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Anomalous origin of the coronary artery from the wrong coronary sinus evaluated with computed tomography: "High-risk" anatomy and its clinical relevance

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Abstract
Objective The aim of the study was to assess coronary arteries arising from the wrong coronary sinus, including CT-evaluated high-risk anatomic features, clinical symptoms and cardiac events during follow-up.
Methods A total of 7,115 patients scheduled for 64-slice or dual-source cardiac CT were screened for the presence of isolated anomalous origin of the coronary artery from the wrong coronary sinus.
Results Anomalous origin of the coronary artery was found in 54 (0.76 %) patients (29 men, 25 women, mean age 60.9± 11.6 years). Sixteen (30 %) patients with abnormal right coronary origin (ARCA) more commonly had a slit-like orifice (15 vs. 3; $p<0.001$), intramural course (15 vs. 3; $p<0.001$) and interarterial course (11 vs. 0; $p<0.001$) than 22 (41 %) and 13 (24 %) individuals with abnormal circumflex artery (ALCx) and left coronary artery (ALCA) origin, respectively. Patients with ALCA presented less frequently with chest pain than subjects with ARCA and ALCx (25 vs. 3; $p=0.03$). Patients with ARCA tended to show higher occurrence of cardiac events in the follow-up than individuals with ALCA and ALCx (5 vs. 4; p=NS).
Conclusions High-risk anatomy features are most common in patients with ARCA and these patients also have higher prevalence of chest pain and cardiac events in the follow-up than individuals with ALCA and ALCx.

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Key Points
- *Multislice computed tomography enables detection and evaluation of the coronary artery anomalies.*
- *Anomalous anatomy of the coronary artery potentially influences the prevalence of adverse events.*
- *Adverse events tend to be most common in anomalous right coronary arteries.*

Keywords Multislice computed tomography · Coronary vessel anomalies · Follow-up studies · Cardiovascular abnormalities · Anatomy

Abbreviations

ALCx	Anomalous origin of the circumflex artery from the right coronary artery sinus
ARCA	Anomalous origin of the right coronary artery from the left coronary artery sinus
ALCA	anomalous origin of the left coronary artery from the right coronary artery sinus
CABG	Coronary artery bypass grafting
ICA	Invasive coronary angiography
PCI	Percutaneous coronary interventions

Introduction

Anomalous origin of the coronary artery is a rare abnormality, which concerns about 1 % of patients [1–5]. The majority of patients with coronary artery anomalies remain asymptomatic, but may also present with clinical symptoms, which usually occur during or shortly after physical exertion. Often the first and only clinical manifestation of coronary artery anomalies is sudden cardiac death [6, 7].

Until the last decade, the detection and evaluation of abnormal coronary arteries were mostly performed using invasive coronary angiography (ICA) [1]. However, the recent development of multidetector cardiac computed tomography (CT) has allowed for non-invasive examination of the coronary arteries, including their origin. CT, in contrast to ICA, enables three-dimensional analysis and also allows for the evaluation of anatomical structures surrounding an abnormally arising and coursing coronary artery. This advantage of CT is important as potential anatomy features responsible for a high risk of sudden cardiac death include a narrowed slit-like orifice, acute take-off angle, intramural course and interarterial course of the anomalous segment [6–10]. Therefore, the evaluation of coronary artery anomalies using CT may not only enable detecting coronary abnormalities but also provide important prognostic information.

The aim of the study was to perform evaluation of coronary arteries with an origin from the wrong coronary sinus, including: CT-based qualitative and quantitative assessment of potential high-risk anatomic features, clinical symptoms and their correlation with anomaly type, and occurrence of adverse cardiac events during follow-up.

Methods

Study population A total of 7,115 patients, who were scheduled for 64-slice CT (Somatom Sensation 64 Cardiac, Siemens, Erlangen, Germany) or dual-source CT (Somatom Definition, Siemens, Erlangen, Germany) because of suspected coronary artery disease, were screened for the presence of anomalous origin of the coronary artery from the wrong coronary sinus. The examinations were performed within 6 consecutive years; 1,021 patients were evaluated using 64-slice CT and 6,094 patients using dual-source CT. The exclusion criteria were prior revascularisation therapy including percutaneous coronary interventions (PCI) and coronary artery bypass grafting (CABG); concomitant other heart defects; contraindications to perform cardiac CT including respiratory failure, severe heart failure, irregular heart rate, pregnancy, known allergy to iodinated contrast agent, impaired renal function (serum creatinine≥1.5 mg/dl) and thyroid disorders [11].

