Human & Veterinary Medicine
International Journal of the Bioflux Society

OPEN ACCESS
Research Article

The prevalence of coronary artery disease in the Romanian population evaluated by coronary CT angiography

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Abstract. Objective: Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality worldwide. Coronary CT angiography (CCTA) represents a non-invasive investigation with high sensibility in evaluating coronary artery stenosis and plaque features. The aim of our study is to assess the prevalence and characteristics of CAD evaluated using CCTA in the Romanian population. Material and Method: We retrospectively reviewed 1027 patients who performed a CCTA examination between January 2014 and February 2019. The indications for CCTA were: atypical angina, typical angina with an inconclusive stress test, patients with intermediate/high-risk for major cardiac events. We excluded from this study the patients with significant arrhythmias which made impossible an optimal evaluation of all coronary segments. Results: Our study population included 552 females and 475 males, with a mean age of 58.3 ± 13.8 years. We analyzed 4108 coronary segments and 2566 coronary plaques were depicted. Obstructive CAD was diagnosed in 23.9% patients (552), while 39.8 % of the subjects had complete absence of coronary stenosis. The majority of significant stenoses (20.9%) involved the proximal segment of the left descending artery, this being also the location of the majority of calcified plaques (18.2%).42.3% patients had 0 coronary artery calcium score (CACS), while CACS > 400 was found in 16.7% individuals. There was a significant difference among genders and the degree of coronary stenosis, with males having more than 3 times higher odds of developing significant luminal narrowing in all the coronary arteries ($p<0.001$), except from left main artery (LM) ($p=0.05$). Plaque analysis also showed a significantly higher proportion of overall affected segments and a higher proportion of non-calcified plaques in males ($p< 0.0001$, $p=0.002$). CACS scores were significantly higher among older patients and among males ($p<0.001$, $p<0.001$). Moreover, there was a significant difference regarding the age and the degree of coronary stenosis, older subjects being more likely to be diagnosed with obstructive CAD (coronary stenosis ≥ 50%). We diagnosed 12.1% (122) patients with coronary artery anomalies, including 11 hemodynamically significant anomalies. Conclusion: To the best of our knowledge, this is the first study performed in Romania regarding the burden of cardio-vascular disease studied by CCTA. This brings priceless information regarding the paradigm of CAD in our country.

Key Words: coronary artery disease, CCTA, prevalence, Romania.

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Introduction

Coronary artery disease (CAD) is the most common cause of death in the developed countries, with one of every six deaths in the USA in 2007 being caused by a coronary event (Roger et al 2011).

Several large population studies have been carried out in order to study coronary artery disease, out of which CONFIRM and MESA have parts that account for the differences between ethnicities, while other authors have studied the situation on a national level (including the represented characteristic ethnicities). Furthermore, a substantial number of studies concern individual traits that might influence the development of CAD.

The most commonly used and validated clinical scores which aim to classify patients according to their cardio-vascular risk are the Updated Diamond-Forrester method and the Duke clinical score, which have been shown to overestimate the prevalence of obstructive CAD, particularly in low-prevalence populations (young people, women) (Takamura et al 2016, Almeida et al 2016, Fujimoto et al 2015, Jensen et al 2012, Genders et al 2012, Lecher et al 2018).

The two scores take into account sex, age, clinical symptoms and risk factors for cardiovascular disease in order to predict the pre-test probability for CAD.

The European Society of Cardiology recommends performing coronary CT angiography (CCTA) in patients with intermediate pre-test probability (15-50%), using CTA as the first-line option due to its high negative predictive value tool for excluding CAD, as well as a second-line option for patients with high pre-test probability with inconclusive stress tests (Matalescot et al 2013). The UK guidelines recommend CCTA as the first-line option

