Cardiac CT Angiography Study of the Prevalence and Short-Term Outcome of Older Patients with Anomalous Origin of the Right Coronary Artery from the Left Sinus of Valsalva with Inter-Arterial Course

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Abstract

Purpose: Anomalous Origin of Coronary Arteries from Opposite Sinus of Valsalva (ACAOS) is prevalent in 1% of the general and 0.4-0.7% of the imaging population. An Inter-Arterial Course (IAC) is considered to be associated with sudden cardiac death, particularly in young athletes predominantly related to anomalous left coronary artery originating from right sinus of Valsalva with IAC. The prognosis of Anomalous Right Coronary Artery from Left Sinus of Valsalva (R-ACAOS) with IAC is not clear. We aimed to assess the prevalence and the short-term prognosis of R-ACAOS in a Cardiac Computed Tomography Angiography (CCTA) population.

Methods: This is a single centre retrospective cohort study encompassing 625 consecutive patients referred for CCTA for suspected Coronary Artery Disease (CAD) between January 2012 and December 2017. We found 10 cases of R-ACAOS with IAC. Each case was matched with two controls for age, gender, severity of CAD, cardiovascular risk factors, and history of revascularisation. Outcome measures of MACE including fatal or non-fatal MI, coronary revascularisation or all cause death.

Results: The prevalence of R-ACAOS with IAC was 1.6%. The cases and controls had a mean age of 65 years; 70% males. The mean ± SD time for MACE was 13±15 months and 29±22 months with a MACE rate of 50% and 40% in cases and controls respectively with a hazard ratio: 1.25(0.055 – 2.84), P=0.59).

Conclusion: R-ACAOS with IAC in older patients has comparable short-term prognosis as in controls. The management of these patients should be similar to those with no R-ACAOS.

Keywords: Angiography; Cardiac CT; Coronary Anomaly; Right Coronary Artery; Prevalence; Short-Term Outcome

Abbreviations

AACAOS: Anomalous Origin of Coronary Arteries from Opposite Sinus of Valsalva; CAD: Coronary Artery Disease; CCTA: Coronary Computed Tomography Angiography; CI: Confidence Interval; HR: Hazard ratio; IAC: Inter-Arterial Course; L-ACAOS: Anomalous Left Coronary Artery Originating from Right Sinus of Valsalva; MACE: Major Adverse Cardiovascular Events; R-ACAOS: Anomalous Right Coronary Artery from Left Sinus of Valsalva, SCD: Sudden Cardiac Death

Introduction

Anomalous Origin of Coronary Arteries from Opposite Sinus of Valsalva (ACAOS) is a rare condition with a prevalence of 1% in general population and between 0.44-0.70% in the cardiac imaging population [1,2]. ACAOS with a course between the aorta...
and pulmonary artery (Inter-Arterial Course (IAC)) is has been associated with increased risk of Sudden Cardiac Death (SCD) in post-mortem studies in particular in young athletes [3-5]. A recent report, however, failed to show significant difference in mortality in middle aged patients compared with matched controls [6]. The excess mortality was seen in those with anomalous origin of Left Coronary Artery from Right Sinus of Valsalva (L-ACAOS) and IAC but less so in those with anomalous origin of Right Coronary Artery from Left Sinus of Valsalva (R-ACAOS) and IAC [3,4]. The association of R-ACAOS with IAC and SCD has not been well recognised.

The widespread use of Multi detector Coronary Computed Tomography Angiography (CCTA) for detection of Coronary Artery Disease (CAD), has led to higher rate of detection of such, coronary artery anomalies [5,7]. The understanding of the prognosis of such coronary anomaly has become even more important therefore. In this study we aimed to assess the prevalence and the short-term prognosis of R-ACAOS in a CCTA population.

Methods

This is a single centre retrospective observational cohort study including 625 consecutive patients who were referred for CCTA between January 2012 and December 2017 for suspected CAD. We identified 10 patients with R-ACAOS during this period (Figure 1). Each patient identified with R-ACAOS and IAC (cases) was matched with two controls (patients without coronary artery anomaly) for age, gender, distribution and degree of CAD on CCTA, cardiovascular risk factors, and history of previous revascularisation. Patients’ demographic data were collected and the outcome of functional tests in R-ACAOS patient were recorded if available.

