

## ORIGINAL ARTICLE

# Primary Congenital Coronary Artery Anomalies: An Angiographic Study in Greece

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**LIST OF ABBREVIATIONS:**

CAAs = coronary artery anomalies  
CABG = coronary artery bypass grafting  
CAD = coronary artery disease  
CT = computed tomography  
LAD = left anterior descending (coronary artery)  
LCx = left circumflex (coronary artery)  
MRA = magnetic resonance angiography  
RCA = right coronary artery

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ABSTRACT

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**BACKGROUND:** Primary congenital coronary anomalies are anatomical variations of the origin, course and termination of coronary arteries, which are not associated with complex congenital heart disease. In Greece, apart from some case reports, there are no published data. Thus, the aim of this study was to assess the prevalence of the different forms of primary congenital coronary artery anomalies in a Greek adult population.

**METHODS:** 5051 coronary arteriographies obtained from January 2008 to December 2010 were retrospectively analyzed. Coronary anomalies were classified as anomalies of origin and course, anomalies of intrinsic coronary anatomy, and anomalies of termination.

**RESULTS:** 123 variations of coronary artery anatomy (incidence 2.44%) were identified. Of these, 76 (61.8%) patients had anomalous origin and course, 25 (20.3%) patients had ectasias, 14 (11.4%) patients had myocardial bridging, and 8 (6.5%) patients had small coronary fistulas. The most common anomalies observed were the separate origin of the left anterior descending (LAD) and left circumflex (LCx) coronary arteries, the ectopic right coronary artery (RCA) and the anomalous LCx from the opposite sinus.

**CONCLUSIONS:** The incidence of primary congenital anomalies in Greece is similar to that reported in other populations. Congenital coronary anomalies do not predispose to accelerated atherosclerosis of the anomalous vessel. Although the majority of coronary anomalies were not associated with symptoms and were detected incidentally during coronary angiography, awareness of these anatomical variants is clinically important for the appropriate management of cardiac patients.

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INTRODUCTION

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Primary congenital coronary anomalies reflect a range of anatomical variations

including the origin, course and termination of coronary vessels, which are not associated with complex congenital heart disease. Coronary artery anomalies (CAAs) have been associated with numerous symptoms, such as angina, dyspnea on exertion, ventricular tachycardia and myocardial infarction.<sup>1-3</sup> After hypertrophic cardiomyopathy, CAAs are considered to be the second major cause of death in young athletes.<sup>4-8</sup>

Routine application of coronary arteriography has led to a better understanding of CAAs, since they are frequently detected as incidental findings. However, all CAAs neither do they produce symptoms, nor do they all lead to sudden cardiac death.

Nevertheless, identification of these anatomical variants is important for the appropriate management of cardiac patients. The lack of suspicion for these rare anomalies is responsible for prolonged catheterization procedures and potential mismanagement of patients with acute cardiac disease.<sup>9</sup> Angioplasty in such complex lesions poses a technical challenge,<sup>10</sup> as it is the case in coronary artery bypass grafting (CABG). There have been reported cases of accidental ligation of an anomalous coronary artery during valve replacement procedures.<sup>11,12</sup> In the era of biventricular pacing, the electrophysiologist must be aware of the coronary anatomy, as these anomalies could be related to variations in the venous system.

Primary congenital anomalies present with a rate of approximately 1% (range: 0.6-5.6%) in various series,<sup>13</sup> depending on the classification criteria. In Greece, apart from some case reports,<sup>14-16</sup> there are no published data. Thus, the aim of the present study was to assess the incidence of primary coronary artery anomalies in a selected adult population submitted to coronary angiography and to also determine whether there is a possible correlation between CAAs and atherosclerosis.

