Computed tomographic characteristics of congenital coronary artery fistulas in an adult population

Anna Maria Michałowska[1, 2], Jarosław Skowroński[3], Ilona Michałowska[4], Paweł Tyczyński[3], Ilona Kowalik[5], Rafal Wolny[3], Maksymilian Przemysław Opolski[3], Marcin Demkow[6], Piotr Hoffman[7], Hubert Lazarczyk[1], Mariusz Kruk[6], Cezary Kepka[6], Mariusz Kusmierczyk[8], Adam Witkowski[3], Jerzy Pręgowski[2]

[1]National Institute of Cardiology, Warszawa, Poland
[2]Department of Diagnostic Radiology, The National Institute of Medicine of the Ministry of Interior and Administration, Warszawa, Poland
[3]Department of Interventional Cardiology and Angiology, National Institute of Cardiology, Warszawa, Poland
[4]Department of Radiology, National Institute of Cardiology, Warszawa, Poland
[5]Department of Coronary Artery Disease and Cardiac Rehabilitation, National Institute of Cardiology, Warszawa, Poland
[6]Department of Coronary and Structural Heart Diseases, National Institute of Cardiology, Warszawa, Poland
[7]Congenital Heart Diseases Department, National Institute of Cardiology, Warszawa, Poland
[8]Department of Cardiac Surgery, Medical University of Warsaw, Warszawa, Poland

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Correspondence to:
Ilona Michałowska, MD, PhD, Department of Radiology, National Institute of Cardiology Alpejska 42, 04–628 Warszawa, Poland,
phone: +48 22 343 41 67,
e-mail: imichalowska@ikard.pl

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ABSTRACT

Background: Coronary artery fistulas (CAFs) are usually congenital coronary artery anomalies of termination.

Aims: This study aimed to assess the prevalence, anatomic characteristics, and clinical significance of CAFs detected by computed tomography (CT) in an adult population.

Methods: We performed 45 817 CT examinations in 39 066 subjects between 2008 and 2020. The electronic database was manually checked using specific keywords to identify patients with CAFs. The CT characteristics of CAFs were evaluated. CAF was defined as clinically significant if it was the most plausible cause of myocardial infarction, infective endocarditis, heart failure, death during follow-up, hospitalization, or if it required either percutaneous or surgical intervention.

Results: Of 39 066 patients, 56 CAFs were detected in 42 subjects (20 men, 47.6%) with a prevalence of 0.11%. Most CAFs originated from the right coronary artery (RCA) (48.2%) and drained into the pulmonary artery (PA) (58.9%). CAFs terminating in the PA were more frequently multiple (P <0.001) and tortuous (P <0.001) as compared to CAFs without PA drainage. Clinically significant CAFs, identified in 7 of 42 patients, were more common in younger (P = 0.03) and male (P = 0.04) subjects and had larger lumen area and diameter at the site of origin (P = 0.03, P = 0.03, respectively).

Conclusions: In the unselected adult population undergoing coronary CT angiography, the RCA and the PA are the most common sites of origin and termination of CAFs, respectively. CAFs draining into the PA are more often multiple and tortuous. Clinically meaningful CAFs are larger and most frequently detected in younger and male patients.

Key words: computed tomography, congenital coronary artery anomalies, coronary artery anomalies of termination, coronary artery fistulas, non-invasive diagnostic technique

INTRODUCTION

Coronary artery fistulas (CAFs) are rare and usually congenital coronary artery anomalies of termination, involving either vessels (coronary-vascular fistula [CVF]) or cardiac chambers (coronary-cameral fistula [CCF]) [1, 2]. With CAF prevalence varying across prior angiographic studies (0.05%–0.17%), their detection has increased with the use of computed tomography (CT) up to 0.91%

WHAT'S NEW?

Congenital coronary artery fistulas (CAFs) are rare coronary artery anomalies of termination, usually detected incidentally. Although CAFs are mainly asymptomatic, some of them might be of clinical importance and lead to myocardial infarction, heart failure, infective endocarditis, or even death. Clinically significant CAFs are not only more frequently detected in younger and male patients but are also larger, and often with wall calcifications. To our knowledge, the current study represents the largest computed tomographic study on congenital coronary artery fistulas in an adult population to date.

[3–6]. Although the vast majority of CAFs are asymptomatic, clinical manifestation of CAFs depends on their size along with the direction and volume of blood flow [7, 8]. Our study aimed to assess the prevalence, anatomic characteristics, and clinical significance of CAFs diagnosed with CT in adults.

METHODS

The study was approved by the Local Ethics Committee and complied with the Declaration of Helsinki. Between February 2008 and November 2020, there were 45 817 coronary CT examinations performed in 39 066 subjects in a single high-volume cardiac center. To select patients with CAF, the electronic database of all coronary CT reports was manually screened with the use of specific keywords. Based on that electronic database, all demographic and clinical data were collected. Information about clinical conditions during follow-up time was obtained based on a telephone survey (February–April 2021). Heart failure (HF) with at least mildly reduced ejection fraction was diagnosed based on the coexistence of classical signs and symptoms of HF together with impaired left ventricular ejection fraction (LVEF) <50% [9, 10]. The probability of pulmonary hypertension (PH) was estimated based on the systolic pulmonary arterial pressure (sPAP) [11]. To assess sPAP, the peak tricuspid regurgitation velocity (TRV) and the TRV-derived regurgitation pressure gradient were measured, after excluding pulmonary stenosis [11]. Exclusion criteria were as follows: (1) poor diagnostic quality of coronary CT; (2) truncated part of fistula on CT examination; (3) known or suspected acquired etiology of fistula; (4) coronary CT performed after surgical or percutaneous treatment of CAF.

