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**Original Article**

# Periodontitis and Age-Related Macular Degeneration: Clinical and Radiographic Insights

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## ABSTRACT

Previous studies have identified oral microorganisms within biopsy samples from individuals with Age-Related Macular Degeneration (ARMD), and bone resorption in the alveolar region has been correlated with this ocular disorder. Hence, this case–control study explored the potential link between ARMD and periodontal disease by assessing both clinical and radiographic periodontal characteristics—primarily between patients and controls, and secondarily within ARMD cases according to their risk factors—to uncover a possible shared pathogenic mechanism. Eighty participants were recruited, comprising 40 ARMD patients and 40 controls without ARMD, matched for gender and age (±3 years) and comparable regarding ARMD-associated risk variables. Each underwent full-mouth periodontal charting, panoramic X-rays, and medical data collection, including ARMD risk information. Data were analyzed with the R statistical language, and group comparisons employed both standard t-tests and Yuen's bootstrap-adjusted test. Participants were all aged 55 years or older, with 50 females and 30 males equally distributed across groups. No statistically significant variation emerged in clinical or radiographic periodontal indices between ARMD and control groups. Within the ARMD cohort, no significant differences were detected between periodontal indicators and ARMD risk factors, except that Clinical Attachment Level scores were notably higher in hypertensive subjects. These results suggest a potential association between periodontal pathology and ARMD among hypertensive patients, indicating hypertension might serve as a shared pathogenic pathway.

**Keywords:** ARMD, Macular degeneration, Periodontal disease, Radiographic

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## Introduction

Age-Related Macular Degeneration (ARMD) is a chronic, degenerative ocular condition primarily affecting elderly populations and threatening central vision. It represents the advanced phase of a range of degenerative alterations in the macula—the central retinal and choroidal region—collectively known as age-related maculopathy [1].

ARMD typically presents with drusen deposits in the macular area, followed by either geographic atrophy or choroidal neovascularization [2], impacting the retinal pigment epithelium first and photoreceptors subsequently, leading to partial or total central vision impairment and eventual legal blindness [1].

Although the exact cause of ARMD remains unclear, the disorder appears to result from an interplay between genetic predisposition and environmental exposures in addition to aging [3, 4]. Early pathological changes in ARMD resemble those in Alzheimer's disease and atherosclerosis [5], suggesting overlapping mechanisms possibly linked to common risk factors such as advanced age, low antioxidant levels [6], elevated Body Mass Index (BMI) [7, 8], tobacco use [9], hypertension, and systemic inflammatory activity [10]. Other recognized risks include sex, ethnicity, diabetes, and abnormal lipid profiles, including total

cholesterol, High-Density Lipoproteins (HDL), and Low-Density Lipoproteins (LDL) [3, 4].

Recent findings have indicated an independent association between ARMD and periodontal disease in individuals aged 40–60 years [10, 11].

Periodontal disease is a multifactorial inflammatory condition driven by microbial infection, commonly manifesting in adulthood and leading to alveolar bone resorption, tissue breakdown, and ultimately tooth loss [12–14].

Growing evidence supports the relationship between periodontal infection and various systemic diseases, including cardiovascular and respiratory diseases, diabetes, albuminuria, obesity, premature birth, chronic obstructive pulmonary disease, and even some cancers such as colorectal malignancy [15, 16]. Periodontal pathogens may contribute directly by entering the circulation through inflamed periodontal tissues, or indirectly through endotoxin-mediated inflammation in distant organs [11, 15, 17].

Notably, associations have been demonstrated between periodontitis and atherosclerosis, and between atherosclerosis and ARMD [10]. Furthermore, alveolar bone loss has been correlated with ARMD [5], and microbial DNA from oral bacteria has been isolated from ocular biopsy material of ARMD patients [10]. These findings point toward a potential shared pathogenic mechanism connecting oral and ocular degeneration.

Given that ARMD is among the most prevalent causes of blindness in elderly populations of developed nations [11, 18], and its incidence continues to rise with population aging [19], understanding its etiology and managing modifiable risk factors is of major importance [10]. Identifying a possible contribution of periodontal disease to ARMD development could enhance comprehension of the oral–systemic health relationship and support an integrated, multidisciplinary approach in ARMD management.

Accordingly, the current case–control study aimed, first, to examine whether an association exists between ARMD and periodontitis by comparing clinical periodontal status and bone loss between ARMD cases and matched controls, and second, to explore in ARMD subjects the possible link between periodontal parameters and known ARMD risk factors, including smoking, lipid levels (cholesterol, HDL, LDL), BMI, diabetes, and hypertension.