CT acquisition The contrast-enhanced ECG retrospectively gated image acquisitions were performed during inspiratory breath hold. The imaging parameters common for 64-slice and dual-source CT were tube voltage of 100-120 kV and effective tube current of 350-400 mA. The collimation and temporal resolution were 2×32×0.6 mm and 165 ms for 64-slice CT, 2×32×0.6 mm and 83 ms for dual-source CT. Electrocardiographically controlled tube current modulation was applied to the majority of patients. The arrival time of contrast agent to the ascending aorta was determined at the level of the carina with use of the test bolus method. Images were reconstructed with a B26f and B46f kernel and an image matrix of 512×512 pixels.

CT analysis The post-processing and study evaluation was performed using a dedicated workstation (Aquarius, TeraRecon, San Mateo, Foster City, CA, USA). Patients were assessed for the presence of an anomalous origin of the coronary artery from the wrong coronary sinus using axial, curved multiplanar (MPR), maximum intensity projection (MIP) and volume-rendered technique (VRT) reconstructions. The analysis was performed in the diastolic phase of the cardiac cycle and the modified American Heart Association 16-segment coronary artery model was utilised [12]. All patients were evaluated for the presence of coronary atherosclerotic lesions. If the lesions occurred, they were assessed for their location and degree of stenosis (≤50 %, >50 % diameter stenosis).

The retrospective CT evaluation concerned qualitative and quantitative analysis of high-risk anatomy features (take-off angle, orifice measurement, presence and length of intramural course, type and length of the proximal course of the anomalous vessel) (Fig. 1). The take-off angle was measured in the plane parallel to the aortic annulus and was specified as the angle between the line parallel to the coronary sinus wall and the line parallel to the proximal course of the coronary artery. An acute take-off angle was defined as an angle showing a value of <45 degrees [10]. Anomalous coronary artery orifices were evaluated for the value of their area, the value of the two orthogonal diameters as well as for the presence and degree of potential stenosis. The reference area was obtained at half the distance between the anomalous artery origin and its return to the correct anatomical position. A slit-like orifice was determined if the value of the maximal orifice diameter exceeded more than twice the value of the orthogonal measurement. Subsequently, the type of the proximal course of the anomalous artery was identified (interarterial, retroaortic, precardiac, subpulmonary) and measured for its length, which was counted as the length between the anomalous coronary artery origin and its return to the correct anatomical position. Finally, anomalous vessels were screened for the presence of the intramural course (within the wall of aorta) and, if shown, its length was measured.

Clinical analysis The analysis concerned demographic data (age, gender), cardiovascular risk factors and the presence of clinical symptoms at the time of the CT examination including chest pain and dyspnoea. The patient's medical histories were also evaluated retrospectively for the presence of arrhythmia, syncope and myocardial infarction. Subsequently, patients were contacted and asked if any cardiac events had occurred during the follow-up. Cardiac events were defined as cardiac

