



Assessment of Calcified Carotid Artery Plaques on Digital Panoramic Radiographs of Middle-aged and Older Asymptomatic Persons in a Turkish Subpopulation and Associated Risk Factors

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Abstract

Background: Vascular calcifications caused by atherosclerosis are frequently observed, especially in aortic and carotid arteries, with large and elastic characteristics. Early detection of calcification in these arteries can play an important role in reducing the clinical pathologies where atherosclerosis may cause, such as stroke and long-time disability.

Objectives: The aim of the present study was to determine the prevalence of calcified carotid artery plaques (CCAPs) on digital panoramic radiographs (DPR) and its association with gender, age, as well as 3 risk factors of cerebrovascular attack including hypertension, cardiovascular diseases, and diabetes mellitus.

Materials and Methods: In this retrospective study, a total of 500 DPRs of subjects 45 years old and older (248 females and 252 males) were evaluated. All the subjects had been referred to the Faculty of Dentistry, Necmettin Erbakan University, Konya, Turkey, during 2014 - 2017 for a routine dental examination. Socio-demographic variables, as well as medical anamnesis, were obtained from the participants and medical records. The radiographs were grouped according to gender, age groups (45 - 60 years old and 61 years old and older), and associated risk factors (diabetes mellitus, hypertension, and cardiovascular diseases).

Results: Of 500 DPRs, 243 (48.6%) were noted to have CCAPs. The 243 individuals who had CCAPs consisted of 119 males (49.0% of all males) and 124 females (51.0% of all females). Of the subjects aged 45 - 60 years old, 87 individuals (17.4%) showed carotid artery calcifications on their DPRs while 156 subjects (31.2%) aged 61 years old and older showed carotid calcification. There were significant differences between age groups, hypertension, cardiovascular diseases, and the prevalence of CCAP, which increased ($P < 0.01$). As the associated risk factor increased, the prevalence of bilateral CCAP also increased ($P < 0.01$).

Conclusions: The existence of bilateral calcified carotid artery plaques on digital panoramic radiographs has a higher prevalence in the subjects who had at least two associated risk factors and older; however, their detection is important to orient the diagnosis and prevention of diseases in asymptomatic high-risk patients.

Keywords: Atherosclerosis, Carotid Artery, Calcification, Diabetes Mellitus, Hypertension, Panoramic Radiography, Risk Factor, Stroke, Vascular Calcification

1. Background

Atherosclerosis is a progressive, inflammatory, and degenerative disease that can cause peripheral vascular disease, coronary artery disease, and ischemic cerebrovascular disease (1). After the accumulation of plaques, constriction of the vascular space and weakening of the underlying media layer occur. The atheromas form the basis of atherosclerosis by being located in the intima layer of the arteries. It consists mainly of lipids and fibrous tissue that accumulate and become calcified on the carotid artery wall and can easily be detected on routine digital panoramic ra-

diographic (DPR) examinations (2). Early detection of calcifications in these arteries can play an important role in reducing the clinical pathologies that atherosclerosis may cause such as stroke and long-time disability (3).

Previous studies have shown that the presence of bilateral calcification is significantly greater than unilaterally (4, 5). Because different arteries in the same individual are exposed to the same etiology, the development of atherosclerotic plaques can also progress bilaterally in the right and left atherosclerosis of the carotid arteries, resulting in the formation of atherosclerotic plaques due to the

similarity of total vessel wall volume and plaque calcification. The most important risk factors for CCAP are hypertension, age, sex, diabetes mellitus, hyperlipidemia, and cigarette smoking (3). The cause of CCAP rates varies from population to population and these risk factors are determined at different frequencies in communities (3, 6).

CCAPs are interpreted as nodular, point, and vertical linear radiopacities that can be seen on the DPR under the mandibular angulus and adjacent to the C3-C4 intervertebral junction level (7). Friedlander and Lande (7) first reported the frequency of carotid atherosclerosis on panoramic radiographs and believed they could be a useful way to identify patients at risk for stroke. CCAPs can be detected with DPRs taken during routine dental examinations, and the detection of calcifications by DPR is emphasized in many studies. In recent years, CCAP has been investigated using DPR in diabetic patients, hypertension patients, postmenopausal women, renal transplant patients, serum levels of low-density lipoprotein (LDL), smoking habits, heavy alcohol intake, obstructive sleep apnea patients, radiotherapy patients, periodontitis, and elderly patients (6, 8). While the prevalence of CCAP in DPRs documented in the literature varies between 3% and 5% of patients without systemic disease (9-12), it ranges between 20% and 38.8% in populations with known risk factors for atherosclerosis (diabetes, menopause, metabolic abnormalities, cardiovascular disease, chronic renal disease, and hypertension) (13-15). In a recent study, it was found that the prevalence of CCAP on panoramic images of 657 male patients with ≥ 45 years of age having a diagnosis of gout was 31% (16).