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## MATERIALS AND METHODS

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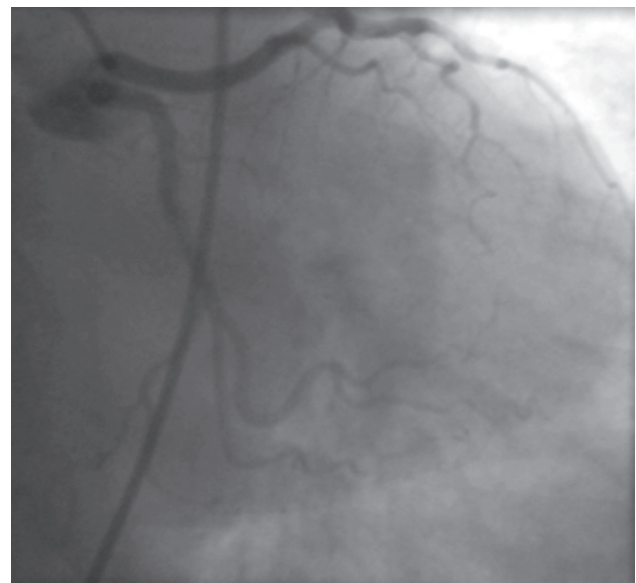
The medical records of patients who underwent coronary arteriography from January 2008 through December 2010 at the Evagelimos General Hospital of Athens were retrospectively reviewed. The main indication for these studies was the evaluation of coronary artery disease. Two independent investigators assessed patient films to determine the incidence of coronary artery anomalies and the concurrent existence of coronary heart disease. In the event of any discrepancy between the investigators, a consensus was reached.

To date, there are no widely agreed upon guidelines for evaluating coronary artery anomalies, although several classification schemes have been proposed. The anatomico-clinical classification criteria proposed by Yamanaka and Hobbs have been the most widely used,<sup>17</sup> despite several concerns.<sup>18</sup> In the present study, coronary anomalies were classified according to the criteria proposed by Angelini and coworkers as: a) anomalies of origin and course, b) anomalies of intrinsic coronary

anatomy, and c) anomalies of termination.<sup>18</sup>

Accordingly, we included variations such as the origin of the right coronary artery (RCA) from an ostium above the sinus of Valsalva (high ostium take-off), myocardial bridging, coronary ectasias and the origins of the left anterior descending (LAD) and left circumflex coronary arteries (LCx) from separate ostia in the left sinus of Valsalva (absence of the left main coronary artery) (Figure 1).

Patients with coronary artery anomalies occurring as part of congenital heart disease were excluded from the study. The presence of significant coronary artery disease (CAD) was defined as a lesion causing more than 50% stenosis of the luminal diameter in an artery or in a major branch.



**FIGURE 1.** Absence of the left main coronary artery. Right anterior oblique view showing the separate origin of the left anterior descending (LAD) and left circumflex (LCx) coronary arteries from different ostia in the left sinus of Valsalva.

## STATISTICAL ANALYSIS

Data are presented as numbers and/or percentages (%). Chi square test was used to assess any significant difference in the presence of CAD between normal and anomalous vessels respectively. All tests are two-sided, statistical significance was set at  $p < 0.05$ . All analyses were carried out using the statistical package SPSS version 13.00 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, Ill., USA).

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## RESULTS

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Data and films from 5051 patients who underwent coronary arteriography were reviewed and 123 variations of coronary ar-

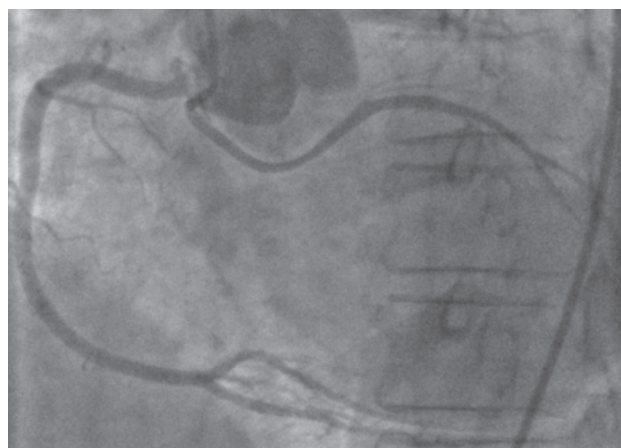
## CONGENITAL CORONARY ANOMALIES

tery anatomy were detected. The overall incidence of recorded coronary anomalies in the study population was 2.44%. The mean age of patients with a coronary anomaly was  $69.4 \pm 11$  years (range, 30 to 84 years). Of these, 99 patients were males and 24 were females (male to female ratio 4.24) (Table 1).

Among the anomalies of vessel origin and course, the separate origin of the LAD and the LCx was the most common anomaly (26 out of 123, incidence 0.55%). The absence of vessel opacification in a territory without collaterals was an indication for such an anomaly.

