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The association of periodontitis with telomere length: a meta-analysis

Qinqin Sun[1†], Jinqing Xiao[1†] and Jinfeng Huo[1*]

Abstract

Background Telomere length (TL) is a biomarker of biological aging and has been linked to various health outcomes; however, its relationship with periodontitis remains inconsistent. This meta-analysis aimed to evaluate the association between periodontitis and TL.

Methods PubMed, Scopus, Medline, and Embase databases were searched for relevant studies published until August 2025. The differences in mean TL between those with and without periodontitis were measured using standardized mean difference (SMD) with 95% confidence intervals (CIs), while standardized beta coefficients (β) and their 95% CIs were applied to assess the strength of the association using a random effects model.

Results Ten observational studies including 22,625 participants were analyzed. The overall results indicated no significant difference in mean TL between individuals with and without periodontitis (SMD = -0.03, 95% CI = -0.09 to 0.03). Additionally, no significant association was observed between periodontitis and TL (β = -0.001, 95% CI = -0.01 to 0.01). Subgroup analysis revealed that patients under 50 years old (SMD = -0.25, 95% CI = -0.41 to -0.09) and Asian patients (SMD = -0.44, 95% CI = -0.82 to -0.06) had significantly shorter TL compared to those without periodontitis. Additionally, periodontitis was significantly inversely associated with TL in these groups (age < 50: β = -0.07, 95% CI = -0.11 to -0.03; Asians: β = -0.20, 95% CI = -0.38 to -0.03).

Conclusion Periodontitis may be linked to shorter TL, indicating that TL could potentially serve as a biomarker for periodontal health.

Keywords Periodontitis, Telomere length, Aging, Meta-analysis

Introduction

Periodontitis is a chronic inflammatory disease characterized by the progressive destruction of the supporting structures of the teeth, including the periodontal ligament and alveolar bone [1]. Periodontitis is recognized as a significant public health challenge worldwide [2]. It is the leading cause of tooth loss among adults [3] and is linked to a higher risk of systemic conditions including cardiovascular disease, diabetes, chronic respiratory illnesses, and cancer [4]. About 50% of adults experience some degree of periodontitis [5], with higher prevalence among males, racial or ethnic minorities, individuals of lower socioeconomic status, and older adults [6].

†Qinqin Sun and Jinqing Xiao are co-1st author.

*Correspondence:
Jinfeng Huo
jinfeng20140923@126.com
[1]Department of Stomatology, Shandong Provincial Third Hospital, Cheeloo College of Medicine, Shandong University, No. 11, Middle Shadowshan Road, Jinan, Shandong 250000, China

The pathogenesis of periodontitis involves a complex interplay between genetic, microbial infection and host immune-inflammatory responses, which can induce oxidative stress and cellular damage [7]. Additionally, obesity, diabetes mellitus, alcohol use, cigarette smoking, and psychological stress are possible risk factors contributing to the incidence and severity of periodontitis [8–10].

Aging is regarded as a key risk factor for periodontitis, as it facilitates the colonization of pathogenic microorganisms, triggers a pro-inflammatory environment, and exacerbates bone loss [11]. Multiple prospective cohort studies have consistently reported that periodontal attachment loss increases with advancing age [12, 13]. Several experimental studies have demonstrated significant individual differences in aging, influenced by a combination of genetic factors and environmental exposures [14]. Ageing is typically measured by chronological age; however, research indicates that people of the same chronological age can differ in their vulnerability to age-related diseases, implying that chronological age does not completely or accurately represent the actual aging process [15]. Telomere length (TL), consisting of TTAGGG nucleotide repeats at chromosome ends, serves as an indicator of biological aging [16]. Telomeres play a crucial role in maintaining genomic stability and cellular replicative capacity [17] and play a key role in the progression of age-related chronic diseases [18]. TL gradually decreases with every cell division because the DNA replication process cannot completely replicate the 5' end of the lagging DNA chain [19]. This process ultimately leads to cellular senescence, a condition that can be hastened by inflammation, oxidative stress, and aging [5]. The variation in the prevalence of periodontitis among populations of the same age may be attributed to differences in TL [6].

Emerging evidence suggests a potential link between periodontitis and telomere attrition. Regarding the association between TL and periodontitis, three studies demonstrated that individuals with chronic periodontitis had shorter TL than healthy individuals [6, 20, 21]. Conversely, two other studies found that TL was comparable in periodontitis patients and healthy subjects [13, 22], and another study found a positive correlation between TL and periodontitis [23]. The inconsistent results are possibly due to differences in study design, population characteristics, and the level of adjustment for covariates. This meta-analysis aims to systematically synthesize existing research to clarify the relationship between periodontitis and TL, thereby providing insights into the potential factors contributing to the heterogeneity across the studies.

Materials and methods

This study was carried out and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [24]. Since this study did not use original data of patients, ethical approval as not required.

Search strategy

We conducted a comprehensive search without any language restrictions for all relevant studies published up to August 2025 across the PubMed, Scopus, Medline, and Embase databases to identify pertinent studies. The following keywords and Medical Subject Headings (MeSH) were employed: ("Periodontitis"[Mesh] OR periodontitis[Title/Abstract] OR periodontal[Title/Abstract] OR periodont*[Title/Abstract] OR periodontal attachment loss[Title/Abstract] OR periodontal disease[Title/Abstract]) AND ("Telomere Shortening"[Mesh] OR "Telomere"[Mesh] OR telomere[Title/Abstract] OR telomere length[Title/Abstract] OR telomeres[Title/Abstract]). References from eligible articles and relevant reviews were also manually examined to identify any studies that might have been missed. The studies were imported into EndNote 8 software, where duplicates were removed. Subsequently, the remaining studies were assessed for eligibility based on the predefined inclusion criteria.

