Prevalence of congenital coronary artery anomalies as shown by multi-slice computed tomography coronary angiography: a single-centre study from Turkey

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Abstract
Objective: Coronary artery anomaly (CAA) is a remarkable etiological factor for sudden cardiac death in young adults. The incidence of CAA is unknown, with most reliable data available based on postmortem/angiography investigations. This study aimed to assess the prevalence of different forms of coronary anomalies, and to investigate the relationships between demographic data and occurrence of CAA.

Methods: A total of 2401 consecutive patients (1805 men; mean age, 56 ± 11.7 years), who were referred between January 2005 and December 2008 for noninvasive multi-slice computed tomography (MSCT) imaging, were retrospectively analysed.

Results: A total of 225 cases (191 men; mean age, 55.9 ± 12) of CAAs were identified (9.37%). Because 11 patients had multiple muscular bridges of the coronary arteries, 236 coronary artery anomalies were found in these 225 patients. Cases were classified into three groups: group 1, coronary anomalies of origin and distribution (n = 36, 1.5%); group 2, anomalies of intrinsic coronary arterial anatomy (n = 180, 7.49%); and group 3, anomalies of coronary termination (n = 9, 0.4%).

Conclusion: The prevalence of CAA was 9.37% in our single-centre study, which is consistent with previous research. A minimally invasive tool, such as MSCT angiography, should be used to identify CAA.

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**Introduction**

Coronary artery anomalies (CAAs) presenting in adulthood are rare and associated with adverse cardiac events, including sudden cardiac death.\(^1\) These anomalies are generally diagnosed incidentally during conventional coronary angiography (CAG). However, CAG is not the ideal modality to define the course of these vessels. Since the early 1990s, a variety of non-invasive techniques have been introduced in coronary artery imaging with an attempt to replace invasive conventional CAG.\(^2\) Multi-slice computed tomography CAG (MSCT-CA) is currently considered the ideal tool to visualize the complex anatomy of coronary arteries three dimensionally.\(^3\)

This study aimed to assess the prevalence of CAAs in patients who underwent 64-slice MSCT-CA to determine their precise localization. This study also aimed to classify CAAs and to investigate the associations between CAAs and parameters, such as age, sex, and other risk factors.

**Patients and methods**

**Population**

A total of 2401 consecutive patients (1805 men, 596 women; mean age, 56 ± 11.7 years; range, 15–88 years) who underwent electrocardiographically-gated 64-slice MSCT-CA from January 2005 to December 2008 were retrospectively reviewed for CAAs. Demographical data and the patients’ history were recorded. The presence of atherosclerotic coronary artery lesions was analysed using a dedicated workstation in a single institution (Maçka Emar, Istanbul, Turkey).

The indications for MSCT-CA were atypical angina, typical angina with an inconclusive stress test, the presence of risk factors and high-risk patients for major coronary events, proximal stent patency at follow-up and bypass graft patency at follow-up.

Patients with unstable angina or acute coronary syndrome, atrial fibrillation, renal insufficiency (without the need for dialysis and a serum creatine level higher than 2.0 mg/dl), a history of contrast allergy and pregnant women were excluded. Verbal and written informed consent was obtained from all of the patients during their cardiovascular evaluation before MSCT-CA.

**Imaging**

Upon presentation to the CT scanner, patients with a heart rate > 70/beats/min received 50 mg atenolol per os (po) 40 min before the study, unless they had known overt heart failure, significant atrioventricular conduction abnormalities (second-degree atrioventricular block) or bronchospastic lung disease. Additional doses (up to a total of 15 mg metoprolol at 5 mg/min, 5 min apart) were administered if the target heart rate (< 65 beats/min) was not achieved and if systolic blood pressure was > 100 mmHg. In patients with major bronchospastic disease or with other contraindications to beta-blocker use, calcium channel blockers were used to control heart rate (intravenous diltiazem at a dose of 5 mg over 1 min repeated up to four times: total dose of 20 mg) every 5 min until the target heart rate was achieved and as long as systolic blood pressure was > 100 mmHg. All of the patients were scanned with a 64-slice CT...
scanner (GE LightSpeed VCT; GE Healthcare). Angiographic scan parameters were as follows: number of slices per rotation was 64; individual detector slice width of 0.625 mm; and 12.5-cm spatial coverage in 5 s at a gantry rotation speed of 330 ms. After the patient was advanced into the scanner bore, the first acquisition consisted of a localizer image of the chest. The second acquisition was a non-contrast scan for calcium scoring. This second acquisition was performed with the following scanning parameters: gantry rotation time of 330 ms, tube voltage of 120 kVp, tube current of 225 mA, prospective gating at 70% of the R–R interval, and collimation of $64 \times 0.625 \text{mm}$. The third acquisition consisted of a test bolus scan, which was performed using a bolus of 20 cc of non-ionic iodinated contrast material (Optiray 350 [ioversol]; Mallinckrodt-Tyco Healthcare, USA). Segmental images were then obtained at 1 image/s over the aortic root. The scan was continued until a threshold of 100 Hounsfield units was reached in a region of interest positioned in the ascending aorta. This allowed graphical estimation of the timing needed for acquisition of the coronary angiogram. The final acquisition was a contrast-enhanced angiogram. Patients were asked to breathe deeply and then hold their breath at end-inspiration. Ioversol was administered according to the following protocol: 5 cc/s, according to the estimated prescan time (prescan time: timing bolus + 9 s [5 s breath hold time + 4 s for filling the distal coronary artery]), followed by a chaser bolus of normal saline (70 cc at a rate of 4 cc/s). The imaging parameters for this scan were as follows: rotation time of 330 ms, tube voltage of 120 kVp, and collimation of $64 \times 0.625 \text{mm}$. Image reconstruction was performed at 10% increments through the R–R cardiac cycle. After acquisition of images, images were transferred to a dedicated GE® AW Workstation for analysis.