for stable CAD, typical and atypical angina and non-anginal chest pain with alteration of the ECG (Oikonomou et al 2018). For patients in which CAD is excluded, there is a minimal risk of future cardiac events (Ghosh et al 2010), with the risk of developing major adverse cardiac events (MACE) of less than 1% up to 7 years (Cheezum et al 2012, Andreini et al 2012).
For patients with diffuse non-obstructive CAD it is recommended to investigate a second set of biomarkers, and provided they are also negative, the patient can be safely discharged (Thomas et al 2015), with the recommendation of secondary preventive therapy. As already mentioned, since non-obstructive CAD is the bad omen of future acute coronary events (Bellasi et al 2007, Anderson et al 2007, Hong et al 2007, Sipahi et al 2010, Bugiardini et al 2006, Raggi et al 2004), CCTA facilitates diagnostic and therapeutic decision-making.
The indication to perform CCTA in patients with suspicion of CAD is not yet consistent across guidelines provided by different associations and the modality to stratify patients according to their risk is not flawless.
Nevertheless, CCTA has its limits and it is not as widespread as it could be, thus further investigations on its potentials are warranted.
The aim of our study is to assess the prevalence and characteristics of coronary artery disease in the Romanian population, evaluated using CCTA. To the best of our knowledge, such a study has not been carried out in our country.

Material and method

Study population

This single center cross-sectional study was conducted using data from the clinical database of Hiperdia - Affidea Imaging Centre, Cluj-Napoca, Romania. Institutional review board approval was obtained for this study.
We retrospectively reviewed 1090 consecutively patients who underwent CCTA between January 2014 and February 2019 in our institution. The indications for CCTA were: atypical angina, typical angina with an inconclusive stress test, patients with intermediate/high-risk for major cardiac events. We excluded from this study the patients with significant arrhythmias which made impossible an optimal evaluation of all coronary segments (n=63 patients). Beside this exclusion criterion, patients with severe renal failure, documented contrast allergy or pregnant women did not perform the CT examination. Finally, 1027 subjects fulfilled the inclusion criteria.
The study was conducted according to the Declaration of Helsinki. It was approved by the institutional Ethical Committee. Informed consent was obtained from all individual participants included in this study.

Scan protocol

All CCTA scans were performed with a 64-sliced multi-detector CT (Sensation 64, Siemens, Forchheim, Germany). The scanning parameters were: slices/collimation 64/0.6 mm, tube voltage 120 kv, 850 mAs, gantry rotation time 330 ms, pitch 0.2, effective slice thickness 0.75 mm and reconstruction increment 0.4 mm. Patients with a heart-rate > 70 bpm received premedication with oral beta-blockers 1-hour prior the examination. Short-acting nitroglycerine sublingual spray was administered to all patients for coronary vasodilatation.
First, a non-contrast enhanced scan was performed in order to assess the coronary artery calcium score (CACS). This scan was followed by the coronary computed tomography angiography (CCTA) to evaluate the coronary artery lumen and to characterize the atherosclerotic plaques. A bolus of 80 ml of iodinated contrast medium was administered intravenously at 5 ml/sec, followed by 40 ml of saline injected at the same rate. After the acquisition, the images were transferred to a dedicated workstation for post-processing, which included multiplanar reconstructions (MPR), maximum intensity projections (MIP) and volume rendering images (VRT).
All CCTA images were assessed by an experienced radiologist who was blinded to the study. CACS was calculated using a semi-automatically software, according to the Agatston method. Plaque composition was classified as: calcified, non-calcified or mixed, with coronary calcified plaque being defined as any structure with a density ≥130 HU.
Coronary atherosclerotic lesions were quantified for stenosis by visual estimation. Coronary artery stenosis was classified as no stenosis, stenosis ≤ 50%, stenosis between 50-70%, stenosis ≥ 70% and total occlusion of a segment.

Statistical analysis

Continuous variables with normal distribution were expressed as means ± standard deviation, those with non-normal distribution as median with 25th-75th percentile range. Normality was tested with the Kolmogorov-Smirnov test. Categorical variables were expressed as counts and percentages. Chi square test was used to compare differences in frequencies of categorical variables. ANOVA and unpaired t-tests were employed to compare means of continuous variables. Whenever the distribution of continuous data was not normal, non-parametric Mann-Whitney test was used for comparison. Multivariate analysis (binary logistic regression model – enter method) was performed to identify whether gender can be considered as independent predictor of significant coronary stenosis. When appropriate, a 95% confidence interval (CI) was calculated. For all comparisons, a p value of <0.05 was considered statistically significant. Statistical analysis was performed with MedCalc for Windows, version 14.8 (MedCalc Software, Ostend, Belgium).

