACAIAC.

Keywords: Coronary Vessel Anomalies; diagnostic imaging; myocardial ischemia; Coronary angiography; Dynamic coronary compression and Coronary Vessels; physiopathology

1. Introduction

Incidence of anomalous aortic origin of the coronary arteries have been reported in 0.14-1.74% of the population as described in the various studies [1]. The course of the anomalous vessel may be intramural, interarterial, intramyocardial, pre-pulmonic, subpulmonic or retroaortic. The interarterial course or 'malignant' course of the artery has been predicted to be a risk factor of Sudden Cardiac Death (SCD) in young athletes. [2,3] Anomalous coronaries have been known to cause various symptoms like dyspnea on exertion, palpitations, arrhythmias and even lead to sudden cardiac death. However, patients can also be entirely asymptomatic.[3,4] The altered physiology of restricted coronary blood flow in interarterial courses have been suggested to be due to various factors like: acute takeoff angle, the slit-like ostium of the coronary, the compression of the intramural segment by the aortic valve commissure and the compression of the artery between the aorta and the main pulmonary artery[5]. Anomalous origin of the Right Coronary Artery (RCA) from the left coronary sinus (AORL) has been reported to be more common compared to anomalous origin of left coronary artery [6-8] The hemodynamic significance of AORL with an Interarterial Course (IAC) differs according to the location of the ostium of anomalous RCA, as the extent of flow reduction depends on the degree of compression of RCA ostium and/or the compression of interarterial RCA segment. Accordingly, RCA ostium located above the pulmonary valve is termed "high interarterial course (HIC)" and an RCA ostium below the pulmonary valve is termed "Low Interarterial Course (LIC)". (Figure 1) In patients with HIC of RCA, coronary segment between the two great vessels. the aorta and main pulmonary artery would be more likely to be compressed during systole, as blood is forced into these vessels, compared to LIC.[5] Oblong or slit like lumen has also been suggested to carry a higher risk of SCD in cases of IAC [9]. An acute angle takeoff of a coronary artery, namely, angle between the proximal coronary artery and the aortic wall of less than 45°, may further compress the coronary artery at its point of takeoff which may lead to SCD [10]. (Figure 2) Keeping in mind of the many risk factors that are proposed, present CT angiogram data can be tailored to demonstrate some of the risk factors in static and dynamic phases, making imaging observations relevant in clinical decision making. This

retrospective study revisits our patients with anomalous coronaries as to their physical dimensions of inter-arterial segment in systolic and diastolic phase.

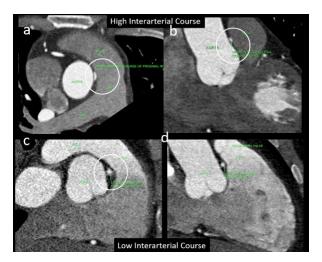


Figure 1: CT coronary angiography MPR images (a, b) demonstrate anomalous inerarterial course of RCA inbetween aorta and proximal main pulmonary artery - High interarterial course.(circle). Images (c,d) show anomalous inerarterial course of RCA inbetween aorta and RVOT - Low interarterial course.

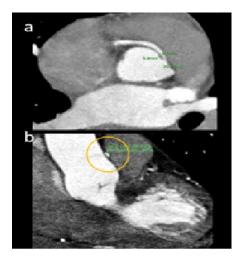


Figure 2: CT coronary angiography MPR image(a) shows acute angle take off (<450) of RCA with anomalous interarterial course. (b) MPR image showing slit like orientation of anomalous interarterial course of RCA.

2. Material and Methods

2.1. Study design

A retrospective descriptive study, was carried out at the imaging services of our institution during the period of June 2016 to May 2018. Study was approved by the Ethics Committee and Medical Research Department. We reviewed

the records of CT coronary angiography data of patients who underwent the procedure as a screening or rule out coronary artery disease. Objective of the study was to detect the prevalence of inter arterial / malignant course of coronary arteries; to study the variations in the IAC of anomalous coronary arteries(ACA); to document change in vessel calibers in systolic & diastolic phases and finally to correlate systolic-diastolic caliber changes with chest pain and results of treadmill test. Technically suboptimal exams were excluded. Patients with occluded or severely diseased coronary arteries with CAD RADS score >2, were also excluded. Relevant clinical and laboratory information was obtained by reviewing the available clinical records.

