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Master’s Thesis

牙周/牙根尖病變和口腔健康狀態與頸動脈鈣化之間的關聯性

Association of periodontal/periapical lesions and oral health status with the carotid artery calcification

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摘要

背景：

炎症是一種重要的保護性反應，涉及免疫細胞、血管和分子媒介，對抗有害刺激至關重要。然而，持續的炎症可能導致各種疾病。本文深入探討頸動脈鈣化、動脈粥樣硬化、牙周病、根尖周圍炎和口腔健康之間的關聯。在現代社會普遍存在的慢性炎症條件明顯影響整體健康，並促成心血管問題。在例行牙科檢查中早期檢測頸動脈鈣化並及時轉介，及早介入治療，可能有助於減少相關疾病的發生。

儘管環口X光攝影並非診斷頸動脈鈣化的直接工具，但它提供有價值的信息，包括對頸部區域的觀察。關於全景X光攝影在檢測頸動脈鈣化的精確度存在爭議，研究結果不一。本文旨在探討牙周疾病、根尖周圍炎、口腔健康和頸動脈鈣化之間的關聯，為臨床醫師和患者提供不同的觀點，增強醫療協助和疾病預防。

材料和方法：

本研究深入探討頸動脈鈣化與口腔健康條件之間的相關性，具體包括牙周組織炎症和根尖病變。利用橫斷式設計和來自國立臺灣大學醫院牙科部的數據，研究旨在了解頸動脈鈣化與牙齒損失、DMFT（蛀牙、缺牙、充填牙齒指數）、齒槽骨損失和根尖病變數量之間的關係。獨立變量包括頸動脈鈣化的存在與否，而依變量包括各種口腔健康參數、社會人口學因素和危險行為。

研究包括972例，利用環口X光攝影圖像進行數據收集。統計分析包括描述性和推論性統計，用於分析頸動脈鈣化、人口統計因素、危險行為和口腔健康參數之間的關係。研究程序包括倫理審查批准、文獻審查、設計修改、病例招募準備、確認數據收集方法以及實際收集病歷和X光。在IRB批准後，研究對674例進行統計分析，旨在提供有關牙周/根尖病變、口腔健康狀態和頸動脈鈣化之間聯繫的相關信息。

結果：

結果呈現了人口統計數據；46.4%為男性，平均年齡為47.1歲。教

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育數據顯示 23.9%高中或以下，15.3%大學，7.1%碩博士學位。還概述了吸煙（24.6%），飲酒（8.2%）和嚼食檳榔（4.5%）的習慣。觀察到 76.7%個案沒有頸動脈鈣化具有頸動脈鈣化則佔 23.0%。
結果也說明了缺牙、DMFT（齲齒、缺失、具填充物之牙齒）、牙根尖病變和齒槽骨缺損。有頸動脈鈣化的病例顯示了略多的缺牙和更高的 DMFT。雖然牙根尖病變略高，但差異不顯著。然而，在有鈣化的病例中，齒槽骨缺損更為嚴重，表明牙周健康較差。

多元迴歸和羅吉斯迴歸分析說明了年齡是影響缺牙、DMFT、牙根尖病變和牙槽骨失的重要因素。在有頸動脈鈣化的分析結果中，年齡、性別和教育水平是顯著的，表明它們的影響。在具有人口統計變量的分析結果中，年齡顯著是影響這項研究中的缺牙、DMFT、牙根尖病變和齒槽骨缺損的最重要因素。

結論：
該研究提供了有關頸動脈鈣化對口腔健康參數的潛在影響的見解，重點關注缺牙、DMFT、根尖病變和齒槽骨缺損。了解這些相互關係有助於提供更好的患者護理和預防措施。

關鍵詞：
頸動脈鈣化、頸動脈粥樣硬化、牙周狀態、根尖病變、環口 X 光攝影、口腔感染

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Abstract

Background:

Inflammation, a crucial response involving immune system, vessels, and molecular compounds, is essential for countering harmful stimuli. However, persistent inflammation can contribute to various diseases. This article delves into the interconnections between atherosclerosis, periodontal disease, apical periodontitis, and oral health. Chronic inflammatory conditions, prevalent in modern society, significantly impact overall health and contribute to cardiovascular issues. Early detection of carotid artery calcification during routine dental check-ups and timely intervention may mitigate the occurrence of related diseases. While panoramic radiography isn't a direct tool for diagnosing carotid artery calcification, it provides valuable information, including observations of the cervical region. The precision of panoramic radiographs in identifying carotid artery calcification is debated, with varying study results. The article aims to explore relationships between periodontal diseases, periapical inflammation, oral health, and carotid artery calcification. This exploration offers a distinctive perspective for clinicians and physicians, enhancing medical assistance and disease prevention education.

Material and methods:

This study delves into the correlation between carotid artery calcification and oral health conditions, specifically periodontal tissue inflammation and periapical lesions. Utilizing a cross-sectional design and data from the National Taiwan University Hospital Dental Department, the research aims to understand how carotid artery calcification relates to tooth loss, DMFT (Decayed, Missing, Filled Teeth index), alveolar bone loss, and the number of periapical lesions. Independent variables encompass the presence of carotid artery calcification, while dependent variables include various oral health parameters, socio-demographic factors, and risk behaviors.