The anomalies of the right coronary artery (RCA) were in general the second most common. An ectopic RCA arising from the posterior sinus of Valsalva was observed in 11 patients (incidence 0.22%). In 9 patients the RCA originated from the proper sinus, but it was located either above the sinotubular junction, or had a lower origination or was near the valve's commissures (incidence 0.18%). In all these cases the vessel's course continued normally along the right atrioventricular groove, supplying the wall of the right ventricle. The anomalous RCA from the left sinus of Valsalva was observed in 9 patients (incidence 0.18%). In each case the course of the anomalous vessel was between the aorta and the pulmonary artery. None of these patients reported a history of syncope or aborted sudden cardiac death.

The anomalous origin of LCx from the RCA, or the right sinus of Valsalva (Figure 2) was the next most common aberration, which was detected in 10 patients (incidence 0.20%). In 7 patients the vessel originated in the right sinus of Valsalva and in 3 patients it arose from the RCA. In every case the course of the vessel was retroaortic, passing behind the aortic root and giving off its branches to the lateral wall of the left ventricle. The LAD in this group was normal in origin, course and termination.



**FIGURE 2.** Anomalous left circumflex coronary artery (LCx) arising from the right sinus of Valsalva. Left anterior oblique view showing an anomalous LCx arising from the right sinus of Valsalva and following a retroaortic course.

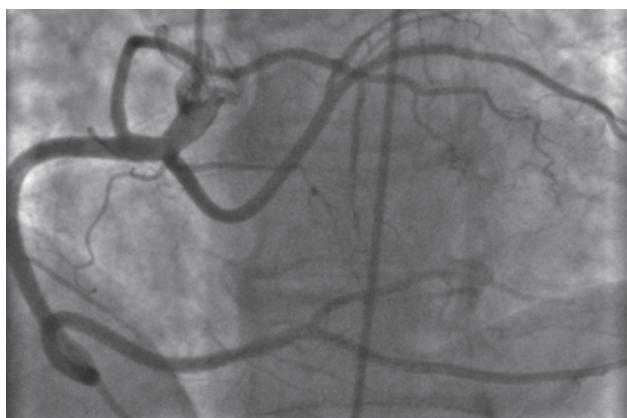
There were also other less common anomalies observed, such as an anomalous left coronary artery originating from the opposite sinus of Valsalva, single RCA (Figure 3) and the LAD arising from the right aortic sinus. From the anomalies of native coronary anatomy, there were 25 cases of coronary ectasias (incidence 0.49%) and 14 cases of myocardial bridging (incidence 0.28%) confined mainly to the mid-segment of the LAD.

Of the anomalies of vessel termination, 8 patients had coronary artery fistulas (incidence 0.16%). These were small, not producing large intracardiac shunts. In most cases these arteriovenous connections originated from the RCA and drained directly into the coronary sinus, into the pulmonary

**TABLE 1.** Incidence of Coronary Artery Anomalies in a Greek Population

Coronary Artery Anomalies		No. of Pts	M	F	Total (%)
Anomalies of origination and course	Absence of Left Main	28	26	2	0.55
	LCx arising from RCA, RSV	10	8	2	0.20
	RCA arising from PSV	11	7	4	0.22
	Ectopic RCA (right cusp)	9	7	2	0.18
	RCA arising from the left cusp	9	8	1	0.18
	Single RCA	3	2	1	0.06
	LCA arising from right cusp	3	2	1	0.06
	LAD arising from right cusp	1	1	0	0.02
	Others	2	0	2	0.04
Anomalies of intrinsic coronary anatomy	Ectasias	25	22	3	0.49
	Myocardial Bridging	14	10	4	0.28
Anomalies of termination	Fistulas	8	6	2	0.16

F = female; LAD = left anterior descending (coronary artery); LCA = left coronary artery; LCx = left circumflex (coronary artery); M = male; PSV = posterior sinus of Valsalva; Pts = patients; RCA = right coronary artery; RSV = right sinus of Valsalva.



**FIGURE 3.** Single coronary artery (Right). Anteroposterior view showing a single coronary artery (Right). The left anterior descending (LAD) and left circumflex (LCx) arteries are arising from the proximal part of a dominant right coronary artery (RCA). *Reproduced with permission from S. Tzikrikas et al. Single Right Coronary Artery, Hellenic J Cardiol 2011; 52: 475.*

artery or into the ventricles.