2.2. Patient preparation and study protocol

According to the protocol patients were pre-medicated with Tab. Metaprolol orally [or Tab. Diltiazem (in asthmatic patients) or Tab. Ivabradine] along with Tab. Alprazolam 0.25 mg to maintain the heart rate between 60-70 bpm and reduce anxiety. Scans were performed with Philips Ingenuity, 128 slice CT scanner (Koninklijke Philips N.V) and contrast was injected with a dual flow injector. Retrospective ECG triggering was used. Iohexol (Omnipaque 350 mg/ml) was injected in the dose of 1-1.5 ml/kg and flow rate of 5.5 ml/sec followed by a saline chase. 'Bolus track' method was used for triggering with ROI at ascending aorta with a triggering threshold of 120 HU. Images were reconstructed on a workstation (Philips's workstation with Intellispace Ver 12.1 software) to generate images in multiple phases with slice thickness of 0.6-0.7 mm. 3D (volume rendering) and curved planar reconstruction (CPR). Technical parameter of CT angiography is provided in Table1. Retrospective reconstruction (0.65mm thickness) of the data was performed in a plane perpendicular to the long axis of ACA. Optimal image representative of vessel cross section was selected. Images were viewed with 2-3X magnification and dimensions and area of IAS of coronary were manually measured at multiple levels by two observers blinded for clinical details and earlier reports. Range of diastolic and narrowest systolic caliber and area of the interarterial segment of anomalous coronary artery was documented. Record of estimated average radiation dose per examination was made.

Scan area	From ascending aorta to diaphragm
Scan length	~12.5 cm
Scan direction	Cranio-caudal
Tube voltage	120 kV
Tube current	900 mAs
CTDIvol (average)	~59 mGy
DLP (average)	~1000 mGy*cm
Rotation time	0.4 sec
Detector coverage	40 mm
Slice width	3 mm
Pitch	0.2 - 0.3
Recon. increment	0.67 mm
Window setting	Window width = 750, Window Level = 90

Matrix Size	512 x 512
Contrast (Omnipaque	1.0 - 1.5 mL / kg + 20-30 mL of
350 mg / mL)	saline chase
Contrast flow rate	5.5 mL / s
Trigger	Bolus tracking
Post threshold delay	5 sec

Table 1: Coronary CTA scan parameters.

2.3. Statistical analysis

Data compiled with Microsoft excel sheet was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and SD. Independent't' test or Mann Whitney U test was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively. Cohen's kappa statistical test was used to evaluate intra and inter observer observation. 'p-value' (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