2. Objectives

In this study, we aimed to determine the prevalence of CCAPs on DPRs of middle-aged and older asymptomatic persons in a Turkish subpopulation and its association with gender, age, and three risk factors of cerebrovascular attack including hypertension, cardiovascular diseases, and diabetes mellitus.

3. Materials and Methods

3.1. Subjects and Sample Size

This retrospective study was approved by the Human Research Ethics Committee of the Faculty of Dentistry, Necmettin Erbakan University, Konya, Turkey (Decision No: 2017.11). Five hundred subjects over 45 years (252 males and 248 females) who applied to the Necmettin Erbakan University Faculty of Dentistry, Konya, Turkey, between

2014 and 2017 and received the digital panoramic radiographs (DPR) for routine dental examinations were retrospectively examined. The DPRs were chosen from the archive of the Necmettin Erbakan University Dentistry Faculty, Oral and Maxillofacial Radiology Department, Konya, Turkey, according to gender, age, and associated risk factors. The DPRs of patients aged 18 years or older showing clearly carotid artery bifurcations on both sides were included in the study. Missing records, radiographs with a poor diagnostic quality or those not including C3 and C4 and individuals with craniofacial conditions, degenerative disease, infection, tumor, traumatic or congenital anomalies or syndromes were excluded from the study. Socio-demographic variables and medical anamnesis were obtained from the participants' medical records.

The original sample size of 500 subjects was determined by a power software based on the assumption of a 37% prevalence based upon a previous study (17) for CCAP, with a 95% power and a 2-sided alpha of 0.05. The estimated sample size was 385 subjects. Considering 23% possible loss to follow-up, 500 subjects were decided to recruit for sample size. There were no missing values.

3.2. Study Design

All the DPRs were obtained with Veraviewepocs 2D CP and 3D R100 P (J Morita MFG Corp., Kyoto, Japan) at 5 to 10 mA and a peak kV between 60 and 80 depending on the subject's jaw size. The radiographs were obtained according to the manufacturer's directions. The radiographs were grouped according to gender, associated risk factors (diabetes mellitus, hypertension, and cardiovascular diseases), and age groups. The radiographs were divided into two groups based on age: 45 - 60 years old and 61 years old or older. The associated risk factors were grouped as (0) no associated risk factor, (1) one associated factor, (2) at least two associated factors. Table 1 shows the distribution of the sample according to gender, associated risk factors, and age.

3.3. Diagnosis of CCAP

We diagnosed CCAPs as nodular radiopacity at or below the intervertebral space between C3 and C4 (Figure 1). For the differential diagnosis of CCAPs, other cervical calcifications such as lymph node calcification, calcified triticeous cartilage, calcified thyroid cartilage, and phleboliths were excluded according to Carter's (5) and Among et al.'s (18) studies. The diagnosis of CCAPs on DPRs was performed by 7 years experienced oral and maxillofacial radiologist (GM) in a darkroom. The assessment of reproducibility was performed on a subsample of 50 randomly selected radiographs. For this purpose, the same investigator examined

Table 1. The Distribution of Sample Size According to Age Groups, Gender, and Associated Risk Factors as Number and Percentage

	N (%)
Age group	
45 - 60 years old	228 (45.6)
≥ 61 years old	272 (54.4)
Gender	
Female	248 (49.6)
Male	252 (50.4)
Diabetes mellitus	
No	261 (52.2)
Yes	239 (47.8)
Cardiovascular diseases	
No	317 (63.4)
Yes	183 (36.6)
Hypertension	
No	312 (63.6)
Yes	182 (36.4)
Associated risk factors	
None	177 (35.4)
One	139 (27.8)
Two	184 (36.8)

the radiographs twice in a period of one month, and the intra-observer variability was calculated.

