

# Relation Between the Incidence of Carotid Artery Calcification and Systemic Diseases

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**Background:** The aim of this study is to investigate the relationship of carotid artery calcifications detected in panoramic radiographs of patients aged 60 or older with isolated systemic diseases.

**Patients and Methods:** From October 2018 to December 2019, 867 panoramic radiographs of patients, who applied to Dicle University Faculty of Dentistry for various dental reasons, were collected for examination. Of these 867 panoramic radiographs, 444 panoramic radiographs were included in this study. Medical data were collected from the archival records of the dental school.

**Results:** The study population consisted of 240 female (54.1%) and 204 male (45.9%) patients. Their mean age was  $66 \pm 7.3$  (range: 60–92) years. Only 39 (8.8%) of the 444 patients had atherosclerotic plaques. Of the 39 patients with carotid artery calcification, 13 (33.3%) were male and 26 (66.7%) were female. As a result of statistical analysis, carotid artery calcification compared to other systemic diseases was found to be significantly more common in patients with hypertension ( $p = 0.009$ ).

**Conclusion:** Carotid artery calcifications detected coincidentally in standard panoramic radiographs of dental patients may be important markers for preventing serious risks such as coronary artery disease, stroke, and death. The relationship between carotid artery calcifications found on dental panoramic radiographs and hypertension was significant. Therefore, it seems that detection of carotid artery calcifications on panoramic images of hypertension patients must be considered by dentists.

**Keywords:** panoramic radiograph, carotid artery calcification, systemic diseases

## Introduction

Atherosclerosis is a progressive inflammatory disease that can cause coronary artery disease, peripheral vascular disease, and ischemic cerebrovascular diseases.<sup>1</sup> The prevalence of atherosclerosis is very high in many countries and a cause of high mortality rates.<sup>2,3</sup> Vascular calcification caused by atherosclerosis is especially common in large and elastic aortic and carotid arteries. Early detection of calcification in these arteries may help to reduce the clinical pathologies caused by atherosclerosis.<sup>4</sup> Thromboembolic material developing due to carotid artery calcification (CAC), whether asymptomatic or symptomatic, may lead to a stroke with a blocking effect on the cerebrovascular system.

The main risk factors for atherosclerosis are considered age, gender, endothelial function, genetic predisposition, smoking, alcohol abuse, diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, obesity and lack of physical activity. Other risk factors include stress, hyperhomocysteinemia, head and neck radiotherapy, obstructive sleep apnea syndrome, and aging.<sup>5</sup>

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Although strokes can be avoided, a major challenge is to develop efficient methods to identify stroke-prone patients. Most non-cardiogenic strokes result from atheroma plaques on panoramic radiographs (PR), in which calcification can be detected in the internal carotid artery.<sup>6</sup>

Radiographically, calcified atheroma plaques are manifested as irregular, circular, or heterogeneous radiopaque masses, unilateral or bilateral. These plates are generally circular and linear when small; when thin and large, it is rectangular.<sup>7</sup> PR is not as useful as Doppler ultrasonography and three-dimensional computed tomography for detecting atherosclerotic plaques in the carotid arteries, especially stenosis of the vessels, but it is less expensive and invasive than other imaging methods. PRs may help in the early diagnosis and evaluation of CACs in patients with or without associated risk factors, thus contributing to reducing the morbidity and mortality rates due to diseases caused by atherosclerosis.<sup>8</sup> Dentists play an important role in their early diagnosis by identifying calcified carotid artery atheroma in PRs. CACs are usually located posterosuperiorly to the angle of the mandible, approximately at the inferior margin of the third cervical vertebra (between C3 and C4) near the hyoid bone; however, their location is not limited to the hyoid bone or the thyroid cartilage.<sup>9</sup> Carotid atherosclerosis is not the only cause of cervical calcification seen anterior to the cervical vertebrae in PRs. Dentists should be able to distinguish CACs from natural anatomical structures and pathological structures. As anatomical structures similar to CACs, calcified tritic or thyroid cartilage, hyoid bone, calcified stylohyoid ligaments, epiglottis might be counted. As pathological structures similar to CACs, calcified lymph nodes, phlebolites, submandibular salivary gland inflammation and tonsil infection might be said.<sup>10</sup>

The aim of this study was to determine the presence of CAC on PRs of patients aged 60 years or older with isolated systemic diseases and to investigate the relationship between its incidence and systemic diseases.