In the course of the study, 3 generations of dual-source CT scanners were used: from 2008 to May 2011 (6414 CT examinations [14%]) – the Somatom Definition; from June 2011 to May 2015 (13 745 CT examinations [30%]) – the Somatom Definition Flash; and from June 2015 to November 2020 (25 658 CT examinations [56%]) – the Somatom Force (all Siemens Healthcare, Forchheim, Germany). The following CT acquisition parameters were used: slice collimation of 64 × 0.6 mm (Definition), 128 × 0.6 mm (Flash), and 192 × 0.6 mm (Force); gantry rotation time of 330 ms (Definition), 280 ms (Flash), and 250 ms (Force); tube voltage of 80–140 kV (Definition, Flash), and 70–120 kV (Force); tube current of 300–550 mAs. Prospective (including high-pitch flash acquisition) or retrospective ECG-gated CT angiography was used. The study protocol was selected by the supervising physician depending on the heart rhythm and clinical indications. A dose modulation technique was used to limit the radiation exposure. Data were routinely reconstructed in the mid- or end-systolic and diastolic phases (35% to 45% and 65% to 75% of the RR intervals). Unless contraindicated, nitroglycerin in a dose of 0.8 mg was administered sublingually immediately before the examination. To achieve a heart rate of 60–75/min (depending on the scanner generation) metoprolol in fractionated doses of 2.5 mg was injected intravenously. After administration of a 10 ml bolus of contrast, the start time of the study acquisition was calculated. The contrast agent (Iomeron 400; Bracco Altana Pharma, Ultravist 370; Bayer Pharma AG; Omnipaque 350 GE) was injected intravenously in two phases — 45–60 ml of contrast and 30 ml of the contrast and saline (30/70%) mixture at the rate of 4.5–6 ml/s (depending on the generation of the CT scanner).

The analysis of the CT scans was performed on a dedicated workstation by a single experienced observer. CAF was defined as an anomalous direct connection between ≥1 coronary artery and a cardiac chamber or a vessel [1]. All CAFs were evaluated based on their site of origin (≥1 main coronary artery: the right coronary artery [RCA], left anterior descending [LAD], or circumflex artery [Cx]) and termination (Figures 1 and 2), as well as morphology: (1) number of CAFs; (2) complexity; (3) size; (4) tortuosity; (5) intramuscular course; and (6) presence of aneurysms, calcifications, vegetations, thrombus in CAF or dissection of CAF (Figure 3). The following definitions of CAF morphologies have been adopted: (1) coronary-cameral fistula — a CAF draining into ≥1 cardiac chamber (right atrium [RA], left atrium, right ventricle [RV], LV); (2) coronary-vascular fistula — a CAF terminating in ≥1 vascular structure (pulmonary trunk [PA], right pulmonary artery, left pulmonary artery, coronary sinus [CS], superior vena cava, inferior vena cava, cardiac veins) [2]; (3) simple CAF — a CAF with 1 origin, consisting of 1 vessel and terminating in 1 structure [6]; (4) complex CAF — a CAF with >1 origin and/or consisting of >1 vessel, and/or terminating in >1 structure [6]; (5) bilateral CAF — a CAF originating from both the RCA and left coronary artery with only 1 termination site [4]; (6) tortuous CAF — presence of ≥3 consecutive bends, i.e., changes in the direction of the vessel by ≥45° in relation to the main stem [12]. In addition, all CAFs were categorized according to their size: small CAF — maximal lumen diameter (LD) of the CAF <2 mm, medium CAF — 2–10 mm, and large CAF — >10 mm [13].

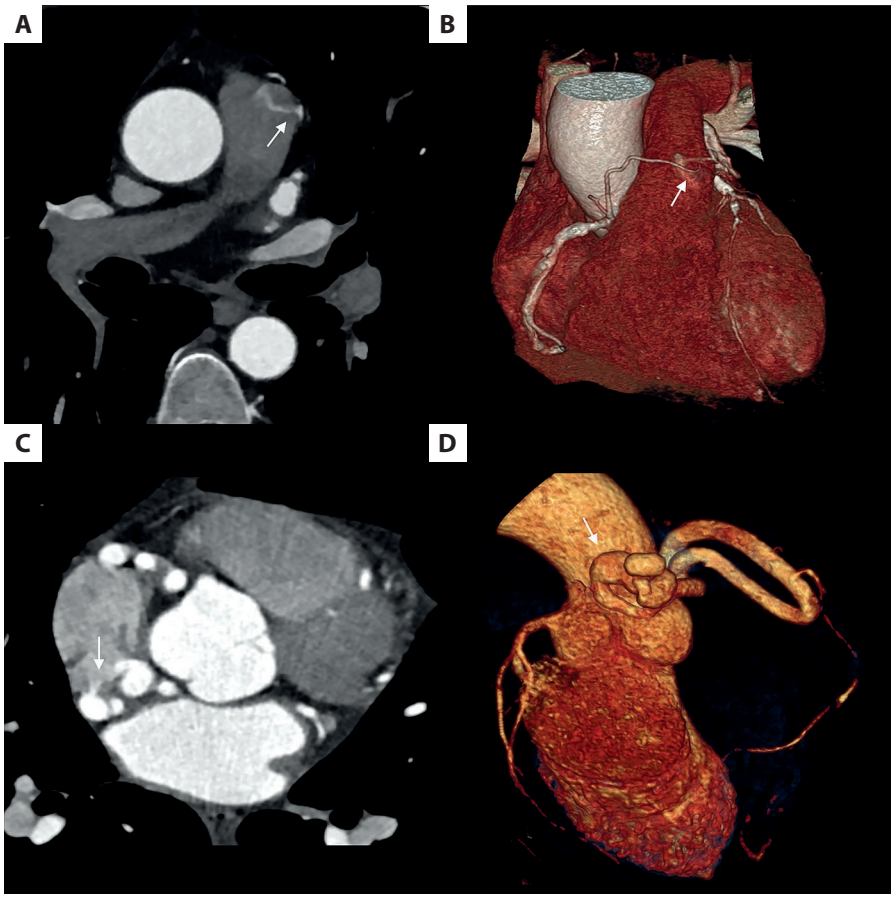

Figure 1. Coronary computed tomography (CT). **A.** Multiplanar reconstruction (MPR). **B.** volume-rendered reconstruction, the coronary artery fistula (CAF) between the right coronary artery (RCA) and the pulmonary artery (white arrows). **C.** MPR. **D.** volume-rendered reconstruction, CAF between the RCA and the superior vena cava (white arrows)