Results

Our study population included 1027 patients. The percentages of the individuals regarding the gender were 53.7% females (552 subjects) and 46.3% males (463 subjects). The mean age of our study group was 58.3 ± 13.8 years. We analyzed a total of 4108 coronary segments. The number of coronary plaques depicted by CCTA was 2566.
Table 1 summarizes the prevalence of coronary stenosis diagnosed in each coronary artery segment. The majority of significant stenoses (>50% luminal narrowing) involved the proximal segment of the left descending artery (LAD) (20.9%). However, total occlusion was more frequent in the mid segments of both left descending artery and right coronary artery (RCA (21.7%). The distal segments of all the three coronary vessels were the least affected by atheromatous deposits.
Regarding the prevalence of coronary artery disease per whole heart, we considered obstructive CAD if there was stenosis ≥ 50% affecting at least one coronary artery. We diagnosed

Table 1. Prevalence of coronary artery stenosis per segment

Coronary segment	No stenosis	Stenosis < 50%	Stenosis 50-70%	Stenosis >70%	Total occlusion
LM	780 (10.2 %)	217 (11.6 %)	25 (5.6 %)	5 (2.2%)	0 (0%)
LAD					
Proximal segment	518 (6.7 %)	351 (18.8%)	104 (23.5 %)	45 (20.2%)	9 (13.0 %)
Mid segment	622 (8.1%)	255 (13.6 %)	87 (19.7%)	48 (21.5%)	15 (21.7%)
Distal segment	901 (11.7 %)	100 (5.3 %)	18 (4.1%)	6 (2.7 %)	2 (2.9 %)
Cx					
Proximal segment	729 (9.5 %)	232 (12.4%)	45 (10.2 %)	19 (8.6 %)	2 (2.9 %)
Mid segment	821 (10.7%)	150 (8.0 %)	32 (7.2%)	15 (6.8 %)	9 (13.0%)
Distal segment	942 (12.3%)	56 (3.0%)	17 (3.9%)	8 (3.6%)	4 (5.8%)
RCA					
Proximal segment	713 (9.3%)	233 (12.4%)	46 (10.4 %)	29 (13.0 %)	6 (8.8 %)
Mid segment	779 (10.2%)	168 (9.0 %)	35 (7.9%)	30 (13.4 %)	15 (21.7%)
Distal segment	860 (11.3%)	109 (5.9%)	33 (7.5%)	18 (8.0 %)	7 (10.2 %)

Abbreviations: LM- left main artery. LAD- left descending artery. Cx – circumflex artery. RCA – right coronary artery
Results are presented as number (%)

Table 2. Distribution of coronary plaques per segment

Coronary segment	No plaque	Non-calcified/ mixed plaque	Calcified plaque
LM	779 (10.1 %)	24 (7.0 %)	224 (10.0 %)
LAD			
Proximal segment	520 (6.7 %)	102 (30.0%)	405 (18.2 %)
Mid segment	653 (8.5%)	62 (18.2 %)	312 (14.0%)
Distal segment	906 (11.8 %)	9 (2.7%)	112 (5.0%)
Cx			
Proximal segment	728 (9.6%)	26 (7.6%)	273 (12.3 %)
Mid segment	821 (10.6%)	21 (6.1 %)	185 (8.3%)
Distal segment	942 (12.2%)	8 (2.3%)	77 (3.5%)
RCA			
Proximal segment	716 (9.3%)	34 (10.0%)	277 (12.4 %)
Mid segment	780 (10.1%)	35 (10.2 %)	212 (9.6%)
Distal segment	859 (11.1%)	20 (5.9%)	148 (6.7%)

obstructive CAD in 23.9% patients (552). 39.8 % (409) of the subjects had complete absence of coronary stenosis, while 2.6 % (27) individuals had occlusion of at least 1 coronary segment. Furthermore, we analyzed the distribution of coronary plaques in all coronary artery segments (Table 2). Calcified plaques were more common in the proximal segments of coronary arteries, with 18.2% of all calcified plaques being identified in the proximal segment of LAD. Also, the majority of the non-calcified and mixed atherosclerotic lesions involved the proximal segment of LAD (30%). The distal segments were more often spared from atherosclerosis.