3.4. Data Analysis

The IBM Statistical Package for the Social Sciences, version 21.0 (IBM Corp., Armonk, N.Y., USA) was used for data statistical analyses. The significance level of 0.05 (or 5%) was considered. The categorical variables were represented as the number (n) and percentage (%) values and compared using the chi-square test. The intra-observer agreements were assessed by calculating Kappa values.

4. Results

The Kappa values for intra-observer reliability were 0.91, 0.89, and 0.93 for the right, left, and bilateral CCAPs, respectively.

The study population consisted of 252 males and 248 females with a mean age of 62.16 ± 9.32 (range: 45 - 89 years) at the time of DPRs taken. There was no significant difference in mean age between males (63.01 ± 9.80 years) and females (61.29 ± 8.75 years) ($P > 0.05$).

Of the 500 individuals, 243 (48.4%) were detected to have CCAP on DPRs. In the right and left sides, 175 (35.0%)

and 180 (36.0%) CCAP were found, respectively. Bilateral CCAP was observed in 111 (22.2%) DPRs (Figure 2). 243 individuals had CCAPs consisting of 119 males (49.0% of all males) and 124 females (51.0% of all females). The prevalence of CCAPs was not significantly different according to gender ($P > 0.05$) (Table 2).

Table 2. The Distribution of Subjects According to the Prevalence of CCAP, Age Groups, Gender, Associated Risk Factors, and P Value

	CCAP		P Value
	No (N: 257) (%) ^a	Yes (N: 243) (%) ^a	
Age group			0.000 ^b
45 - 60 years	141 (28.2)	87 (17.4)	
≥ 61 years old	116 (23.2)	156 (31.2)	
Gender			0.591
Female	124 (24.8)	124 (24.8)	
Male	133 (27.0)	119 (23.4)	
Diabetes mellitus			0.089
No	144 (28.8)	117 (23.4)	
Yes	113 (22.6)	126 (25.2)	
Cardiovascular diseases			0.005 ^b
No	178 (35.6)	139 (27.8)	
Yes	79 (15.8)	104 (20.8)	
Hypertension			0.000 ^b
No	186 (37.2)	132 (26.4)	
Yes	71 (14.2)	111 (22.2)	
Associated risk factors			0.000 ^b
None	114 (22.8)	63 (12.6)	
One	68 (13.6)	71 (14.2)	
Two	75 (15.0)	109 (21.8)	

Abbreviation: N, numbers of subjects.

^a%; percent of subjects.

^b $P < 0.01$

Subjects with CCPA were on average 64.38 ± 9.41 years-old, whereas the subjects without CCPA were on average 60.05 ± 8.75 years-old. Of the subjects aged 45-60 years, 87 individuals (17.4%) showed carotid artery calcifications on their DPRs while 156 subjects (31.2%) aged 61 years or older showed carotid calcification. The distribution of CCAPs according to age groups, is given in Table 2. A highly significant difference was detected between the two age groups of subjects regarding the prevalence of CCAPs ($P < 0.001$) (Table 2).

While 177 subjects (35.4%) had no associated factor, 323 subjects (64.6%) had at least one associated risk factor. In 243 subjects with CCAP, 63 subjects (25.9%) had no associated risk factor, 71 (29.2%) had one associated factor, and