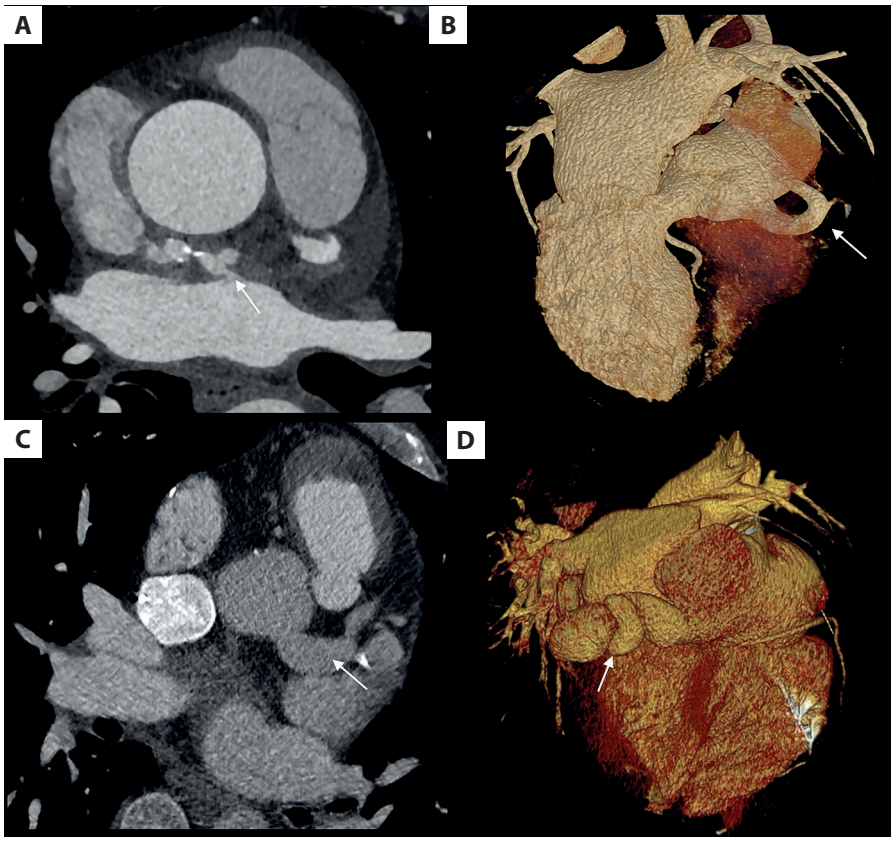

Figure 2. Coronary CT. **A.** MPR. **B.** Volume-rendered reconstruction, CAF between the RCA and the left atrium (white arrows). **C.** MPR. **D.** Volume-rendered reconstruction, CAF between the circumflex artery and the coronary sinus (white arrows)

Abbreviation: see Figure 1

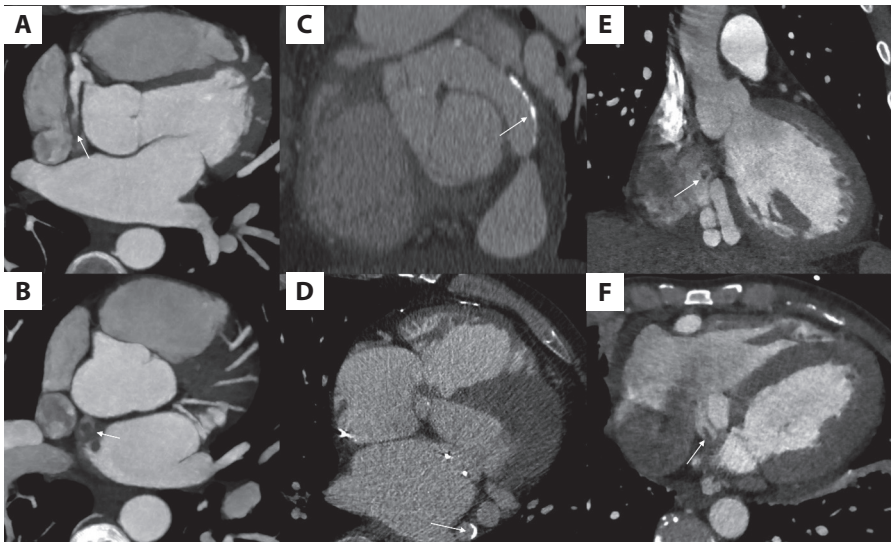

Figure 3. Coronary CT, MPR. **A.** Cross-sectional view, CAF between the RCA and the LA (arrow). **B.** Distal segment of CAF with thrombus (arrow). **C.** Oblique cross-section, calcification within CAF (arrow). **D.** Cross-sectional view, calcification within CAF (arrow). **E–F.** Vegetation at the site of termination of CAF draining into the right atrium (arrow), frontal view (**E**), cross-sectional view (**F**)

Abbreviation: see Figure 1

Within every CAF, the following morphological features were described: (1) aneurysm — segmental dilatation of the artery ≥50% of the reference vessel diameter [13]; (2) calcification — presence of regions with >130 Hounsfield units attenuation in the fistula wall [14]; (3) vegetation — hypodense, homogeneous, irregular mass in the lumen of the fistula [15]; (4) thrombus – low-attenuated structure within the lumen of the fistula [16]; (5) dissection — linear, hypodense structure within the vessel lumen, separating the false and true canals [17]. To distinguish between vegetation and a thrombus, clinical data were used — in patients with clinical signs of infective endocarditis (IE), vegetation was diagnosed.