A CCTA examination also includes calculating the coronary artery calcium score (CACS). Therefore, we classified our study population into 5 groups according to their CACS. Our results show that 42.3% of the subjects who performed a CCTA examination had 0 calcium score, which means no calcified plaques in any coronary artery. A percentage of 8.8% of the patients had CACS between 1- 10, 16.8% individuals were diagnosed with a CACS between 11-100, 15.4% of the subjects received a total CACS between 101-400 and finally a CACS > 400 was found in 16.7% of the total population.

We performed univariate analysis to determine if there is any association between the CACS and the age and the gender, respectively (Table 3). Our findings indicate that older patients had significantly higher CACS ($p<0.001$). Moreover, there was a significant difference among the CACS of the two genders, male subjects being more likely to have higher CACS ($p<0.001$).

Table 4 summarizes the results regarding the association between gender, age and the severity of coronary artery disease evaluated at CCTA. We found significant differences in the frequencies of obstructive coronary stenosis involving LAD, Cx and RCA among the two genders ($p<0.001$, $p<0.001$, $p<0.001$). However, no notable difference was identified among the females and the males in respect to LM stenosis ($p=0.08$). Obstructive CAD (at least one coronary artery with stenosis ≥ 50%) was more frequently diagnosed among male subjects (34.8% males vs. 15.4% females, $p<0.001$). Our results also show that three vessel disease (three vessels with stenosis>70%) affected slightly more males (3.2 % vs. 0.7%, $p=0.0008$). Furthermore, plaque analysis showed a significantly higher proportion of overall affected segments in males (1594 vs 972, $p< 0.0001$) with a higher proportion of non-calcified plaques in males compared to females (62% vs 42.4%, $p=0.002$). Regarding the age, patients diagnosed with obstructive CAD were significantly older than people with non-obstructive coronary stenosis ($p<0.001$, regardless the coronary artery). Also, older people were more likely to develop 3 vessel diseases ($p<0.001$). However, our findings show that patients depicted with non-calcified/mixed plaques were significantly younger (53.14 ± 9.43), while calcified plaques would rather develop among older people (65.54 ±10.63).

After adjustment for age, there remained a strong association between male sex and luminal narrowing ≥ 50% in LAD, Cx and RCA. Male patients had more than 3 times higher odds of developing obstructive stenoses on any of these 3 vessels (Table 5). Our study population also included patients with previous known coronary artery disease. Therefore, we evaluated the

Table 3. Association between age, gender and coronary artery calcium score (CACS)

Variable	CACS					
	0	**1-10**	**10-100**	**100-400**	**>400**	**p**
Age	49.2±12.0	58.1±9.2	62.6±10.6	65.2±9.9	71.2±9.44	<0.001
Gender						
Male	143 (33 %)	40 (44.4%)	81 (46.8 %)	91 (57.6%)	120 (69.8 %)	<0.001
Female	291 (67.0%)	50 (55.6 %)	92 (53.2%)	67 (42.4%)	52 (30.2%)	

*Statistically significant p<0.05; Results are presented as mean±SD, or number (%)

Table 4. Association between gender, age and coronary artery CT findings

Variable	Female	Male	p	Age	p
LM			0.08		<0.001*
Stenosis < 50%	541 (98.0 %)	456 (96.0%)		59 [48-67]	
Stenosis ≥ 50%	11 (2.0%)	19 (4.0 %)		71.5 [65.5-76.25]	
LAD			<0.001*		<0.001*
Stenosis < 50%	485 (87.9 %)	334 (70.3%)		58 [47-65]	
Stenosis ≥ 50%	67 (12.1%)	141 (29.7 %)		68 [59-75]	
Cx			<0.001*		<0.001*
Stenosis < 50%	527 (95.5 %)	411 (86.5%)		59 [48-66.25]	
Stenosis ≥ 50%	25 (4.5%)	64 (13.5%)		70 [62-77.5]	
RCA			<0.001*		<0.001*
Stenosis < 50%	513 (92.9 %)	392 (82.5%)		58 [48-66]	
Stenosis ≥ 50%	39 (7.1%)	83 (17.5 %)		70 [62-77]	
Three vessel disease			<0.001*		<0.001*
Yes	4 (0.7 %)	15 (3.2%)		59 [49-67]	
No	548 (99.8%)	460 (96.8%)		70 [63-77]	
Plaques	972	1594	<0.001*		<0.001*
Non-calcified/Mixed	98 (10.1 %)	243 (15.2%)	0.002*	53.14 ±9.43	
Calcified	874 (89.9%)	1351 (84.8 %)		65.54 ±10.63	