Selection criteria

Studies included in this meta-analysis met the following criteria: (1) included studies were observational in design (case-control, cohort, cross-sectional), (2) included patients diagnosed with periodontitis and considered subjects without periodontitis as control group, (3) examined the association between TL and periodontitis, regardless of the specimen type used for TL measurement, (4) reported sufficient data including sample size, unstandardized regression coefficient, and correlation coefficient to estimate standardized beta coefficients (β) with 95% confidence intervals (CIs) for the relationship between periodontitis as exposure and TL as outcome, (5) measured TL from leukocytes or gingival crevicular epithelium cells. Excluded studies were review articles, republished studies, letters, editorials, studies lacking enough data, or those that did not use TL as a biological marker of aging. Two researchers independently assessed eligibility, with disagreements resolved by a third author.

Data extraction and quality assessment

Data extracted from each study included: the first author's name, study design, publication year, country of origin, sample size, TL measurement methods, DNA source, participants' ethnicity, average age, gender distribution, body mass index (BMI), prevalence of current

smokers, diabetes, hypertension, level of education, number of cases, mean TL, effect sizes for the associations, and variables adjusted for in the analyses. When multiple estimates for the association were reported, the one adjusted for the most covariates was selected. If essential data were missing, corresponding authors were contacted directly. Two reviewers independently extracted the data and evaluated study quality, resolving any disagreements through discussion with a third reviewer. The methodological quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS), which evaluates studies across three main domains: Selection, Comparability, and Outcome or Exposure. Studies scoring between 7 and 9 stars on the NOS were classified as high quality, those scoring 5 to 6 stars as moderate quality, and those with less than 5 stars as low quality [25].

Statistical analysis

Standardized beta coefficients (β) with their 95% CIs were used as the effect size to evaluate the association between periodontitis (exposure) and TL (outcome). Standardized mean difference (SMD) with 95% CI was used to assess the differences in mean TL between patients with and without periodontitis. For studies where TL was the outcome, effect sizes were originally reported using different statistical measures, such as regression coefficients, correlation coefficients, or mean differences between exposed and non-exposed groups. To enable pooling of these effect sizes, we converted them into β with corresponding 95% CIs using the formulas provided in supplementary file 1. Statistical heterogeneity among studies was assessed using Cochran's Q test and the I^2 statistic, with $I^2 \geq 50\%$ indicating significant heterogeneity. Data were pooled using a random-effects model according to the DerSimonian and Laird method [26, 27]. To explore sources of heterogeneity, subgroup analyses were conducted according to study quality, sex, median sample size (≥ 700 vs. <700 participants), geographic region (Asian vs. non-Asian), obesity status (BMI ≥ 30 vs. <30 kg/m²), median age (≥ 50 vs. <50 years), and adjustment for covariates including age, BMI, diabetes, hypertension, education, income, ancestry, sex, and smoking status. Meta-regression analyses examined the impact of racial composition (percentages of Black and White participants), prevalence of diabetes and hypertension, proportion of participants with advanced education (college level or above), percentage of smokers, participant sex (% male), and study quality score on the pooled effect size. Sensitivity analyses were performed by sequentially removing each study to assess their influence on the overall pooled estimates. Additional sensitivity analyses excluded one study that measured TL from gingival crevicular epithelium cells (while others used leukocyte TL) and another study that used Southern blot for TL measurement (versus quantitative PCR in others). Publication bias was evaluated using funnel plots and Egger's test [28]; if bias was detected ($P < 0.05$), the trim-and-fill method was applied to adjust the pooled effect size. Analyses were conducted using Stata version 15.1 (StataCorp LLC, Texas, USA), with all tests two-sided and a significance threshold of 0.05.

Results

Study characteristics

The databases systematic search initially retrieved 163 studies, with 42 duplicates excluded. Following title and abstract screening, additional 97 unrelated citations were removed. Subsequently, 24 potentially relevant studies were subjected to full-text review. During this phase, 14 more publications were excluded due to various reasons, including being, duplicate publications, review studies, studies focusing on telomerase gene expression, or having irrelevant exposures or outcomes. List of studies that were retrieved in full text but excluded at the eligibility stage is presented in Table S1. A total of 10 studies [6, 13, 20–23, 29–32], published between 2004 and 2025, with a combined sample of 22,625 subjects, were ultimately analyzed. Figure 1 presents the study selection process. Data to estimate the mean difference in TL between patients with and without periodontitis were available from seven studies [6, 20, 22, 29–32], while all included studies provided data to assess the association of periodontitis with TL using standardized beta regression. Among the studies, two focused on Asian populations [22, 31], while eight involved non-Asian populations [6, 13, 20, 21, 23, 29, 30, 32]. Nine studies measured TL with the use of the qPCR method, while one study [22] employed the Southern blotting technique for TL measurement. The study by Sonoki et al. [31] used gingival crevicular epithelium cells as the source for DNA, whereas the other studies applied peripheral blood leukocytes for TL assessment. The average age of participants ranged from 27.9 ± 4.8 years to 74.3 ± 7.6 years. All studies had a cross-sectional design, except for the study conducted by Thomson et al. [13], which was a prospective cohort study. According to the NOS, the included studies exhibited moderate to high methodological quality, with total scores between 4 and 9 (Table S2). The detailed reporting of periodontitis case definitions and severity classifications is presented in Table S3. Key details include: the Centers for Disease Control and Prevention and American Academy of Periodontology (CDC/AAP) criteria used in 5 studies [6, 21, 22, 30, 32], with severe periodontitis defined as ≥ 2 interproximal sites with clinical attachment loss (CAL) ≥ 6 mm (not on same tooth) + ≥ 1 interproximal site with PD ≥ 5 mm; custom PD/CAL thresholds (> 4 mm PD + bleeding in Sonoki et al. [31]; ≥4 mm CAL/PD in Masi et al. (2011) [20]; partial/full-mouth protocols (e.g., 2–6