The minimal and maximal LD and lumen area (LuA) of CAFs were measured at the site of origin and termination, as well as at the narrowest and widest segments of the CAFs. In addition, the end-diastolic RV and LV dimensions were measured in a four-chamber CT view, and the ratio of RV/LV dimensions was calculated to identify RV enlargement as an indicator of its volume overload (RV/LV ≥1.0) [18].

CAF was defined as clinically significant if it was the most plausible cause of myocardial infarction, IE, HF, death within the follow-up time, hospitalization, or if it required either percutaneous or surgical intervention.

The presence and severity of atherosclerotic lesions in coronary arteries were assessed according to the Coronary Artery Disease — Reporting and Data System (CAD-RADS), which ranges from CAD-RADS 0 (no atherosclerosis) to CAD-RADS 5 (total occlusion in at least one vessel) [19].

Statistical analysis

Normality was assessed with the Shapiro-Wilk test and visual evaluation of histogram skewness. Continuous variables with normal distribution were presented as means (standard deviations, SD) and non-normally distributed variables as medians with interquartile ranges (IQR). The significance of differences between the mean values of the three groups was verified by one-way analysis of variance and Tukey's post-hoc test, applied when the null hypothesis of the general test was rejected. The significance of differences between the mean values of the 2 groups was analyzed using Student's t-test. To assess the conformity of skewed distributions of continuous variables for 3 or 2 groups, non-parametric analysis of variance Kruskal-Wallis, non-parametric multiple comparison tests, and Mann-Whitney tests were used. To assess the difference within the group, the Wilcoxon rank-sum test was used.

The results of categorical variables were shown as counts and relative frequencies (percentages). The χ^2 test of independence or Fisher's exact test were used for binary comparison. The χ^2 test for equal proportion was used to verify the homogeneity of proportion. The Cochran-Mantel-Haenszel modified ridit score was applied to the analysis of categorical variables, with >2 categories (whereby nominal variables were compared using General Association *P*-value and ordinal variables were compared using row mean score *P*-value).

All *P*-values were two-tailed and a *P*-value of <0.05 was considered statistically significant. Statistical analysis was performed using SAS, version 9.4. (SAS Institute Inc, Cary, NC, US).

RESULTS

Among 39 066 patients, CAFs were diagnosed in 52 subjects. After exclusion of 10 patients due to the potentially acquired nature of CAFs (n = 7) and non-diagnostic evaluation of the site of termination of CAFs (n = 3), the final study cohort included 42 patients (20 men, 47.6%) with 56 CAFs. The prevalence of CAFs was 0.11% (42/39 066). In the majority of subjects (73.8%), CAFs were incidental findings. Table 1 displays the baseline characteristics, while Table 2 shows CT morphology of CAFs. Six of 42 (14.3%) patients required surgical or percutaneous closure of CAFs, whereas the remaining patients were treated conservatively. During the median 22.5-month (4.75–103.5) follow-up, 7 (16.7%) patients died.

Table 1. Baseline characteristics

	CAF (n = 42)
Age[a], years	57.5 (13.8)
Sex, male	20 (47.6)
BMI, kg/m^2	27.8 (7.2)
Hypertension	23 (54.8)
Diabetes mellitus	4 (9.5)
Dyslipidemia	13 (31.0)
Smoking history	5 (11.9)
Presence of atherosclerosis:	
CAD-RADS <3	30 (71.4)
CAD-RADS 3 (50%–69%)	6 (14.3)
CAD-RADS 4/5 (≥70%)	6 (14.3)
Concomitant congenital heart diseases	2 (4.8)
Previous history of AF (acute/chronic)	10 (23.8)
Supraventricular arrhythmias	5 (11.9)
Ventricular arrhythmias	2 (4.8)
Heart failure	12 (28.6)
Previous history of myocardial infarction	4 (9.5)
Pulmonary hypertension	5 (11.9)
Previous history of IE	3 (7.1)
Previous history of sudden cardiac arrest	1 (2.4)
Previous history of PCI	4 (9.5)
Death during follow-up	7 (16.7)
Follow-up, months	22.5 (4.75–103.5)

Values are presented as n (%), means (SD), or medians (IQR)

[a]Age of the patients at which the CT examination was performed

Abbreviations: AF, atrial fibrillation; BMI, body mass index; CAF, coronary artery fistula; CAD-RADS, Coronary Artery Disease – Reporting and Data System; CT, computed tomography; IE, infective endocarditis; IQR, interquartile range; n, number of patients; PCI, percutaneous coronary intervention; SD, standard deviation

Table 2. CAF morphology evaluated with computed tomography

CAFs		n (%)
Fistula origin	RCA	27 (48.2)
	LAD	19 (33.9)
	Cx	10 (17.9)
Fistula drainage site		
	PA	33 (58.9)
	CS	6 (10.7)
	LA	5 (8.9)
	RPA	3 (5.4)
	SVC	3 (5.4)
	LPA	2 (3.6)
	RA	2 (3.6)
	IVC	1 (1.8)
	MCV	1 (1.8)
Number of CAFs per patient	1	30 (71.4)
	>1	12 (28.6)
Size of CAF	<2 mm	1 (1.8)
	2–10 mm	45 (80.4)
	>10 mm	10 (17.9)
Type of CAF	CVF	48 (85.7)
	CCF	8 (14.3)
Complexity of CAF	Simple	29 (51.8)
	Complex	27 (48.2)
Tortuosity of CAF		44 (78.6)
Intramuscular course		0
Presence within CAF	Aneurysmal formation	9 (16.1)
	Calcification	5 (8.9)
	Vegetation	2 (3.6)
	Thrombus	1 (1.8)
	Dissection	0