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The study includes 972 cases, utilizing panoramic radiographic images for data collection. Statistical analyses, including descriptive and inferential statistics, are employed to analyze relationships between carotid artery calcification, demographic factors, risk behaviors, and oral health parameters. The research procedure involves ethical approval, literature review, design modification, case recruitment preparations, confirmation of data collection methods, and the actual collection of medical records and X-rays. Following IRB approval, statistical analysis is performed on 674 cases, aiming to offer insights into the correlation between periodontal/periapical lesions, oral health status, and carotid artery calcification.

Results:
There's table presents demographic data; 46.4% are male, average age is 47.1. Educational data reveal 3.1% with primary school or below, 20.8% secondary school, and 22.4% with university or above. It also outlines smoking (24.6%), drinking (8.2%), and betel nut chewing (4.5%) habits. Carotid artery calcification is observed in 76.6% without.
There're tables detail missing teeth, DMFT, root apex lesions, and alveolar bone loss. Cases with calcification show slightly more missing teeth and higher DMFT. Although periapical lesions are slightly higher, the difference is not significant. However, alveolar bone loss is more severe in cases with calcification, indicating poorer periodontal health. Multiple regression and logistic regression analyses identify age as a significant factor impacting missing teeth, DMFT, periapical lesions, and alveolar bone loss. In logistic regression with carotid artery calcification, age is significant factor, suggesting their influence. Age is notably the most significant factor in logistic regression with demographic variables, affecting missing teeth, DMFT, periapical lesions, and alveolar bone loss in this study.

Conclusions: In conclusion, the study provides insights into the potential impact of carotid artery calcification on oral health parameters, with a focus on missing teeth, DMFT, root apex lesions, and alveolar bone loss.

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Understanding these correlations can contribute to better patient care and preventive measures.

Keywords: carotid artery calcification, carotid artery atheromas, periodontal status, periapical lesion, panoramic radiographs, oral infection

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1 Introduction

1.1 Background and motivation

Inflammation is a protective response within the human body that involves immune system, vessels, and organic mediators. It is a complicated organic reaction of the human body dealing with microbial invasion and is part of the host immune response against such threats. When the body is infected or damaged, the inflammatory response is initiated by the tissues to counteract danger signals. It aims to isolate the infected or damaged site, attempt to restore the body's balance, and involves processes such as wound healing and defense against pathogens in the body's internal equilibrium regeneration.

As mentioned above, inflammation is an essential process in the body's repair mechanism, playing a crucial role in many diseases. Whether it's a common cold with symptoms like runny nose and sore throat, the expectation is to restore normal body function. However, if the body undergoes uncontrollable and persistent inflammation overload due to various reasons (such as microbial infections, improper lifestyle like smoking and diet, genetics, and environmental pollutants), it can cause the initiation of several diseases, including:

1. Fatty Liver Disease: or hepatic steatosis, is the accumulation of fat in the liver, often associated with obesity and other metabolic disorders. It can lead to liver inflammation and, if untreated, may progress to more severe liver conditions.
2. Endometriosis: A condition characterized by the growth of tissue resembling the uterine lining outside the uterus, typically leading to pain and fertility issues.
3. Type 2 Diabetes Mellitus: A chronic disorder that change the way human dealing with sugar, leading to high blood sugar levels.
4. Inflammatory Bowel Disease: A collection of disorders that lead to persistent inflammation in the digestive tract, encompassing conditions such as Crohn's disease.
5. Asthma: A chronic respiratory condition marked by airway inflammation, resulting in recurring episodes of coughing, chest tightness, and wheezing.
6. Rheumatoid Arthritis: An autoimmune disorder causing joint pain, edema, and loss of mobility, often affecting multiple joints.

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7. Alzheimer's and Parkinson's Diseases: Neurodegenerative disorders affecting the brain. Alzheimer's is characterized by memory loss, and Parkinson's involves movement-related symptoms.
8. Cancer: A categories of diseases which is notorious for uncontrolled cell growth and migration of abnormal cells.
9. Atherosclerosis: The condition where arteries become narrowed and hardened due to a buildup of plaque, potentially leading to heart attacks or strokes.

The aforementioned conditions, if allowed to persist and develop unchecked, can potentially result in significant irreversible consequences for individuals, severely impacting both their physical health and quality of life. From a societal perspective, it can also lead to substantial expenditures on healthcare resources. If methods for early detection and timely intervention and treatment can be implemented, it may have a positive impact on the overall development of human civilization, making the world a more ideal place.

Due to the author's expertise and regular interaction with patients, inflammatory diseases in the oral cavity are frequently encountered. One cannot overlook conditions such as periodontitis and periapical disease.[1, 2]. According to the World Health Organization, about 35-50% of people around the world are affected by periodontitis[3]. As for our country, there’s reports show that 56.2% of adults were affected by periodontitis who got CPI score >=3 and the prevalence was higher in the older generation.[4, 5] has been shed focus on and a bunch of reports has published to discuss this issue.[6-10] Recent research and clinical studies have identified links between periodontitis and various systemic inflammatory conditions, such as atherosclerosis, type 2 diabetes mellitus, and arthritis [9, 11].
Apical periodontitis is a form of local inflammation affecting the periapical tissues, typically stemming from pulp disease. This condition can develop as a result of dental caries development, trauma, or clinical dental treatment[12]. Apical periodontitis is primarily caused by an infected pulp. The inflammatory response triggered by pathogenic microbes is responsible for the destruction of periapical tissues[13]. Modern lifestyles characterized by a hectic pace and high work pressures have given rise to many diseases, with cardiovascular-related conditions being particularly prevalent. Conditions such as hypertension, abnormal lipid levels, stroke, and

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atherosclerosis can significantly impact the quality of life and even pose life-threatening risks. Atherosclerosis, in particular, can lead to arterial calcification, commonly observed in the carotid artery region. Atherosclerosis is a continuous inflammatory process. When endothelial cells of the blood vessels are damaged due to metabolic factors, hypertension, viral or bacterial infections, etc., it triggers subsequent inflammatory responses involving platelets, genetic factors, phagocytes, smooth muscle cells, and T cells.