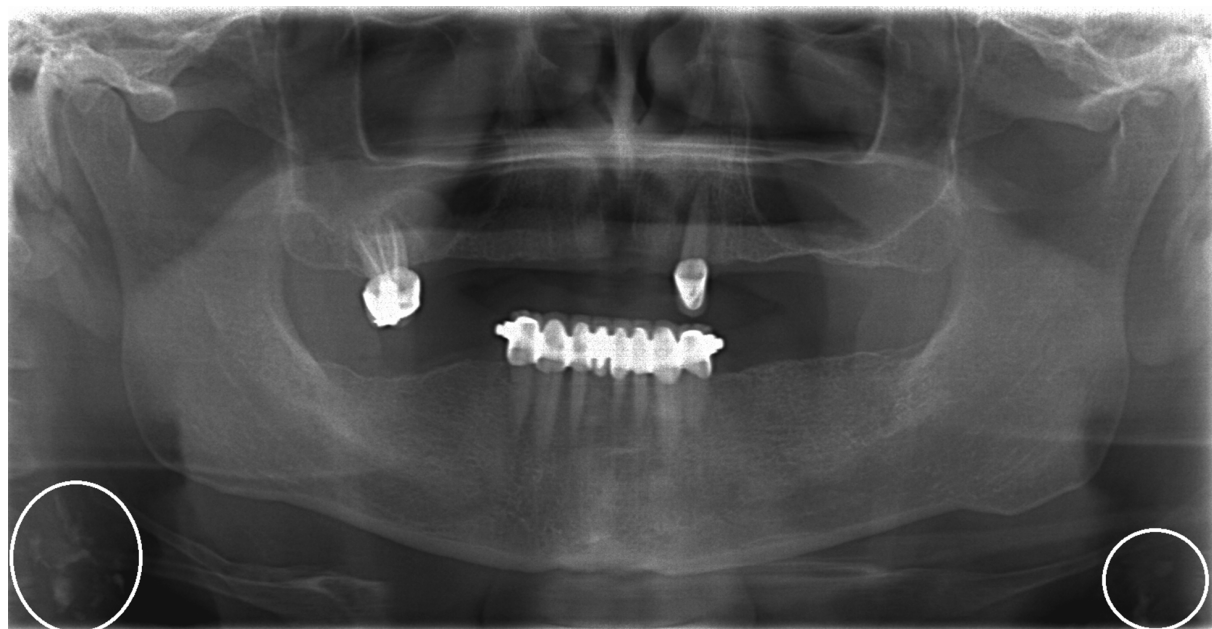


Figure 1. Bilateral calcified carotid artery plaques (CCAPs) (white circles) adjacent to the intervertebral space between C3 and C4 as shown on the DPR in a subject with the cardiovascular disease

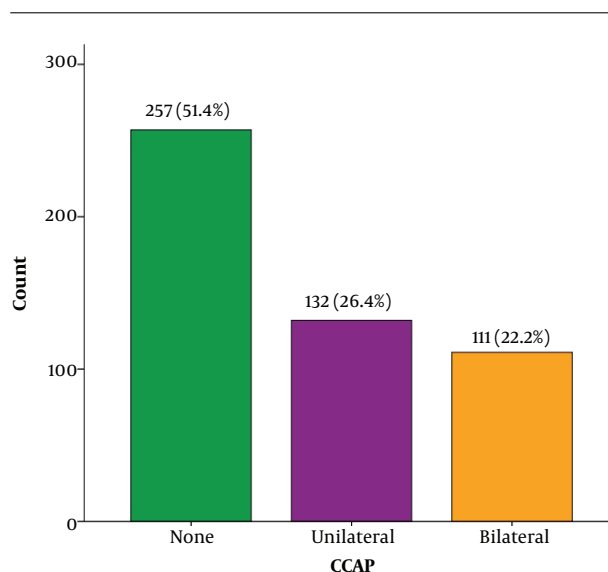


Figure 2. The bars show the numerical distribution of CCAPs as none, unilateral, or bilateral

109 subjects (44.9%) had at least two associated factors, as shown in Figure 3. According to the chi-square test, there was a significantly greater prevalence in subjects who had at least two associated risk factors ($P < 0.01$) (Table 2). One hundred twenty-six subjects (25.2%) with diabetes mellitus

had CCAP while 117 patients (23.4%) without diabetes mellitus showed CCAP. No significant differences were found between subjects with and without diabetes mellitus in terms of the prevalence of CCAP ($P = 0.089$). One hundred four subjects (20.8%) with a history of cardiovascular diseases displayed CCAP while 139 cases (27.8%) without cardiovascular diseases exhibited CCAP with a significant difference between the two groups ($P < 0.01$) (Table 2). One hundred eleven individuals (22.2%) of those with a history of hypertension displayed calcification. However, 132 patients (26.4%) of those without any history of hypertension displayed calcification. According to the chi-square test, there were significant differences between the two groups for the prevalence of CCAP ($P < 0.01$) (Table 2).