Values are presented as n (%)

Abbreviation: CCF, coronary-cameral fistula; CS, coronary sinus; CVF, coronary-vascular fistula; Cx, circumflex artery; IVC, inferior vena cava; LA, left atrium; LAD, left anterior descending; LPA, left pulmonary artery; MCV, middle cardiac vein; n, number; PA, pulmonary artery; RA, right atrium; RCA, right coronary artery; RPA, right pulmonary artery; SVC, superior vena cava; other — see Figure 1

The most common origin of CAFs was the RCA (48.2%), followed by the LAD (33.9%) and the Cx (17.9%) (Table 2). The site of origin was neither related to demographic characteristics, clinical presentation, nor CAF morphology (Table 3 and Supplementary material, *Table S1*). Additionally, there was no significant relationship between the site of origin and the size of the CAF. The pulmonary artery (PA) was the predominant drainage site of CAFs (58.9%). Furthermore, IE was more often diagnosed in patients with CAFs draining into the right-side cardiac structures compared with CAFs with drainage in the left-side cardiac structures as well as with CAFs terminating in the pulmonary arteries ($P = 0.006$). CAFs terminating in the PA as well as into the right and left pulmonary arteries were more often multiple (63.2% vs. 11.1%; $P < 0.001$), complex (71.1% vs. 0%; $P < 0.001$), tortuous (92.1% vs. 50.0%; $P < 0.001$), and bilateral (57.9% vs. 0%; $P < 0.001$) as compared to CAFs draining into either the left-side or right-side cardiac structures. CAFs draining into the right structures and vasculatures of the heart were significantly larger at the site of origin (average lumen diameter [LD_{avg}]: 6.8 vs. 2.4; $P = 0.008$), site of termination (LD_{avg} 18.7 vs. 3.94; $P < 0.01$) as well as at their narrowest segment (LD_{avg} 4.65 vs. 1.55; $P = 0.004$) in comparison to CAFs terminating in the pulmonary vasculature or the left-side structures of the heart (Table 3).

Supplementary material, *Table S2* displays the comparison between CAFs ≤10 mm and >10 mm. Large CAFs were not only more often found in younger patients ($P = 0.03$), subjects with PH ($P = 0.03$) and/or IE ($P = 0.004$), but also were more frequently treated by surgical or percutaneous closure ($P = 0.04$). Furthermore, CAFs >10 mm were more often calcified and usually drained into the CS ($P < 0.001$ for both). The site of origin and termination of CAFs ≤10 mm and >10 mm are shown in Figure 4.

Atherosclerosis was detected in 22 of 42 (52.4%) subjects with CAFs, in whom 6 (27.3%) atherosclerotic lesions were classified as CAD-RADS 1, 4 (18.2%) as CAD-RADS 2, 6 (27.3%) as CAD-RADS 3, 5 (22.7%) as CAD-RADS 4, and 1 (4.5%) as CAD-RADS 5. Percutaneous coronary intervention (PCI) was performed in 4 subjects (18.2%). The comparison between clinical manifestation of patients with versus without atherosclerosis is shown in Supplementary material, *Table S3*, while *Figure S1* depicts the presence of atherosclerotic lesions based on the sites of origin and termination of CAFs.

Clinically significant CAFs were diagnosed in 7 of 42 patients (16.7%), of whom 3 subjects died (42.9%). Four of 7 of these patients (57.1%) had HF resulting from CAFs while in 3 patients (42.9%) IE was confirmed. Of all patients with clinically significant CAFs, 3 patients required percutaneous

Table 3. Tomographic characteristics of coronary artery fistulas based on their site of origin and termination

Tomographic evaluation	CAFs originating from RCA (n_F = 27)	CAFs originating from LAD (n_F = 19)	CAFs originating from Cx (n_F = 10)	*P*-value	CAFs terminating in the right structures of the heart (n_F = 13)	CAFs terminating in the pulmonary trunk and pulmonary arteries (n_F = 38)	CAFs terminating in the left structures of the heart (n_F = 5)	*P*-value
	(1)	(2)	(3)		(4)	(5)	(6)	
Number of CAFs, >1	13 (48.1)	10 (52.6)	3 (30.0)	0.500	1 (7.7)	24 (63.2)	1 (20.0)	0.001
Large CAFs, >10 mm	6 (22.2)	1 (5.3)	3 (30.0)	0.19	8 (61.5)	1 (2.6)	1 (20.0)	<0.001
Complex CAF	13 (48.1)	12 (63.2)	2 (20.0)	0.09	0	27 (71.1)	0	<0.001
Tortuous CAF	21 (77.8)	16 (84.2)	7 (70.0)	0.67	7 (53.8)	35 (92.1)	2 (40.0)	0.001
Aneurysm formation	5 (18.5)	3 (15.8)	1 (10.0)	0.82	1 (7.7)	7 (18.4)	1 (20.0)	0.65
Vascular calcification within CAF wall	2 (7.4)	1 (5.3)	2 (20.0)	0.39	3 (23.1)	1 (2.6)	1 (20.0)	0.06
Presence of thrombus in CAF	1 (3.7)	0	0	0.58	0	0	1 (20.0)	0.09
CAF origin site								
LuA, mm^2	7.2 (4.1–14.0)	3.6 (2.4–6.2)	7.6 (3.8–31.0)	0.08	36.0 (5.5–95.0)	4.4 (3.0–7.8)	7.5 (2.1–29.0)	0.02 4 vs. 5: 0.02
LD_{avg}, mm	3.05 (2.2–4.3)	2.05 (1.8–2.8)	3.3 (2.0–6.3)	0.08	6.8 (2.3–11.0)	2.4 (1.9–3.2)	3.15 (1.5–6.5)	0.02 4 vs. 5: 0.02
CAF drainage site								
LuA, mm^2	4.4 (3.2–12.9)	3.5 (2.7–7.2)	4.7 (1.3–18.7)	0.51	18.7 (4.4–38.0)	3.7 (2.8–6.7)	5.7 (1.3–8.5)	0.04 4 vs. 5: 0.03
LD_{avg}, mm	2.35 (2.1–4.1)	2.15 (1.75–3.1)	2.55 (1.3–4.9)	0.40	4.9 (2.3–7.5)	2.2 (1.9–3.1)	2.5 (1.3–3.3)	0.04 4 vs. 5: 0.03
Widest segment of CAF								
LuA, mm^2	10.4 (5.7–63.0)	12.0 (5.2–19.0)	8.8 (3.8–124.0)	0.79	124.0 (7.8–213.0)	10.1 (5.4–14.5)	7.8 (5.7–47.0)	0.13
LD_{avg}, mm	3.65 (2.65–8.95)	3.6 (2.6–4.8)	3.35 (2.15–13.15)	0.74	13.15 (3.2–16.4)	3.5 (2.6–4.3)	3.25 (2.5–8.0)	0.11
Narrowest segment of CAF								
LuA, mm^2	2.6 (1.7–5.5)	1.8 (1.5–2.8)	2.4 (1.3–11.1)	0.15	15.0 (3.0–36.0)	2.2 (1.4–2.2)	2.1 (1.3–5.5)	0.008 4 vs. 5: 0.006
LD_{avg}, mm	1.85 (1.45–2.6)	1.55 (1.2–2.0)	1.45 (1.3–3.75)	0.23	4.65 (2.0–6.8)	1.58 (1.3–1.8)	1.55 (1.3–2.6)	0.01 4 vs. 5: 0.01
RV, cm	4.1 (0.7)	4.1 (0.7)	4.5 (0.9)	0.31	4.4 (0.8)	4.1 (0.7)	4.1 (0.8)	0.33
LV, cm	4.6 (0.9)	4.7 (1.0)	4.5 (0.9)	0.92	4.8 (0.8)	4.6 (1.0)	4.3 (1.1)	0.62
RV/LV	0.9 (0.2)	0.9 (0.2)	1.0 (0.2)	0.20	0.9 (0.1)	0.9 (0.2)	1.0 (0.3)	0.51