### CT image analysis

The CT data set was analysed by two independent experienced readers who were blinded to the patients’ clinical data. For analysis of the coronary arteries, the original axial dataset pre- (for calcium scoring) and post-contrast was examined. Volume rendering images and curved multi-planar reconstructions were also used for analysis. Types of abnormal coronary arteries were classified using the patients’ demographic data according to the American Heart Association scheme.

This scheme clearly describes the coronary artery map used by the Bypass Angioplasty Revascularization Investigation study for segmentation of coronary arteries, and was used to define and classify individual CAAs. The types of abnormal coronary artery, including its origin, proximal course, intrinsic coronary anomalies and termination anomalies as seen by MSCT-CA, were collected.

### Statistical analysis

Statistical analysis was performed using SPSS, version 15.0 (SPSS Inc., Chicago, IL, USA). Normality of distribution was evaluated with the Kolmogorov–Smirnov test. Normally distributed data are expressed as mean ± standard deviation and Q1–Q3 if data were not normally distributed. Results were analysed with the Student’s $t$ test for quantitative data that were normally distributed and with the Mann–Whitney $U$-test for quantitative data that were not normally distributed. Categorical data were analysed with the chi-square or Fisher’s exact test (when Levene’s test was significant). $P$-values $< 0.05$ were considered statistically significant.

This study was approved by the No. 1 Clinical Research Ethics Committee of Istanbul at Istanbul University with no D-012 on November 10, 2009. The study conformed to the guiding principles of the Declaration of Helsinki.
Results

MSCT-CA was performed without any complications in all of the patients. Table 1 shows demographic data for all patients who underwent MSCT-CA. A total of 225 (9.37%) patients were identified as having CAAs and a total of 236 CAAs were found because 11 patients had more than one type of anomalies of coronary arteries. In one patient, the left circumflex artery (CX) arose from the right anterior sinus of Valsalva with a muscular bridge. The CX arose from the right anterior sinus with coronary ectasia in one patient. One patient had coronary ectasia with a coronary aneurysm. Two patients had coronary aneurysms with a muscular bridge and six patients had coronary ectasia with muscular bridges at the same time. The details of coronary anomalies are shown in Table 2 and demographic data of the patients with coronary anomalies are shown in Table 3. The frequency of male sex was significantly higher than that of female sex ($P < 0.001$). Patients with CAAs had a significantly greater degree of atherosclerotic changes and stenosis than did control patients with normal coronaries ($P = 0.001$, $P = 0.007$).

Patients with CAAs were divided into the following subgroups: group 1, coronary anomaly of origin and distribution (AOC) ($n = 36$, 1.5%); group 2, anomaly of intrinsic coronary arterial anatomy (AICA) ($n = 191$, 7.9%); and group 3, anomalies of coronary termination ($n = 9$, 0.4%). AOCs were identified in 36 cases (1.5%). Table 4 shows the demographic characteristics of these patients. AICAs were the most common abnormality ($n = 180$, 7.49%) including the three main problems of muscular bridges, coronary ectasias, and coronary aneurysms (Table 5). There were significant differences in atherosclerotic and sclerotic changes in coronary arteries in the AOC ($P = 0.015$, $P = 0.04$) and AICA subgroups ($P = 0.007$ for a muscular bridge, $P = 0.001$ for coronary ectasia, $P = 0.046$ for coronary aneurysm). When patients with CAAs were compared with patients with normal coronary arteries, the AOC and the AICA subgroups were less symptomatic ($P < 0.001$). Muscular bridges and coronary aneurysms were most commonly localized in the proximal and middle segments of the left coronary artery, but coronary ectasia was more frequently situated in the right coronary artery (RCA).

Anomalies of coronary termination (coronary artery fistulas) were detected in only nine (0.4%) patients. Among these patients, fistulas from coronary arteries to the right heart chambers were the most common.

### Table 1. Demographic data of the patient population.

| Variables                          | n = 2401 | %    |
|-----------------------------------|----------|------|
| Age, years                        | 56 ± 11.7| (15–88) |
| Sex (M/F)                         | 1805/596 | 75.2/24.8 |
| Categorized BMI                   | 575      | 23.9 |
| Normal (BMI < 25)                 | 1196     | 49.8 |
| Overweight (BMI 25–30)            | 630      | 26.2 |
| Obese (BMI > 30)                  | 1170     | 48.7 |
| Hypertension                      | 522      | 21.7 |
| Diabetes mellitus                 | 874      | 36.4 |
| Smoker                            | 1349     | 56.2 |
| Hyperlipidaemia                   | 1357     | 56.5 |
| Family history                    | 394      | 16.4 |
| Patients with known CAD           | 186      | 7.7 |
| Patient who underwent CABG        | 209      | 8.7 |
| Patients who underwent stent implantation |        |     |
| Symptomatic                       | 823      | 34.3 |

Abbreviations: M, male; F, female; BMI, body mass index; CAD, coronary artery disease; CABG, coronary artery bypass grafting.

*Calculated as weight in kilograms divided by the square of height in meters ($kg/m^2$).