5. Discussion

In the world population, atherosclerosis is the primary cause of myocardial infarctions and strokes, determining the death of thousands of persons (about 50.0% of all deaths). There are many etiologic factors such as diabetes mellitus, obesity, arterial hypertension, inadequate diet, eating habits, chronic renal disease, menopause, radiotherapy of the head and neck, and the obstructive sleep apnea syndrome (19). If these factors are diagnosed early, morbidity and mortality rates may decrease (20). CCAP

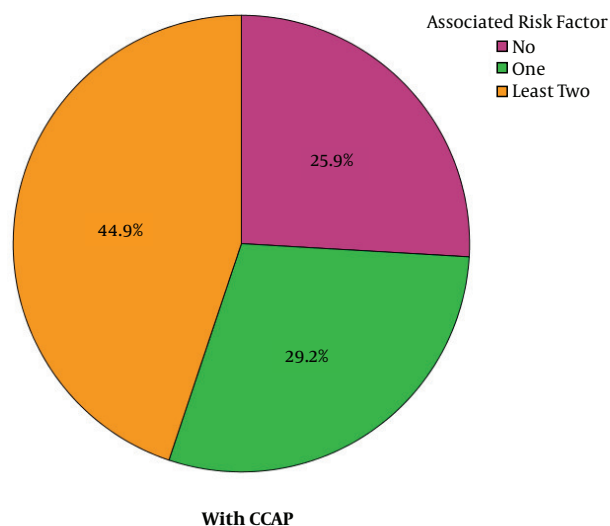


Figure 3. The graphic shows the distribution of associated risk factors in subjects with CCAPs as percentages

may be one of the key indicators of future coronary artery disease, stroke, and death (5).

The Doppler ultrasonography is accepted as the gold standard to detect atherosclerotic plaques in the carotid arteries. However, panoramic radiography is a very cheap, easy, and non-invasive method in comparison with other imaging methods. Panoramic radiographs routinely used as a part of the assessment of subjects with dental problems are discovered to be valuable in detecting atherosclerosis (21). CCAPs may appear as nodular radiopaque masses or radiopaque vertical lines inferior and/or posterior of the gonial region of the mandible and close to the level of the C3-C4 intervertebral intersection in the panoramic radiograph, independent of the hyoid bone (22). However, these patterns should be discriminated from other radiopacities in this region such as tonsilloliths, salivary calculi, the stylohyoid complex, calcified lymphoid tissue, and the triticeous cartilage (7, 14, 22, 23).

In the literature, the reliability of panoramic radiographs in the detection of CCAPs is controversy, and the diagnostic accuracy ratios vary between 62.3 and 81.5% (24, 25). While some studies reported that the conventional panoramic radiographs had a low reliability in the detection of CCAPs (4, 26), the others stated that especially panoramic radiographs were good screening tools for the detection of CCAPs (27). Khambete et al. (27) stated that DPRs were very useful in detecting calcified atheromatous plaques with high sensitivity and specificity. Bayer et al. (10) concluded that while panoramic radiography was not considered a definitive test for atherosclerosis, the pres-

ence of calcification on a panoramic radiograph should be directed to a specialist for further diagnosis. Hence, the DPRs may be seen as a risk predictor of the consequent cardiovascular events (28).

In the literature, the prevalence of CCAP determined on panoramic radiographs varied from 0.43% to 5% (15, 29). In individuals with systemic diseases, the prevalence was higher than in the general population, reaching up to 38.8% (30). In the current study, the prevalence of CCAPs was 48.6%. This result is prominently higher than the literature. This may be due to the different age range, sex, ethnic factors, environment, lifestyle, and the high proportion of individuals with associated risk factors (64.6%) in our sampling group. Else, the prevalence may have been high in our study because DPRs altered contrast and intensity and offered image enhancement that helped better perceive atheromatous plaques.

Taheri and Moshfeghi (31) reported that the prevalence of CCAPs was 40.9% on the right side, 31.8% on the left side, and 27.3% on both sides. Whereas Ohba et al. (11) reported calcification involvement to be 3 times more prevalent on the right side than on the left side in a Japanese population, Uthman and Al-Saffar (15) reported a non-significant relationship of CCAP with the side involved. In the present study, 36.0% of the patients presented with calcifications on the left side while 35.0% had right-sided calcifications and 22.2% showed bilateral calcifications. No statistically significant relationship ($P > 0.05$) was found between the presence of CCAP and the side of involvement. The distinction in the side involvement can be explained by the way that carotid bifurcation level contrasts in connection to the cervical vertebrae and also the right and left sides. In addition, bifurcation levels on the level of C5 may not be noticeable on the panoramic radiographs.