Values are presented as n (%), means (SD), or medians (IQR)

Abbreviations: avg, average; LuA, lumen area; LD, lumen diameter; LV, left ventricle, transverse diameter in the 4-chamber view; n_F, number of fistulas; RV, right ventricle, transverse diameter in the 4-chamber view; RV/LV, right-to-left ventricular diameter ratio; SD, standard deviation; other — see Figures 1 and 2

closure of CAFs, 2 subjects with coexisting structural heart diseases underwent surgical repair of CAFs, and in 2 cases, CAFs were treated conservatively due to active IE (n = 1) or the presence of a thrombus within CAF (n = 1). The comparison between clinically significant and clinically insignificant CAFs is shown in Table 4. The presence of clinically significant CAFs was more common in younger (P = 0.03) and male (P = 0.04) patients and was associated with PH (P = 0.03). Also, the CT analysis revealed larger lumen area and diameter at the site of origin (P = 0.03, P = 0.03, respectively) and higher wall calcifications (P = 0.003) in clinically meaningful CAFs.

In 15 patients (35.7%) stress myocardial perfusion imaging was performed – predominantly in subjects with moderate CAFs (12/15). Eight patients underwent magnetic resonance imaging, 6 single-photon emission computed tomography, and 1 both magnetic resonance imaging and single-photon emission computed tomography. In all subjects, no significant myocardial perfusion defects were detected.

DISCUSSION

In this study, we evaluated the prevalence, clinical significance, and anatomic characteristics of CAFs detected on coronary CT in the unselected adult population. Our main findings are as follows: (1) the most common site of origin and termination of CAFs are the RCA and PA, respectively; (2) large CAFs are usually single and calcified, and most commonly drain into the CS, whereas CAFs terminating in the PA are frequently multiple, tortuous, and complex; (3) clinically significant CAFs are usually large, mainly terminate in the RA or CS and are most frequently found in younger and male patients.

The prevalence of CAFs differs based on the study group, diagnostic methods, and applied definitions. To our knowledge, our report represents the largest computed