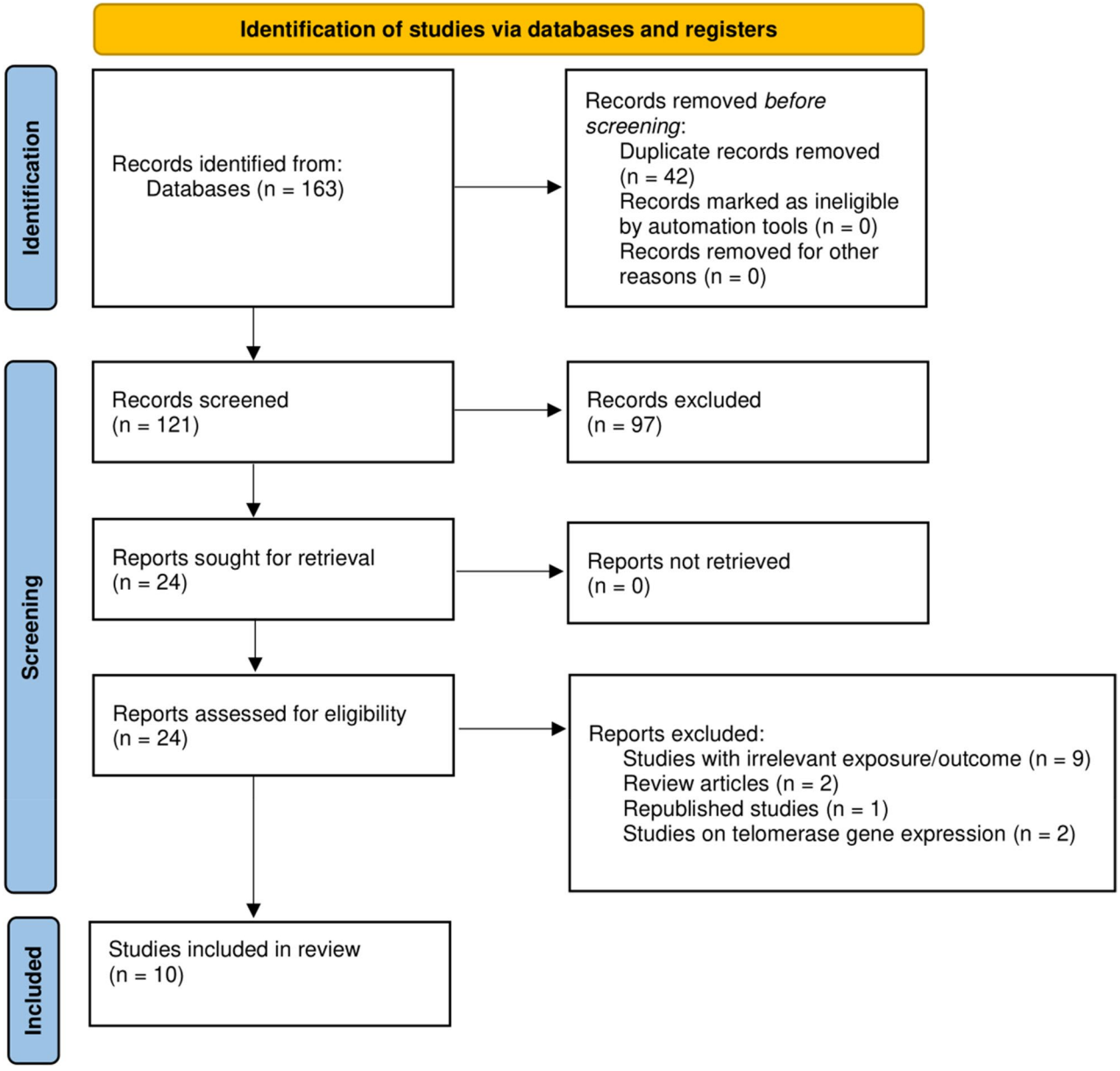

Fig. 1 Flow diagram of the study

sites/tooth, specific quadrants); and basic periodontal examination (BPE)/World Health Organization (WHO) index in Masi et al. (2014), with scores 3–4 for moderate/severe [29]. In analyses, mild cases were generally excluded or combined with none; moderate/severe were pooled as primary exposure due to low number of severe cases. The characteristics of the eligible citations are summarized in Table 1.

Quantitative analysis

Figure 2 presents a forest plot of the pooled effect sizes and subgroup analyses by sex for the mean difference in TL between patients with and without periodontitis. The analysis found no significant difference in the mean TL between patients with and without periodontitis (SMD = −0.03, 95% CI = −0.09 to 0.03), though notable heterogeneity was observed across studies (I^2 = 43.0%, P = 0.08). In the subgroup analysis, patients younger than 50 years (SMD = −0.25, 95% CI = −0.41 to −0.09) and Asian patients (SMD = −0.44, 95% CI = −0.82 to −0.06) showed significantly shorter telomere lengths compared to those without periodontitis (Table 2).