## Materials and Methods

*Study framework and participants*

This observational case–control investigation was reviewed and authorized by the Ethical Committee of the Azienda Ospedaliero–Universitaria San Giovanni di Dio e Ruggi d'Aragona (Protocol No. 34/2013, May 6, 2013; reconfirmed Resolution No. 776, August 6, 2014). The study was carried out in accordance with the ethical standards set forth in the Declaration of Helsinki.

The case group comprised 40 patients clinically identified with Age-Related Macular Degeneration (ARMD) at the Ophthalmology Department of the Azienda Ospedaliero–Universitaria San Giovanni di Dio e Ruggi d'Aragona in Salerno, Italy. These individuals also attended the same institution's Odontostomatology Unit between May 2014 and March 2019. The control group consisted of 40 participants without ARMD who presented for regular dental evaluation within the same period. Controls were age- (±3 years) and gender-matched to ARMD cases and exhibited comparable levels of BMI, blood pressure, hypertension, and total cholesterol to ensure consistency across groups.

Eligibility criteria required participants to be at least 18 years old and have three or more teeth. Those younger than 18, pregnant, fully edentulous, or diagnosed with malignant disease were excluded, as were individuals with active infections (oral or systemic), osteonecrosis of the jaws induced by medication, recent periodontal therapy, or use of antibiotics or corticosteroids during the prior three months. ARMD patients with advanced cataracts or any ocular disorder interfering with OCT evaluation and controls experiencing visual issues at the time of examination were not included.

All eligible subjects signed informed consent forms and underwent dental and periodontal evaluation, panoramic imaging, and medical record collection.

*ARMD diagnosis and classification criteria*

Before enrollment, ARMD cases received a complete ophthalmologic work-up, which included testing of best-corrected visual acuity using the ETDRS logMAR scale, slit-lamp inspection, intraocular pressure assessment, and fundus examination. Optical coherence tomography (OCT) was performed with the Spectralis SD-OCT device (Heidelberg Engineering, Heidelberg, Germany) to confirm diagnosis.

All imaging was executed by the same experienced operator using the Spectralis OCT (software v6.0), applying the 30″ horizontal enhanced depth imaging (EDI) mode centered on the fovea. Each scan represented the mean of 100 automatically aligned frames with eye-tracking enabled and automatic real-time (ART) imaging set to 100 [20].

Subsequent ARMD grading followed the National Health and Nutrition Examination Survey (NHANES

III) protocol [10]. Control participants did not undergo ophthalmologic testing.

*Definition and assessment of periodontal disease*

Periodontal evaluation—including full-mouth charting and panoramic radiography—was conducted for both groups at the Odontostomatology Unit of the same hospital in Salerno.

Each participant's total number of teeth was documented. Periodontal charting recorded Clinical Attachment Level (CAL) and Periodontal Pocket Depth (PPD) in millimeters, along with Gingival Index (GI) [21] and Plaque Index (PlI) [22], obtained from six locations per tooth. A single blinded and calibrated clinician performed all assessments under standardized light conditions using a UNC-15 periodontal probe (Hu-Friedy, Chicago, IL, USA). Tooth mobility and furcation involvement were also noted. Full-Mouth Plaque Score (FMPS%) and Full-Mouth Bleeding Score (FMBS%) [23] were subsequently calculated.

Radiographic images were evaluated to determine Radiographic Bone Loss (RBL) following Tonetti *et al*. [24], and alveolar bone resorption was categorized according to Karesvuo *et al*. [5]. Radiographic interpretation was carried out by a different blinded examiner independent of the clinical examiner.

Diagnosis and staging of periodontitis for both ARMD and control subjects were based on the 2017 World Workshop classification for periodontal and peri-implant conditions [24].

*Clinical and medical record collection*

Comprehensive medical data, including known ARMD-related risk indicators, were gathered for every participant to ensure proper matching between the two groups. Variables included demographic and anthropometric details (age, gender, height, weight, BMI), smoking status, medical history of hypertension (verified through antihypertensive prescriptions), diabetes diagnosis and HbA1c level for diabetic patients, total cholesterol, HDL, LDL, triglycerides, and C-reactive protein. In addition, information regarding previous ocular diseases, cancers, infections, antibiotic or corticosteroid intake, and periodontal therapy within the past three months was recorded [3, 4, 25].