*Statistically significant p<0.05; Results are presented as number (%),median [25th-75th percentile] or mean±SD

Table 5. Association between significant coronary artery stenosis (>50%) and male gender

Coronary stenosis ≥ 50%	Male sex (unadjusted)		Male sex (age-adjusted)	
	OR (95% CI)	**P**	**(95 % CI)**	**P**
LM	2.05 (0.96 – 4.35)	0.06	2.08 (0.97 – 4.49)	0.05
LAD	3.05 (2.21– 4.21)	<0.001*	3.62 (2.57– 5.10)	<0.001*
Cx	3.28 (2.03– 5.30)	<0.001*	3.73 (2.25– 6.16)	<0.001*
RCA	2.78 (1.86– 4.16)	<0.001*	3.21 (2.10– 4.93)	<0.001*

*Statistically significant p<0.05

frequency of coronary artery bypass grafts (CABG) and coronary stents. 57 patients (5.5%) had CABGs with 52.6% subjects having saphenous vein (SV) grafts and 47.4% individuals having left internal mammary artery (LIMA) graft. There was a significant difference between the patency of the two types of grafts (96.3% patent LIMA grafts vs. 33.3% patent SV grafts, p<0.001). Coronary stents were found in 49 patients (4.8%), with the majority of them (91.8%) being patent.

Another aspect of coronary artery anatomy that was evaluated was coronary dominance. 87.1% patients had right coronary dominance, while left coronary dominance was identified in 7.2% individuals and 5.7% patients were found having codominance. There was no significant difference among genders regarding the coronary dominance (p=0.09).

Last but not least, we assessed the presence of coronary artery anomalies (CAA). In total, 122 CAAs were identified (12.1% patients). We classified the CAAs according to their hemodynamic significance and we depicted 111 (91.0%) benign CAAs and 11 (9.0%) malignant CAAs. Considering the anatomical criteria, we discovered 26 (21.3%) anomalies of origin and course and 96 (78.7%) anomalies of intrinsic coronary arterial anatomy, with two-third of CAAs being myocardial bridges.

Discussion

Our study aimed to provide a detailed fresco of the burdensome coronary artery disease phenomenon in a representative population from Romania.

Atherosclerosis (ATS) is a systemic chronic inflammatory process which has been shown to develop from infancy. Plaque formation ranges from an initial small lesion which contains foam cells to a calcified one and finally, to a fibrotic plaque without lipid core (Cai et al 2002). Several studies have proved that acute coronary syndromes (ACS) occur in asymptomatic patients (Khosa et al 2013), precipitated by rupture, erosion or ulceration (Hausleiter & Maier 2006) of a non-stenotic plaque. This raised the concern that assessment of only the vessel lumen by invasive coronary angiography (ICA) could underestimate the presence of the so-called "vulnerable plaques" which might undergo positive remodeling, rendering the lumen normal in the early stages and revealing only 1-5% of disease (Nissen & Yock 2001), thus allowing the progression of the disease. Regarding this aspect, several investigations of the coronary plaque burden and plaque subtypes have been gaining attention, among which CCTA.

The development of CAD seems to differ as pertaining to some inherent, immutable personal factors (sex, familial history, age) and other acquired factors (hypercholesterolemia, diabetes mellitus, hypertension, etc.). The complicated combination of certain factors and the effects they may have on one another provide some recognizable patterns and some that are not yet fully understood.

As pertaining to age, some authors (Faletra et al 2009) have shown that increased age is associated with the presence of more plaques. On the other hand, the older the patient, the bigger the CACS, not reflecting only the true plaque burden, but rather the plaques' natural evolution (Stary et al 1995, Detrano et al. 1996, Mautner et al 1994). Our study sample reflects the same pattern, with older patients having a significantly higher CACS ($p<0.001$).