This interaction can result in rigidity of the blood vessel wall, accompanied by formation of atheromas or plaques. Atheromatous plaques is caused by calcification of endothelial intima, which can lead to elasticity loss, obstruction, or other degenerative changes [14, 15].This leads to the occlusion and loss of flexibility in the vessels. If the affected vessel supplies the brain through the carotid artery, it may cause a stroke. If it is a coronary artery supplying the heart, it may result in a heart attack.[16, 17]

Absolutely, there're a range of risk factors associated with atherosclerosis. These factors account for the occurrence and development of this condition, increasing the likelihood of arterial plaque formation and related complications. The identified risk factors include:

Diabetes Mellitus: Elevated blood sugar levels can contribute to endothelial damage and inflammation.[18]

Obesity: Excess body weight, especially around the abdominal area, is associated with increased risk.[19]

Arterial Hypertension: High blood pressure puts stress on the arterial walls, promoting damage and atherosclerosis.[20]

Smoking: Tobacco taken contains a bunch of chemicals that can have harmful impact upon vessels and account for the development of atherosclerosis.[21]

Alcoholism: Excessive alcohol consumption may contribute to elevated blood pressure and other cardiovascular issues.[22]

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Inadequate Diet: Diets rich in saturated fats, total cholesterol, and low in essential nutrients can contribute to atherosclerosis.[23]

Periodontitis: Inflammatory conditions in the oral cavity, such as periodontitis, have been linked to higher incidence of CAD.[24]

Chronic Renal Disease: Impaired kidney function can be associated with increased cardiovascular risk.[25]

Menopause: Changes in hormonal levels during menopause can influence cardiovascular health.[26]

These risk factors underscore the importance of lifestyle modifications, regular health check-ups, and preventive measures to mitigate the impact of atherosclerosis and reduce the likelihood of associated complications.

Calcification plaques often exhibit partial calcification, creating radio-opacity that allows observation through panoramic radiography. Some literature indicates an association between carotid artery calcification (atheromatous lesions) and cardiovascular diseases[27], further linked to mortality and various symptoms (symptomatic carotid atherosclerosis, ischemic stroke, blindness, cognitive impairment, severe complications).[28] According to the 2022 national mortality statistics, the top ten causes of death in order are (1) malignant neoplasms (cancer), (2) heart diseases, (3) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (COVID-19), (4) pneumonia, (5) cerebrovascular diseases, (6) diabetes mellitus, (7) hypertensive diseases, (8) accidents and injuries, (9) chronic lower respiratory diseases, and (10) nephritis, nephrotic syndrome, and nephropathy.

It is evident that heart diseases and cerebrovascular diseases are significant concerns, ranking second and fifth, respectively. Detecting carotid artery calcification early during routine dental check-ups and intervening promptly may reduce the occurrence of related diseases. Typically, the diagnosis of carotid artery calcification is made using ultrasonography with Doppler and computerized tomography. Although panoramic radiography, commonly used in dental clinical practice, is not a direct tool for diagnosing carotid artery calcification, it can provide valuable information.

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Panoramic radiography is widely taken in dental daily practice to assess the severity of alveolar bone destruction and the presence of periapical lesions. Due to its non-invasiveness and ease of access, it is a commonly employed imaging tool. Additionally, panoramic radiography covers not only the dental and maxillary areas but also extends to the cervical spine, trachea, and carotid artery regions. Thus, besides evaluating alveolar bone destruction and periapical lesions, panoramic radiography allows observation of the morphology of the sinuses, maxillary sinus, jawbone, trachea, and carotid arteries. Due to the radiopaque nature of calcified structures, highly calcified objects like dental calculus and pulp stones are more easily observed. In clinical practice, carotid artery calcification is occasionally observed through panoramic radiography in the cervical region, presenting with variable morphologies, appearing granular at times or covering the carotid artery wall, and varying in quantity, either as isolated occurrences or in clusters.

The precision of panoramic radiographs in detecting carotid artery calcification has been the subject of ongoing evaluation. [29, 30] In one study involving 104 patients who underwent Doppler ultrasonography for various reasons, a cardiologist assessed the incidence of calcification and stenosis of the carotid arteries. Subsequently, the same patients underwent panoramic radiographs. The research findings suggest that panoramic radiographs lack sufficient sensitivity and positive predictive value to be considered precise or suitable tests for detecting calcification or carotid arterial stenosis[31].

In contrast, a different study reviewed 83 panoramic radiographs, from which two experienced evaluators identified 32 exams with suspected carotid artery calcification. Subsequent ultrasonography as well as Doppler assured the presence of calcification in 29 exams (90%) as identified by the experts. This indicates that with careful diagnostic evaluation, panoramic radiography can yield positive results [32].

