

Sensitivity and accuracy of panoramic radiography in identifying calcified carotid atheroma plaques

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Abstract

Atherosclerosis is a chronic inflammatory disease that can cause death and physical and/or mental disabilities. It represents a serious public health problem owing to the high healthcare costs involved in rehabilitating patients. Among the different methods available for diagnosing atherosclerotic disease, color Doppler examination may be considered the “gold standard.” On the other hand, panoramic radiography of the jaws (PRJ) is a diagnostic resource commonly used by dentists, and the obtained images allow examining other structures apart from the maxilla and the mandible. **Aim:** To evaluate the sensitivity and accuracy of panoramic radiography in identifying calcified carotid atheroma, and compare the results to those obtained with color Doppler examination. **Methods:** Forty-two cervical regions were evaluated in panoramic radiographs and color Doppler scans. The kappa test ($p < 0.05$) was used to assess agreement between the examinations. Data were tested for sensitivity, specificity and negative predictive value, as well as positive and negative likelihood ratios. **Results:** The kappa value was 0.11. The sensitivity and specificity of PRJ were 73.9 and 36.8%, respectively, and the positive and negative likelihood ratios were 1.2 and 0.7, respectively. **Conclusions:** Although a low correlation between PRJ and color Doppler examination was observed, as shown by the kappa test, the sensitivity of PRJ in identifying calcified carotid atheroma was considered acceptable.

Keywords: stroke, carotid artery diseases, radiography, panoramic.

Introduction

Atherosclerosis is an inflammatory disease that produces circulatory changes caused by fat deposits on the walls of the arteries. When the carotid arteries are involved, it can cause stroke – a cerebral vascular accident (CVA) – that can be ischemic or hemorrhagic¹. The formation of atheromatous plaques in the carotid artery – also called calcified carotid atheromatous plaques (CCAP) – is not a simple and inevitable degenerative process resulting from advanced age, but rather a chronic inflammatory disease that can develop into an acute clinical condition owing to plaque rupture, rendering the patient susceptible to thromboembolism or stroke².

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Stroke is the third leading cause of death in the United States, accounting for over 150,000 deaths/year, ranking only behind cardiovascular disease and cancer³⁻⁴. By 2009, it was the first cause of death in Brazil, claiming over 300,000 deaths/year⁵. It represents a serious public health problem because it causes death and physical and/or mental disabilities – approximately 60% of survivors suffer from such disabilities⁶ – and have high costs involved in treating and rehabilitating patients.

The main risk factors said to favor or accelerate the atherosclerotic process are: heredity, dyslipidemia, smoking, hypertension, diabetes, viral infections, elevated homo-cysteine (an amino acid derived from eating meat and dairy products) in the blood, obesity, sedentary lifestyle and stress⁷. Preventive measures and early diagnosis are key factors to reduce the prevalence of the disease. However, a non-invasive, inexpensive and reliable diagnostic method still lacks. Angiography, which considered the “gold standard” for diagnosing this disease, is an invasive method that can cause major complications⁸, and Color Doppler (also known as Laser Doppler flowmetry or Duplex Scan), although fast, accurate, noninvasive and painless⁹, is not yet widely accessible to all strata of society because of its high costs (Figures 1A, 1B).