*Assessed considering symptoms in accordance with American College of Cardiology/American Heart Association guidelines.
Table 2. Prevalence of coronary artery anomalies.

| Type of coronary anomaly                                      | n  | %    |
|--------------------------------------------------------------|----|------|
| 1. Anomalies of origination and course                       |    |      |
| Absent left main trunk (split origination of the LMCA)      | 4  | 0.17 |
| Anomalous location of the coronary ostium within the aortic root or near the actual aortic sinus of Valsalva (for each artery): high, low, commissural | 1  | 0.04 |
| Anomalous location of the coronary ostium outside normal “coronary” aortic sinuses | 3  | 0.12 |
| Anomalous origination of the coronary ostium from opposite, facing the “coronary” sinus |    |      |
| a. RCA arising from the left anterior sinus                  | 12 |      |
| b. LAD arising from the right anterior sinus                  | 0  |      |
| c. CX arising from the right anterior sinus                   | 11 |      |
| d. LMCA arising from the right anterior sinus                 | 2  |      |
| Single coronary artery                                       | 2  | 0.08 |
| 1. Conal artery arising from the LMCA                        | 1  | 0.04 |
| 2. Anomalies of intrinsic coronary arterial anatomy           | 191| 7.9b |
| Congenital ostial stenosis or atresia (LMCA)                 | 1  |      |
| Coronary ectasia                                             | 53 |      |
| Coronary aneurysm                                            | 32 |      |
| Coronary hypoplasia                                          | 1  |      |
| Intramural coronary artery (muscular bridge)                 | 100|      |
| Double LAD                                                   | 4  |      |
| 3. Anomalies of coronary termination (fistulas)               | 9  | 0.4  |
| 4. Anomalous collateral vessels                               | 0  | 0    |
| Total                                                        | 236| 9.37a|

aCAAs are listed by classification among a total of 225 patients with 236 coronary artery anomalies. The total prevalence was 9.37% (225/2401).
bOne patient had a CX arising from the right anterior sinus of Valsalva together with a muscular bridge, one patient had a CX arising from the right anterior sinus together with a coronary ectasia, one patient had coronary ectasia together with a coronary aneurysm, two patients had coronary aneurysms together with a muscular bridge and six patients had coronary ectasia together with muscular bridges. Because of this overlapping in 11 patients, the total rate of anomaly of intrinsic coronary arterial anatomy was high (191/2401).

Abbreviations: LMCA, left main coronary artery; RCA, right coronary artery; CX, left circumflex artery; LAD, left anterior descending coronary artery.

Figure 1 shows different demonstrative anomalies found in our patient population.

Discussion

Prevalence

The prevalence of CAA reported by MSCT-CA and by conventional CAG studies varies from 2.04% to 18.4% depending on the definition used and on the focus of the study.7,8 Different results of the incidence of CAA from the literature are shown in Table 6. Unfortunately, most of the previous studies focussed on AOCs.9-16 These studies did not use the same classification system to define CAA. Some groups included solely AOCs in their study population, while others included AOCs together with coronary
termination anomalies (i.e., using a modified classification). This difference in classification systems is the major cause of dissimilar incidences reported in these studies. The classification criteria for CAA have been widely discussed. Angelini et al. reported a classification that covers all possible coronary anatomical variations independently from their clinical and haemodynamic importance. Altin et al.’s study compared the incidence of CAA in the same patient population. This incidence was calculated according to Angelini et al.’s classification and a modified classification, with two different frequencies of 1.4% and 2.7%, respectively. This finding indicates the importance of the classification system that is used for calculating the incidence of CAA.

In the current study, the prevalence of coronary anomalies was 9.37% (225/2401), including all types of coronary anomalies with specified classification (as described by Angelini et al.). The current study showed that the incidence of AOCs was

Table 3. Demographic data of patients with or without CAAs.

| Coronary anomaly | + | - | P | \( \chi^2 \) |
|------------------|---|---|---|-----------|
| **Sex**          | Female | 34 | 15.1 | 562 | 25.8 | \( P < 0.000 \) | 12.54 |
|                  | Male  | 191 | 84.9 | 1614 | 74.2 |              |       |
| **Diabetes**     | +    | 45  | 20.0 | 477  | 21.9 | \( P = 0.506 \) |       |
|                  | -    | 180 | 80.0 | 1699 | 78.1 | \( \chi^2 = 0.44 \) |       |
| **Hypertension** | +    | 97  | 43.1 | 1073 | 493  | \( P = 0.077 \) |       |
|                  | -    | 128 | 56.9 | 1103 | 50.7 | \( \chi^2 = 3.13 \) |       |
| **Hyperlipidaemia** | + | 111 | 49.3 | 1238 | 56.9 | \( P = 0.030^a \) | 4.73  |
|                  | -    | 114 | 50.7 | 938  | 43.1 | \( \chi^2 = 4.73 \) |       |
| **Smoker**       | +    | 74  | 32.9 | 800  | 36.8 | \( P = 0.250 \) |       |
|                  | -    | 151 | 67.1 | 1376 | 63.2 | \( \chi^2 = 1.32 \) |       |
| **Family history** | + | 113 | 50.2 | 1244 | 57.2 | \( P = 0.045^a \) | 4.00  |
|                  | -    | 112 | 49.8 | 932  | 42.8 | \( \chi^2 = 4.00 \) |       |
| **Categorized BMI, normal (BMI < 25)^b** | + | 52  | 23.1 | 523  | 24.0 | \( P = 0.915 \) | 0.177 |
|                  | -    | 115 | 51.1 | 1081 | 49.7 |              |       |
| **Categorized BMI, overweight (BMI 25–30)^b** | + | 58  | 25.8 | 572  | 26.3 | \( P < 0.05 \) |       |
|                  | -    | 190 | 74.2 | 1624 | 74.0 | \( \chi^2 = 10.6 \) |       |
| **Atherosclerotic changes in the coronary arteries** | + | 35  | 15.6 | 552  | 25.4 | \( P = 0.01^a \) | 7.15  |
|                  | -    | 153 | 64.4 | 1246 | 58.8 | \( \chi^2 = 7.15 \) |       |
| **Stenotic changes in the coronary arteries^c** | + | 72  | 30.0 | 873  | 41.2 | \( P < 0.007^a \) | 4.73  |
|                  | -    | 40  | 17.8 | 783  | 36.0 | \( \chi^2 = 4.73 \) |       |
| **Symptomatic^d** | + | 185 | 82.2 | 1393 | 64.0 | \( P < 0.000^a \) | 30.0  |
|                  | -    | 185 | 17.8 | 783  | 36.0 |              |       |

\(^aP < 0.05; \) correlations between patients with or without coronary anomalies by the chi square test.

\(^b\)Calculated as weight (kg) divided by the square of height (m).