![R-ACAOS with IAC](image)

Figure 1: CCTA: 3D rendering and multi planar reconstruction of the coronary arteries showing R-ACAOS with IAC in one of our patients.

R-ACAOS with IAC: Anomalous Right Coronary Artery Originating from The Left Sinus of Valsalva with Inter-Arterial Course; RSoV: Right Sinus of Valsalva; LSoV: Left Sinus of Valsalva; LMCA: Left Main Stem Coronary Artery; MPA: Main Pulmonary Artery; LA: Left Atrium, RA: Right Atrium.

Outcome data in both cohorts were collected from the Hospital’s electronic data management system. Primary outcome was the rate of Major Adverse Cardiovascular Events (MACE) defined as fatal or non-fatal myocardial infarction, coronary artery revascularisation and all cause death.

IBM-SPSS v. 22 was used for data analysis. Categorical variables were expressed in percentage values whereas continuous variables as mean ± SD or median, as appropriate. We performed Kaplan-Meier event-free survival analysis comparing the time to the first MACE. Event-free survival curves were compared between cases and controls using Kaplan-Meier plots and Cox regression with robust variance estimate, accounting for clustering among matched cases and controls. Hazard Ratios (HR) with 95% Confidence Intervals (CI) are presented.

Our study complied with ethical standards set in the declaration of Helsinki with prior written consent of the patients.

Results

We found 10 patients with R-ACAOS with IAC amongst 625 consecutive CCTA patients with a prevalence of 1.6%. Out of these 10 patients 8 patients also had additional high risk features (3 patients had intramural course and 5 of them had slit like origin). The baseline characteristics of cases and controls are summarised in Table 1.

![CTA rendering of R-ACAOS with IAC](image)

We found the mean age of 65 years (range 43-78 years) in R-ACAOS with IAC group and 65 years (range 41-85 years) in the control group. The gender distribution in both cohorts included 70% males and 30% females. Their symptoms on presentation were chest pain (80%) and exertional breathlessness (20%). None of the patients presented with sustained or non-sustained arrhythmia, syncope, family history of SCD or known coronary artery anomaly. Both groups were matched for their anthropometric variables, risk factor profile, distribution and the extent of CCTA base CAD and history of previous revascularisation. The mean follows up was 15.1 months (range: 1-49) and 34.7 months (range: 2-62) for the cases and controls, respectively.
Baseline Characteristic | Cases (n = 10) | Controls (n = 20)  
--- | --- | ---  
Age in years (mean, range) | 65, 43-78 | 65, 41-85  
Gender  
• Male | 7 | 14  
• Female | 3 | 6  
Risk factors  
• Diabetes Mellitus | 1 | 4  
• Hypertension | 4 | 9  
• Hypercholesterolemia | 4 | 10  
Coronary Artery Disease In Non-Anomalous Coronaries (CCTA) | 5 | 10  
Previous revascularisation | 1 | 2  
Symptoms  
• Effort breathlessness | 2 | 4  
• Chest pain | 8 | 16  

Table 1: Baseline characteristics of cases (R-ACAOS with IAC) vs. controls. CCTA: Coronary Computed Tomography Angiography >50% luminal stenosis. R-ACAOS with IAC: anomalous right coronary artery originating from the left sinus of Valsalva with inter-arterial course. Note: there was no difference between the two groups.

Pre-existing CAD in non-anomalous coronary arteries was present in 50% of the cases and controls defined as >50% luminal stenosis in at least one of the major epicardial coronary arteries. Five out of 10 cases underwent functional testing based on their clinical needs (2 exercise perfusion scintigraphy and 3 dobutamine stress echocardiography) for ischaemia detection and found to have no inducible ischaemia in the anomalous RCA territory. No death occurred in either group during the follow up period. 50% (n = 5) of the cases and 40% (n = 8) of the controls had MACE. These were associated with the non-anomalous coronary related revascularisation and non-fatal myocardial infarction (Table 2). There was only one R-ACAOS with IAC patient (10%, n = 1/10) who underwent revascularization including the anomalous RCA after informed patient’s decision. Mean time ± SD for MACE was 13 ± 15 months for cases and 29 ± 23 months for controls. This difference in MACE between cases and controls was statistically non-significant (HR: 1.25 CI: 0.5506 - 2.8379, P = 0.5937).