There is a "female advantage" in the development of CAD, as Makaryus well puts it (Makaryus et al 2015), women developing CAD almost a decade later in life (Lansky et al 2012), but the incidence CAD in postmenopausal women reaches that of men at around 75 years-old (Lerner& Kannel 1986) and it can even exceed that of men according to the Framingham study (Hayward et al 2000, Kannel 2002). The majority of authors posits that estrogen plays a protective role in the premenopausal women, but there have been surprising reports that show that combination hormone therapy in post-menopausal women is associated with increased risk of cardio-vascular disease (Rossow et al 2002, Manson et al 2003, Wassertheil-Smoller et al 2003, Hulley et al 1998), proving that one hormone is not a one-size-fits-all solution. Furthermore, women also seem to have smaller vessel size, less collateral flow, lower coronary flow reserve, more vascular stiffness (Pepine et al 2006, Jacobs 2009), and increased endothelial dysfunction (Taddei et al 1996).

On the other hand, females have an overall greater mortality rate (Lloyd-Jones et al 2009), likely due to the atypical presentation which often deflects evaluation towards non-cardiac causes (Shaw et al 2010) and a less aggressive treatment (Bellasi et al 2007). With more advanced disease in females, comes a higher risk of death (Grunau et al 2014), more adverse events at 6 months (Dey et al 2009), more hospitalizations for angina and heart failure compared to men (Lloyd-Jones et al 2009, Dey et al 2009).

The sex of the patient has also been shown to be correlated with the predominant type of plaques. Since "vulnerable plaques" (usually non-calcified, non-stenotic) are the primary culprit involved in the precipitation of ACS, plaque characterization is gaining a lot of focus. Even though males have been proved to have a higher CACS (Otaki et al 2015, Makaryus et al 2015, Blaha et al 2009), and a higher total burden of plaques (Otaki et al 2015), it is in fact women who have the majority of the non-calcified plaques (Plank et al 2014). Our findings are partly in concordance with these findings, male subjects having a higher likelihood of a greater CACS ($p<0.001$). In contrast, we found a higher proportion of non-calcified plaques in males (62% vs. 42.4%, $p = 0.002$) compared to females. These results are nevertheless in line with the results of Rivera (Rivera et al 2009) and Grunau (Grunau et al 2014), the latter pondering if the results in increased number of certain plaque subtypes in men isn't in fact a selections bias, since men have an increased total plaque burden. Lastly, we also found that the majority of three-plaque disease (with >70% stenosis) is more common in males (3.2% vs. 0.7%, $p = 0.008$).

Nevertheless, Sheen Yen Tay (Tay et al 2017) raises the problem of adjacent plaques in different stages of evolution, showing that patients with high CACS should likely have a similar charge in non-calcified plaques (Schmermund & Erbe, 200l). This situation is posing a conundrum, forcing scientists to direct efforts into defining CAD in relation to the sex of the patient, as well as evaluating plaque structure.

Generally, the CACS is subdivided in 5 categories (absolute values in Agatston units: 0, 1-10, 11-100, 101-400, >400), which translates into the calcification grade (none, minimum, mild, moderate, severe). These categories are used to estimate the risk for a cardiovascular event in an age, sex and race-matched group, values expressed in percentiles that are calculated in general population databases, mainly the Multi-Ethnic Study of Atherosclerosis (<25th percentile, 25th-50th percentiles, 50th-75th percentiles, 75th-95th percentiles, >95th percentile) (MESA) (McClelland et al 2006).

Even though CACS can independently predict CAD (Mitsutake et al 2006), coronary artery calcium score value alone is at times inconclusive, since up to 16% of significant stenosis diagnosed on ICA had no calcification on 64-MDCT (Rosen et ak. 2009) and up to a third of asymptomatic patients with a CACS = 0 may have non-calcified plaques (Plank et al 2014). Also, the CONFIRM registry shows that 13% of patients with CACS = 0 had non-obstructive CAD, while 3.5% had significant obstructive CAD (Villines et al 2011). In asymptomatic and symptomatic patients with suspected CAD, adding CACS increases the prediction value of future ACS (Ghosh et al 2010, Detrano et al 2008, Greenland et al 2004), although other authors disagree (Lemer et al 1986).