In the present study, the prevalence of CCAPs was not significantly different according to gender, consistent with the findings of studies carried out by Atalay et al. (24), Ohba et al. (11), Bayram et al. (9), Uthman and Al-Saffar (15), and Gonçalves et al. (32). However, this finding is not similar to the results of Tamura et al.'s (12) study. We believe that this difference is probably due to ethnic factors, nutritional habits, or lifestyle.

As age progresses, it is stated that individuals have increased CCAP prevalence on panoramic radiographs (29, 33). The CCAP could be seen in a large age range, but they are more often found in patients aged above 45 years (32). When associating age information, the present study demonstrated a statistically significant ($P > 0.001$) higher prevalence of CCAP in subjects aged 61 years old or older. In addition, the prevalence of CCAP was 17.4% in subject age 45 - 60 years (Table 2). On the other hand, Taheri and Moshfeghi (31) reported no significant differences between

age and CCAP. These differences could be due to that they studied only postmenopausal women. These results suggest that despite statistically significant findings related to age, CCAP must be searched in panoramic radiographs of patients of any age.

Individuals with CCAP on their DPRs have an increased risk of future vascular events. (34) Cohen et al. (28) and Taheri and Moshfeghi (31) found 81 and 86% of subjects with CCAP displaying at least one related factor, respectively. There were similar findings indicating that 64.6% of the subjects with at least one associated risk were identified with CCAP on their DPRs. In the studies carried out by Carter et al. (35) and Friedlander et al. (6), individuals with type 2 diabetes were determined to have a high prevalence of CCAP visualized on panoramic radiographs. These results are not similar to our findings. In the present study, the prevalence of CCAP was not high in subjects with diabetes mellitus, consistent with other studies (11, 24). Whereas MacDonald et al. (36) emphasized that hypertension is one of the most important factors in atheroma formation, Johansson et al. (37) found no significant difference in the prevalence of CCAP between individuals with and without hypertension. Bayram et al. (9) also stated that there was no significant relationship between cardiovascular disease and coronary risk factors and CCAP. Garoff et al. (38) observed that carotid calcifications were seen in PRs in 84% of patients with carotid stenosis $\geq 50\%$. Fukuta et al. (39) reported that 29.3% of patients with cardiovascular diseases had CCAPs, and the prevalence rate was 14.7 times higher than in those without cardiovascular diseases. In a study conducted by Barona-Dorado et al. (40), they stated that patients with risk factors (cardiovascular disease, diabetes, and hypertension) had a greater prevalence than patients who showed no radiographic atheroma. In the present study, the prevalence of CCAP was high in subjects without hypertension and cardiovascular diseases (Table 2). However, there were significant differences between the subjects with and without hypertension and cardiovascular diseases in terms of the prevalence of CCAP. This may result from our non-homogeneous sample in terms of hypertension and cardiovascular diseases. The contradictory results found by our study and other studies may arise from different sample sizes, ethnicity, lifestyle, and nutritional factors.

We could not find a published study in the literature evaluating the carotid plaques in radiographs in the Turkish subpopulations. However, this study had some limitations. First, our sample consisted of subjects who referred to our dental clinic for dental examination. This implies that our sample was not representative of Turkish adults in general. Second, the study had a retrospective design. Hence, it was not possible to obtain the patient's entire his-

tory such as height, weight, BMI, smoking habits, heavy alcohol intake, medicine use for diseases, or duration of drug use.

In conclusion, one of the signs of cardiovascular problems is the presence of CCAP. Although panoramic radiography is not the gold standard for atherosclerosis, a positive finding on radiography requires referral to a specialist for further diagnosis. Thus, the dentist can really save lives by careful evaluation of panoramic radiography. Finally, we can conclude that the existence of bilateral CCAPs on DPRs has a higher prevalence in subjects who had at least two associated risk factors and their detection is important to orient the diagnosis and prevention of diseases in asymptomatic high-risk patients. Other studies need to confirm the presence and severity of different calcifications presented here. The dentist should carefully examine the area of the carotid artery on the panoramic radiographs not only in patients with a systemic disease but also in asymptomatic patients. In addition, the comprehensive prospective studies on this issue are needed for the different markers that propose atherosclerosis in the absence of classical risk factors.

Footnotes

Conflict of Interests: The authors declare that they have no conflicts of interest.

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