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1.2 Purpose

As mentioned above, atherosclerosis, periodontal disease, and apical periodontitis are all inflammation-related diseases. The interconnection among them has piqued the author's curiosity, leading to the conceptualization and experimental design of this article. The objective of this article is to use panoramic radiography to explore the relationships between periodontal diseases, periapical inflammation, oral health, and carotid artery calcification, all of which are inflammatory conditions. The aim is to provide clinical dentists and physicians with a different perspective and insights through the data and information gathered from this research. This, in turn, may enable them to offer more comprehensive medical assistance and education on disease prevention when dealing with patients in their medical interventions.

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2 Material and methods

This study aims to investigate the correlation between carotid artery calcification and oral health conditions, periodontal tissue inflammation, and periapical lesions. The research seeks to explore the correlation between carotid artery calcification and factors such as tooth loss, DMFT (Decayed, Missing, Filled Teeth index)[33], the extent of alveolar bone loss, and the number of periapical lesions.

2.1 Study design

The purpose of the article is to explore the relationship between carotid artery calcification and oral health, periodontal health, and periapical lesions. The study adopts a cross-sectional study design, and the samples are collected from the database of the Dental Department at the National Taiwan University Hospital. The data and panoramic X-rays or periapical X-rays were collected from patient records dated between July 1, 2021, and August 2, 2021.

The research focuses on understanding the impact of carotid artery calcification on oral health, periodontal health, and periapical lesions. The independent variables in the research framework include disease factors (presence of carotid artery calcification). The dependent variables include tooth loss (Missing), DMFT index, the degree of alveolar bone loss, and the count of periapical lesions as well as socio-demographic factors (age, gender, education level), and risk behaviors (smoking, alcohol consumption, betel nut chewing).

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2.2 case selection

The study subjects consist of 972 cases, and the data were collected from panoramic radiographic images taken at the Dental Department of National Taiwan University Hospital from July 1, 2021, to August 2, 2021. After screening and exclusion, the analysis was conducted using panoramic X-rays and periapical X-rays to determine the number of missing teeth, DMFT index, the number of periapical lesions, and the extent of alveolar bone loss. Moreover, the existence and location of carotid artery calcification were identified.

Panoramic Radiography

All panoramic radiographs (PRs) were captured at the Faculty of Dentistry, National Taiwan University, Taipei, Taiwan, using Planmeca ProMax systems from Finland. The exposure settings varied from 1 to 7.5 mA and 60 to 70 kV, adjusted according to each patient's size. According to the former study about carotid artery calcification observation[34], radiopaque nodular masses located near the vertebrae around the C3–C4 level, or the retromandibular area, typically at a 45° angle from the mandibular angle, were classified as carotid artery calcifications . Two well-trained dentists assessed all panoramic radiographs (PRs) for the presence of CAC.

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2.3 Data extraction and Statistical Analysis

The collection of oral conditions and basic information was conducted by two trained dentists who jointly interpreted panoramic X-rays or periapical X-rays in the dental setting. These images provided information about missing teeth, DMFT (Decayed, Missing, Filled Teeth), degree of alveolar bone loss, and the presence of periapical lesions. Subsequently, we recorded and organized this data for statistical analysis. The collection of demographic factors (age, gender, and education) and risk behavior factors (smoking, alcohol consumption, and betel nut chewing) primarily came from the medical records of the cases.

This study involved a total of 972 medical records. After organizing and coding the collected data, statistical analysis was performed using SPSS 28 for Windows. The statistical analysis methods were as follows:

Descriptive statistics: Descriptive statistics were used to present the demographic information (age, gender, education) and behavioral data (smoking, drinking, and betel nut chewing) of the study subjects, including the number, percentage, mean, standard error, and other statistical values, describing the distribution of each variable among the cases.

Inferential statistics: Inferential statistics, including Independent Sample t-test, Chi-Squared Test of Independence, One-way Analysis of Variance (One-way ANOVA), post-hoc tests, multiple regression analysis, and logistic regression analysis, were employed to analyze the relationships between carotid artery calcification, demographic factors, and risk behavior factors with the number of missing teeth, DMFT, the number of periapical lesions, and the degree of alveolar bone loss. All statistical analyses were performed using SPSS statistical analysis software (SPSS 28 for Windows), with a significance level set at 0.05.

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2.4 Study procedure

Firstly, we submitted an application for review of ethical to the Institutional Review Board (IRB) of the National Taiwan University Hospital. While awaiting IRB review, we continued to conduct a literature review, extracting the necessary data through literature collection, analysis, and summarization. Simultaneously, we referred to previously successful research methods and cases. During this stage, we discussed the original research design with our supervisor based on the foundation of the literature review, examining whether modifications were necessary.

Next, we confirmed the preparations required for case recruitment, including the location, process, timing, contact details, and the confirmation of dental practitioners, physicians, and other relevant personnel assisting in case recruitment. We also confirmed the data collection methods and the use of research tools. After IRB approval, we began collecting the estimated number of cases from the database of the Dental Department of the National Taiwan University Hospital. The study collected medical records and panoramic X-rays or periapical X-rays of teeth taken from July 1 to August 2, 2021, totaling 974 cases. Subsequently, we screened and excluded 301 cases from the initially collected 974 cases based on exclusion criteria. The final number of cases included in the study for statistical analysis was 673. Cases related to smoking, drinking, and betel nut chewing were also included in the study following the aforementioned steps.

Finally, we conducted statistical analysis on the remaining cases to explore their interrelationships or differences.

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3 Results

3.1 Distribution of Sociodemographic and Risk Behavior Factors

The demographic variables in this study include age, gender, and education level, and their distribution is shown in Table 1. Of the cases, 46.4% are male, while 53.5% are female. The average age of the cases is 47.1 years.