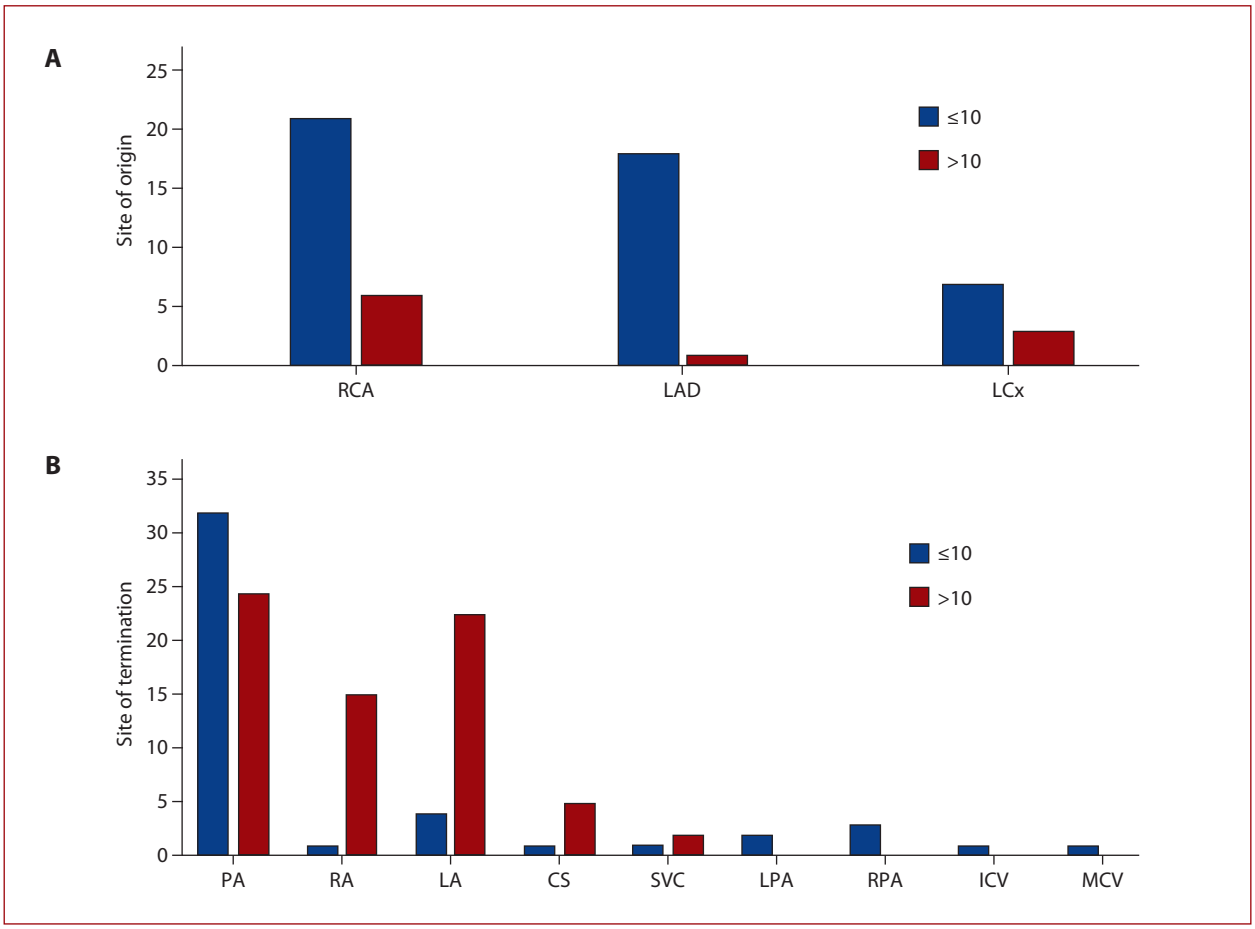

Figure 4. Site of origin (**A**) and termination (**B**) of CAFs ≤10 mm and >10 mm

Abbreviations: CS, coronary sinus; Cx, circumflex artery; IVC, inferior vena cava; LAD, left anterior descending; LA, left atrium; LPA, left pulmonary artery; MCV, middle cardiac vein; PA, pulmonary artery; RA, right atrium; RCA, right coronary artery; RPA, right pulmonary artery; SVC, superior vena cava

tomographic study to date in adults, and the CAF prevalence of 0.11% is in line with the previous tomographic and angiographic studies [3–6, 19–21].

CAFs usually drain into the low-pressure right-sided structures of the heart and less frequently into those on the left. Importantly, there are contradictory data regarding the most common site of origin (RCA or LAD) and termination (RV or PA) of CAFs [1, 4–5, 7, 21–23]. In our study, the most frequent site of origin of CAFs was the RCA, whereas the most common site of termination was the PA. Moreover, most of our CAFs including clinically significant CAFs were single, which corroborates the earlier report [4].

The fistula drainage site rather than the site of origin has more clinical significance [1, 24]. Indeed, PH and IE were more often observed in patients with CAFs terminating in right-sided structures of the heart in our cohort replicating previous reports [2]. Valente et al. in their study noted that most CAF patients with clinically significant complications, such as myocardial infarction, HF, or thrombus formation, had CAFs draining into the CS [25], which was similar to our findings. Of all CAFs terminating in the CS in this study, 50% were clinically significant, and the CS was more often the drainage site of large CAFs.

The size of the fistula has clinical significance — small CAFs are usually incidental findings due to their asymptomatic clinical course, whilst large CAFs often cause symptoms and are related to progressive enlargement of the native vessel [1, 8, 26–28]. In our study, the predominance of medium-sized CAFs was observed. The most common drainage site of CAFs ≤10 mm was the PA, while CAFs >10 mm mostly drained into the CS, which is in line with earlier echocardiographic studies [28]. Large CAFs are not only clinically significant but also more common in younger patients. In addition, CAFs >10 mm were more often calcified and usually drained into the CS.

Clinical manifestations in CAF patients may be related to the presence of atherosclerosis and/or valvular heart disease [8, 29]. In contrast, clinical symptoms of myocardial ischemia in patients with CAFs and without any or with non-significant atherosclerotic lesions might be explained by decreased myocardial perfusion resulting from the coronary steal phenomenon [24]. Interestingly, 4 of 42 patients (9.5%) in our cohort had myocardial infarction despite not having coronary atherosclerosis. Another potential but rare cause of acute myocardial infarction or ventricular arrhythmia in CAF patients is thrombus

Table 4. Comparison between clinically significant and clinically insignificant CAFs