Figure 3 shows a forest plot of the standardized β coefficients, including overall results and sex-specific subgroups, examining the association between TL and periodontitis.No significant overall association was

Table 1 Characteristics of studies

Study (year)	Country	Study type	Male (%)	Sample size	Mean TL	Source of DNA	TL assessment	Age (mean ± sd)	Mean BMI (Kg/m^2)	Smokers (%)	Advanced education (college and above) (%)	Diabetes (%)	Hypertension (%)	Ancestry composition	Adjustment
Sonoki (2024) [31]	Japan	Cross-sectional	32	25	392.6 ± 232.8 kb	Gingival crevicular epithelium cells	qPCR	72.4 ± 7.8	NR	NR	NR	NR	NR	NR	Not adjusted
Thomson (2016) [13]	New Zealand	Prospective cohort	54	734	6277 ± 3723 bp	Peripheral blood leukocytes	qPCR	NR	NR	36	NR	NR	NR	NR	Sex, socio-economic status, smoking, cannabis use, and age
Song (2021) [21]	USA	Cross-sectional	52	3478	5763 ± 2123 bp	Peripheral blood leukocytes	qPCR	49.5 ± 29.4	NR	20.6	46.9	10	30.9	79.84% White, 17.4% Black, 2.6% others	Age, sex, race/ethnicity, family income to poverty ratio, education, smoking, BMI, and cardiometabolic comorbidity includding diabetes and hypertention
Shen (2025) [23]	USA	Cross-sectional	50.5	2521	5459 ± 2544 bp	Peripheral blood leukocytes	qPCR	74.3 ± 7.6	27.8 ± 4.9	17.4	30.3	23.7	48.6	81.5% White, 12.3% Black, 6.2% others	Sex, age, race, education, poverty income ratio, BMI, smoking, diabetes, and hypertension
Sanders (2015) [6]	USA	Case-control	49	356	5807 ± 3684 bp	Peripheral blood leukocytes	qPCR	62.6 ± 5.5	NR	20	40.4	17	35.6	52.5% White, 47.5% Black	Age, sex, race, income, smoking, BMI, and number of retained natural teeth
Nguyen (2022) [30]	USA	Cross-sectional	49.8	3454	5823 ± 668 bp	Peripheral blood leukocytes	qPCR	30 to 80	NR	9	NR	NR	NR	47.9% White, 17.3% Black, 34.8% others	Not adjusted
Masi (2011) [20]	UK	Case-control	41.3	563	7670 ± 2632 bp	Peripheral blood leukocytes	qPCR	46.9 ± 8.2	NR	35.4	NR	NR	NR	65.8% White, 34.2% others	Age, race, sex, and smoking
Masi (2014) [29]	UK	Cross-sectional	59.5	630	5977 ± 3977 bp	Peripheral blood leukocytes	qPCR	54.2 ± 16.0	29.1 ± 7.6	15.3	NR	100	NR	65.8% White, 31.3% others	Age, sex, ethnicity, diabetes type, smoking, waist circumference, circulating levels of endotoxin, medication use, insulin, and CRP
Nguyen (2025) [32]	USA	Cross-sectional	NR	10,793	5706 ± 612 bp	Peripheral blood leukocytes	qPCR	≥ 30 years	NR	NR	NR	NR	NR	NR	Not adjusted
Takahashi (2004) [22]	Japan	Case-control	33.3	71	8350 ± 1190 bp	Peripheral blood leukocytes	Sothern blot	27.9 ± 4.8	NR	NR	NR	NR	NR	100% white	Age

NR not reported, *qPCR* quantitative polymerase chain reaction, *TL* telomere length, *BMI* body mass index, *bp* base pairs