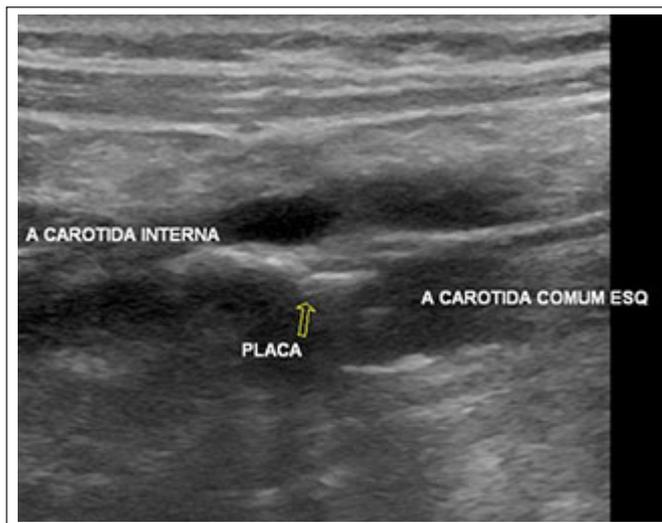


Fig. 1A - Color Doppler – CCAP

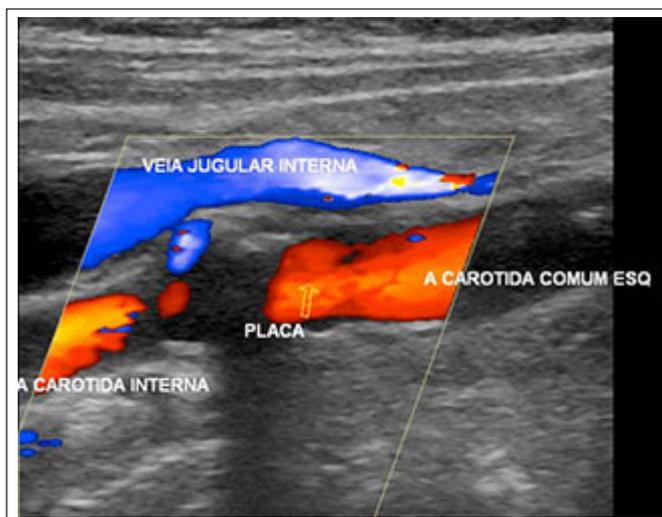


Fig. 1B - Color Doppler – CCAP

Since 1981, the presence of radiopaque images on panoramic radiographs has been described as a sign of the presence of CCAP¹⁰⁻¹¹, indicating that this examination could contribute to the early diagnosis of stroke risk. There are studies reporting that partially calcified atherosclerotic lesions can be observed in panoramic radiographs of the jaws (PRJ)¹²⁻¹³. The image of the calcification is described as a nodular, radiopaque mass in one or more areas, either elongated or triangular, of various sizes, measuring from 1.5 to 4.0 cm, and as observable below and posteriorly to the angle of the mandible, adjacent to the intervertebral spaces between C2, C3, and C4^{8,14-15} (Figures 2A, 2B).



Fig. 2A - Panoramic Radiography of the Jaws



Fig. 2B - Panoramic Radiography of the Jaws - CCAP

Some studies have reported calcifications in dental panoramic radiographs between the second, third and fourth cervical vertebrae, which were later confirmed by color Doppler examination as atheromatous plaques¹⁶⁻¹⁷. Because panoramic radiography may be able to detect CCAP during routine examinations, thus enabling proper referral of patients for appropriate treatment, it has the potential to promote a significant reduction in the morbidity rate caused by this disorder, and a substantial reduction in the healthcare costs associated with atherosclerosis¹⁸. Nevertheless, because panoramic radiographs cover several different anatomical areas, developing the ability to perform differential diagnosis of the structures that comprise the carotid region is of utmost importance. This ability involves comprehensive anatomical knowledge of structures such as the hyoid bone, epiglottis, calcified submandibular and styloid ligaments, and triticeous

cartilage, as well as of pathological processes such as sialoliths, phleboliths, and calcified lymph nodes¹⁹.

In view of these considerations, it is reasonable to assume that PRJ has a great potential in identifying CCAP, or should at least be further investigated as a diagnostic tool for atherosclerosis. Nevertheless, there is still controversy in the literature about its use as a reliable method for this purpose, and great divergence in results. This could be explained by the different methodologies used and because the methods used for comparative analysis of panoramic radiographs in these studies are not considered the “gold standard,” and are based solely on radiographic interpretation for diagnostic conclusion.

Based on the methodological limitations of the existing studies, on the fact that dentists use panoramic radiographs routinely, and on the fact that early detection of patients at risk for developing atherosclerosis is an important public health goal, the purpose of the present study was to evaluate the sensitivity and accuracy of PRJ in identifying CCAP compared with color Doppler examination.

Material and methods

Sample

In this study, the accepted ethical principles governing human experimentation were followed closely, after approval was obtained from the Ethics Committee of the Federal University of Maranhão (Protocol n. 2311-005753/2009-57).

The sample was calculated based on the estimated prevalence of calcification in the carotid artery, approximately 2%. The following parameters were used for calculating sample size: significance level of 0.05 and maximum permissible error of $\pm 5\%$, thus producing $n = 31$.

In the period from August 2009 to June 2010, panoramic two dental radiologists evaluated PRJ of patients of both genders in a clinic commissioned by the Public Health System in the city of São Luis, MA, Brazil. Radiographic diagnosis of CCAP was considered conclusive when there was agreement between both examiners regarding the presence of CCAP and the side in which its presence was detected. Twenty-one panoramic radiographs were considered by the examiners as undoubtedly positive for the diagnosis of CCAP, on at least one side, thus leading to an analysis of 42 cervical regions ($n = 42$).

The inclusion criteria for all participants of this study was the detection of an image suggestive of CCAP on at least one side of the PRJ in patients who were at least 40 years of age, and who agreed to undergo color Doppler angiography.