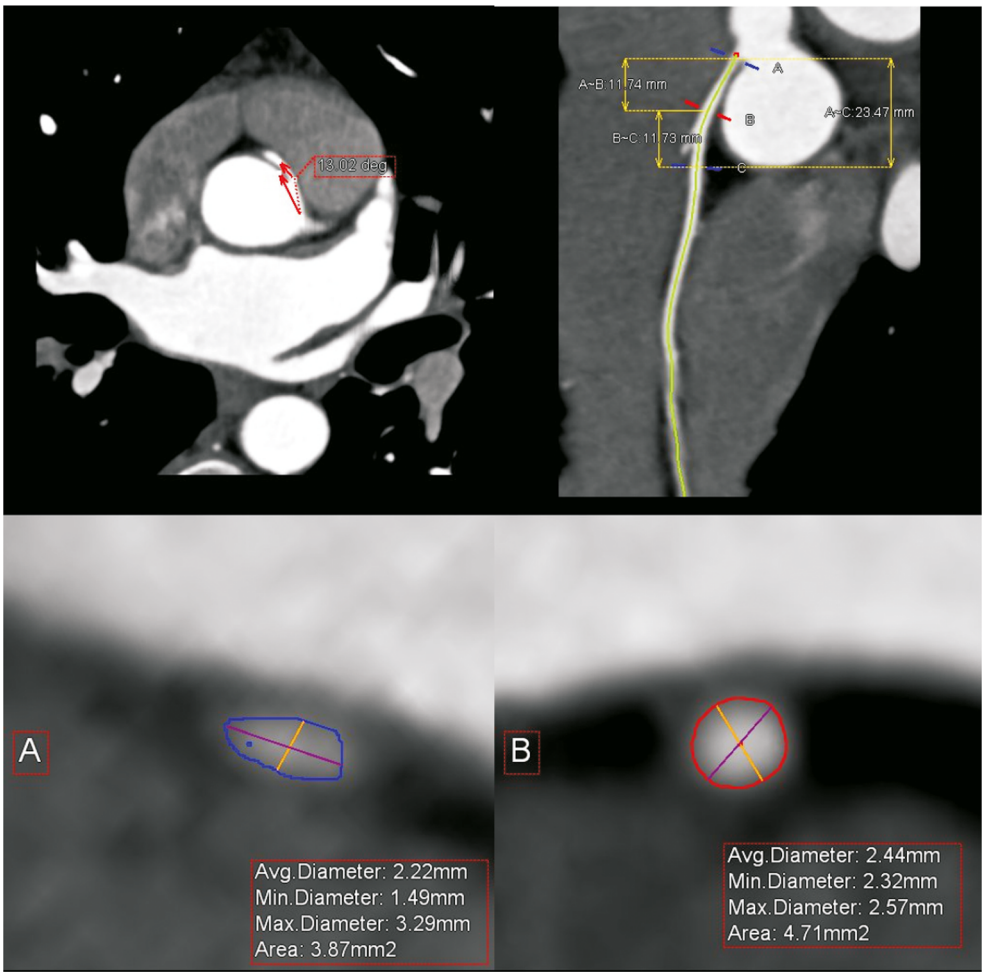

Fig. 1 Multiplanar reconstructions (*MPR*) including curved multiplanar reconstructions (*CMPR*) were used to evaluate (a) the take-off angle of the anomalous vessel, (b) the area and two orthogonal diameters of the anomalous orifice (**A**) and reference area (**B**), (c) the length between the anomalous coronary artery origin and its return to the correct anatomical position (**A**–**C**)

death, myocardial infarction, coronary revascularisation (PCI and CABG) or hospitalisation due to unstable angina or exacerbation of heart failure. Written informed consent from the patients was not required for this study because this was a primarily retrospective study.

Statistical analysis Next, an analysis of the relationship between the data derived from CT, clinical symptoms and follow-up results was performed. Continuous variables were presented as the mean ± standard deviation and compared using one-way analysis of variance (ANOVA). In the qualitative analysis of high-risk anatomic features, the chi-square test with Yates' modification was used. $P<0.05$ was considered statistically significant. Survival plots free of cardiac events were created using the Kaplan-Meier method. The statistical analysis was performed using the Statistica 10 software (StatSoft Inc.).

Results

Main characteristics An anomalous origin of the coronary artery from the wrong coronary sinus was found in 54 (0.76 %) patients. Among them, 29 (54 %) were male and 25 (46 %) female. The mean age of the group of patients with anomalies was 60.9±11.6 years; 22 (41 %) patients presented an anomalous origin of the circumflex artery from the right coronary artery sinus (ALCx), 16 (30 %) patients showed an anomalous origin of the right coronary artery from the left coronary artery sinus (ARCA), 13 (24 %) patients had an anomalous origin of the left coronary artery from the right coronary artery sinus (ALCA), and 3 (5 %) patients presented an anomalous left coronary artery originating from the noncoronary artery sinus. The detailed characteristics of the study group are presented in Table 1.