Although the educational level data is not available for 323 cases in the medical records, or the information about education level is unclear according to the cases' family members, based on the complete data collected from 312 cases, 21 individuals (3.1%) have an education level of primary school (including illiterate and barely literate), 140 individuals (20.8%) have completed secondary school, and 151 individuals (22.4%) have completed university or above. This indicates that more than half of the patients have received higher education.

Risk behavior factors include smoking, drinking, and betel nut chewing, and their distribution is shown in Table 1. In smoking habits, although 270 cases (40.3%) do not specify whether they have a smoking habit, among the remaining 404 cases, 100 individuals (24.6%) have a smoking habit (including former smokers), while 304 individuals (74.7%) do not smoke. In drinking habits, although 299 cases (44.3%) do not specify whether they have a drinking habit, among the remaining 375 cases, 55 individuals (8.2%) have a drinking habit (including former drinkers), while 320 individuals (47.5%) do not drink. In betel nut chewing habits, although 276 cases (41.0%) do not specify whether they have a betel nut chewing habit, among the remaining 398 cases, 31 individuals (4.5%) have a betel nut chewing habit (including former betel nut chewers), while 367 individuals (54.5%) do not chew betel nuts.

Regarding the distribution of carotid artery calcification, this article categorizes cases based on X-ray observations into groups: those without carotid artery calcification, those with carotid artery calcification. In the dataset of 674 cases, it is observed that the number of cases without carotid artery calcification is 526 (78.0%), and cases with carotid artery calcification are 145 (21.5%). Examples of X-rays are illustrated in figures 1, 2, 3, and 4.

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3.2 Correlation between Carotid Artery Calcification and Tooth Loss, DMFT, Apical Periodontitis, and Alveolar Bone Loss

Tables 2 present the distribution and averages of missing teeth, DMFT (Decayed, Missing, Filled Teeth), root apex lesions, and alveolar bone loss for cases with and without carotid artery calcification. According to the statistical data in Table 2, the average number of missing teeth for cases with carotid artery calcification (5.63±6.27) was slightly higher than for those without carotid artery calcification (4.56±5.85), but the p-value > 0.05 indicates no significant difference. It might suggest that the carotid artery calcification groups have more missing teeth. According to the statistical data in Table 2, the average number of DMFT for cases with carotid artery calcification (10.47±8.38) was slightly higher than for those without carotid artery calcification (8.63±7.85), and the p-value < 0.05 indicates there's significant difference. It might suggest that the carotid artery calcification groups have more DMFT. According to the statistical data in Table 2, the average number of apical lesions for cases with carotid artery calcification (0.64±0.736) was slightly higher than for those without carotid artery calcification (0.52±0.684), but the p-value > 0.05 indicates no significant difference. It might suggest that the carotid artery calcification groups have more apical lesions. Data of Table 2 implies that cases with carotid artery calcification generally have more decayed teeth and fillings, indicating a potentially poorer oral health status. These findings imply that carotid artery calcification does impact oral health.

Regarding the degree of alveolar bone loss, as shown in table 3, among the 145 cases with carotid artery calcification, 16 had no alveolar bone loss, 52 had mild loss, 41 had moderate loss, and 36 had severe loss. In the 526 cases without carotid artery calcification, the distribution was 154, 172, 113, and 86, respectively. Furthermore, the proportions of cases with carotid artery calcification were higher in mild, moderate, and severe alveolar bone loss categories, except for the absence of alveolar bone loss, where the proportion was higher for cases without carotid artery calcification. Furthermore, as shown in table 4, it was observed that in the group with carotid artery calcification, the number and percentage of people with alveolar bone loss was more than those without bone loss. Although in the group without CAC, the

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number of individuals with perodontal bone loss (n=371) was also higher than those without bone loss (n=154), the proportion of alveolar bone loss was higher in patients with carotid artery calcification. These data suggest that alveolar bone loss is worse in cases with carotid artery calcification, indicating poorer periodontal health in these cases.

To investigate whether missing teeth, DMFT, root apex lesions, and alveolar bone loss are primary influencing factors in cases with carotid artery calcification, we conducted multiple regression analysis and logistic regression analysis, distinguishing between cases with and without carotid artery calcification. Age, gender, education level, smoking habits, drinking habits, and betel nut-chewing habits were used as independent variables, while missing teeth, DMFT, root apex lesions, and alveolar bone loss served as dependent variables (refer to Table 5). The statistical results revealed that, in our study, both demographic and risk factors significantly predicted missing teeth, DMFT, periapical lesions, and alveolar bone loss (R^2 = 0.259, R^2 = 0.352, R^2 = 0.081, R^2 = 0.304). For the cases, the most important independent variable predicting missing teeth, DMFT, periapical lesions, and alveolar bone loss was age (β=0.162, β=0.248, β=0.006, β=0.028), and it was statistically significant ($p<0.05$), indicating that age has a statistically significant impact on missing teeth, DMFT, and root apex lesions.
According to the data in Table 6, in the Logistic Regression Analysis model with carotid artery calcification (CAC) and demographic variables, 26.3% can be explained by independent variables. We found that age (OR=1.078; $p<0.05$) remained statistically significant among all variables, while all other factors were not statistically correlated with the independent variables. This suggests that age is the most significant influencing factor for missing teeth, DMFT, periapical lesions, and alveolar bone loss in cases of this study.