Radiographic examination

PRJ was performed using the standard positioning technique, Orthophos 3 Ceph X-ray equipment (Sirona Dental Systems GmbH, Germany) and 15 x 30 cm panoramic film (Eastman Kodak Co., Rochester, NY, USA). The films were processed automatically (Revell-XTec Ltd., São Paulo, SP, Brazil), with appropriate developer and fixer solutions (Kodak Brazilian Trade and Industry Ltd., Sao José

dos Campos, SP, Brazil).

Interpretation of the radiographic images was performed by two dentists, with less than three years of experience as radiology specialists, and in an environment with dimmed light and using a light box. The presence of CCAP could be unilateral or bilateral. Both sides of each one of the 21 patients were evaluated, for a total of 42 cervical exams ($n = 42$).

Doppler Examination

All 21 patients with positive radiographic exams for CCAP on at least one side of the PRJ were subjected to Doppler examination at the Presidente Dutra University Hospital, São Luis, MA, Brazil. A Duplex Scan equipment (General Electric, New York, USA) was used owing to its reliability in demonstrating blood flow in the artery under study. A physician specialized in angiology had previously determined the presence of stenosis and/or obstruction caused by an atheromatous plaque. In the same way as done in the radiographic examination, both sides of each exam were evaluated, also totaling 42 cervical analyses ($n = 42$).

Statistical methods

Data were analyzed statistically using BioEstat 5.0 software, according to criteria adopted by the related literature²⁰. The kappa agreement test ($p < 0.05$) was used to assess and compare sensitivity, specificity, negative predictive value (NPV), accuracy (ACC), positive likelihood ratio (PLR) and negative likelihood ratio (NLR) for the different examinations. The kappa values and their interpretations were < 0 (no agreement), 0 to 0.19 (very weak agreement), 0.20 to 0.39 (poor agreement), 0.40 to 0.59 (moderate agreement), 0.60 to 0.79 (substantial agreement), and 0.8 to 1.0 (excellent agreement), following criteria previously approved²¹.

The sensitivity test was used to match the PRJ's ability to detect the disease when its presence was confirmed, i.e., to assess how many positive and negative results were found using PRJ for the cases found positive in the color Doppler examination (“gold standard”)¹⁸. Sensitivity was calculated as follows:

$$\text{Sensitivity (\%)} = \frac{\text{true positives}}{\text{true positives} + \text{false negatives}} \times 100.$$

The specificity test was used to identify the true negatives determined by PRJ in individuals who were genuinely healthy, as revealed by the Doppler examination. It was calculated as follows:

$$\text{Specificity} = \frac{\text{true negatives}}{\text{true negatives} + \text{false positives}} \times 100.$$

The NPV for PRJ was calculated to assess how many test results among those that proved negative were actually negative according to the Doppler examination. It was calculated as follows:

$$\text{NPV (\%)} = \frac{\text{true negatives}}{\text{true negatives} + \text{false negatives}} \times 100.$$

PRJ's accuracy was defined as the proportion of successful examinations, i.e., the total number of true

positives and true negatives, as confirmed by the Doppler examination. It was calculated as follows:

$$ACC = (\text{true positives} + \text{true negatives}) / \text{total}.$$

The likelihood ratio is a means of describing the performance of a diagnostic test. It expresses how many times the result of a given test is more likely (or less likely) to occur in affected subjects compared to unaffected subjects. If a test is dichotomized (positive/negative), two types of likelihood ratio describe its ability to separate those affected from those not affected: one associated with a positive test and another associated with a negative test, respectively calculated as follows:

$$PLR = \text{sensitivity} / (1 - \text{specificity}), \text{ and}$$

$$NLR = (1 - \text{sensitivity}) / \text{specificity}.$$

Results

Of the 42 cervical analyses (L and R sides of 21 patients), 17 images visualized on the PRJ were confirmed by the Doppler examination (true positives), with 6 non-visualized sides (false negatives). PRJ identified 12 images of CCAP that were not confirmed by the Doppler examination (false positives), with 7 sides that were truly without disease (true negatives) (Table 1).

Table 1 - Assessment of the agreement between panoramic radiography and color Doppler in identifying calcified carotid atheroma plaques (n, %).