The overall incidence of CAD in patients with CAAs was 58.54% (Table 2). With the exception of the anomalous origin of LAD from the opposite sinus of Valsalva, rarely was the anomalous artery the only one affected. There was no significant difference in CAD incidence when this was confined to anomalous vessels only, or whether this was confined to normal vessels only. On the other hand, there was a significant difference between the incidence of diffuse CAD and the incidence of CAD in a localized vessel whether it was normal or anomalous ( $p < 0.005$ ) (Table 3).

**DISCUSSION**

Coronary artery anomalies are rare anatomical variations.<sup>19</sup> The most extreme case of primary congenital anomaly is the origin of one or both coronary arteries from the pulmonary artery. These conditions result in obligatory ischemia and are associated with decreased survival.<sup>20</sup> The anomalous origin of the left coronary artery from the pulmonary artery, also known as the Bland-White-Garland syndrome is observed in 1 to 300000 births.<sup>21</sup> Most of these patients die within the first year of life.<sup>22</sup> In sporadic cases, the presence of collaterals from the hypertrophied RCA permits survival through adulthood without symptoms. The anomalous origin of the RCA from the pulmonary artery is less common. It rarely presents with overt symptoms, as the right ventricle is a low-pressure chamber and there is no serious ischemia.<sup>19</sup>

The anomalous origins of the left or right coronary artery

**TABLE 3.** Comparison of the presence of significant coronary artery disease (CAD) between normal and anomalous vessels in the Greek Cohort

	N	%	p-value
<b>CAD in anomalous vessel only</b>	12	9.76	
<b>CAD in normal vessel only</b>	10	8.13	
<b>CAD in normal and anomalous vessels</b>	50	40.65*	<0.0005
<b>No significant CAD</b>	51	41.46*	

\*  $p < 0.0001$  vs CAD in anomalous vessel only and CAD in normal vessel only

**TABLE 2.** Incidence of Coronary Artery Disease (CAD) in Patients with Coronary Artery Anomalies in the Greek Cohort

		CAD in anomalous vessel only	CAD in normal vessel only	CAD in normal and anomalous vessels	No significant CAD
Absence of Left Main	28	4 (14.29%)	0 (0.00%)	15 (53.57%)	9 (32.14%)
LCx arising from RCA, RSV	10	2 (20.00%)	1 (10.00%)	5 (50.00%)	2 (20.00%)
RCA arising from PSV	11	0 (0.00%)	3 (27.27%)	4 (36.36%)	4 (36.36%)
Ectopic RCA (right cusp)	9	0 (0.00%)	1 (11.11%)	3 (33.33%)	5 (55.56%)
RCA arising from the left cusp	9	0 (0.00%)	2 (22.22%)	3 (33.33%)	4 (44.44%)
Single RCA	3	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (66.67%)
LCA arising from right cusp	3	1 (33.33%)	1 (33.33%)	1 (33.33%)	0 (0.00%)
LAD arising from right cusp	1	1 (100.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Others	2	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (100.00%)
Ectasias	25	3 (12.00%)	0 (0.00%)	10 (40.00%)	12 (48.00%)
Myocardial Bridging	14	0 (0.00%)	0 (0.00%)	6 (42.86%)	8 (57.14%)
Fistulas	8	1 (12.50%)	2 (25.00%)	2 (25.00%)	3 (37.50%)

CAD = coronary artery disease; F = female; LAD = left anterior descending (coronary artery); LCA = left coronary artery; LCx = left circumflex (coronary artery); M = male; RCA = right coronary artery; RSV = right sinus of Valsalva; PSV = posterior sinus of Valsalva.