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4 Discussion

DMFT is one of the most commonly used methods in dental epidemiology to assess the prevalence of dental caries and the treatment modality of individuals. This index involves a clinical examination of the oral cavity using a probe and mirror, calculating the number of decayed teeth (D), missing teeth (M), and filled teeth (F), and summing up these values to obtain the DMFT. Data from a study on the correlation between DMFT and oral health conditions and related factors indicate that the frequency of dental floss use, socioeconomic status,[35, 36] . This indirectly suggests that DMFT is an important indicator for assessing the condition of teeth in an individual's oral cavity and their personal oral hygiene habits.

The amount of bone tissue is regulated by the equilibrium between bone accumulation by osteoblasts and bone consumption by osteoclasts. Under normal physiological conditions, bone formation and bone resorption are in balance. However, patients with periodontal disease may experience excessive bone resorption, leading to destruction of the alveolar bone[37, 38].

This study determines the extent of periodontal disease based on the extent of alveolar bone loss. The criteria for assessing the extent of alveolar bone loss and root apex lesions were primarily determined by two professional dentists. The extent of alveolar bone loss was categorized into classes below: no alveolar bone loss, <1/3 alveolar bone loss,1/3~1/2 alveolar bone loss, 1/2~ 2/3 alveolar bone loss, and >2/3 alveolar bone loss .Within these categories., we considered cases with no bone loss and those with bone loss < 1/3 as without periodontal disease , cases with 1/3~1/2 alveolar bone loss as mild periodontal disease , 1/2~ 2/3 alveolar bone loss as moderate periodontal disease and >2/3 alveolar bone loss as severe periodontal disease cases.
In the literature review, the correlation between CAC and periodontal disease is mentioned. A meta-analysis suggests that hyperlipidemia is associated with the incidence of periodontal disease, with reports indicating significantly elevated total cholesterol, low-density lipoprotein, and triglyceride levels in patients with periodontal disease compared to individuals free from periodontitis. Moreover, the impact of bacteria is not to be overlooked. Periodontal pathogenic bacteria can invade the bloodstream due to loss of periodontal attachment or even routine oral hygiene practices, causing bacteremia. P. gingivalis and Actinobacillus

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actinomycetemcomitans are commonly found in this context. Animal experiments have shown that individuals infected with these oral pathogens will accelerate the formation of atherosclerosis and accumulation of fat in the blood vessels[39]. All these findings suggest a correlation between periodontal disease and the presense of carotid artery calcification or its risk factors.

The correlation between carotid artery calcification and cardiovascular disease has been highlighted in various studies. Carotid artery calcification involves the deposition of calcium within the carotid artery walls, forming calcified plaques, a phenomenon associated with atherosclerosis.[27] The rigid arterial walls are susceptible to the development of atherosclerotic plaques, contributing to vascular narrowing and damage to vessel walls. If these conditions occur in the coronary arteries (primary vessels of coronary heart disease), it can lead to cardiovascular events like heart attacks or strokes.[27]

Carotid artery calcification has been identified as highly related to cardiovascular and cerebrovascular disease [40]. These conditions contribute significantly to human mortality and are among the causes of mortality in developed countries. Moreover, there have been reports indicating the correlation between carotid calcification and coronary artery disease (CAD) [41-43].

Oral infections, such as apical periodontitis or periodontitis, are quite common, as previously mentioned, and their etiology and mechanisms have been explored. Studies employing RNA sequencing data analyze the bacterial composition of the blood of individuals with and without coronary artery disease (CAD). The identification of subgingival plaque components in the blood of patients with coronary artery calcification supports the theory that pathogens from subgingival plaque may travel from the oral environment to the vascular sites via the bloodstream. This mechanism intensifies inflammatory responses, potentially exacerbating or contributing to the onset of systemic diseases, including CAD, indicating a positive link between periodontal disease and CAD [44-46].

In other studies, the correlation between oral infections and cardiovascular disease has also been mentioned [47]. Studies showed much information correlating periodontal disease to a versatile of cardiovascular diseases, including coronary heart disease, stroke, and others. Inflammation is one of the key factors in oral and systemic

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infections, like periodontitis, and cardiovascular disease [48, 49].Oral inflammation is triggered by bacteria present in biofilms that form on human teeth, constituting the oral microbiome. On the contrary, vascular inflammation is triggered by factors such as hyperlipidemia, smoking, and various other identified and unidentified causes. The mechanisms correlating oral infections to cardiovascular disease revolve around the effect of oral bacteria on the vasculature. To investigate the impact of oral bacteria in the development of atherosclerosis, several mechanistic as well as animal model studies have been undertaken, aiming to show that these bacteria contribute to atheromatous disease [50, 51].

Periodontal bacteria have the ability to enter systemic vascular tissues, and their presence has been detected in affected tissues. There is evidence indicating the presence of active periodontal pathogen at the affected region. Regarding the migration of these organisms to vascular sites, two methods of intrusion of cardiovascular tissues by oral bacteria have been recognized: bacteremia, as previously discussed, and phagocyte-mediated bacterial migration from the periodontal lesion to the distal target tissues. [52]. A recent study suggests that dendritic cells ingest periodontal bacteria from infected periodontal pockets and transport the bacteria through the bloodstream to be accumulated in cardiovascular region. [53].