CT data Six (11 %) patients underwent a CT examination using a 64-slice scanner and 48 (89 %) using a dual-source device. All examinations using a dual-source scanner were performed with ECG-controlled tube current modulation. The mean radiation dose obtained during the examination was 11.4±3.5 mSv for a 64-slice and 13.2±3.3 mSv for a dual-source device. Coronary artery atherosclerosis was present in 31 (57 %) patients; among them 9 had significant (>50 % diameter stenosis) lesions. The majority of significant lesions

Table 1 Group characteristics

Characteristics	All patients (n=54)	ALCA (n=13)	ARCA (n=16)	ALCx (n=22)	LCA from noncoronary sinus (n=3)
Female	25	7	6	10	2
Male	29	6	10	12	1
Age (years)	60.9±11.6	60.8±12.3	57.9±11.8	63.6±10.1	56.7±19.5
Hypertension	39	10	9	18	2
Cigarette smoking	16	3	5	6	2
Diabetes mellitus	8	1	1	6	0
Hypercholesterolaemia	35	9	10	13	3
BMI (body mass index)	28.1±4.2	29.1±4.9	26.7±3.6	28.6±4.3	25.4±1.5

occurred in patients with ALCx (5 subjects), 80 % (4 cases) of them in the proximal part of the anomalous artery. Among subjects with ARCA and ALCA, significant lesions occurred in three and one patient, respectively.

Clinical data Thirty-one (57 %) patients presented with chest pain, and typical angina occurred in 18 (33 %) of cases. A history of dyspnoea, arrhythmia, syncope and myocardial infarction occurred in 33, 5, 5 and 3 patients, respectively. Patients with ALCA presented less frequently with chest pain than subjects with ARCA and ALCx (25 vs. 3; p=0.03).

Coronary anatomy Patients with ARCA more commonly had a slit-like orifice (15 vs. 3; p<0.001), intramural course (15 vs. 3; p<0.001), acute take-off angle (p=0.018) and interarterial course (11 vs. 0; p<0.001) than individuals with ALCA and ALCx (Table 2). The mean value of the take-off angle was lower (p<0.001) in patients with ARCA compared to those with ALCA and ALCx and measured 21.5±7.0, 51.1±26.8 and 47.4±22.3 degrees, respectively (Fig. 2a). The most common course of the proximal part of the anomalous artery was retroaortic (27 patients), which concerned all 22 patients with ALCx and 5 patients with anomalous left coronary artery origin. A subpulmonary course of the anomalous segment occurred in 14 patients, whereas the precardiac course, which was the least frequent, was present in 14 cases. Subjects with ALCx showed the longest abnormal course of the anomalous artery (59.9±15.6 mm), while the length of this course in patients with ALCA and ARCA had a lower value (p<0.001) and measured 43.9±15.4 mm and 31.1±12.9 mm, respectively (Fig. 2b). The value of the anomalous coronary artery orifice area was highest in patients with ALCA, intermediate in subjects with ALCx and lowest in those with ARCA [13.7±7.3 mm^2, 6.3±2.8 mm^2 and 5.7±2.2 mm^2 (p=0.004), respectively] (Fig. 2c). The ratio of the anomalous coronary artery orifice and reference area had the lowest value (p=0.003) in subjects with ARCA (0.87±0.40) and a higher value in patients with ALCA (1.47±0.53) and ALCx (1.14±0.33) (Fig. 2d). Of the 22 (41 %) patients who showed stenosis of the anomalous coronary artery orifice, half of them (11 patients) were subjects with ARCA.

Follow-up Follow-up analysis, which was successfully performed in 52 (96 %) patients, showed 9 cardiac events. Events that occurred among patients with ARCA were cardiac death in one patient and coronary artery bypass grafting, which occurred in four cases (all 5 patients had a course between the aorta and pulmonary artery). Hospitalisation due to unstable angina or exacerbation of heart failure was observed in four patients (among them, 3 patients had ALCx and 1 presented with ALCA). Patients with ARCA tended to show a higher occurrence of cardiac events in the follow-up than individuals with ALCA and ALCx (5 vs. 4; p=NS). The mean duration of the follow-up period in the study group was 895±565 days. The time of survival free of cardiac events was 255±309 days for the entire group, 472±449 days for patients with ALCx, 170±180 days for subjects with ARCA and 26 days for the patient with ALCA (Fig. 3).