from the opposite sinus of Valsalva are also hemodynamically significant anomalies that could occasionally produce ischemia. The left main coronary artery in its course from the right to the left ventricle can take four paths, prepulmonic, interarterial, septal and retroaortic.<sup>19</sup> The course between the aorta and the pulmonary artery has been responsible for angina, episodes of ventricular tachycardia and sudden cardiac death.<sup>18,23-26</sup> The pathophysiological mechanism is not completely understood. In the past, the scissors-like theory had been proposed.<sup>27-29</sup> Others suggested the presence of an ostial ridge,<sup>24,28,30,31</sup> that causes obstruction and consequently ischemia during exercise, while Maddoux et al regard spasm as an additional mechanism.<sup>32</sup> The majority of the investigators argue over a slit-like ostium along with the acute angulation of the anomalous artery that could result in significant obstruction during vigorous exercise. Angelini et al<sup>18</sup> performing intravascular ultrasound examination and dobutamine stress test in a series of ten patients observed that the initial part of the artery is intussuscepted in the medial layer of the aorta and is susceptible to spasm and phasic worsening during systole. The remaining possible paths are usually considered benign, although there have been reports associating the septal course with episodes of ventricular tachycardia or ischemia.<sup>33</sup> The anomalous right coronary artery, due to the low systolic pressures in the right chambers, does not seem to produce significant symptoms and the incidence of sudden cardiac death is accordingly low.<sup>28</sup>

Apart from these obvious cases of aberration, the anatomical variations of the coronary arteries, which are mainly asymptomatic and incidental findings in coronary angiography, may have important clinical implications. During catheterization, when only the LAD is opacified, thus leaving a large part of the left ventricle unperfused, the angiographer should not conclude that the LCx is totally obstructed. A more careful manipulation of the catheter could reveal an LCx with a separate ostium, a common variation well described. Angioplasty in such anomalous arteries often imposes a technical challenge.<sup>34</sup> During valvuloplasty there has been reported the compression of an anomalous coronary artery that follows a retroaortic path.<sup>11,12,35</sup> Accidental ligation of an anomalous coronary artery could lead to periprocedural myocardial infarction.

In our study, 123 coronary angiographies out of 5051 patients revealed a primary congenital anomaly, an incidence of 2.44% which is higher than usually reported (Table 4).<sup>17,18,36-47</sup> The study with the largest angiographic population was that of Yamanaka et al,<sup>17</sup> who reported an angiographic incidence of 1.3%. However, since there is no clear-cut classification and widely adopted criteria, there are differences in the methodology of these studies. Some of them include the absence of left main,<sup>17,18,36-39</sup> others exclude it as they regard it to be a common variation and not an anomaly.<sup>40-47</sup> The study with a clearly stated methodology and the strictest criteria for assessing coronary normality/abnormality is that of Angelini et al,<sup>18</sup> who reported an incidence of 5.6% in a population of 1950 patients. Eid et

**TABLE 4. Incidence of Coronary Artery Anomalies (CAAs) in Different Angiographic Populations**

Study	Year	Country	Total	CAAs	%
Engel <sup>36</sup>	1975	USA	4250	51	1.2
Chaitman <sup>41</sup>	1976	CAN	3750	31	0.8
Kimbiris <sup>42</sup>	1978	USA	7000	45	0.6
Donaldson <sup>37</sup>	1983	ENG	9153	82	0.9
Wilkins <sup>46</sup>	1988	USA	10661	95	0.9
Yamanaka <sup>17</sup>	1990	USA	126595	1686	1.3
Topaz <sup>45</sup>	1992	USA	13010	87	0.7
Cieslinski <sup>39</sup>	1993	GER	4016	39	1.0
Kardos <sup>38</sup>	1997	HUN	7694	103	1.3
Angelini <sup>18</sup>	1999	USA	1950	110	5.64
Garg <sup>44</sup>	2000	IND	4100	39	0.9
Pillai <sup>43</sup>	2000	EIRE	11411	60	0.5
Kaku <sup>40</sup>	2000	JPN	17731	56	0.3
Eid <sup>47</sup>	2009	LEB	4650	34	0.7
Present study	2013	GRE	5051	123	2.44

al in their arteriographic study in an adult Lebanese population found an overall incidence of 2.04%, before excluding the absence of the left main coronary artery.<sup>47</sup> In the present study, the Angelini classification system was used, as it is comprehensive and strictly anatomical. Thus, the incidence of 2.44% in this series could reflect the true incidence of primary congenital anomalies in this country.