The preceding discussion elucidates the association between carotid artery calcification and cardiovascular diseases. Subsequently, the link between oral infections and cardiovascular diseases is studied, suggesting that inflammation takes a enormous role in both conditions[54]. The literature review suggests that natural molecules which could resolve inflammation may mitigate the inflammatory component of the estimated periodontitis–CVD link with no bactericidal medication involved, presenting an intriguing departure from clinical practice[55].

In certain animal experiments, rabbits fed a 0.5% cholesterol diet for 13 weeks developed significant lipid deposits and displayed atherogenic changes in the aorta. Periodontal inflammation triggered by P. gingivalis notably increased lipid accumulation in this design[56] . These findings support the idea of periodontitis as a local inflammatory impact contributing to CVD progression. Additionally, the role of inflammation in the development of periodontitis and CVD is emphasized. The

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control of inflammation is crucial, especially mentioning the remarkable impact upon the cardiovascular system of COX inhibitors usage.

Recent discoveries in inflammation resolution pathways provide opportunities for modifying inflammation without using unnatural pathways[57]. Proinflammatory mediators such as prostaglandins and leukotrienes, as well as newly identified pro-resolution mediators like lipoxins[58], resolvins[59-61], and protectins[62, 63] derived from essential fatty acids, constitute a genuine group of endogenous anti-inflammatory and pro-resolving compounds. These compounds have recently proven to have potential in dealing with many inflammation-related pathways of disease[64, 65].

There're studies concentrated on exploring the impact of resolvins on tissue regeneration. In the experiment, alveolar bone destruction and further inflammation were induced utilizing ligature and P. gingivalis applications around teeth of leporidae. Subsequently, resolvin1(RvE1) was applied right onto the target site three times a week of a duration of 6 weeks. The control sites, which did not receive any treatment, exhibited significant inflammatory infiltrate, collagen loss, and bone destruction. In contrast, the study group, which received RvE1, showed no inflammatory reaction, osteoclast expression, or bony destruction. Moreover, there was nearly total regeneration of both bone structure and gingival tissues that had been lost due to the disease[66].

This news is indeed uplifting. If inflammation-related diseases can be treated from a systemic perspective by controlling inflammation, instead of using antibiotics to kill all microorganisms, it would not only reduce the side effects associated with antibiotics but also offer a glimmer of hope for treating various diseases, including arthritis[67], colitis[68], peritonitis, asthma[69], dermatitis[70], infantile eczema[71], diabetic wounds[72], and retinopathies[73], benefiting all of humanity. In the future, more experimental designs and even clinical trials will be needed to thoroughly uncover the correlation between anti-inflammatory molecules and diseases, unveiling the mysterious aspects of inflammatory diseases. This will pave the way for a brighter future, enabling humanity to take an early step toward complete healing of many chronic inflammatory conditions.

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5 Conclusions

In conclusion, the interconnectedness of oral health, periodontal disease, periapical lesions, and cardiovascular diseases is evident. The significant correlation between carotid artery calcification and cardiovascular diseases, including coronary artery diseases, underscores the importance of thorough dental examinations. Vigilance for warning signs, comprehensive information gathering, and appropriate referrals for further examination and treatment during routine dental check-ups can contribute to the early prevention of life-threatening conditions such as coronary artery diseases and strokes. This approach not only helps maintain patient health but also reduces medical costs and enhances overall quality of life, ensuring a happier life for individuals.[74]

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6 Tables and figures

Table 1、Distribution of demographic variables in study group

variables	groups	N or mean	percentage(%) or SD
Age		47.1	22.7
Gender	Male	313	46.4
	Female	360	53.5
	Missing	1	0.1
Education level	University and higher	151	22.4
	Secondary school	140	20.8
	Primary school	21	3.1
	Others	39	5.8
	Missing	323	47.9
Occupation	Employed	124	18.4
	Unemployed or others	169	25.1
	Others	381	56.5
Alveolar bone loss	No	170	25.2
	Mild	224	33.2
	Moderate	155	23.0
	Severe	122	18.1
	Missing	3	0.4
Apical lesion	0	376	55.8
	1-3	227	33.7
	4-6	61	9.1
	Over 7	6	0.9
	Missing	4	0.5
Carotid artery calcification	No	526	78.0
	Yes	145	21.5
	Missing	3	0.5
Systemic disease	No	184	27.3
	Yes	490	72.7

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Smoking	No	304	74.7
	Yes	100	24.6
	Not mentioned	3	0.7
	Missing	267	39.6
Drinking	No	320	47.5
	Yes	55	8.2
	Not mentioned	3	0.4
	Missing	296	43.9
Betel nut chewing	No	367	54.5
	Yes	31	4.5
	Not mentioned	2	0.3
	Missing	274	40.7

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Table 2、The distribution and mean values of cases with or without carotid artery calcification(CAC), as well as Missing, DMFT, and apical lesions.