| MACE | Cases (n = 10) | Control (n = 20)  
--- | --- | ---  
Revascularization: Anomalous artery: | 1 | 0  
Non-Anomalous artery: | 3 | 6  
Myocardial infarction | 1 | 2  
Death | 0 | 0  

Table 2: MACE in patient with R-ACAOS with IAC vs. Controls. R-ACAOS with IAC: anomalous right coronary artery originating from the left sinus of Valsalva with inter-arterial course. MACE: Major Adverse Cardiovascular Events. Note: there was no difference in the cumulative MACE rate between two groups.

Discussion

In this study, we found 1.6% prevalence of R-ACAOS with IAC in our 625 consecutive CCTA cohort which is higher than that found in other imaging population [2]. During the short term follow up of 15 months we found no statistically significant difference in the MACE rate in the cases as compared with matched controls. Admittedly our population was slightly older (65 years) compared to those previously reported cases. The MACE events were all due to the diseased, non-anomalous coronary arteries related revascularisation and non-fatal myocardial infarction. There was no anomalous coronary artery related MACE.

Our findings of a non-significant difference in MACE rate between cases and controls (50% vs 40%), are in agreement with a recent study by Grani, et al. [5]. In their study they found 33 patients of ACAOS with IAC and showed a non-significant difference in cardiovascular mortality compared to the control group. Their combined MACE rate in both ACAOS with IAC groups (L-ACAOS and R-ACAOS) was 17.5% vs 21.3% in controls which is lower than in our study. Higher MACE rate in our patients is probably confounded by the older age of our patients and a smaller sample size. However, there is an agreement in the nature of major cardiovascular events which were entirely attributed to non-anomalous coronary revascularisations rather than deaths.

Benign nature of R-ACAOS with IAC was also found by other investigators showing a <1% mortality in the conservatively managed R-ACAOS population between 1.3-5 years follow up [7,8]. Cheezum et al. in their systematic review in autopsy cases found a coronary event related SCD rate of 22% in patients with R-ACAOS as compared to 60% SCD rates in L-ACAOS which occurred predominantly during high level of exercise in younger population [9].
In our study, five patients of R-ACAOS with IAC, who underwent functional tests, showed no inducible ischemia in the anomalous RCA territory. This finding is not surprising as prior reviews have highlighted the prevalence of low sensitivity and high specificity of functional tests in this patient population [10-12].

Although, our study is in agreement with earlier reports showing low incidence of adverse events in R-ACAOS, there is a need for future research in identifying the best risk stratification tools to aid indication and timing of coronary artery revascularisation, in particular in patients taking part in competitive sport activities.

With the evidence available to us to date it is safe to recommend watchful waiting approach and a conservative management strategy in patients with coronary artery anomaly [7,8]. Our study provides additional observational evidence in support of patients with R-ACAOS with IAC would not require different management strategy from that of those with no coronary anomaly. This would be in keeping with the 2008 and 2011 ACC and AHA guidelines [13,14].

Limitations

As a retrospective study it may have inherent shortcoming of selection bias for the MACE rate detection. The low prevalence of this coronary anomaly and a small sample size can influence our results too. However, we tried to minimize it by matching the cases with twice the number of controls according to their anthropometric and cardiovascular variables. The follow up period is short and allows us to make comments only on the short-term outcome of these older patients with R-ACAOS. Our results can also give room for speculation on the reason of the dis-similarity of the short-term prognosis between the groups. May well be that the younger patients with R-ACAOS with IAC could have events during high intensity exercise in their young age and therefore our patients may represent a preselected cohort with more benign outcome. Only a limited number of our patients had ischemia testing. This is due to the observational nature of this study when functional test was requested on the basis of patients’ clinical need at the clinician’s discretion. We believe that our study could be a part of a larger systematic review or meta-analysis in this very selected group of ACAOS patients.

Conclusion

Our study showed the prevalence of R-ACAOS with IAC in the CCTA population as 1.6%. R-ACAOS with IAC is not associated with increased rate of short-term MACE in patient with relatively older age. Management of these patients should be guided by the extent of ischemia and on prognostic grounds similar to those with no R-ACAOS.

References