	Clinically insignificant CAFs (n_P = 35)	Clinically significant CAFs (n_P = 7)	*P*-value
Age[a], years	59.5 (13.0)	47.1 (13.8)	**0.03**
Sex, male	14 (40.0)	6 (85.7)	**0.04**
BMI, kg/m^2	29.1 (7.5)	24.1 (4.2)	0.1
Hypertension	18 (51.4)	5 (71.4)	0.43
Diabetes mellitus	4 (11.4)	0	>0.99
Dyslipidemia	13 (37.1)	0	0.08
Smoking history	3 (8.6)	2 (28.6)	0.19
Presence of atherosclerosis:			
CAD-RADS <3	23 (65.7)	7 (100)	0.19
CAD-RADS 3 (50%–69%)	6 (17.1)	0	
CAD-RADS 4/5 (≥70%)	6 (17.1)	0	
Concomitant congenital heart diseases	2 (5.7)	0	>0.99
Clinical presentation			
Previous history of AF (acute/chronic)	7 (20.0)	3 (42.9)	0.33
Supraventricular arrhythmia	4 (11.4)	1 (14.3)	>0.99
Ventricular arrhythmia	2 (5.7)	0	>0.99
Pulmonary hypertension	2 (5.7)	3 (42.9)	**0.03**
Previous history of sudden cardiac arrest	0	1 (14.3)	0.17
Previous history of PCI	4 (11.4)	0	>0.99
Tomographic evaluation	(n_F = 46)	(n_F = 10)	
Large CAFs, >10 mm	5 (10.9)	5 (50.0)	**0.03**
Type of CAF, CVFs	43 (93.5)	5 (50.0)	**0.003**
Complex CAF	24 (52.2)	3 (30.0)	0.3
Bilateral CAF	20 (43.5)	2 (20.0)	0.29
Tortuous CAF	37 (80.4)	7 (70.0)	0.43
Aneurysm formation	7 (15.2)	2 (20.0)	0.65
Vascular calcification within CAF	1 (2.2)	4 (40.0)	**0.003**
Presence of visible thrombus	0	1 (10.0)	0.18
CAF origin site			
LuA, mm^2	4.92 (2.5–9.1)	18.25 (4.4–96.0)	**0.03**
LD_{avg}, mm	2.4 (1.9–3.4)	4.8 (2.4–11.0)	**0.03**
CAF drainage site			
LuA, mm^2	3.9 (2.8–8.4)	16.7 (2.8–38.0)	0.12
LD_{avg}, mm	2.3 (2.0–3.0)	4.6 (1.9–7.2)	0.11
Widest segment of CAF			
LuA, mm^2	8.9 (4.2–14.5)	75.0 (25.0–213.0)	**0.003**
$LD_{avg,}$ mm	3.4 (2.3–4.3)	10.2 (5.9–16.4)	**0.002**
Narrowest segment of CAF			
LuA, mm^2	2.3 (1.4–3.2)	4.25 (1.8–34.0)	0.06
LD_{avg}, mm	1.6 (1.3–2.0)	2.3 (1.7–6.5)	**0.02**
RV, cm	4.01 (0.70)	4.73 (0.73)	**0.005**
LV, cm	4.51 (0.96)	5.16 (0.47)	**0.004**
RV/LV	0.91 (0.17)	0.92 (0.14)	0.88

Values are presented as n (%), means (SD,) or medians (IQR)
[a]Age of the patients at which the CT examination was performed
Abbreviations: avg, average; LuA, lumen area; LD, lumen diameter; LV, left ventricle, transverse diameter in the 4-chamber view; n_F, number of fistulas; n_P, number of patients; RV, right ventricle, transverse diameter in the 4-chamber view; RV/LV, right-to-left ventricle diameter ratio; other — see Table 1

formation within CAF, which, in our study, was observed in 1 patient [30].

Despite the mostly asymptomatic clinical course of CAFs, the probability of clinical manifestations increases with age due to the development of atherosclerosis in coronary arteries [7, 8, 24]. Canga et al. suggested that CAFs >1.5 mm, originating from the proximal segments of coronary arteries might increase the progression of coronary atherosclerosis and further the risk of myocardial infarction [22]. However, there was no association between the site of origin and termination and the presence as well as the severity of atherosclerotic lesions in our study. Significant coronary artery disease (≥50%) was more often seen in patients with smaller CAFs.

Clinically relevant complications of CAFs, such as IE, HF, myocardial infarction, or rupture of aneurysm, might be the first clinical manifestation of CAFs and may even lead to sudden cardiac death [1, 2, 7, 8, 26]. According to a 10-year analysis of available literature conducted by Said et al., clinically significant complications of CAF more often

occur in men [2]. This is in line with our results, whereby clinically relevant CAFs were more frequently found in younger male subjects.

Coronary artery aneurysms associated with fistula develop in up to 26% of cases of congenital CAFs detected by coronary angiography [1, 4, 29]. While tomographic analysis of CAFs conducted by Ouchi et al. reported the prevalence of aneurysms at 48.4%, in our study, aneurysms associated with CAFs were found in 16.1% of cases [6]. Although rupture of CAF aneurysms is extremely rare, it is associated with very high mortality [27]. In the present study, all CAFs with aneurysms were tortuous.

The presence of CAFs predisposes to IE, which is seen in up to 12% of patients with CAFs and might be the cause of death [8, 26]. While IE could be the first clinical manifestation of CAFs, the development of IE is seen in both coronary-cameral and coronary-vascular fistulas [26]. In our study, IE was present in 7.1% of patients and was more often seen in CAFs draining into the right-side structures of the heart as well as in large CAFs.

Due to the most common asymptomatic clinical course, the majority of CAFs do not require invasive treatment [31]. In our study patients with clinically relevant CAFs and with large CAFs required surgical or interventional treatment. According to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines patients with symptomatic small and medium CAFs should undergo CAF closure, as well as patients with large CAFs regardless of clinical manifestation [32]. Percutaneous interventions are less invasive and usually better tolerated [33]. Surgical treatment is preferable in patients with CAFs and structural heart diseases necessitating surgical repair and in subjects with large CAFs, CAFs with high blood flow as well as in cases of complex CAFs or the presence of large aneurysms [34]. Albeit, in some cases, the closure of CAFs might be challenging and require a multi-disciplinary approach [35, 36].

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In conclusion, although CAFs are usually asymptomatic incidental findings on CT scans, clinically significant CAFs are larger and more frequently detected in younger and male patients.

This study has several limitations. First, it was a single-center and retrospective report of patients referred to tertiary sites. Second, three generations of dual-source CT with similar spatial resolution but different time resolution were used during the study. Finally, CT examinations were selected manually from the electronic database based on the predefined keywords.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

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