Blood pressure values measured on the examination day were noted and compared with those reported by each participant's attending physician.

*Statistical workflow and data handling*

All data were processed and analyzed using R software (version 3.5.3). The tidyverse package facilitated data cleaning and visualization, while WRS2 supported robust statistical computation. Between-group comparisons relied on traditional t-tests. To validate the robustness of the findings in the presence of heteroscedasticity and potential outliers, Yuen's trimmed mean test with bootstrap calibration (1,999 resamples) was additionally applied [26].

Power calculations employed the pwr package for standard t-tests and the Luh and Guo method [27] for trimmed t-tests under unequal variance assumptions. Following Cohen's effect size guidelines, it was estimated that detecting a standardized difference of 0.8 at a power of 0.80 and $\alpha = 0.05$ would require 26 cases and 26 controls. With 40 participants per group, the current study achieved a statistical power of 0.94. For categorical data, identifying a difference of 0.5 necessitates 32 per group; thus, with 40 in each group, the achieved power reached 0.88.

## Results and Discussion

*Demographic profile of participants*

The study included 80 individuals in total—40 with Age-Related Macular Degeneration (ARMD) and 40 without the disease as matched controls. Age, gender, and exposure to ARMD risk indicators did not differ significantly between the two groups. Every participant was 55 years of age or older and had been age-matched within a three-year range. The average age for patients with ARMD was 75.8 years, while the control group averaged 71.2 years. Out of all participants, 50 were female and 30 were male, with an even gender distribution between cases and controls. The two groups were also comparable concerning predisposing factors for ARMD.

Within the ARMD cohort, 28 individuals had early-stage non-exudative ARMD, and 12 showed advanced disease, including 8 neovascular and 4 with geographic atrophy. Representative Optical Coherence Tomography (OCT) images are displayed in **Figures 1 and 2**.

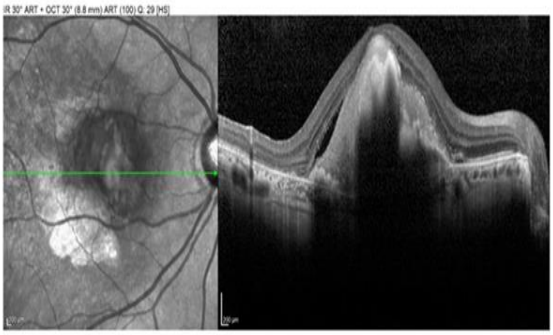


**Figure 1.** OCT image depicting neovascular ARMD.

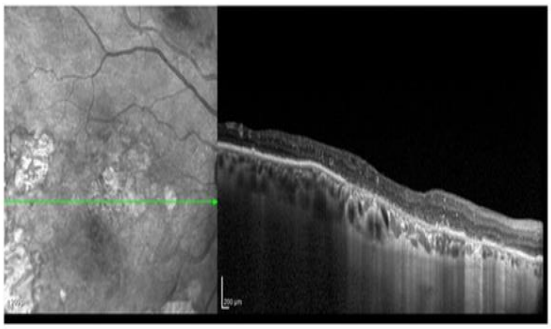


**Figure 2.** OCT image showing the atrophic (geographic) form of ARMD.

*Oral and periodontal assessment*

The results for average tooth count, mean clinical attachment level (mCAL), mean probing pocket depth (mPPD), full-mouth plaque score (FMPS%), and full-mouth bleeding score (FMBS%) are summarized for both groups in **Table 1**. The values of CAL and PPD were first averaged across each participant's teeth and then across individuals. Since participants presented with different numbers of teeth, the dataset exhibited heteroscedasticity, which was accounted for during statistical processing, as specified in the Data Management and Statistical Analysis section.

**Table 1.** Distribution of mean tooth number, mCAL, mPPD, FMPS%, and FMBS% for case and control subjects.
SD: Standard deviation.

| Group | *Average Number of Teeth (±SD)** | *Average Clinical Attachment Level (±SD)** | *Average Probing Pocket Depth (±SD)** | *Full-Mouth Bleeding Score (±SD)** | *Full-Mouth Plaque Score (±SD)** |
|---|---|---|---|---|---|
| **ARMD Cases** | 17.48 (±7.73) | 3.48 (±1.28) | 2.63 (±0.70) | 94.1% (±0.19) | 93.9% (±0.18) |
| **Non-ARMD Controls** | 17.33 (±6.68) | 3.19 (±1.56) | 2.34 (±0.64) | 74.4% (±0.37) | 81.3% (±0.31) |

The interdental CAL at the site with the most severe attachment loss, determined following Tonetti *et al*. (2018), is shown in **Table 2**. Nearly 95% of all participants had circumferential CAL values of 5 mm or greater. The classification of alveolar bone loss based on Tonetti *et al*. [24] and Karesvuo *et al*. [5] is presented in **Table 3**. Every individual—both among ARMD cases and controls—displayed generalized periodontitis, affecting at least 30% of their teeth.