	Doppler		Total
	Sick (%)	Healthy (%)	
PRJ +	17 (73.9)	12 (63.2)	29 (69.0)
PRJ -	6 (26.1)	7 (36.8)	13 (31.00)
Total	23 (100)	19 (100)	42 (100)

Kappa = 0.11 / p = 0.2265

PRJ: Panoramic radiography of the Jaws

We found a kappa value of 0.11 (p = 0.2265), indicating that the agreement between the Doppler and the PRJ examinations was weak and not significant (Table 1). The sensitivity calculated for PRJ was 73.9%, indicating that 73 out of 100 patients with the disease were correctly identified and 26 were considered erroneously healthy. The calculated specificity was 36.8%, indicating that 36 out of 100 patients with the disease were identified as healthy and 63 were considered erroneously sick.

The NPV of PRJ was found to be 53.8%, indicating that 53 out of 100 patients who had a negative result in the PRJ examination actually did not have CCAP, or, stated differently, 53.8% of the diagnoses found to be negative by PRJ were correct, and 46.2% of the diagnoses initially considered negative by PRJ were actually positive in the color Doppler examination.

The likelihood ratios were as follows: PLR = 1.2 and NLR = 0.7. The higher the PLR, the better the test, and, in order to be considered a good test, the PLR should be significantly higher than 1. This would mean that a positive outcome is more likely to be a true-positive than a false-positive. The

lower the NLR (closer to 0), the better the test. This would mean that a negative result is more likely to be a real negative than a false negative.

The accuracy found for PRJ was 57.1%, indicating that this examination provided a correct diagnosis – a true positive or a true negative – in 57 out of 100 patients. The sensitivity and accuracy results obtained with the use of PRJ for the identification of calcifications in the carotid artery indicate that this test could contribute to reducing the risk of patients suffering a stroke (Table 2).

Table 2 - Accuracy (ACC) of the panoramic radiography in identifying calcified carotid atheroma plaques (n, %).

	Doppler		Total
	Present	Absent	
PRJ +	17 (a)	12 (b)	29 (a + b)
PRJ -	6 (c)	7 (d)	13 (c + d)
Total	23 (a + c)	19 (b + d)	42 (N)

PRJ: Panoramic radiography of the Jaws

ACC = [(a + d)/N]*100

ACC = 57.1%

Discussion

When atheromatous plaques of the carotid bifurcation region are identified, the first feature to note is the size of the obstruction. If it blocks less than 60% of the artery, simply inhibiting platelet aggregation associated with thrombus formation can treat the patient. When the obstruction is greater than 60%, invasive procedures are required to remove the plaque²². Panoramic radiography is limited to identifying CCAPs, and cannot evaluate its exact location, or the degree of the obliteration¹³.

The main limitation of this study was that the population evaluated consisted of a selective group (patients with an image suggestive of CCAP detected in panoramic radiographs), rather than the general population. Nonetheless, this bias can also be considered one of its strengths, from a methodological standpoint, because it compared the sensitivity and accuracy of PRJ to that of the “gold standard” method (Doppler) in identifying the presence of atherosclerotic plaques, considering that PRJ is an exam commonly requested by dentists, in which the occasional presence of CCAP is a radiographic finding.

The NPV found in this study was not substantial (63.2%), considering that atherosclerotic diseases are among the major causes of death worldwide. However, the sensitivity of PRJ in identifying CCAP was significant (73.9%) when compared to angiographic examination (color Doppler imaging), which is considered the “gold standard” (Figure 3)

Although the sensitivity of PRJ in identifying CCAP was 73.9%, its accuracy was only 57.1% and its specificity was 36.8%, a trend confirmed by the kappa test (0.11). Thus, PRJs should not be suggested as a diagnostic imaging examination for the identification of CCAP, as proposed by some authors. The results of the present study

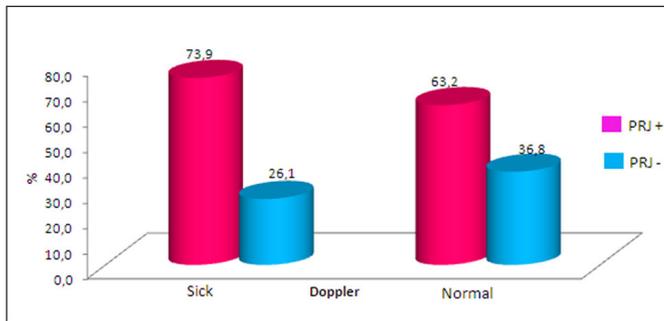


Fig. 3 - Assessment of the agreement between panoramic radiography and color Doppler in identifying calcified carotid atheroma plaques (n, %).

corroborate those of previous studies¹⁹, which stated that a radiopacity between C2, C3 and C4 in a panoramic radiograph does not always represent a CCAP.