Table 2 The prevalence of high-risk anatomy in patients with anomalous origin of the coronary artery from the wrong coronary sinus

Feature	ALCx (n=22)	ARCA (n=16)	ALCA (n=13)	p value
Intramural course (n=18)	3	15	0	<0.001
Slit-like orifice (n=16)	1	15	0	<0.001
Acute take-off angle (n=35)	12	6	7	0.02
Interarterial course (n=11)	0	11	0	<0.001

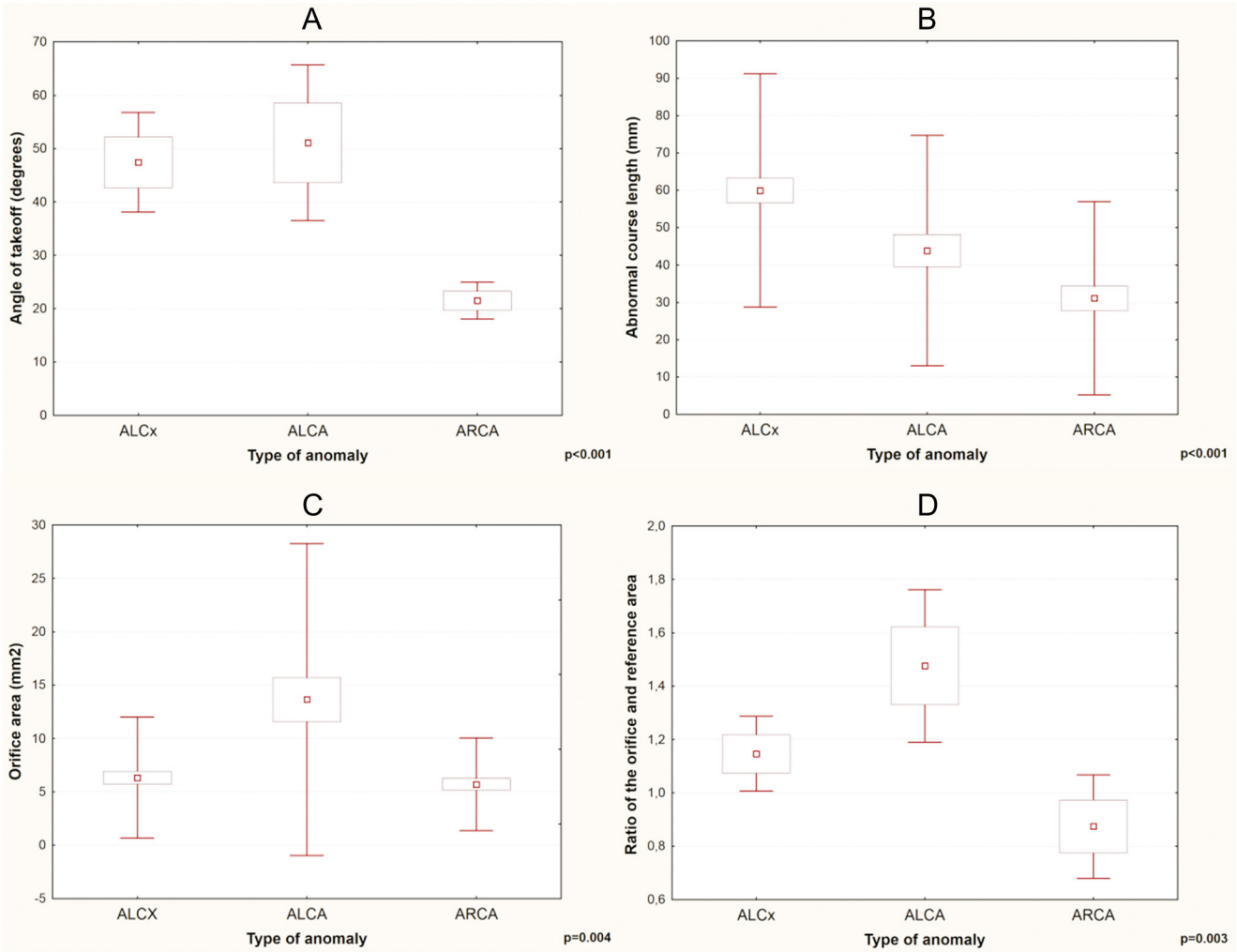

Fig. 2 Box-and-whisker plot: take-off angle (degrees) (**a**), orifice area (mm^2) (**b**), abnormal course length (mm) (**c**) and ratio of the orifice and reference area (**d**). Continuous variables are presented as mean ± standard deviation, mean±1.96 * standard deviation

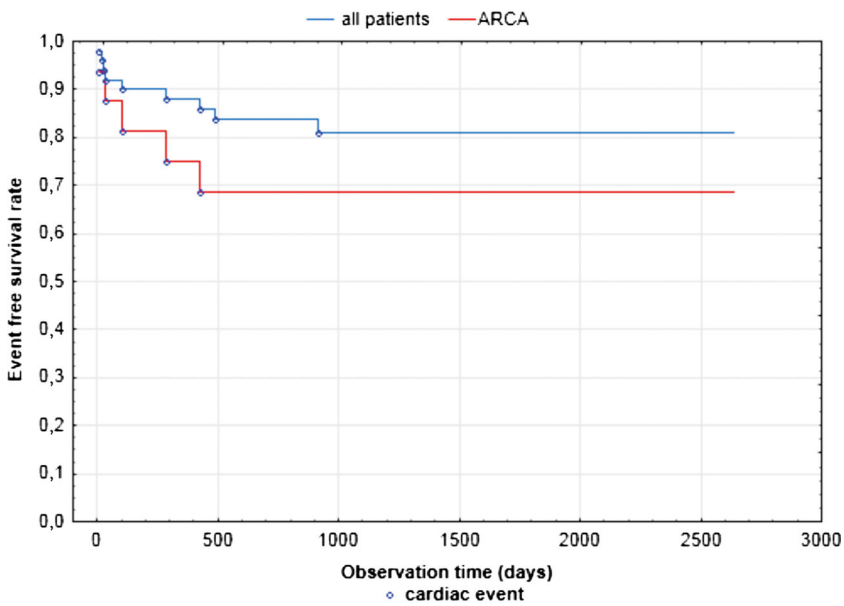

Fig. 3 Kaplan-Meier plot of survival free of cardiac events. A comparison of all patients with an anomalous coronary artery originating from the wrong coronary sinus and patients with an anomalous right coronary artery originating from the left coronary artery sinus (ARCA)

Discussion

The present study demonstrates a high prevalence and coexistence of high-risk anatomy features in patients with an anomalous origin of the coronary artery. Taylor et al. [7] published an autopsy study in which they analysed anomalous origins of the coronary artery in patients who died of sudden cardiac death. In this analysis the authors showed that abnormally originating coronary arteries with a longer intramural course present more frequently than others with an acute take-off angle and coronary artery orifice stenosis. In another analysis, Kaushal et al. [9] discovered the coexistence of an intramural course and reduced coronary artery orifice area (if compared to the orifices of non-anomalous coronary arteries). With regard to high-risk anatomic features, our results are consistent with studies by Taylor et al. [11] and Kaushal et al. [12], as those analyses also showed the coexistence of anatomical disturbances such as intramural course, acute take-off angle and a stenotic, slit-like orifice. In our study, the intramural course involved 18 (35 %) patients, mostly those with ARCA. However, in a study that analysed a group of deceased young athletes, Basso et al. [6] showed a less frequent intramural course that was present only in three (11 %) cases and concerned only patients with ALCA. This discrepancy may result from the fact that Basso performed a pathologic evaluation of adolescents, while our analysis is based on the CT examination of an older population. Our study is the first to analyse the length of the proximal course of the anomalous vessel. The difference of this length between the types of anomalies proved to be statistically significant and resulted from the different anatomical locations of the specific anomalous vessels.