## Patients and Methods

The study included patients admitted to the Department of Oral and Maxillofacial Surgery. Study was planned on PRs which had received for various dental reasons between October 2018–December 2019. Data regarding their age, sex, previous systemic diseases, drugs used, and chronic diseases and their courses were collected. Informed consent forms were obtained from all the patients for using their data. The study was approved by the Ethics Committee of the

Faculty of Dentistry of Dicle University (Protocol No: 53/ November 22, 2018). The number of PRs obtained was 844.

The inclusion criteria of the study are written below:

1. Male and female patients 60 years and older
2. With isolated systemic disease diagnosed at least 5 years ago (Hypertension, diabetes, coronary artery disease, hyperlipidemia, atherosclerosis)
3. Radiographs where the image resolution allows the examination of the regions in the working grab
4. Patients who do not have regular smoking and alcohol use habits

A number of patients were excluded from the study according to the following criteria

1. Patients with two or more systemic diseases, ie multiple systemic diseases
2. Diagnosis of systemic disease less than five years prior to the study
3. Systemic or physical disability due to obvious inherited causes
4. Lack of image clarity due to misuse of the panoramic X-ray system
5. Smoking and alcohol use (Patients who are addicted and use regularly)
6. Body mass index (BMI) > 30

A total of 444 PRs were finally included according to these criteria. All PRs included in the study were examined by a radiologist with 17 years of experience and using the same monitor, considering differential diagnosis. The research procedure extended over four sessions, spaced by a fifteen day period. The patient's data were analyzed according to age, sex, systemic disease, and presence of atheroma plaque. The relationship between the frequency of atheroma plaques and systemic diseases was analyzed.

## Panoramic Radiography

All PRs were taken at the Faculty of Dentistry, Dicle University, Diyarbakır, Turkey, using Planmeca ProMax (Helsinki, Finland) panoramic X-ray systems. The exposure value ranges were 1–7.5 mA and 60–70 kV, depending on each patient's size. According to the differential diagnosis of CAC described by Friedlander and Lande,<sup>10</sup> radiopaque nodular masses independent of the hyoid bone adjacent to the cervical vertebrae at or below the C3–C4 intervertebral disc level or the retromandibular area, generally at an angle of about 45° from the mandibular angle, were regarded as



**Figure 1** Diagrammatic illustration of a panoramic radiograph indicating the carotid artery atheromas disposed bilaterally (arrows).



**Figure 2** Panoramic radiography image suggesting the presence of common carotid artery calcifications (arrows).

CAC. To minimize observation discrepancies, all PRs were evaluated by the same radiologist (Figures 1 and 2).

## Statistical Analysis

Statistical analysis was performed using SPSS Statistics 21.0 (Statistical Package for Social Science Inc., Chicago, USA). Numerical variables were expressed as means $\pm$ standard deviations. The Kolmogorov–Smirnov test was used to determine whether the cases fit the normal distribution. The Mann–Whitney *U*-test was used for those that did not comply with the normal distribution. The independent-test was performed for the normal distribution. The chi-square test was used for categorical variables. The effect of the independent variables was evaluated by multivariate linear regression analysis. A value of  $P < 0.05$  was considered statistically significant.

## Results

The study population consisted of 240 female (54.1%) and 204 male (45.9%) patients. Their mean age was  $66 \pm 7.3$  (range: 60–92) years (Table 1). Regarding the distribution of systemic diseases, the most common was hypertension, followed by diabetes, coronary artery disease, atherosclerosis, and hyperlipidemia (Table 2).

**Table 1** Distribution of Demographic Features

Demographic Features		Mean $\pm$ SD (Min–Max)
Age		66.0 $\pm$ 7.3 (60–92)
		n (%)
Gender	Male	240 (54.1%)
	Female	204 (45.9%)

**Table 2** Distribution of Systemic Diseases in Patients That Included in This Study

Systemic Diseases	n (%)
Hypertension	168 (37.8%)
Coronary artery disease	70 (15.8%)
Atherosclerosis	50 (11.3%)
Hyperlipidemia	37 (8.3%)
Diabetes mellitus	119 (26.8%)

On PRs, CACs were round, irregular, or heterogeneous radiopaque between or just below the vertebrae C3 and C4 (Figure 1). Only 39 (8.8%) of the 444 patients had atherosclerotic plaques. The remaining 405 patients (91.2%) had no observed of atheroma plaques.