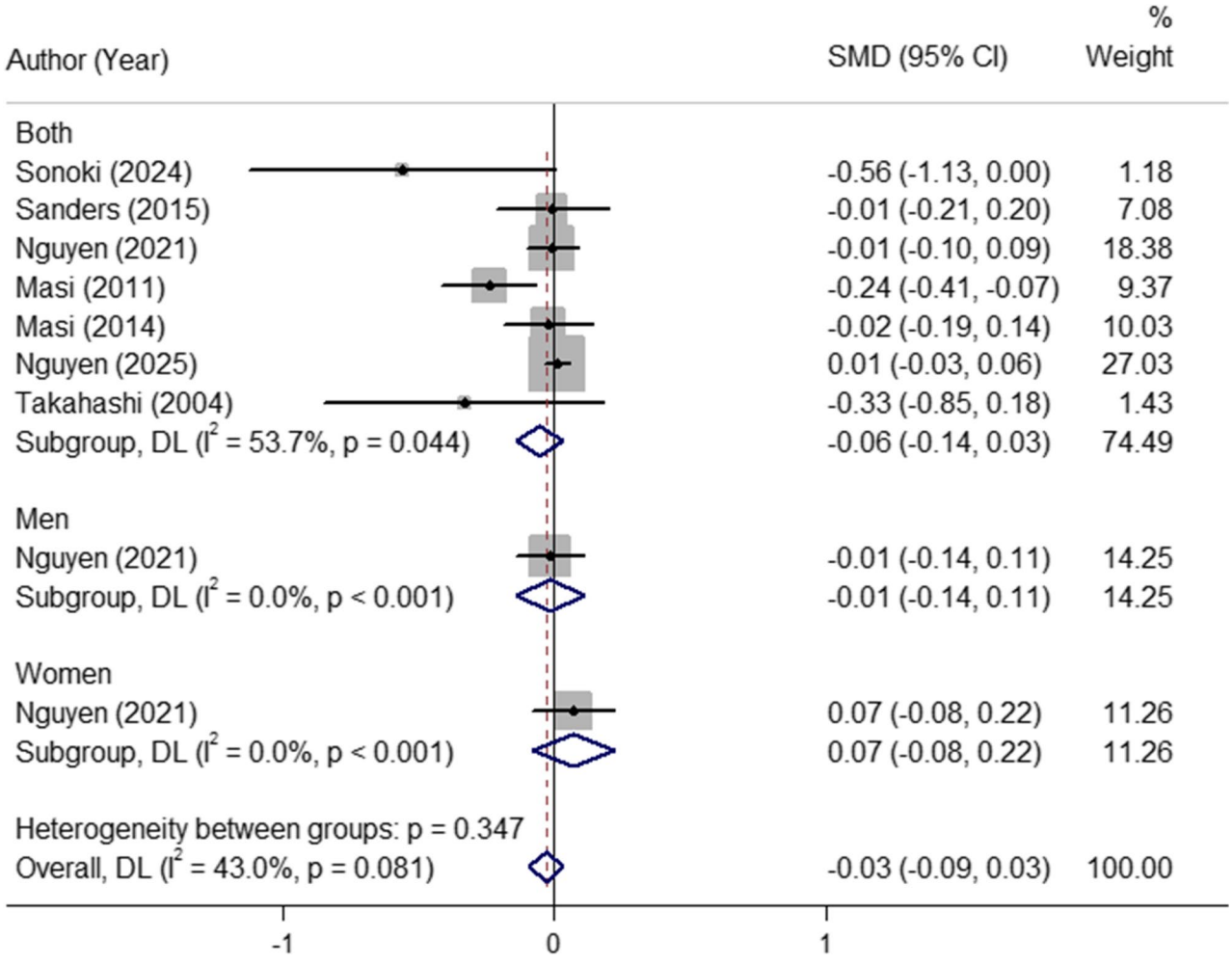

Fig. 2 Overall and subgroup analysis by the gender of participants for the association between serum vitamin D and telomere length

found between periodontitis and TL (β = −0.001, 95% CI = −0.01 to 0.01). There was significant heterogeneity among the studies (I^2 = 67.9%, $P < 0.001$). In subgroup analyses, periodontitis was significantly inversely linked to TL in patients aged < 50 years (β = −0.07, 95% CI = −0.11 to −0.03), in Asian populations (β = −0.20, 95% CI = −0.38 to −0.03), and in studies with smaller sample sizes (β = −0.11, 95% CI = −0.22 to −0.001) (Table 2). No significant associations were found in subgroups defined by gender, obesity status, or level of covariate adjustment (Table 2).

Meta-regression analysis

The results of meta-regression analysis are presented in Table S4. The meta-regression analyses revealed that the associations were not influenced by factors such as the racial composition of the studied population, smoking status, quality of studies, education level, study quality score, participants' sex ratio (% males), or history of diabetes and hypertension, with all P-values being ≥ 0.10.

Sensitivity analysis

None of the individual studies significantly influenced the overall pooled estimates in the sensitivity analysis. Additionally, excluding the study by Sonoki et al. [31], which measured TL from gingival crevicular epithelium cells, and the study by Takahashi et al. [22], which used Southern blotting for TL measurement, did not change the results. When studies at clearly higher risk of bias (NOS score ≤ 4) were exclude, the main results did not changes remarkably (SMD for TL= −0.03, 95% CI = −0.08 to 0.02; β for association= −0.001, 95% CI = −0.02 to 0.01).

Publication bias

A significant publication bias was identified in studies investigating the mean difference in TL between patients with and without periodontitis ($P = 0.04$; Fig. 4). Nonetheless, the trim-and-fill analysis, which adjusts for publication bias, showed no change in the pooled effect sizes (SMD for TL= −0.029, 95% CI = −0.091 to 0.034; β for association= −0.002, 95% CI = −0.010 to 0.007),

Table 2 Overall and subgroup analysis for the association between periodontitis and telomere length