**Table 2.** Interdental CAL values (maximum loss site) following Tonetti *et al*. (2018).

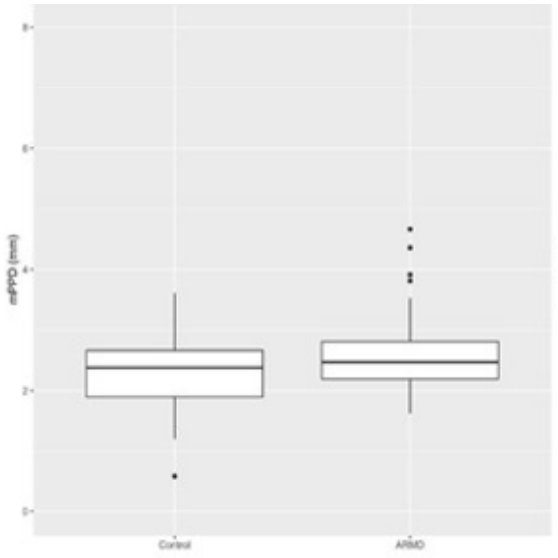
| Clinical Attachment Level at Maximum Loss Site | ARMD Cases n. (%) | Non-ARMD Controls n. (%) |
|---|---|---|
| **1–2 mm** | 0 (0%) | 0 (0%) |
| **3–4 mm** | 2 (5%) | 2 (5%) |
| **≥5 mm** | 38 (95%) | 38 (95%) |

**Table 3.** Alveolar bone loss stages based on Karesvuo *et al*. (2013) and Tonetti *et al*. (2018).

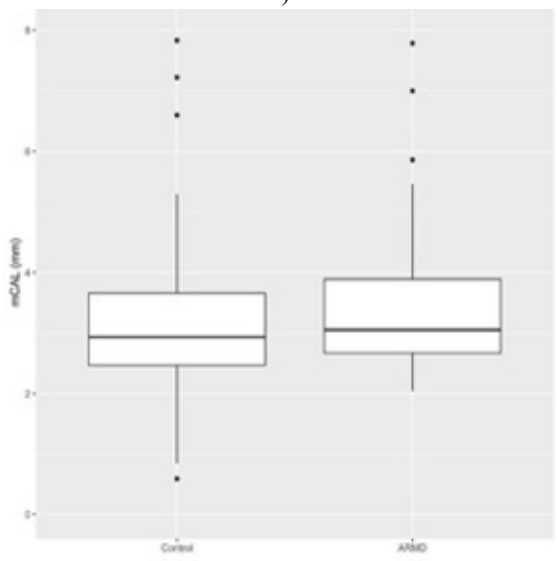
| Alveolar Bone Loss (Bone Pocket) *Based on Karesvuo et al. 2013* | ARMD Cases n. (%) | Non-ARMD Controls n. (%) |
|---|---|---|
| **Class 0: No bone pocket** | 5 (12.5%) | 6 (15%) |
| **Class 1: Bone pocket beyond the middle third of the root** | 26 (65%) | 24 (60%) |
| **Class 2: Bone pocket beyond the apical third of the root** | 9 (22.5%) | 10 (25%) |
| **Radiographic Bone Loss (RBL) Based on Tonetti *et al.* 2018** | ARMD Cases n. (%) | Non-ARMD Controls n. (%) |
| **Coronal third (<15%)** | 2 (5%) | 3 (7.5%) |
| **Coronal third (15% to 33%)** | 3 (7.5%) | 3 (7.5%) |
| **Extending to middle or apical third of the root (>33%)** | 35 (87.5%) | 34 (85%) |

*Group comparison of periodontal indicators*

When comparing the ARMD and control cohorts, no significant differences were identified in tooth number, PPD, CAL, or radiographic bone loss categories **(Figure 3)**.




a)




b)

**Figure 3.** Comparative representation of mean PPD (mPPD) and mean CAL (mCAL) values between ARMD and control groups (not statistically significant at α = 0.05).