Variables	N(%)	Missing Mean±SD	$p^{§}$	N(%)	DMFT Mean±SD	$p^{§}$	N(%)	Apical lesions Mean±SD	$p^{§}$
CAC									
No	526	4.56±5.85	0.067	526	8.63±7.85	0.013	526	0.52±0.684	0.114
Yes	145	5.63±6.27		145	10.47±8.38		145	0.64±0.736	

§ Two independent samples *t* test

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Table 3、The distribution of carotid artery calcification(CAC) and different extent of alveolar bone loss

		Alveolar bone loss				
Variable	N(%)	No	Mild N(%)	Moderate N(%)	Severe N(%)	$p^{§}$
CAC						
No	526(78.4)	154(29.3)	172(32.8)	113(21.5)	86(16.4)	< 0.0001
yes	145(21.6)	16(11.0)	52(35.9)	41(28.3)	36(24.8)	

§ Chi-square test

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Table 4、comparison of cases with or without carotid artery calcification(CAC) and alveolar bone loss

variable	N(%)	Without alveolar bone loss N(%)	With alveolar bone loss N(%)	$p^{§}$
CAC				
No	526(78.4)	154(29.3)	371(70.7)	< 0.0001
yes	145(21.6)	16(11.0)	129(89.0)	

§ Chi-square test

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Table 5、Multiple Regression Analysis of variables including carotid artery calcification(CAC) and missing, DMFT, periapical lesion, and alveolar bone loss

variable	Missing			DMFT			Periapical lesion			Alveolar bone loss		
	B	SE	*p*	B	SE	*p*	B	SE	*p*	B	SE	*p*
Male	1.669	0.870	0.056	0.818	1.024	0.425	0.135	0.103	0.190	0.530	0.130	<.001
Age	0.162	0.025	<.001	0.248	0.029	<.001	0.006	0.003	0.032	0.028	0.004	<.001
Education (ref=Others)												
Primary	-0.240	2.023	0.906	0.422	2.380	0.859	-0.399	0.239	0.097	0.011	0.301	0.971
Secondary	-0.950	1.680	0.572	0.151	1.976	0.939	-0.162	0.199	0.415	0.168	0.250	0.502
University or higher	-2.769	1.803	0.126	2.666	2.121	0.210	-0.438	0.213	0.041	0.194	0.268	0.470
Having jobs	-0.661	0.792	0.405	1.523	0.932	0.104	-0.058	0.094	0.534	0.039	0.118	0.742
Smoking	0.040	1.119	0.971	0.859	1.316	0.514	-0.059	0.132	0.654	0.194	0.166	0.244
Drinking	-0.433	1.319	0.743	0.955	1.552	0.539	0.243	0.156	0.120	0.280	0.196	0.155
Betel nut chewing	0.341	1.576	0.829	0.115	1.854	0.951	-0.263	0.186	0.160	0.199	0.234	0.395
CAC	-0.957	0.873	0.274	0.720	1.027	0.484	-0.106	0.103	0.306	0.145	0.130	0.264
	R squared = 0.259			R squared = 0.352			R squared = 0.081			R squared = 0.304		

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Table 6、Logistic Regression Analysis with carotid artery calcification(CAC) and demographic variables

Independent Variable	B	SE	Odds ratio	P-Value
Male	0.531	0.424	1.700	0.211
Age	0.075	0.013	1.078	0.000
Education (reference=Others)				
Primary school	1.257	1.342	3.516	0.349
Secondary school	0.713	0.926	2.040	0.441
University or higher	0.918	0.968	2.504	0.343
Having jobs	0.162	0.387	1.176	0.675
Smoking	0.631	0.689	1.880	0.360
Drinking	0.135	0.808	1.145	0.867
Betel nut chewing	-0.351	0.900	0.704	0.696
CAC	0.633	0.494	1.882	0.201

Pseudo R Square = 0.263

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Figure 1、case without CAC

Figure 2、case with right side CAC

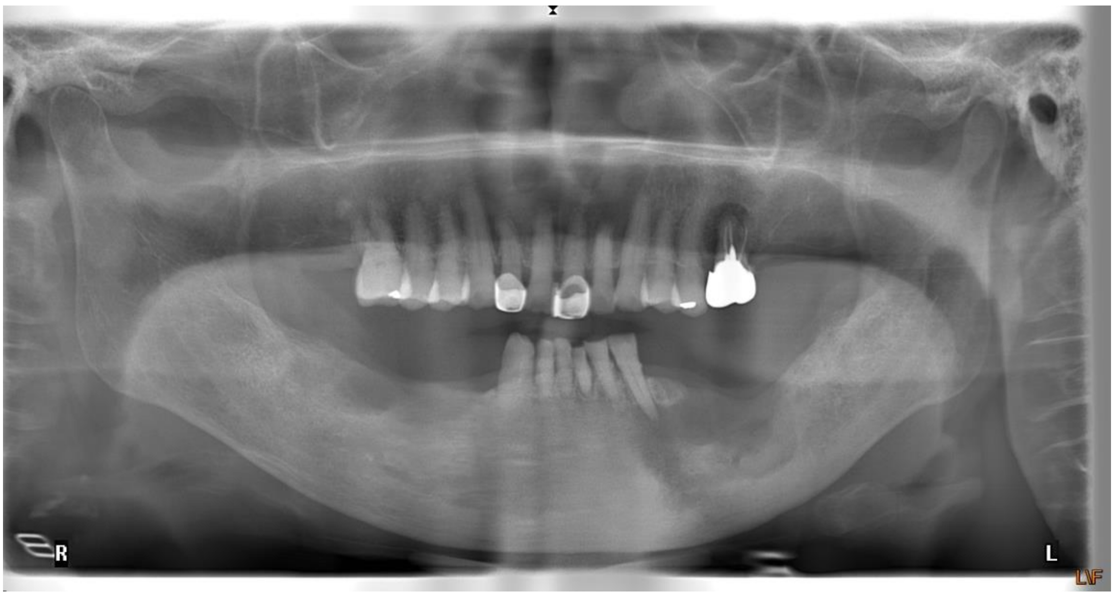

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Figure 3、case with left side CAC

Figure 4、case with bilateral CAC

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