	Test of association				Test of heterogeneity		
	Subgroup variable	**Subgroups**	**Studies**	***SMD*/β**	**95%CI**	**I^2 (%)**	***P***
Standardized mean difference of relative TL between patients with and without periodontitis		Overall	7 (9 effect sizes)	−0.03	−0.09 to 0.03	43.0	0.08
	Gender	Men	1	−0.01	−0.14 to 0.11	-	-
		Women	1	0.07	−0.08 to 0.22	-	-
		Both	6	−0.06	−0.14 to 0.03	53.7	0.04
	Sample size	≥ 700 participants	2	0.01	−0.03 to 0.05	0.0	0.75
		< 700 participants	5	−0.14	−0.29 to 0.01	45.5	0.11
	Geographic region	Asian	2	−0.44	−0.82 to −0.06	0.0	0.55
		Non-Asian	5	−0.01	−0.07 to 0.04	31.5	0.18
	Quality of studies	High	3	−0.04	−0.16 to 0.09	0.0	0.50
		Low/moderate	4	−0.03	−0.11 to 0.05	59.8	0.02
	Age	≥ 50 years	3	−0.07	−0.25 to 0.12	41.0	0.18
		< 50 years	2	−0.25	−0.41 to −0.09	0.0	0.73
		NR	2	0.01	−0.03 to 0.05	0.0	0.75
Standardized β regression for the association of periodontitis with TL (outcome)		Overall	10 (18 effect sizes)	−0.001	−0.01 to 0.01	67.9	< 0.001
	Gender	Men	4	−0.01	−0.04 to 0.02	43.8	0.14
		Women	4	−0.02	−0.07 to 0.02	75.5	0.007
		Both	10	−0.001	−0.01 to 0.01	72.0	< 0.001
	Sample size	≥ 700 participants	5	0.01	−0.01 to 0.02	46.5	0.11
		< 700 participants	5	−0.11	−0.22 to − 0.001	75.8	0.002
	Geographic region	Asian	2	−0.20	−0.38 to −0.03	0.0	0.48
		Non-Asian	8	−0.001	−0.01 to 0.01	73.9	< 0.001
	Quality of studies	High	6	−0.001	−0.01 to 0.01	75.9	< 0.001
		Low/moderate	4	−0.001	−0.02 to 0.02	73.7	0.01
	Age	≥ 50 years	5	0.001	−0.01 to 0.01	81.7	< 0.001
		< 50 years	3	−0.07	−0.11 to −0.03	7.8	0.33
		NR	2	−0.02	−0.07 to 0.02	0.0	0.77
	BMI	≥ 30 Kg/m^2	2	−0.03	−0.10 to 0.05	88.7	0.003
		< 30 Kg/m^2	2	0.01	−0.001 to 0.02	0.0	0.79
	Adjusted for age	Yes	7	−0.001	−0.02 to 0.01	78.3	< 0.001
		No	3	−0.001	−0.03 to 0.03	50.5	0.13
	Adjusted for BMI	Yes	4	−0.001	−0.02 to 0.01	82.4	< 0.001
		No	6	−0.01	−0.04 to 0.02	65.8	0.01
	Adjusted for diabetes	Yes	3	−0.001	−0.02 to 0.01	84.3	0.002
		No	7	−0.02	−0.05 to 0.02	68.4	0.004
	Adjusted for hypertension	Yes	2	−0.02	−0.07 to 0.04	84.3	0.01
		No	8	−0.001	−0.02 to 0.01	64.3	0.06
	Adjusted for education	Yes	2	−0.02	−0.07 to 0.04	84.3	0.01
		No	8	−0.001	−0.02 to 0.01	64.3	0.06
	Adjusted for income	Yes	3	−0.03	−0.10 to 0.04	81.5	0.004
		No	7	−0.001	−0.02 to 0.01	60.9	0.01
	Adjusted for ancestry	Yes	5	−0.001	−0.02 to 0.01	83.3	< 0.001
		No	5	0.001	−0.02 to 0.03	42.0	0.14
	Adjusted for sex	Yes	6	−0.001	−0.02 to 0.01	80.9	< 0.001
		No	4	−0.001	−0.04 to 0.03	47.6	0.12
	Adjusted for smoking	Yes	6	−0.001	−0.02 to 0.01	80.9	< 0.001
		No	4	−0.001	−0.04 to 0.03	47.6	0.12

SMD standardized mean difference

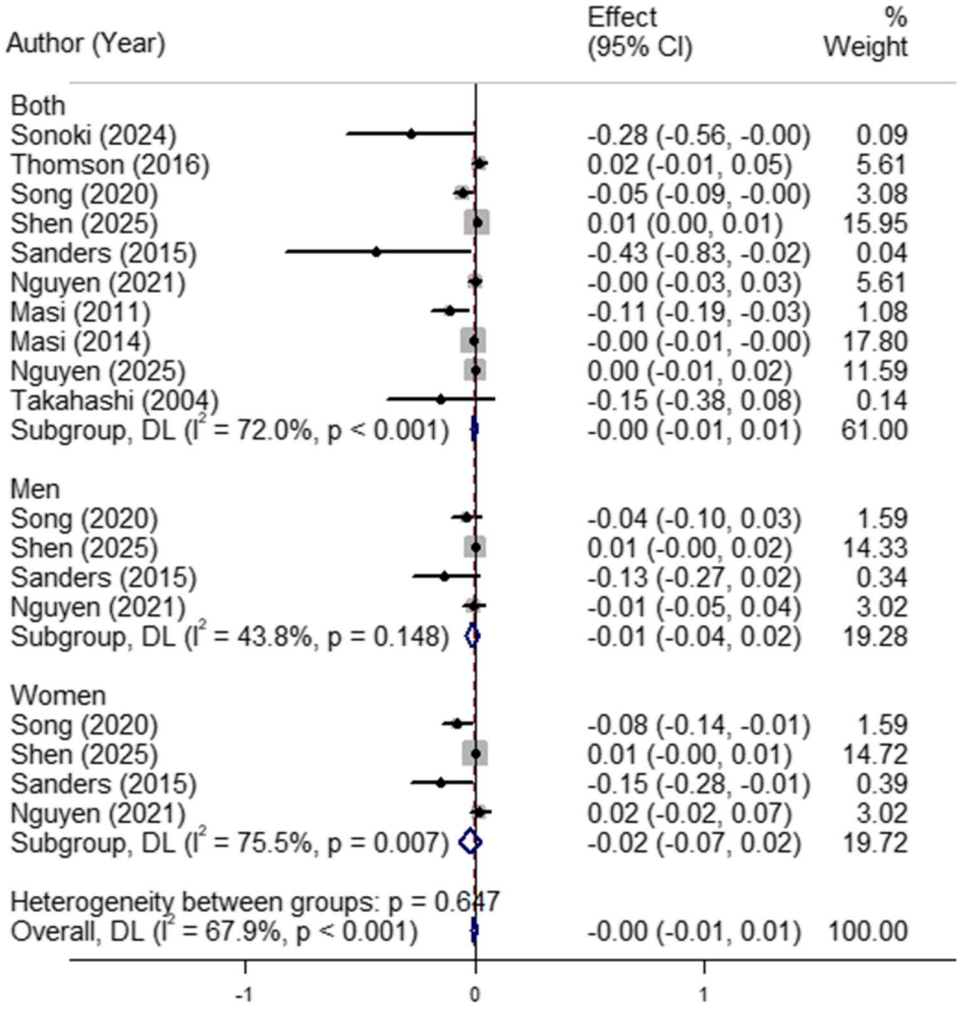

Fig. 3 Sensitivity analyses by excluding one study at a time

supporting the robustness of the findings (Figure S1 and Figure S2).