\(^c\)Based on luminal stenosis > 50%.

\(^d\)Assessed considering symptoms in accordance with American College of Cardiology/American Heart Association guidelines.

Abbreviations: M, male; F, female; BMI, body mass index.
1.5% (36/2401), which is in line with previous studies.\textsuperscript{7,9,18} Reports from Turkey generally identify the incidence of AOCs by conventional CAG.\textsuperscript{10,11,17,19,20} Because conventional CAG is not the gold standard for the diagnosis of CAA, interpretation of these results is not accurate. To render different results comparable, investigators should use a strict classification system for coronary anomalies and include dedicated staff for analysis. The real prevalence of coronary anomalies is difficult to determine intrinsically because the techniques used for diagnosis are costly and time-consuming.

Among our population, 12 patients with AOCs had the RCA arising from the left anterior sinus of Valsalva. Eleven of the remaining 24 patients had the CX arising from the right anterior sinus of Valsalva (Table 2). Chaitman et al.\textsuperscript{13} reported that

| Table 4. Demographic data of patients with or without coronary anomaly of origin and distribution. |
|---------------------------------------------------------------|
|                                                                                           |
| | Coronal anomaly | + | - | n | % | n | % | $\chi^2$ | $P$ |
| | Sex | F | 6 | 16.7 | 590 | 24.9 | 0.254 |
| | | M | 30 | 83.3 | 1775 | 75.1 | 1.30 |
| | Diabetes | + | 1 | 2.8 | 521 | 22 | 7.22 |
| | | - | 35 | 97.2 | 1844 | 78 | 4.83 |
| | Hypertension | + | 11 | 30.6 | 1159 | 49 | 4.38 |
| | | - | 25 | 69.4 | 1206 | 51 | 1.19 |
| | Hyperlipidaemia | + | 17 | 47.2 | 1332 | 56.3 | 2.75 |
| | | - | 19 | 52.8 | 1033 | 43.7 | 1.19 |
| | Smoker | + | 15 | 41.7 | 859 | 36.3 | 0.508 |
| | | - | 21 | 58.3 | 1506 | 63.7 | 0.438 |
| | Family history | + | 13 | 36.1 | 1344 | 56.8 | 0.013 |
| | | - | 23 | 63.9 | 1021 | 43.2 | 6.193 |
| | Categorized BMI, normal (BMI $<25$) | + | 12 | 33.3 | 563 | 23.8 | 0.171 |
| | | - | 21 | 66.7 | 1177 | 76.2 | 3.53 |
| | Categorized BMI, overweight (BMI 25–30) | + | 19 | 52.8 | 1177 | 49.8 | 5.82 |
| | Categorized BMI, obese (BMI $>30$) | + | 5 | 13.9 | 625 | 26.4 | 0.015 |
| | Atherosclerotic changes | + | 21 | 58.3 | 1793 | 75.8 | 0.015 |
| | | - | 15 | 41.7 | 572 | 24.2 | 5.86 |
| | Stenotic changes in the coronary arteries | + | 13 | 36.1 | 1386 | 60.1 | 0.004 |
| | | - | 23 | 63.9 | 922 | 39.9 | 8.44 |
| | Symptomatic | + | 8 | 22.2 | 815 | 34.5 | 0.125 |
| | | - | 28 | 77.8 | 1550 | 65.5 | 2.358 |

$^a$Correlations between patients with or without anomalies of origination and course by the chi square test. $^b$Calculated as weight in kilograms divided by the square of height in meters. $^c$Based on luminal stenosis $>50%$. $^d$Assessed considering symptoms in accordance with American College of Cardiology/American Heart Association guidelines.

Abbreviations: M, male; F, female; BMI, body mass index.
**Table 5.** Demographic data of patients with or without anomalies of intrinsic coronary arterial anatomy (by subgroup classification, such as muscular bridge, coronary ectasia and coronary aneurysm).