Of the 39 patients with CAC, 13 (33.3%) were male and 26 (66.7%) were female. Their medical records were examined and analyzed for possible systemic risk factors. CAC was found to be significantly more common in patients with hypertension compared to other systemic diseases ( $p = 0.009$ ; Table 3). Twenty-two of these patients (56.4%) had hypertension, 6 (10.5%) had diabetes, 6 (4.4%) had atherosclerosis, 3 (6.1%) had coronary artery disease, and 2 (3.3%) had hyperlipidemia (Table 4).

As a result of multivariate analysis of the effects of age, gender and systemic diseases on atheroma plaque, it was observed that age and gender had no effect, but those with systemic disease had a significant effect on the development of atheroma plaque (Table 5).

**Table 3** Atheroma Plaque Distribution on the Panoramic X-Ray in the Patients That Included in This Study

		n (%)	
Atheroma plaque (-)		405 (91.2%)	
Atheroma plaque (+)	Hypertension	22 (56.4%)	p: 0.009
	Other diseases	17 (43.6%)	
	Total	39 (8.8%)	

**Table 4** Atheroma Plaque Percentages That Seen in Systemic Diseases

Systemic Diseases	Atheroma Plaque (n) (%)	p
Hypertension	22 (14.8%)	0.057
Coronary artery disease	3 (6.1%)	
Atherosclerosis	6 (4.4%)	
Hyperlipidemia	2 (3.3%)	
Diabetes mellitus	6 (10.5%)	

**Table 5** Multivariate Analysis Results Evaluating the Effect of Age, Gender and Systemic Diseases on Parameters

	t	p	95% CI (Lower/Upper)
Systemic diseases	-2.123	0.034	-0.033/-0.001
Age	-1.069	0.286	-0.006/0.002
Gender	0.033	0.973	-0.052/0.054

## Discussion

The objective of this study was to determine the relationship of CACs detected in a PRs of patients aged 60 or older with isolated systemic diseases. We found that CAC was significantly higher in patients with hypertension, which is a systemic disease.

Friedlander and Lande<sup>11</sup> were the first to describe the presence of calcification in the common carotid artery region using PR for routine dental diagnoses. Friedlander and Baker<sup>12</sup> reported that asymptomatic patients at risk of a stroke could be identified by PRs. Almost 5% of PRs of patients over the age of 30 show detectable CAC.<sup>12</sup> In our study, 8.8% CAC was detected.<sup>13</sup> However, the higher CAC rate in our study compared to the literature may be due to the group of patients included in the study over 60 years of age. CAC may appear in the form of a nodular or verticolinear radiopacity inferior to the angulus mandible, adjacent to the cervical 3–cervical 4(C3–C4) intervertebral junction.<sup>14</sup> Cohen et al<sup>15</sup> pointed out that PR is an important marker for detecting atheroma plaque formation in the carotid artery and suggested that patients with CAC should be evaluated for cerebrovascular and cardiovascular risks. Sisman et al reported hyperlipidemia in 31.58% of their patient population with CAC.<sup>8</sup> In this study, although more atheroma plaques were found in patients with hypertension than in those with other systemic diseases, this did not reach the level of statistical significance. Nevertheless, hypertension was significantly higher than the other systemic diseases among patients with atheroma plaques. Therefore, we should be alerted in terms of atheroma

plaque in patients with hypertension and vice versa for hypertension in patients with atheroma plaques.

CAC may cause ischemic cerebrovascular attacks due to severe stenosis and obstructions.<sup>16</sup> In Western societies, this is the underlying reason for approximately 50% of all deaths. Cerebrovascular accidents, or strokes, are the third most common etiology of death in the United States today, preceded only by cardiovascular disease and cancer.<sup>17–19</sup> Over 750,000 new or recurrent strokes occur in the United States annually. Atherosclerosis and its more dramatic consequences are stroke and heart attack; are important health problems in other countries as well. In Turkey, too, strokes are the third etiology of death, after cardiovascular disease and cancer.<sup>20</sup> Carotid artery disease may not show symptoms until severe contraction or complete obstruction of the carotid arteries occurs. In some people, stroke is the first sign of the disease.<sup>19</sup> Therefore, the diagnosis of CAC is very important. Friedlander and Cohen<sup>21</sup> reported that 26% of men (mean age 66 years) with CAC diagnosed by PR experienced an adverse vascular event (myocardial infarction, stroke, revascularization, transient ischemic attack, or angina).