Our results differ from those of a previous study²³ that found PRJ sensitivity and specificity values of 22.2% and 90.0%, respectively, for identifying CCAP using CT as the “gold standard.” The authors also concluded that panoramic radiographs could be considered a diagnostic method with moderate accuracy and low sensitivity for the detection of CCAP. This difference may be explained by the different “gold standards” adopted for comparison with PRJ.

In a previous study²⁴, PRJ presented low sensitivity and no accuracy for detecting calcification or stenosis. Only one dental radiologist interpreted the panoramic radiographs in that study, and the authors used two different radiographic x-ray apparatuses (Siemens Corp., Iselin, New Jersey, USA or Gendex Corp., Milwaukee, Wisconsin, USA) for image acquisition. In contrast, the authors also mentioned that the Doppler images were obtained at various locations, and interpreted by different radiologists.

A study assessing the performance of digital PRJ in forty patients with carotid atherosclerotic disease diagnosed by angiography found NPV and sensitivity values of 46% and 60%²⁵, which differ from those found in our study (53.8% and 73.9%, respectively). One possible explanation for this divergence in results is the different characteristics of the projection devices used, particularly the rotation system, the section thickness and the apparatus calibration¹⁹.

A survey⁸ conducted at the Health Department of the city of Valença, RJ, Brazil, reviewed panoramic radiographs and Doppler images of 16 patients to investigate whether there was agreement between the diagnosis of CCAP in the Doppler color and in the PRJ images. The results indicate substantial agreement between these tests ($\kappa = 0.78$), contrasting with those of the present study. This difference may be explained by the different sample sizes and by the different number of evaluators used to assess the panoramic radiographs.

In another study⁸, calcifications were observed in 9.4% of PRJs, but not confirmed by the color Doppler examination, and were considered false positives; in the same study, 3.1% of results were considered false negatives, meaning that the color Doppler examination revealed the presence of calcifications that went undetected in the PRJs. In contrast,

the present study showed even higher values for false positives (63.2%) and false negatives (36.8%).

It is noteworthy that the identification of CCAP in panoramic radiographs may not be a simple task. Published articles^{8,23}, and ours alike, have used dental radiologists in their methodology, leading one to believe that false results, whether positive or negative, could be even greater if the radiographic analysis were performed by general dentists, less trained to visually identify pathologies. A previous study⁸ showed that a general dentist, who is more familiar with evaluating the maxilla, mandible and temporomandibular joint cannot adequately perform the identification of CCAP in panoramic radiography. In that study⁸, dental radiologists found evidence of calcification in the carotid artery in 9 out of 1,818 panoramic radiographs examined, whereas the general dentist, examining the same panoramic radiographs, failed to identify any of these calcifications.

Misinterpretation could be linked to the various anatomical structures existing in the cervical region studied, representing differential diagnoses. In 1981, when the panoramic radiograph was described for the first time as an aid in identifying patients at risk for stroke, calcification in the region of the carotid artery bifurcation was identified in 2% of cases, of which 88% were actually carotid artery calcifications and the remaining 12% were calcified lymph nodes or salivary calculi¹¹.

Although PRJ may not be considered a reliable method to detect calcifications in the carotid artery, it should be used as a referral for the Doppler²⁵ examination (the “gold standard”) and other specialists⁸.

Merely detecting calcifications or stenosis of the carotid artery in PRJ is of limited value in assessing the risk of stroke, insofar as it does not take into account plaque vulnerability²⁶⁻²⁸. According to a recommendation of the American Heart Association, physicians should routinely assess the vulnerability of all major arterial plaques²⁷, including their morphology, as well as biochemical and molecular factors, none of which can be identified by means of panoramic radiography.

Dental clinicians should refer all patients with atheroma-like lesions to a physician, since early aggressive treatment has been shown to reduce strokes, fatal or otherwise¹¹. On the other hand, owing to the wide divergence of results observed, it remains unclear whether dentists could be adequately trained to reduce the number of false positive diagnoses to an acceptable level. Otherwise, unnecessary referrals to physicians could occur, leading to unnecessary tests and increased healthcare spending²⁹. We believe that knowledge of this topic should be generalized, and general dentists should be trained in identifying carotid artery alterations.

Within the limitations of the present study, PRJ presented good sensitivity and only moderate accuracy in identifying calcified carotid atheroma plaques compared with color Doppler examination. These results were confirmed by the observed positive likelihood and negative likelihood ratios. These results support previous findings and point to enhancing the prospects of an interdisciplinary approach,

where dentists can refer their patients to other specialists, who, in turn, may reach a definitive diagnosis based on specific tests and prescribe the proper treatment.

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