Discussion

This meta-analysis examined the relationship between periodontitis and TL. While no significant association was found in the overall analysis, the results showed that periodontitis is inversely related to TL in patients younger than 50 years old, Asian populations, and studies with smaller sample sizes. This relationship was not influenced by factors such as the racial composition of the studied population, smoking habits, education level, study quality, obesity, degree of covariate adjustment, participant gender, or histories of diabetes and hypertension.

Only a limited number of studies have explored the link between periodontitis and TL, and their findings have been inconsistent. The cross-sectional study conducted by Song et al. involving 3,478 participants provided evidence supporting a significant link between periodontitis and shorter TL in females [21]. Masi et al. compared leukocyte TL between 356 individuals with periodontitis and 257 healthy controls, finding that TL was significantly shorter in the periodontitis group. This association remained significant after adjusting for factors such as smoking habits, ancestry, gender, and age [20]. In a nested case-control study matched by ancestry, gender, study site, and age, leukocyte TL was found to be significantly shorter in periodontitis cases compared to controls, supporting the association between periodontitis and accelerated cellular aging [6]. On the contrary, Thomson et al. reported that despite both periodontitis and TL being age-dependent, there was no apparent link between them [13]. Additionally, a cross-sectional study by Shen et al. including 2,521 U.S. adults (aged 61–85, with 50.5% men) found a positive relationship between periodontitis and TL [23]. Variability in study results may be attributed to differences in patient characteristics, racial backgrounds, and sample sizes.