Studies on the frequency of CAC have reported varying rates, ranging from 3% to 20%.<sup>22–24</sup> In our study, the rate was 8.8%. This result was found to be compatible with the literature. Bayram et al<sup>25</sup> evaluated the PRs of 4106 patients and reported the presence of CAC in 88 (2.1%). If we compare our results with the two studies, the reason for the higher rate in our study; The presence of an isolated systemic disease can be explained by regional differences, diet, lifestyle and the average age of our patients. Pornprasertsuk-Damrongsri and Thanakun found CAC in 2.5% of the PRs in a Thai dental patient population.<sup>10</sup> In that study, the patients were aged 50 or older. We believe that the higher rate in our study is due to the fact that our patients were 60 or older. Carter et al<sup>7</sup> evaluated the prevalence of CAC in PRs from 1175 dental patients at the University of New York and reported a prevalence of 3.6%. Tamura et al<sup>26</sup> retrospectively investigated the prevalence of CAC in 2568 PRs from a Japanese population and reported a rate of 4.13%.

The most important risk factors for CAC are hypertension, age, sex, diabetes mellitus, hyperlipidemia, atherosclerosis, and smoking.<sup>27</sup> The differences in these factors between populations explain the different rates of CAC from society to society. Ethnicity, diet, and lifestyle are among other factors. In this study, we analyzed hypertension, hyperlipidemia, coronary artery disease, diabetes mellitus, and atherosclerosis as risk factors.<sup>28</sup>



In our study, the incidence of CAC was twice as high in female (26) than in male (13) patients. Bayram et al<sup>25</sup> reported that its incidence in women was approximately three times higher than in men. In Pornprasertsuk-Damrongsri and Thanakun's<sup>10</sup> study, the male-to-female ratio was 1:0.8, which is consistent with that in our study.

Regarding diseases and lifestyle factors associated with CAC, hyperlipidemia, hypertension, cardiovascular diseases, smoking, obesity, renal disease, diabetes mellitus, obstructive sleep apnea syndrome, and periodontitis have been reported.<sup>8</sup> In our study, hypertension was observed in 56.4% of the 39 patients who had atherosclerotic plaque, diabetes in 15.3%, atherosclerosis in 15.3%, coronary artery disease in 7.7%, and hyperlipidemia in 5.1%. The high prevalence of hypertension and diabetes among patients with CAC is in line with other studies' findings. Pornprasertsuk-Damrongsri and Thanakun<sup>10</sup> reported hypertension in 52.9% of their patient population with CAC, diabetes mellitus in 29.4%, hyperlipidemia in 14.7%, and smoking in 2.9%. Lewis and Brooks<sup>29</sup> reported hypertension 77.8% and diabetes mellitus 22.2% as risk factors. Cohen et al<sup>15</sup> examined the PRs of 1879 male patients over 55 years of age and reported that only 3.8% had CAC. In that study, 53.5% of the patients with CAC had hypertension, 36.6% had hyperlipidemia, 22.5% had diabetes mellitus, and 54.9% were smokers. Constantine et al evaluated the PRs of 5780 patients and reported the presence of CAC in 623 (10.8 %).<sup>30</sup> In our study, the rate was 8.8%. The reason for the high prevalence of CAC compared to our study may be due to the differences in nutritional habits socially.

## Conclusion

CACs detected coincidentally in standard PRs of dental patients may be important markers for preventing serious risks such as coronary artery disease, stroke, and death. Therefore, it seems that detection of CAC on panoramic images of hypertension patients must be considered by dentists. It is necessary to be alerted in terms of atheroma plaque in patients with hypertension and vice versa, in terms of hypertension in patients with atheroma plaques. We believe that more extensive studies are needed in this regard. We think that the patient should be warned in terms of hypertension in patients with CAC on dental PRs.

## Disclosure

The authors report no conflicts of interest in this work.

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