3. Results

A total of 6299 CT angiograms were reviewed. The prevalence of IAC of coronary artery abnormality was seen in 0.77% (49 patients). We excluded 13 patients with CAD-RADS score of 2 or more, leaving 36 patients for the analysis. We recorded anatomical variations and caliber of interarterial coronary course (subtypes of IAC, slit like course and acute angle takeoff) with chest pain and TMT findings. The results of the study are described below. The mean age of the patient was 50.18 ±11.15 years with 72.2% of patients being male. 35 patients (97.2%) had AORL with an interarterial course and 1 patient (2.8%) had LMCA arising from the right anterior sinus with AC. In AORL, 22 patients (62.8%) had HIC and 13 patients (37.2%) had LIC. Only one patient of LMCA originating from right anterior sinus had LIC. In patients with HIC, acute angulation at the origin was present in all patients (22 patients) and slit-like opening/course was present in 77.3% (17 of 22 patients). In patients with LIC, acute angulation at the origin was present in 85.7% (12 of 14 patients) and slit-like course was present in 28.6% (4 of 14 patients). (Table 2) There was a statistically significant difference in slit-like course distribution between two groups (p value 0.004) and there was no significant difference in acute angle takeoff at the origin distribution between two groups (p value 0.068). In patients with HIC, chest pain was present in 68.2% (15 of 22 patients) and TMT was positive in 45.5% (10 of 22 patients). In patients with LIC, chest pain was present in 64.3% (9 of 14 patients) and TMT was positive in 14.3% (2 of 14 patients). There was no significant difference in occurrence of chest pain (p value 0.809) and TMT findings between two groups (p value 0.053). In HIC, mean systolic area and diameter was $5.236 \pm 1.369 \text{ mm}^2$ and 1.500 ± 0.495 mm respectively. In LIC, mean systolic area and diameter was 7.629 ± 3.879 mm² and 2.171 ± 0.897 mm respectively. This difference in systolic area (p value 0.012) and diameter (p value 0.007) between high and low group was statistically significant. The mean diastolic area was $6.873 \pm 1.516 \text{ mm}^2$ and mean diastolic diameter was 1.995 ± 0.509 mm in patients with HIC. The mean diastolic area was 8.500 ± 4.017 mm² and mean diastolic diameter was 2.379 ± 0.885 mm in patients with LIC. This difference in diastolic area (p value 0.093) and diameter (p value 0.108) between high and low group was not statistically significant. There was good intra and interobserver variations (85% and 83%) in the vessel diameter or area measurements. In HIC, percentage change in mean area and diameter was 23.692 ± 14.962 % and 24.706 ± 14.276 % respectively. In LIC, percentage change in mean area and diameter was 11.007 ± 9.306 % and 9.632 ± 7.794 % respectively. This difference in percentage change in area (p value 0.008) and diameter (p value 0.001) between HIC and LIC was statistically significant. (Table 3). Imaging appearance of the anomalous artery with negative TMT and without significant arterial compression in systolic and diastolic phase is illustrated in Figure 3. In patients with positive TMT, slit like course was present in 83.3% and among those with negative TMT 45.8% had slit like course. This difference was statistically significant (p value 0.031). However, no association was found between the angulation at the AORL origin and TMT results. Among those with positive TMT, the mean systolic area was seen to be 5.4 mm2, mean systolic diameter 1.5 mm, mean diastolic area 7.7 mm2 and mean diastolic diameter 2.1 mm. Whereas in TMT negative patients mean systolic area was seen to 6.4 mm2, mean systolic diameter 1.8 mm, mean diastolic area 7.3 mm2 and mean diastolic diameter 2.1 mm. Imaging appearance of the anomalous artery with positive TMT and significant arterial compression in systolic and diastolic phase is illustrated in Figure 4. The percentage change in mean systolic area was 29.800 ± 13.852 % in those with positive TMT, and in those with negative TMT percentage change in mean area was 13.239 ± 11.226 %. This difference in percentage change in area between those with positive and negative TMT findings was statistically significant (p value <0.001). In patients with positive TMT, percentage change in mean diastolic diameter was 30.605 ± 13.301 % and in those with negative TMT percentage change in mean diameter was 12.964 ± 10.586 %. This difference in percentage change in diameter between those with positive and negative TMT findings was statistically significant (p value <0.001) (Table 4). Associations of other parameters in relation to TMT results are shown in Table 5.

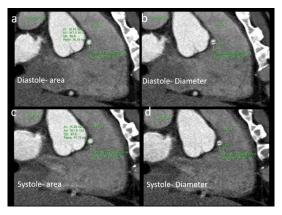


Figure 3: CT coronary angiography MPR image of 48 years old male with history of chest pain and negative TMT, showing systolic (c,d) (Area – 16.2 mm²; Diameter – 4.0 mm) and diastolic (a,b) (Area – 18.2 mm²; Diameter – 4.3 mm) phases of low interarterial course of RCA without significant change in caliber during cardiac cycle.

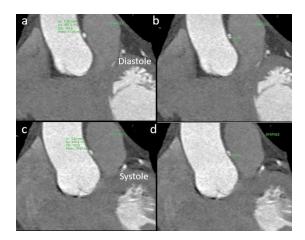


Figure 4: CT coronary angiography MPR image of 38 years old male with history of chest pain and positive TMT, showing systolic (c,d) (Area -5.5 mm^2 ; Diameter -1.6 mm) and diastolic (a,b) (Area -7.5 mm^2 ; Diameter -2.3 mm) phases of high interarterial course of RCA with significant change in caliber during cardiac cycle.

		Group				
		Hi	gh	Low		
		Count	%	Count	%	
Sex	Male	8	36.40%	2	14.30%	
	Female	14	63.60%	12	85.70%	
Coronary origin	LMCA from right 8 coronary cusp		36.40%	2	14.30%	
	RCA from left coronary cusp	14	63.60%	12	85.70%	
	<30 years	2	9.10%	0	0.00%	
	31 to 40 years	4	18.20%	3	21.40%	
A ===	41 to 50 years	5	22.70%	5	35.70%	
Age	51 to 60 years	7	31.80%	4	28.60%	
	>60 years	4	18.20%	2	14.30%	
	Mean ± SD	48.82 ± 12.783		49.29 ± 9.667		

Table 2: Age, Sex and Coronary origin location distribution between high and low coronary origin groups.