Approximately 85% or more of participants exhibited radiographic bone loss extending into the middle or apical portion of the root, consistent with Tonetti *et al*. [24]. In addition, over 60% of subjects were categorized within bone loss classes 1 and 2, according to Karesvuo *et al*. [5] **(Table 3)**.

*Periodontal parameters and ARMD risk variables among cases*

When the analysis was limited to ARMD patients, the potential associations between tooth count, probing pocket depth (PPD), clinical attachment level (CAL), and radiographic bone loss with gender, tobacco use, body mass index (BMI), cholesterol levels, and diabetes were examined. None of these comparisons reached statistical significance.

Similarly, when assessing tooth number against blood pressure distribution, no relevant statistical association was identified. In addition, the comparisons between hypertensive and non-hypertensive ARMD subjects revealed no significant variations in tooth count, PPD, or radiographic bone loss categories. However, CAL values were notably elevated among hypertensive ARMD participants, with a p-value of 0.005, a mean difference of −0.980, and a 95% confidence interval ranging from −1.577 to −0.383, as displayed in **Figure 4**.

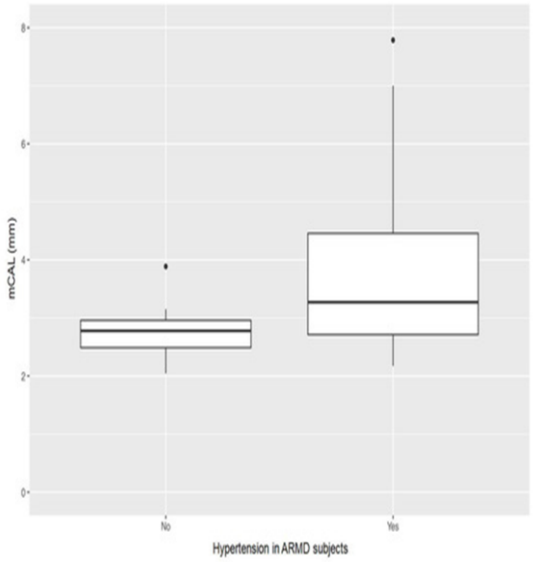



**Figure 4.** Mean CAL (mCAL) comparison between hypertensive and non-hypertensive ARMD subjects (significant at α = 0.05).

This case-control study explored the potential relationship between periodontitis and Age-Related Macular Degeneration (ARMD) by comparing both clinical and radiographic periodontal outcomes in ARMD patients and controls, and by analyzing how these parameters related to established ARMD risk determinants—including smoking status, cholesterol, HDL/LDL levels, BMI, diabetes, and hypertension—within the case group, to detect any plausible pathogenic association between the two disorders.

The case and control cohorts, matched beforehand for age and sex, also showed comparable results in BMI, blood pressure, cholesterol, and triglyceride profiles, ensuring their clinical comparability. All ARMD subjects were 55 years or older, aligning with Jonas *et al*. [28], who documented an ARMD onset range of 45–85 years, with incidence rising sharply beyond 75 years across all ethnicities.

*Comparison of periodontal parameters between cases and controls*

Assessment of clinical periodontal indicators (CAL and PPD) showed no statistically meaningful differences between the ARMD and non-ARMD groups, suggesting that the degree of periodontal compromise was similar across both. The overall poor control of local etiologic factors, reflected in elevated FMPS and FMBS values, along with the high prevalence and severity of periodontitis in both groups, may account for this similarity. Furthermore, the slightly higher FMPS% and FMBS% values noted in ARMD participants could plausibly result from reduced brushing efficiency caused by visual impairment.

In contrast, Brzozowska *et al*. [29] observed a higher occurrence of dental and periodontal lesions among ARMD patients, proposing a link between oral conditions and ARMD susceptibility. However, their investigation was retrospective and lacked a control group, differing fundamentally from the current study's controlled design.

Wagley *et al*. [10] also found an association between ARMD and periodontal disease in Caucasian patients aged 40–60, but not in those older than 60, using a disease definition from the U.S. National Institute of Dental and Craniofacial Research. Similar findings were later echoed in an Asian cohort aged ≥40 years by Shin *et al*. [11], applying the WHO Community Periodontal Index. The divergence between those findings and the present results may be attributable to different diagnostic standards, as the current study employed the 2017 classification of periodontal and peri-implant diseases and conditions [24], which is more contemporary and widely endorsed.