|                      | +               | -               | Statistic |
|----------------------|-----------------|-----------------|-----------|
|                      | n   | %       | n   | %       | χ²   | P     |
| Muscular bridge      |     |         |     |         |      |       |
| Sex                  |     |         |     |         |      |       |
| F                    | 17  | 17 579  | 25.2| P = 0.064|      |       |
| M                    | 83  | 83 1722 | 74.8| P = 0.193| χ² = 3.422|       |
| Diabetes             |     |         |     |         |      |       |
| +                    | 27  | 27 495  | 21.5| P = 0.016| χ² = 1.69|       |
| −                    | 73  | 73 1806 | 78.5|            |      |       |
| Hypertension         |     |         |     |         |      |       |
| +                    | 51  | 51 1119 | 48.6| P = 0.643|      |       |
| −                    | 49  | 49 1182 | 51.4|            |      |       |
| Hyperlipidaemia      |     |         |     |         |      |       |
| +                    | 50  | 50 1299 | 56.5| P = 0.203|      |       |
| −                    | 50  | 50 1002 | 43.5|            |      |       |
| Smoker               |     |         |     |         |      |       |
| +                    | 29  | 29 845  | 36.7| P = 0.116|      |       |
| −                    | 71  | 71 1456 | 63.3|            |      |       |
| Family history       |     |         |     |         |      |       |
| +                    | 56  | 56 1301 | 56.5| P = 0.915|      |       |
| −                    | 44  | 44 1000 | 43.5|            |      |       |
| Categorized BMI, normal (BMI < 25)b | + 15 | 15 560  | 24.3| P = 0.096|      |       |
| Categorized BMI, overweight (BMI 25–30)b | + 57 | 57 1139 | 49.5| χ² = 4.69|      |       |
| Categorized BMI, obese (BMI > 30)b | + 28 | 28 602  | 26.2|            |      |       |
| Atherosclerotic changes in the coronary arteries | + 87 | 87 1727 | 75.1| P = 0.007a|      |       |
|                      | − 13 | 13 574  | 24.9| χ² = 7.40|      |       |
| Stenotic changes in the coronary arteriesc | + 71 | 71 1328 | 59.2| P = 0.018a|      |       |
|                      | − 29 | 29 916  | 40.8| χ² = 5.55|      |       |
| Symptomaticd         | + 17 | 17 806  | 35  | P < 0.000a|      |       |
|                      | − 83 | 83 1495 | 65  | χ² = 13.82|      |       |
| Coronary ectasia     |     |         |     |         |      |       |
| Sex                  |     |         |     |         |      |       |
| F                    | 10  | 10 586  | 25  | P = 0.310|      |       |
| M                    | 43  | 43 1762 | 75  | χ² = 1.03|      |       |
| Diabetes             |     |         |     |         |      |       |
| +                    | 9   | 17 513  | 21.8| P = 0.396|      |       |
| −                    | 44  | 44 1835 | 78.2| χ² = 0.722|      |       |
| Hypertension         |     |         |     |         |      |       |
| +                    | 23  | 43.4 1147| 48.9| P = 0.432|      |       |
| −                    | 30  | 56.6 1201| 51.1| χ² = 0.617|      |       |
| Hyperlipidaemia      |     |         |     |         |      |       |
| +                    | 31  | 58.5 1318| 56.1| P = 0.732|      |       |
| −                    | 22  | 41.5 1030| 43.9| χ² = 0.117|      |       |
| Smoker               |     |         |     |         |      |       |
| +                    | 17  | 32.1 857 | 36.5| P = 0.508|      |       |
| −                    | 36  | 67.9 1491| 63.5| χ² = 0.438|      |       |
| Family history       |     |         |     |         |      |       |
| +                    | 27  | 50.9 1330| 56.6| P = 0.408|      |       |
| −                    | 26  | 49.1 1018| 43.4| χ² = 0.685|      |       |
| Categorized BMI, normal (BMI < 25)b | + 15 | 28.3 560 | 23.9| P = 0.722|      |       |
| Categorized BMI, overweight (BMI 25–30)b | + 24 | 45.3 1172| 49.9| χ² = 0.653|      |       |
| Categorized BMI, obese (BMI > 30)b | + 14 | 26.4 616 | 26.2|            |      |       |
| Atherosclerotic changes in the coronary arteries | + 50 | 94.3 1764| 75.1| P = 0.001a|      |       |
|                      | − 3  | 5.7 584  | 24.9| χ² = 10.35|      |       |
| Stenotic changes in the coronary arteriesc | + 43 | 81.1 1356| 59.2| P = 0.001a|      |       |
|                      | − 10 | 18.9 935 | 40.8| χ² = 10.36|      |       |
| Symptomaticd         | + 4  | 7.5 819  | 34.9| P < 0.001a|      |       |
|                      | − 49 | 92.5 1529| 65.1| χ² = 17.18|      |       |

(continued)
the prevalence of AOCs was 0.83%. They also found that the RCA arising from the left anterior sinus of Valsalva was the most common type of anomaly with a prevalence of 70%.\textsuperscript{13} Other studies have also postulated that the CX arising from the right anterior sinus of Valsalva or split origination of the left main coronary artery is the most common type of AOC.\textsuperscript{8,9} Additionally, the RCA arising from the left anterior sinus of Valsalva has been reported as the most common type of AOC.\textsuperscript{19} These studies included important data. However, because of the differences in the study populations, the techniques used, and their limitations, they are not eligible for comparison with the current study.

**Clinical relevance**

Although CAA is the second most common cause of exercise-related sudden death in athletes younger than 35 years, many patients with coronary anomalies are asymptomatic and are diagnosed at post-mortem.\textsuperscript{1} Similarly, in the present study, patients with CAA and the subgroup including patients with coronary ectasia and a muscular bridge were less symptomatic compared with patients without coronary

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**Table 5.** Continued.

|                                | +     | –     | n   | %   | n   | %   | Statistic |
|--------------------------------|-------|-------|-----|-----|-----|-----|-----------|
| **Coronary aneurysm**          |       |       |     |     |     |     |           |
| **Sex**                        |       |       |     |     |     |     |           |
| M                              | 31    | 96.9  | 1774| 74.9| 25  | 78.1| \(\chi^2 = 8.18\) |
| F                              | 1     | 3.1   | 595 | 25.1|     |     |           |
| **Diabetes**                   |       |       |     |     |     |     |           |
| +                              | 7     | 21.9  | 515 | 21.7| 25  | 78.1| \(\chi^2 = 0.00\) |
| –                              | 25    | 78.1  | 1854| 78.3|     |     |           |
| **Hypertension**               |       |       |     |     |     |     |           |
| +                              | 12    | 37.5  | 1158| 48.9| 25  | 78.1| \(\chi^2 = 0.201\) |
| –                              | 20    | 62.5  | 1211| 51.1| 25  | 78.1|           |
| **Hyperlipidaemia**            |       |       |     |     |     |     |           |
| +                              | 14    | 43.8  | 1335| 56.4| 25  | 78.1| \(\chi^2 = 1.63\) |
| –                              | 18    | 56.2  | 1034| 43.6| 25  | 78.1|           |
| **Smoker**                     |       |       |     |     |     |     |           |
| +                              | 13    | 40.6  | 861 | 36.3| 25  | 78.1| \(\chi^2 = 0.617\) |
| –                              | 19    | 59.4  | 1508| 63.7| 25  | 78.1|           |
| **Family history**             |       |       |     |     |     |     |           |
| +                              | 15    | 46.9  | 1342| 56.6| 25  | 78.1| \(\chi^2 = 0.268\) |
| –                              | 17    | 53.1  | 1027| 43.4| 25  | 78.1|           |
| **Categorized BMI, normal (BMI < 25)\textsuperscript{b}** |       |       |     |     |     |     |           |
| +                              | 7     | 21.9  | 568 | 24  | 25  | 78.1| \(\chi^2 = 0.809\) |
| **Categorized BMI, overweight (BMI 25–30)\textsuperscript{b}** |       |       |     |     |     |     |           |
| +                              | 15    | 46.9  | 1181| 49.9| 25  | 78.1| \(\chi^2 = 0.425\) |
| **Categorized BMI, obese (BMI > 30)\textsuperscript{b}** |       |       |     |     |     |     |           |
| +                              | 10    | 31.2  | 620 | 26.1| 25  | 78.1|           |
| **Atherosclerotic changes in the coronary arteries** |       |       |     |     |     |     |           |
| +                              | 29    | 90.6  | 1785| 75.3| 25  | 78.1| \(\chi^2 = 0.046\) |
| –                              | 3     | 9.4   | 584 | 24.7| 25  | 78.1|           |
| **Stenotic changes in the coronary arteries\textsuperscript{c}** |       |       |     |     |     |     |           |
| +                              | 22    | 68.8  | 1377| 59.6| 25  | 78.1| \(\chi^2 = 3.98\) |
| –                              | 10    | 31.3  | 935 | 40.4| 25  | 78.1|           |
| **Symptomatic\textsuperscript{d}** |       |       |     |     |     |     |           |
| +                              | 7     | 21.9  | 816 | 34.4| 25  | 78.1| \(\chi^2 = 0.137\) |
| –                              | 25    | 78.1  | 1553| 65.6| 25  | 78.1|           |