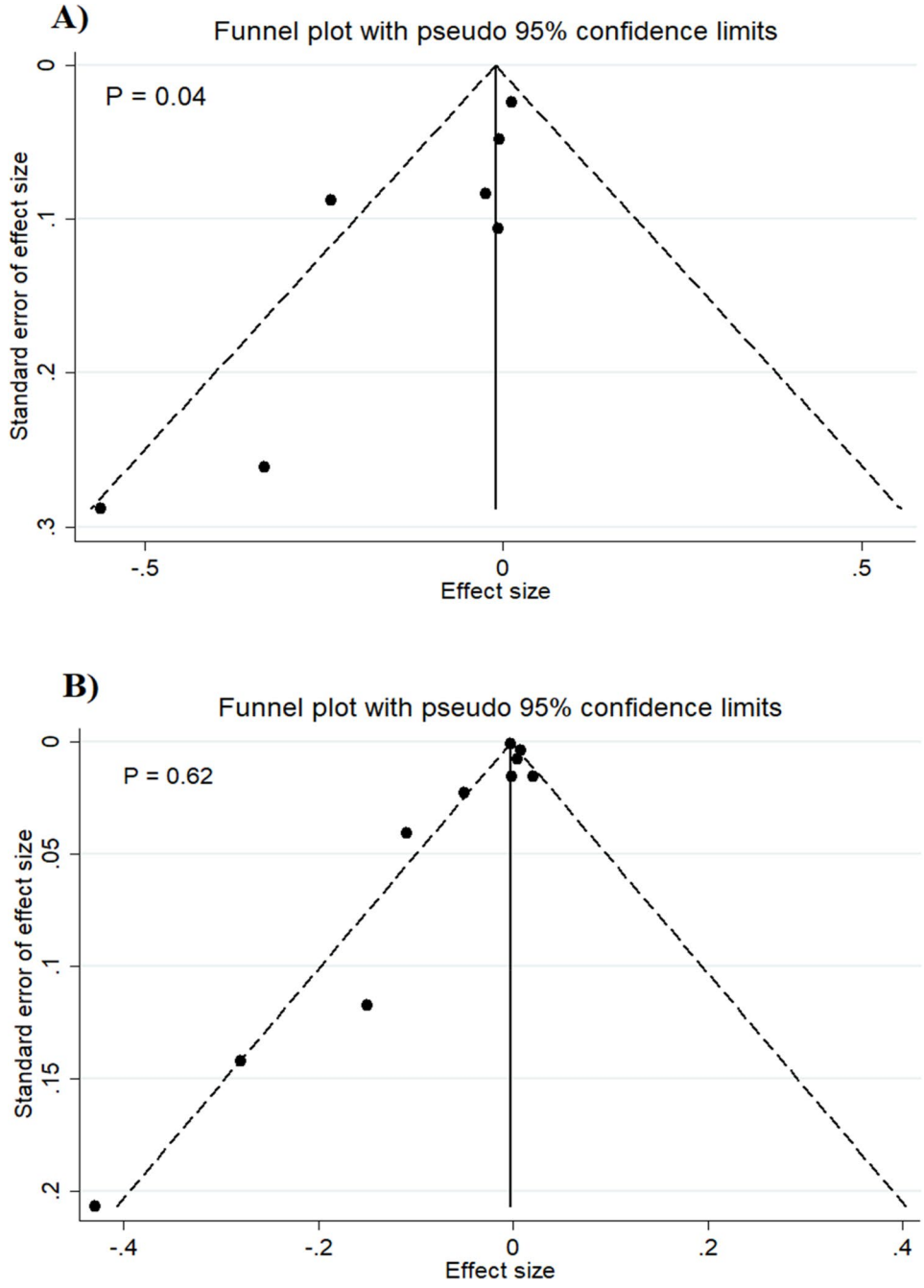

Fig. 4 Funnel plot for publication bias

The present study suggested that periodontitis may be correlated to accelerated TL shortening in younger patients and Asian populations, but not in older patients and non-Asians, which may be explained by several factors. Younger individuals tend to have less cumulative exposure to confounding aging processes, making the relationship between periodontitis and cellular aging more apparent in this group. Additionally, younger patients naturally have longer telomeres where shortening is more detectable [33]. Nguyen et al. [30] supported our findings by demonstrating that periodontitis progressively reduces TL up to age 50. Interestingly, they also observed that TL in patients with periodontitis gradually increased after age 50, with TL in patients over 70 comparable to those of the general population. An explanation could be that chronic periodontal disease may alter the age-related loss of immune cells and immune aging by favoring a subset of lymphocytes with more normal TL. This shift could lead to reduced immune response diversity, increased autoimmune and chronic

inflammatory diseases, and greater infection risk in aging individuals with periodontitis [30]. Furthermore, Sanders et al. attributed the lack of association between periodontitis and TL change in patients aged 53 to 73 to the possibility that most telomere shortening had already occurred earlier in life during the initial stages of the disease [6]. The finding in Asian populations could be due to genetic, environmental, or lifestyle factors that modulate the impact of periodontitis on TL, as well as potential differences in disease severity, immune response, or susceptibility to oxidative stress and inflammation across ethnic groups. The findings were also supported by studies with lower sample sizes. Smaller studies may capture more homogeneous samples or control confounding factors more tightly, making the association clearer. Importantly, this relationship was not affected by other variables such as smoking, education, obesity, gender, or histories of diabetes and hypertension, indicating that the link between periodontitis and TL in these groups is likely specific rather than confounded by common risk factors. Future research is needed to clarify the mechanisms behind these age- and ethnicity-specific associations.

Mechanistically, periodontitis could contribute to telomere shortening primarily through chronic inflammation and oxidative stress, both key features of periodontitis, which accelerate telomere shortening and cellular aging [20]. Telomeres protect DNA integrity but progressively shorten with each cell division [19]. In periodontitis, persistent inflammation caused by bacterial pathogens triggers the release of inflammatory cytokines and reactive oxygen species that increase oxidative damage to DNA, including the telomeric regions, promoting faster telomere erosion [34]. This leads to premature cellular senescence and impaired regenerative capacity in periodontal tissues. Additionally, bacterial components, such as lipopolysaccharides from periodontal pathogens, may directly induce telomere shortening in local gingival epithelial and endothelial cells [31]. Shortened telomeres in immune cells can also impair immune function, potentially exacerbating periodontal disease progression [5]. Thus, telomere shortening reflects the biological aging effects of chronic periodontal inflammation and damage at the cellular level, linking periodontitis with accelerated cellular senescence and systemic aging processes. The finding of shorter TL in individuals with periodontitis may offer a biological rationale for the observed increased mortality rate in these patients compared to the general population [35]. Furthermore, understanding the biological link between periodontitis and cellular aging underscores the importance of comprehensive periodontal care not only for oral health but also for its potential impact on overall aging and systemic diseases, such as cancers and cardiovascular disease. This meta-analysis does not conclude that telomere length measurement predicts periodontitis risk as causality could not be inferred; it identifies an association suggesting accelerated cellular aging as a mechanistic link from periodontal inflammation. Established risk factors remain primary for clinical screening, with telomere findings offering biological insights warranting prospective validation.

This is the first meta-analysis investigating the association between periodontitis and TL. The analysis included a large sample size of 22,625 subjects, enhancing the statistical power and reliability of the findings. Extensive subgroup and meta-regression analyses were conducted to assess the influence of multiple demographic and clinical factors on the pooled effect sizes, aiding identification of potential sources of heterogeneity across studies. Of the 10 included studies, 8 were financially funded primarily by governmental funders, while 2 studies reported that no funding was received. Moreover, the authors of all included studies reported no conflicts of interest (Table S5). This funding profile minimizes the risk of industry bias influencing the evidence base in our meta-analysis. However, our study has several limitations. First, significant heterogeneity was observed among the included studies, which may limit the generalizability of the results. Subgroup analyses indicated that this heterogeneity is arise from differences in sample size, geographic region, and age of participants. Second, although the search strategy was unrestricted by date or language, significant publication bias was detected, suggesting that some small studies might have been overlooked. However, the trim-and-fill analysis adjusting the results for publication bias showed that the impact of publication bias was not significant on the pooled effect sizes. Third, the results of subgroup analyses should be interpreted with caution due to the small number of studies in certain subgroups. Lastly, the observational nature of the included studies and potential residual confounding from unmeasured factors might influence the results, and the cross-sectional design of the majority of the included studies limits causal inference. Therefore, causality could not be inferred from this study. Future research with longitudinal designs and more rigorous control for confounders is warranted to validate these findings.

Conclusion

In conclusion, this study indicated that periodontitis might be negatively associated with TL, a biomarker of cellular aging. Further research is needed to confirm these findings and to reveal the practical clinical implications. Future studies are encouraged to further clarify the biological mechanisms involved and to investigate potential interventions aimed at reducing the negative impacts of periodontitis on TL.

Abbreviations

TL	Telomere length
SMD	Standardized mean difference
CIs	Confidence intervals
β	Standardized beta coefficients
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
MeSH	Medical Subject Headings
BMI	Body mass index
NOS	Newcastle-Ottawa Scale
qPCR	quantitative PCR

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Supplementary Material 5.

Supplementary Material 6.

Supplementary Material 7.

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All data generated or analyzed during this study are included in this published article. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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