Another plausible explanation lies in age variation: both ARMD and control groups in this study consisted of older participants (≥55 years), matched within a three-year range, whereas the earlier studies examined younger populations. Shin *et al*. [11] postulated that in middle-aged individuals, the inflammatory mechanisms linked to both ARMD and periodontitis—possibly under genetic influence—are more pronounced, while in older subjects, oxidative stress and degenerative processes overshadow such inflammatory contributions. Hence, in the current dataset, this shared inflammatory component may have been masked by the participants' higher age.

Regarding radiographic periodontal assessment, alveolar bone loss was analyzed using both Tonetti *et al*. [24] and Karesvuo *et al*. [5] classification systems. No significant difference emerged between cases and controls under either approach. Conversely, Karesvuo *et al*. [5] reported greater bone loss in ARMD patients than in controls. This discrepancy might be explained by age mismatch in their research, as their control group was younger, whereas the current one was age-matched (±3 years).

Furthermore, based on the radiographic bone loss data from Karesvuo *et al*. [5, 30], their population appeared to have healthier periodontal conditions than ours, likely due to fewer local etiologic influences. This remains speculative, as Karesvuo *et al*. did not provide information regarding plaque accumulation or gingival inflammation. In the current analysis, however, the presence of active local factors and gingival inflammation in both groups—evidenced by FMPS% and FMBS% **(Table 1)**—could have masked the effect of other systemic risk factors.

*Periodontal indicators in relation to ARMD risk factors among cases*

In this study, when analyses were restricted to ARMD patients, periodontal measures—including tooth count, CAL, PPD, and radiographic bone levels—were examined against potential ARMD risk factors such as smoking, cholesterol, HDL/LDL, BMI, diabetes, and hypertension.

Among these, only hypertensive patients exhibited significantly higher CAL values compared to non-hypertensive participants. Interestingly, previous research has linked hypertension primarily with moderate periodontitis, as defined by earlier criteria of the American Academy of Periodontology and the Centers for Disease Control [31], whereas in this study, most ARMD patients presented with stage III or IV periodontitis [24]. Some studies, however, did not find any association between periodontal disease and hypertension [32]. Moreover, hypertension has been previously identified as a risk factor for cardiovascular disease and ARMD, each recognized independently [11, 33, 34].

No significant differences in PPD were observed between hypertensive and non-hypertensive ARMD cases. Similarly, tooth counts did not differ significantly between the two subgroups. This is notable because earlier work suggested that fewer teeth may correlate with higher cerebrovascular or cardiovascular risk [35] or with increased hypertension risk in post-menopausal women [36]. Reduced dentition could influence hypertension either through the systemic pro-inflammatory effects of periodontal disease [32, 37] or due to altered dietary intake resulting from fewer teeth, as initially proposed by De Stefano *et al*. [38] and Appel *et al*. [39], and later supported by Lowe *et al*. [40] and Zhu and Hollis [41].

Furthermore, Shin *et al*. [11] reported that fewer teeth were associated with higher systolic blood pressure. This relationship was assessed in the current study but was not observed. The lack of significant associations between tooth number, systolic pressure, and hypertension in both cases and controls may be explained by the overall low tooth counts and widespread residual ridge resorption in the study population [42].

## Conclusion

Although mounting evidence suggests a possible link between periodontitis and ARMD [10, 43, 44], and previous studies have shown alveolar bone loss and periodontal pathogens in ARMD patients, the present analysis did not detect significant differences in either clinical or radiographic periodontal parameters between cases and controls, thus not supporting a direct association.

The elevated CAL in hypertensive ARMD patients suggests that hypertension could act as a potential pathogenic bridge between ARMD and periodontal disease.

Nonetheless, further research with larger cohorts is necessary to confirm this hypothesis. The strict diagnostic criteria applied in this study, while ensuring methodological rigor, limited the sample size, representing a potential limitation, together with possible selection and confounding biases inherent to case-control designs.

A more detailed understanding of the pathophysiological mechanisms linking ARMD onset and progression with periodontal disease may guide the development of patient-centered preventive strategies targeting the leading cause of blindness among elderly populations in industrialized nations. Such insights could foster an integrated, multidisciplinary approach, combining dental care and medical management to optimize outcomes for older patients.

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**Conflict of Interest:** None

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**Ethics Statement:** None

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