\(aP < 0.050.\)

\(b\)Calculated as weight in kilograms divided by the square of height in meters.

\(c\)Based on luminal stenosis \(> 50\%\).

\(d\)Assessed considering symptoms in accordance with American College of Cardiology/American Heart Association guidelines.

Abbreviations: M, male; F, female; BMI, body mass index.
**Figure 1.** (A) Split origination of the LMCA. Multi-slice computed tomography coronary angiography (MSCT-CA) image shows the absence of the LMCA and the separate origins of the LAD and CX. (B) RCA arising from the left anterior sinus of Valsalva. (C) Anomalous origin of the CX from the right anterior sinus of Valsalva. (D,E) LMCA arising from the right anterior sinus of Valsalva. Image shows the opening of the LMCA and its interarterial course between the ascending aorta and the pulmonary artery. (F) A volume rendering image of MSCT-CA shows a single coronary artery originating from the right sinus of Valsalva. This was classified as the type RI pattern, with passage of the LMCA between the pulmonary artery and aorta. (G) Image shows coronary ectasia of the proximal segment of the LAD, which is indicated with a white arrow. (H) Volume rendering image of the coronary arteries shows no atherosclerotic lesion, but hypoplasia of the LMCA with compensatory enlargement of the RCA. (I) Intramural coronary artery (muscular bridge). MSCT-CA image shows an example of proximal and mid segments of the LAD with myocardial bridging, which is indicated with white arrows.

Abbreviations: RCA, right coronary artery; CX, left circumflex artery; LAD, left anterior descending coronary artery; LMCA, left main coronary artery.
anomalies. Most patients with an anomalous origin of a coronary artery from the aorta are symptom-free.\textsuperscript{14,21} A proposed mechanism of sudden death is believed to be episodic myocardial ischaemia. However, this mechanism cannot explain the clinical course because this hypothesis mainly proposes recurrent and rapid deterioration during exercise, but not the infarct size, as the responsible factor.

Shirani \textit{et al}.\textsuperscript{15} reported that sudden cardiac death cases with a single coronary artery were all free of signs of myocardial ischaemia or asymptomatic. Similarly, Datta and colleagues\textsuperscript{14} reported that no patients with an anomalous coronary artery diagnosed by MSCT were symptomatic. These results could explain why coronary anomalies are generally diagnosed incidentally.

\textbf{Table 6. Incidence of CAA as shown by CAG and MSCT studies in various populations.}

| Authors         | n   | Coronary anomaly (n) | (%)  |
|-----------------|-----|----------------------|------|
| Incidence of coronary artery anomalies according to CAG studies |     |                      |      |
| Eid \textit{et al}.\textsuperscript{8}     | 4650 | 95                   | 2.04\textsuperscript{a} |
| Yamanaka \textit{et al}.\textsuperscript{9} | 126595 | 1686             | 1.3\textsuperscript{a} |
| Tuncer \textit{et al}.\textsuperscript{10}  | 70850 | 73                   | 0.3\textsuperscript{a} |
| Aydinlar \textit{et al}.\textsuperscript{11} | 12059 | 100                  | 0.8\textsuperscript{a} |
| Chaitman \textit{et al}.\textsuperscript{13} | 3750  | 31                   | 0.8\textsuperscript{a} |
| Angelini \textit{et al}.\textsuperscript{31} | 1950  | 110                  | 5.6 |
| Topaz \textit{et al}.\textsuperscript{19}   | 13010 | 80                   | 0.6 |
| Gu¨ntekin \textit{et al}.\textsuperscript{20} | 2398  | 55                   | 2.3\textsuperscript{b} |
| Incidence of coronary artery anomalies according to MSCT studies |     |                      |      |
| Cademartiri \textit{et al}.\textsuperscript{7} | 543  | 100                  | 18.4 |
| Srinavastan \textit{et al}.\textsuperscript{16} | 1495 | 11                   | 0.8\textsuperscript{a} |
| Shi \textit{et al}.\textsuperscript{22}     | 242  | 16                   | 6.6\textsuperscript{a} |
| Ten Kate \textit{et al}.\textsuperscript{18}  | 1000 | 10                   | 1\textsuperscript{a} |
| Knickelbine \textit{et al}.\textsuperscript{37} | 4543 | 201                  | 4.4\textsuperscript{b} |
| Zeina \textit{et al}.\textsuperscript{26}   | 300  | 78                   | 26\textsuperscript{c} |

\textsuperscript{a}Studies including coronary anomalies of origin and distribution only.
\textsuperscript{b}Studies including coronary anomaly of origin and distribution and anomalies of coronary termination.
\textsuperscript{c}Studies including muscular bridges only.