	Chest pain						
	Yes		No			P value	
		Mean	SD	Mean	SD		
Createlie	Area	6.279	2.825	5.942	3.006	0.743	
Systolic	Diameter	1.842	0.778	1.6	0.68	0.367	
Diastolic	Area	7.788	2.8	6.942	2.933	0.406	
	Diameter	2.271	0.73	1.892	0.563	0.124	
Percentage change in caliber	Area difference	20.587	15.807	15.103	10.514	0.097	
	Diameter difference	19.87	14.398	16.793	14.044	0.546	

Table 3: Area and diameter comparison of interarterial segment between patients with and without chest pain.

		Positive		Negative		P value
		Mean	SD	Mean	SD	
Crestalia	Area	5.542	1.812	6.479	3.235	0.359
Systolic	Diameter	1.542	0.623	1.871	0.789	0.217
Diastolic	Area	7.758	1.921	7.379	3.223	0.711
	Diameter	2.192	0.601	2.121	0.748	0.778
Percentage change in caliber	Area difference	29.8	13.852	13.239	11.226	<0.001*
	Diameter difference	30.605	13.301	12.964	10.586	<0.001*

Table 4: Area and diameter comparison of interarterial segment between patients with positive and negative TMT findings

		ТМТ				
		Positive		Negative		P value
		Count	Percentage Count Percentage			
Coronary	LMCA from right coronary cusp	0	0.00%	1	100.00%	0.473
Origin	RCA from left coronary cusp	12	34.30%	23	65.70%	

Acute angulation at the	No	0	0.00%	2	100.00%	0.303
origin	Yes	12	35.30%	22	64.70%	
Slit-like	No	2	13.30%	13	86.70%	0.031*
orifice	Yes	10	47.60%	11	52.40%	0.031

Table 5: Association between various parameters with TMT.

4. Discussion

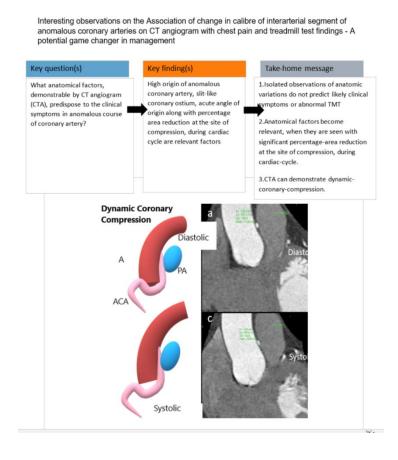
To our knowledge, this is a unique study correlating the measurement of change in vessel caliber in anomalous coronaries during the cardiac cycle. We did not come across imaging or angiography studies with similar intent in the literature. Anomalous coronary arteries have been reported to cause various cardiac symptoms and various mechanisms have been hypothesized as to the pathophysiology. Physical exertion in such individuals can lead to accentuation of precarious hemodynamic state leading to restricted blood flow, even myocardial ischemia, and sudden death. [11-14] However, it has been observed that many patients may remain entirely asymptomatic. Hence it is imperative to identify the patients at risk of potential myocardial ischemia thus selecting candidates for surgical intervention.[15-17] This study documents location of ostium and path of ACA, variation in the systolic-diastolic diameter-area of their interarterial segment in our patients and correlate observations with chest pain/TMT results. The significant 'percentage change' in mean area and diameter of the artery in individuals with HIC and LIC concurs with the hypothesis proposed by Lee et al, which state that hemodynamic significance of AORL with an interarterial course differs according to the location of ostium of the ACA due to greater compression of the interarterial segment of ACA with high origin [5]. We did not observe any significant correlation based on location of ACA ostium in relation to TMT findings. However, we noted significant positive correlation in the change in vessel caliber in the interarterial course of coronary arteries in the cardiac cycle and TMT findings. Our observations may suggest that anatomical classification into HIC and LIC may not adequately categorize the ischemic risk, on the other hand, absolute percentage of arterial compression does. Therefore, it is logical to suggest that, along with type of IAC, the degree of compression also should be taken into consideration when predicting risk assessment and making decision on management strategies.