The incidence of coronary artery disease (CAD) among the patients in our study was 55.48%. With the exception of one case of anomalous LAD from the opposite sinus, the anomalous artery was the only one affected in approximately 10% of the cases. The prevalence of CAD in patients with CAA has been extensively studied. From the first pathological studies, it has been reported that the patients with CAA suffer from accelerated atherosclerosis. Wilkins et al suggested that the anomalous course of the RCA is responsible for the increased incidence of CAD in these vessels.<sup>46</sup> Samarendra has also reported that the anomalous LCx is subject to accelerated atherosclerosis.<sup>48</sup> However, the majority of the studies did not succeed in proving this hypothesis. In fact, they are more inclined towards the conclusion that coronary artery variations are not an independent risk factor for coronary artery disease.<sup>17,44,45,47</sup> In the present study, we also could not find an association between atherosclerosis and CAAs. It seems that atherosclerosis is a diffuse metabolic process that affects equally both normal and anomalous vessels.

One of the most interesting findings in our study was the increased incidence of the anomalous right coronary artery. This can be attributed to a variety of reasons. This

could be an inevitable bias of the retrospective nature of our study. When the ostium of RCA is close to the valve's commissure, it can be misdiagnosed as coming off the adjacent sinus. Secondly, this aberration could be attributed to genetic variations, which are actually quite common. There have been well-described variances in the origin of the conus artery among different geographic populations.<sup>49</sup> Topaz et al found an increased incidence of anomalous right coronary artery.<sup>45</sup> As their population consisted mainly of patients of Hispanic origin, they concluded that this could be the result of genetic variation. Eid et al, have also found an increased incidence of anomalous RCA and attributed it to geographical variation as well.<sup>47</sup> When strict classification criteria were applied, the anomalous RCA was the most common anomaly observed after the absence of the left main.<sup>18</sup> For many years the diagnosis of the CAAs was based exclusively on coronary arteriography, a procedure that is still considered the gold standard.<sup>19</sup> Unfortunately, the visualization of the exact course of the vessels is not always easy, even for the experienced operator.<sup>50,51</sup> The radiation exposure, the use of iodine-contrast agents and the interventional nature of the study limit its effectiveness as a screening test. Nowadays there are other modalities that can serve this purpose. Echocardiography has been proposed as a screening test in young asymptomatic individuals engaged in vigorous activities.<sup>52,53</sup> After implementing protocols for detection of clinically silent CAAs, Lytrivi et al concluded that when specifically sought, a wide range of anomalies can be screened for successfully with echocardiography.<sup>54</sup> The main disadvantage is that only the proximal course can be visualised and that a high degree of suspicion is needed. With computed tomography (CT) the course of the entire vessel can be easily visualized. In a blinded study which compared the efficacy of CT angiography to invasive angiography, the results were surprising. The diagnosis had to be revised in 2 out of 30 patients with CAAs who had undergone invasive angiography in the past.<sup>55</sup> The authors conclude that such a modality permits reliable detection and better classification of CAAs without the invasive nature of the traditional coronary angiography. The magnetic resonance imaging angiography (MRA) has similar specificity and sensitivity,<sup>56,57</sup> without the radiation exposure. Most experts committees consider MRA as the first choice modality for detecting CAAs,<sup>52,53,58,59</sup> especially in the pediatric population.

To the best of our knowledge, this is the first report of CAAs in a large angiographic population in Greece, published in a peer-reviewed journal. We have found an overall incidence of 2.44%, which is higher than usually reported. As there are no accepted guidelines, we followed an anatomical classification which attempted to include the entire spectrum of CAAs, rather base inclusion on more arbitrary criteria which may result in entry bias. As such, the reported incidence might reflect the true incidence of CAAs in Greece.

In accordance with previous studies, the majority of the

coronary anomalies detected did not produce symptoms and were identified as incidental findings during coronary angiography. We also found that CAAs are not associated with accelerated atherosclerosis and are not an independent risk factor for coronary heart disease.

Nevertheless, CAAs are one of the most confusing topics in cardiology practice. The literature is full of case reports and national series, but adequate explanation and understanding with regards to the underlying pathophysiology, the precipitating factors and the clinical implications of each coronary anomaly still remain elusive. The newer imaging modalities promise higher diagnostic accuracy without the need for an interventional approach. There is still a need for a large multi-center registry, so that the true incidence of CAAs in the general population can be recorded, and their pathophysiology clarified and guidelines for their management become implemented.

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