\textbf{Demographic data}

The aetiology of coronary anomalies is unknown and whether a hereditary background is involved has yet to be determined. In the current study, male sex was associated with CAA, which is in accordance with other studies that reported a male predominance (58%–80\%).\textsuperscript{8,10,14,16,18,22,23,24} Similarly, Basso \textit{et al}. reported that 80% of deaths caused by CAA in young athletes occur in male patients.\textsuperscript{1} The current study showed a frequency of 96.9% of male patients with aneurysmal coronary artery dilatation, similar to that reported by Swaye \textit{et al}. (88.2%).\textsuperscript{25}

Eid \textit{et al}.\textsuperscript{5} reported no association between atherosclerotic comorbidities, lipid profiles, and significant atherosclerotic lesions in patients with normal or anomalous coronary
arteries. Other studies have also shown no association between anomalous coronary arteries, such as myocardial bridging, coronary ectasia, and aneurysmal dilatation of the coronary arteries, with coronary artery disease risk factors, such as diabetes, hypertension, hyperlipidaemia and smoking.

**Increased risk of coronary atherosclerotic disease**

Whether coronary anomalies predispose to early atherosclerosis or precede lethal influences is unknown. The current study showed a significantly higher incidence of coronary atherosclerotic changes and stenotic changes in anomalous versus normal coronary arteries. This finding has not been demonstrated by previous studies. However, these results should be interpreted with caution because of their different haemodynamic and pathophysiological properties. Angelini et al. showed no association between the location of atherosclerotic coronary disease and anomalies of coronary anatomy/course. Many other studies have also reported similar results showing no association between AOC, such as single coronary artery and, an increased incidence of atherosclerosis. In patients with a single coronary, if atherosclerosis occurs in the common trunk, the clinical consequences would be unusually severe because of the lack of collateral circulation.

However, the discussion is quite different for intrinsic coronary arterial anatomy abnormalities. Recent studies have focussed on the occurrence of atherosclerotic plaques in myocardial bridge localization. They reported that the tunnelled segment was unusually affected by atherosclerosis, unlike the proximal epicardial segment, where atherosclerotic plaques were commonly found. There have been some reports on haemodynamic hypotheses on the association between a tunnelled coronary segment (intramyocardial segment) and ischaemia. However, the contribution of haemodynamic factors caused by a tunnelled segment on atheromatous plaque formation is still controversial. The current finding of a higher incidence of atherosclerotic changes and stenotic coronary lesions in this subgroup of patients with muscular bridges supports the hypothesis stating that the intramyocardial segment is an anatomical risk factor for coronary artery disease.

Coronary artery dilatations are usually associated with an underlying factor, which is atherosclerosis in Western countries and Kawasaki disease in Japan. The most common cause of coronary dilatation is thought to be atherosclerosis. The current study supports the idea that coronary artery dilatation is an anomaly that develops based on atherosclerotic disease. Coronary artery ectasia is also associated with hyperlipidaemia, systemic hypertension, and male sex.

The current study has some limitations. Although the sample size in the current study is not small, this study was not able to determine the actual prevalence of CAA because the study group consisted of a relatively select group of patients (asymptomatic high-risk patients, asymptomatic patients with risk factors, high-risk patients for atherosclerotic lesions and symptomatic cardiac patients). Comparisons with other modalities, such as conventional CAG, or collecting long-term follow-up data are outside of the scope of this study.

**Conclusion**

Based on recent advances in imaging technology, especially those that can provide high-quality measurements for the diagnosis of CAA, MSCT-CA is currently the main method of identifying CAA. The reason why MSCT-CA is the main method of identifying CAA is because of its capacity to gather a large amount of information on the complex
three-dimensional anatomy of vessels. In conclusion, the prevalence of CAAs was 9.37% in our select group of patients and the most common coronary artery anomalies were AICAs. Male sex showed a high tendency for occurrence of CAA and AICA, and thus it may be considered as a predisposition to atherosclerosis of the coronary arteries.

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References
1. Basso C, Maron BJ, Corrado D, et al. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. J Am Coll Cardiol 2000; 35: 1493–1501.
2. Ohnesorge B, Flohr T, Becker C, et al. Cardiac imaging by means of electrocardiographically gated multisection spiral CT: initial experience. Radiology 2000; 217: 564–571.
3. Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American heart association committee on cardiovascular imaging and intervention, council on cardiovascular radiology and intervention, and committee on cardiac imaging, council on clinical cardiology. Circulation 2006; 114: 1761–1791.
4. Scanlon PJ, Faxon DP, Audet AM, et al. ACC/AHA guidelines for coronary angiography123: A report of the American college of cardiology/American heart association task force on practice guidelines (Committee on coronary angiography) developed in collaboration with the society for cardiac angiography and interventions. J Am Coll Cardiol 1999; 33: 1756–1824.
5. Click RL, Holmes DR Jr, Vlietstra RE, et al. Anomalous coronary arteries: location, degree of atherosclerosis and effect on survival–a report from the coronary artery surgery study. J Am Coll Cardiol 1989; 13: 531–537.
6. Angelini P, Velasco JA and Flamm S. Coronary anomalies: incidence, pathophysiology, and clinical relevance. Circulation 2002; 105: 2449–2454.
7. Cademartiri F, La Grutta L, Malagò R, et al. Prevalence of anatomical variants and coronary anomalies in 543 consecutive patients studied with 64-slice CT coronary angiography. Eur Radiol 2008; 18: 781–791.
8. Eid AH, Itani Z, Al-Tannir M, et al. Primary congenital anomalies of the coronary arteries and relation to atherosclerosis: an angiographic study in Lebanon. J Cardiothorac Surg 2009; 4: 58.
9. Yamanaka O and Hobbs RE. Coronary artery anomalies in 126,595 patients undergoing coronary arteriography. Cathet Cardiovasc Diagn 1990; 21: 28–40.
10. Tuncer C, Batyraliev T, Yilmaz R, et al. Origin and distribution anomalies of the left anterior descending artery in 70,850 adult patients: multicenter data collection. Catheter Cardiovasc Interv 2006; 68: 574–585.
11. Aydinlar A, Çiçek D, Sentürk T, et al. Primary congenital anomalies of the coronary arteries: a coronary arteriographic study in Western Turkey. Int Heart J 2005; 46: 97–103.
12. Garg N, Tewari S, Kapoor A, et al. Primary congenital anomalies of the coronary arteries: a coronary arteriographic study. Int J Cardiol 2000; 74: 39–46.
13. Chaitman BR, Lespérance J, Saltiel J, et al. Clinical, angiographic, and hemodynamic findings in patients with anomalous origin of the coronary arteries. Circulation 1976; 53: 122–131.
14. Datta J, White CS, Gilkeson RC, et al. Anomalous coronary arteries in adults: depiction at multi-detector row CT angiography. Radiology 2005; 235: 812–818.
15. Shirani J and Roberts WC. Solitary coronary ostium in the aorta in the absence of other major congenital cardiovascular anomalies. *J Am Coll Cardiol* 1993; 21: 137–143.