Specific anatomic characteristics in patients with IAC of coronary arteries on CTA and relation between major adverse cardiac events have been studied earlier. [18] However, there was no relevant literature on the assessment of change in vessel caliber during the cardiac cycle in patients with IAC of coronary arteries, thus we believe that results of our study bridge the information lacunae, providing more accurate basis for the patient management. This information should be explored in more detail in future while deciding the treatment strategy of this specific patient group. Ashrafpoor et al. assessed in their study, the relation between major adverse cardiac events and anatomical criteria determined by coronary CTA. A significantly smaller minimal lumen area was seen in their patients with adverse coronary events (3.6 mm² vs 9.0 mm²) [18]. Our observations suggest that difference in minimal lumen area

(systolic phase lumen) was not a significant factor (5.4 mm² vs 7.4 mm²). In fact, only three patients in our study had a minimal lumen area ≤3.6 mm², one had negative TMT, second had positive TMT (borderline symptoms) and the third had a positive TMT (symptomatic, minimal lumen area of 1.7mm² and area difference of 55% and 35% change in diameter). Third patient underwent reinsertion of the anomalous RCA onto right coronary cusp and remains asymptomatic on follow up. Thus we do not recommend single measurement of the interarterial segment, as a sole criteria for assessing significance. [18] Many studies have assessed the anatomic parameters of ACA with IAC in young patients. One such study comparing the "high-risk" morphologic characteristics of anomalous aortic origins of RCA vs left coronary artery showed no significant differences with respect to any morphologic features Traditionally it is believed that slit like course and acute ostial angulation were significant risk factors in SCD. We were not able to confirm positive correlation with positive stress testing, similar to observation by Palmieri et al. [20] Regarding 'percentage change in caliber' with stress testing results, we could not arrive at an absolute cut off value that can serve as a decisive factor in choosing management options. Higher percentage of change in coronary caliber in symptomatic individuals, along with anatomical factors, can contribute to the risk of SCD The positive TMT findings in patients with significant change in vessel caliber is an indication that the increased myocardial activity, exaggerates vascular compromise, leading to higher risk of myocardial ischemia. As surgery is currently indicated only in symptomatic patients, identifying the patients who would benefit from surgery in a timely manner is critical [15,16]. There is also the problem of lack of existing universal guidelines for treatment of ACIAC in asymptomatic patients with wide variation in recommendations ranging from surgical repair in all teenagers to a recommendation to a small subset of patients based on clinical and imaging criteria [21-24]. Though exercise testing is routinely performed in ACIAC, a negative exercise test does not provide significant reassurance or predict adverse cardiac events in previously asymptomatic patients [25]. It is imperative that we need to follow up cases of borderline risk, as well designate low risk or 'no increased risk' category to the appropriate patient group. Risk stratification thus seems to be of paramount importance. We hope our criterion of dynamic assessment of interarterial coronary segment caliber may offer much needed help in solving the patient management dilemma. Our study, being a retrospective in nature, of a relatively rare entity, has few limitations. There is limited availability of all relevant clinical physiological parameters, which are critical in this complex context. Inclusion of stress thallium study or a stress MRI certainly serve better than TMT results in patient risk stratification. Since a large majority of subjects are asymptomatic, often the anomaly detected incidentally, adding expensive and demanding studies may pose a great challenge. In the recent past, we have noted a major improvement in imaging infrastructure with better, more specific image acquisition-analysis options, since our study. Current options are likely to prove to be more accurate, versatile (Flow dynamics) and allow significant reduction in radiation dose. Our CTA protocol resulted in an approximate radiation dose of 8-10mSv per exam, as against the current ECG phase specific, dose modulated protocols (2-3.1 mSv per exam). [27] Thus there is immediate scope for dose reduction. Including suggested recommendations to study protocol may provide unequivocal proof of ischemia in the prospective surgical candidates, making decision for surgery straightforward.

5. Conclusion

The dynamic assessment of change in coronary arterial caliber during cardiac cycle in patients with IAC of coronary arteries is a novel concept in assessment of anomalous coronary arteries. Percentage change in vessel caliber is a potential criterion that can be used in the risk assessment for coronary ischemia when considering medical and interventional management in patients with anomalous coronary arteries with an IAC. Inclusion of dynamic study protocols is likely to provide more predictable outcome parameters for patient selection for definitive procedures. Rapid evolution and greater availability of investigative infrastructure has made assessment accurate and more affordable. Further exploration of the concept, substantiation of observations and defining predictive objective cut-off values of significance will ensure optimal management of the patients.



Graphical Abstract

Authorship statement

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [VR] and [KG]. Intra-observer reading performed by Dr. VR and inter-observer readings done by (VR and KG). The first and final draft of the manuscript was written by [VB] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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