The type and incidence of clinical symptoms in the evaluated group are comparable with previously published analyses concerning coronary anomalies [1, 6, 8, 13, 14]. In our study, patients with ALCA presented less frequently with chest pain than individuals with other types of anomalies. First of all, it is a result of higher blood flow through an anomalous left coronary artery than through other types of anomalous arteries. A higher prevalence of chest pain in patients with ARCA compared to those with ALCA may result from a more common occurrence of high-risk anatomy features in the first group. A similar observation was reported by Kaushal et al. [9] who discovered a higher prevalence of chest pain in patients with a longer intramural course. In our study, patients with ARCA had an intramural course more frequently and this may explain the presence of chest pain in this group. Higher values of the coronary orifice area and less common ostial stenosis in patients with ALCA also support this theory.

The lower incidence of chest pain in patients with ALCA than in those with ALCx may be due to the more common presence of significant (>50 % diameter stenosis) coronary atherosclerotic lesions in the latter group. This theory supports the study by Samarendra et al. [15], who noted the predisposition of the anomalous circumflex artery to selective atherosclerosis. Moreover, the analysis cited above was performed in a group with an average age exceeding 60 years. This is in accordance with our study in which cardiovascular risk factors (including older age) together with the presence of an anomalous coronary artery anatomy were responsible for the high prevalence of coronary atherosclerosis in patients with ALCx. On the other hand, in the study by Frescura et al. [10], no correlation between the coexistence of coronary atherosclerosis and coronary anomalies was reported. Further studies need to be performed to determine whether the presence of an anomalous circumflex coronary artery origin is responsible for the higher prevalence of coronary atherosclerosis than in vessels with normal origin.

To date, most of the analyses concerning coronary anomalies [4, 6, 9] were performed in young populations without concomitant cardiovascular risk factors, which makes them different from our study. However, the analysis by Taylor et al. [7], which also took older patients into account, showed that the presence of coronary atherosclerosis was responsible for sudden cardiac death only in patients older than 30 years, while anomaly-related cardiac death occurred in younger individuals. According to the study mentioned above, there is no single anatomical factor responsible for the occurrence of sudden cardiac death in patients with an anomalous coronary origin. It is rather related to the presence of several anatomical disturbances that cause a decrease in coronary flow and lead to cardiac arrest.

In the follow-up, four patients with ARCA underwent coronary artery bypass grafting. This strategy was consistent with that in the ACC/AHA guidelines [16] to perform surgical interventions in patients with ARCA and a course of the anomalous segment between the aorta and pulmonary artery with concomitant obstructive atherosclerosis. The second group, according to the prevalence of cardiac events in our study, was patients with ALCx. The occurrence of three cardiac events in this group should be related to the presence of obstructive atherosclerosis. This theory supports the study by Taylor et al. [7], in which cardiac death in patients older than 30 years happened because of significant atherosclerotic lesions. A small number of cardiac events in the follow-up is an important limitation of our study; however, patients with ARCA tended to have a shorter cardiac event-free survival time compared to the entire evaluated group. The fact that follow-up was not performed in the whole evaluated group is also a limitation of this analysis. Nevertheless, in contrast to previous analyses [17–21], in our study we not only detected coronary anomalies but also provided important prognostic information.

Other study limitations are the lack of non-invasive ischaemia imaging stress testing as well as the absence of ICA results including fractional flow reserve evaluation. Lastly, in an attempt to reduce radiation exposure, more CT studies are now being performed using prospective gating as well as reduced tube voltage [22].

Conclusions

In the evaluated group with a mean age exceeding 60 years, high-risk anatomic features are most common in patients with anomalous right coronary artery origin from the left coronary sinus. This implies a higher prevalence of chest pain and cardiac events in the follow-up in patients with ARCA than in individuals with ALCA. Subjects with ALCx show more common significant coronary atherosclerosis than those with ALCA, which results in more frequent angina and cardiac events. Patients with ALCA have the least occurrence of high-risk anatomic features and obstructive coronary artery atherosclerosis, which results in the lowest incidence of chest pain and adverse cardiac events in the follow-up in this group.

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