16. Srinivasan KG, Gaikwad A, Kannan BR, et al. Congenital coronary artery anomalies: diagnosis with 64 slice multidetector row computed tomography coronary angiography: a single-centre study. *J Med Imaging Radiat Oncol* 2008; 52: 148–154.

17. Altin C, Kanyilmaz S, Koc S, et al. Coronary anatomy, anatomic variations and anomalies: a retrospective coronary angiography study. *Singapore Med J* 2015; 56: 339–345. (doi: 10.11622/smedj.2014193.

18. Ten Kate GJ, Weustink AC and de Feyter PJ. Coronary artery anomalies detected by MSCT coronary angiography in the adult. *Neth Heart J* 2008; 16: 369–375.

19. Topaz O, DeMarchena EJ, Perin E, et al. Anomalous coronary arteries: angiographic findings in 80 patients. *Int J Cardiol* 1992; 34: 129–138.

20. Güntekin U, Sağlam E, Tuncer M, et al. Kliniğimizde Kardiyak Kateterizasyon Yapılan hastalarda Koroner Arter Anomalisi Sıklığı ve Koroner Anomalilerin Dağılımı. *MN Kardiyoloji* 2009; 16: 19–24.

21. Cieslinski G, Rapprich B and Kober G. Coronary anomalies: incidence and importance. *Clin Cardiol* 1993; 16: 711–715.

22. Shi H, Aschoff AJ, Brambs HJ, et al. Multislice CT imaging of anomalous coronary arteries. *Eur Radiol* 2004; 14: 2172–2181.

23. Maron BJ and Zipes DP. Introduction: eligibility recommendations for competitive athletes with cardiovascular abnormalities—general considerations. *J Am Coll Cardiol* 2005; 45: 1318–1321.

24. Taylor AJ, Rogan KM and Virmani R. Sudden cardiac death associated with isolated congenital coronary artery anomalies. *J Am Coll Cardiol* 1992; 20: 640–647.

25. Swayne PS, Fisher LD, Litwin P, et al. Aneurysmal coronary artery disease. *Circulation* 1983; 67: 134–138.

26. Zeina AR, Blinder J, Sharif D, et al. Congenital coronary artery anomalies in adults: non-invasive assessment with multidetector CT. *Br J Radiol* 2009; 82: 254–261.

27. Duygu H, Zoghi M, Nalbantgil S, et al. Myocardial bridge: a bridge to atherosclerosis. *Anadolu Kardiyol Derg* 2007; 7: 12–16.

28. Aksu T, Uygur B, Durukan Koşar M, et al. Coronary artery ectasia: its frequency and relationship with atherosclerotic risk factors in patients undergoing cardiac catheterization. *Anadolu Kardiyol Derg* 2011; 11: 280–284. ([in Turkish, English Abstract].

29. Baman TS, Cole JH, Devireddy CM, et al. Risk factors and outcomes in patients with coronary artery aneurysms. *Am J Cardiol* 2004; 93: 1549–1551.

30. Pahlavan PS and Niroomand F. Coronary artery aneurysm: a review. *Clin Cardiol* 2006; 29: 439–443.

31. Angelini P, Villason S, Chan AV, et al. Normal and anomalous coronary arteries in humans. In: Angelini P and Fairchild VD (eds) *Coronary artery anomalies: a comprehensive approach*. Philadelphia: Lippincott Williams & Wilkins, 1999, pp.27–150.

32. Ishii T, Asuwa N, Masuda S, et al. The effects of myocardial bridge in coronary atherosclerosis and ischaemia. *J Pathol* 1998; 185: 4–9.

33. Möhlenkamp S, Hort W, Ge J, et al. Update on myocardial bridging. *Circulation* 2002; 106: 2616–2622.

34. Díaz-Zamudio M, Bacilio-Pérez U, Herrera-Zarza MC, et al. Coronary artery aneurysms and ectasia: role of coronary CT angiography. *Radiographics* 2009; 29: 1939–1954.

35. Falsetti HL and Carroll RJ. Coronary artery aneurysm. A review of the literature with a report of 11 new cases. *Chest* 1976; 69: 630–636.

36. Giannoglou GD, Antoniadis AP, Chatzizisis YS, et al. Prevalence of ectasia in human coronary arteries in patients in northern Greece referred for coronary angiography. *Am J Cardiol* 2006; 98: 314–318.

37. Knickelbine T. Identification of unexpected nonatherosclerotic cardiovascular disease with coronary CT angiography. *JACC Cardiovasc Imaging* 2009; 2: 1085–1092.