The hemodynamic consequence of plaques is also found in relation to the sex of the patients. It seems that women have more non-obstructive CAD (<50% stenosis), with obstructive CAD in pre-menopausal women accounting for only one third of cases compared to men in the same age group (Lemer et al 1986). The high rate of non-obstructive CAD in females and difference in remodeling (Taylor et al 2010, Hausleiter et al 2006) leads to investigation of an alternative diagnosis, thus delaying appropriate intervention. In patients over the age of 75, regardless of sex, the incidence of obstructive CAD becomes similar (Lemer et al 1986). Furthermore, non-obstructive CAD in women is tied to more adverse effects (Hang et al 2012). In our study, male patients' odds of developing obstructive stenoses on any of the 3 coronaries were 3 times higher, even after adjustment for age. Interestingly, it was shown that symptomatic patients without known CAD diagnosed by CCTA with significant stenosis (>50%) had a higher mortality even after adjustment for age, gender, classical cardiac risk factors and CAC (Ostrom et al 2008).

On the other hand, the development of ACS in asymptomatic patients correlates with higher morbidity, higher mortality and higher frequency of other ACS (Fleg et al 1990, Deedwania et al 2001, He et al 2000), and actually the prevalence of CAD in asymptomatic high-risk patients is high (Plank et al 2014).

As far as treatment is concerned, statins have been proven to be effective in patients with extensive or high-risk plaques (Thomas et al 2015), with non-calcified plaques having a better response to medical therapy (Nicholls et al 2007) and they should be taken into account in patients with CACS greater than 0 (Divakaran et al 2014). Should the medical therapy fail, PCI or CABG are the final therapeutic strategies, especially in patients with higher non-calcified plaque burden, a status which inflicts a worse outcome with regard to these invasive therapies (Plank et al 2014, Otaki et al 2012) . Our study shows that 5.5% of patients underwent CABG intervention and 4.8% had a PCI performed. LIMA grafts represented the majority of patent grafts, while an overwhelming number of PCIs were patent (91.8%).

As all methods, regardless of the passion with which CCTA is promoted, this investigation has its proved limitations that have to be taken into consideration. Firstly, due to its high negative predictive value and low sensitivity, CTA cannot estimate the functional impact of stenosis, with almost half of patients with significant stenosis on CTA not showing signs of ischemia (Blankstein et al 2010). Also, CCTA is limited in detecting obstructive CAD in patients with calcium scores >600, high pre-test probability and known CAD (Arbab-Zadeh et al 2012), while overestimating the CACS when compared to intravascular ultrasound (Leber et al 2006).

Finally, we report several limitations to our own study, which should entail future investigations. The study was a retrospective one and enrolled patients whose investigations were performed in a university-related clinic, which attracts a high number of patients with complicated pathology. Secondly, since the clinic is a privately owned one, not all clinical data were available. Thus, the medical treatment and the correlation with the invasive angiography results was not studied. Also, our study includes both patients with and without plaques, resulting in an expected selection bias, given that men have a higher total plaque burden.

Conclusion

This study brings priceless information regarding the paradigm of CAD in Romania, the majority of which is in line with previous studies.

Our study proves once again that there is a "female advantage" in play, with males having a higher atherosclerotic burden (higher CACS, higher proportion of non-calcified plaques) and that they had a higher frequency of obstructive coronary stenosis on all coronary arteries (except LM). Also, obstructive coronary stenosis was diagnosed in older patients, regardless the involved artery. However, non-calcified/mixed plaques, which tend to be more vulnerable, were more likely to develop among younger subjects.

Acknowledgement

The authors would like to thank Oana Ţenter for proofreading the article.

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Citation	Popa LE, Molnar A, Rancea R, Feier DS, Lebovici A, Zaharie A, Petresc B, Buruian MM. The prevalence of coronary artery disease in the Romanian population evaluated by coronary CT angiography. HVM Bioflux 2019;11(2):78-86.
Editor	Antonia Macarie
Received	16 April 2019
Accepted	6 May 2019
Published Online	23 May 2019
Funding	None reported
Conflicts/ Competing Interests	None reported