The impact of periodontitis on physical fitness: a systematic review

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ABSTRACT

This study aimed to review the evidence regarding the impact of periodontitis on physical fitness. An electronic search was performed in six electronic databases, protocol records and other sources. Eligibility criteria included observational studies on the impact of periodontitis on physical fitness as primary outcome. The quality of primary studies was assessed. GRADE was used to assess the quality of responses. Seven studies were included. Six reported a significant relationship between periodontitis or mean probing depth/clinical attachment loss and physical fitness. The increase in clinical attachment loss and probing depth/clinical attachment loss was associated with decreased handgrip strength and chance to reach the highest physical fitness test score, respectively. Increased mean probing depth was associated with $\dot{V}O_{2peak}$ (maximum oxygen consumption over 30 seconds during the test) and exercise duration. Higher $\dot{V}O_{2max}$ (maximum oxygen consumption during exercise) was associated with lower risk of severe periodontitis and combined highest $\dot{V}O_{2max}$, and lowest body mass index was associated with lower risk of severe periodontitis. Associations with mean probing depth were most convincing for $\dot{V}O_{2peak}$ and exercise duration. The methodological quality of the studies was high, and the level of evidence ranged between "2" and "3". Periodontitis and unfavorable periodontal parameters were associated with worse PF.

Practice Relevance:

- The findings regarding the interaction between periodontitis and physical fitness underscore the importance for dentists to make evidence-based decisions when personalizing the treatment of periodontitis.
- The current scarcity of clinical trials examining the impact of periodontal treatment on physical fitness highlights a significant area for future research within the academic community.

Keywords: exercise; periodontal disease; periodontitis; physical fitness

CDHA Research Agenda category: risk assessment and management

INTRODUCTION

Periodontitis is defined as a non-communicable chronic inflammatory disease (NCD) associated with a dysbiotic biofilm characterized by the progressive destruction of the dental support apparatus[1]. Also, gingivitis and periodontitis are a continuum of the same inflammatory disease[2]. Periodontitis affects more than 50% of the world's adult population and increases even more with age[3], being considered the highly common chronic inflammatory NCD, with a prevalence of its severe form between 7% and 11%[4]. In addition, severe periodontitis is considered the 6th most prevalent human disease, according to the 2010 global burden of disease study, with a standardized prevalence of 11.2%[5].

Cardiorespiratory fitness is defined as the ability of the cardiovascular and pulmonary system to deliver oxygen to sustain musculoskeletal function during exercise. Previous studies suggested that reduced levels of systemic inflammation markers are linked to improved cardiorespiratory fitness[6, 7]. Also, it is important to emphasize that chronic periodontitis is associated with low-grade systemic inflammation[8] that is either directly induced via dislocation of periopathogenic bacteria into the bloodstream[9], thus triggering an immune response, or indirectly via increased levels of locally produced proinflammatory mediators[10]. In this context, it is hypothesized that periodontal diseases may impact physical fitness (PF).

Physical activity was inversely associated with periodontal disease in cross-sectional[11–15] and prospective[16] studies. Although physical activity may affect periodontal health by improving insulin sensitivity[12, 15, 16], and reducing inflammation[17], obesity[12, 17] and stress[11, 18], the opposite remains uncertain; to our knowledge, there are only few studies assessing associations between periodontitis and cardiorespiratory fitness. Thus, a potentially causal association between periodontitis and cardiorespiratory fitness would be of special interest, as it would also provide a possible mechanism linking periodontitis with cardiovascular diseases[19] and cardiovascular mortality[20].

At first glance, the current literature (although very limited) seems to support a relationship between periodontitis and PF. Various methodological issues comprising inappropriate confounder adjustment, small sample sizes, restriction to younger persons (20–49y), classification bias when identifying periodontally diseased participants (e.g., partial-mouth periodontal examination protocol), disuse of extent or severity estimates of periodontitis, and study design issues complicate well-founded conclusions[21]. While the impact of periodontitis on PF has been reported, the level of evidence for this association has not yet been established. Thus, this study aimed to (1) systematically review the evidence on the impact of periodontitis on PF, (2) identify methodological limitations and the need for more well-designed studies.

MATERIALS AND METHODS

Protocol and registration

This study was conducted according to the EQUATOR Network website (http://www.equator-network.org/), including the PRISMA 2020 statement[22] (https://prisma-statement.org). The protocol for this SR was structured in accordance with PRISMA-P[23] - the review protocol was registered in the PROSPERO database (http://www.crd.york.ac.uk/PROSPERO): #CRD42023390818. There were no deviations from the initial protocol.

Focused question

This systematic review aimed to answer the focused question: What is the effect of periodontitis on physical fitness? The question addressed in this review followed the PECOD principle:

- P (population): Humans without gender and age restrictions.
- E (exposure): Periodontitis.
- C (comparator): Absence of periodontitis.
- O (outcome): Any impact of periodontitis on PF that will be objectively evaluated through exercise tests, regardless of test types.
- D (study design): Observational studies, such as analytical cross-sectional studies (comparative studies), case-control and cohort studies.

Study selection criteria

We included in this systematic review only observational studies that assess the impact of periodontitis on PF as primary outcome. We excluded studies that: A) Questionnaire-based study; B) Inaccurate or unavailable information related to the diagnosis of periodontitis; and C) Unavailability of the study full text copy. Unpublished data were not included. No restrictions were placed on the language or date of publication when searching the electronic databases.

Information sources

An extensive literature search was performed among six electronic databases, namely MEDLINE via PubMed (http://www.ncbi.nlm.nih.gov/sites/pubmed), Web of Science – WOS (https://www.webofknowledge.com) accessed through the Clarivate Analytics (https://clarivate.com), Cochrane Central Register of Controlled Trials (CENTRAL) (https://www.cochranelibrary.com), Embase (https://www.embase.com) and Scopus (http://www.scopus.com) through Elsevier (https://www.elsevier.com), and LILACS via VHL (https://bvsalud.org). Other sources (grey literature) was consulted through System for Information on Grey Literature in Europe (SIGLE) through OpenGrey (https://easy.dans.knaw.nl/ui/datasets/id/easy-dataset:200362/tab/2) databases. The protocol registration databases ClinicalTrials.gov was also assessed. Handsearch was performed in specialized periodontics periodicals with a relevant impact factor and in reference lists of selected articles. Experts were identified using expertscape.com (https://expertscape.com) and contacted for other data sources.

Search strategy

Database search strategies included MeSH terms, entry terms and keywords to query in PubMed, Web of Science, Cochrane Library, other sources (gray literature), and protocol record. The search strategies for Embase, Scopus and LILACS databases added Emtree, Index and DeCS/MeSH terms, respectively. All terms were combined by the Boolean operators "OR" and "AND" connecting the key concepts in a “building blocks” strategy (Table 1). The electronic searches were performed in January 2024 and databases alerts were created to identify studies published after the time of the search, until the manuscript submission process.

Selection process

The retrieved articles were exported to Endnote® Web (www.myendnoteweb.com) and duplicates were removed by the program. Then, the references were exported to rayyan™ reference manager (https://www.rayyan.ai) for manual removal of duplicates and blind selection process of studies. The selection process was conducted in two phases: Phase 1, two researchers independently examined the titles and abstracts of all retrieved references, applying the inclusion criteria; and Phase 2, the same two reviewers independently applied the exclusion criteria in the full text screening. The full texts were evaluated and judged in the entire document. Inter-reviewer reliability in the study selection process was determined by the Cohen κ test, assuming an acceptable threshold value of 0.80[24]. Before the search was conducted, the researchers held a meeting to establish a protocol for handling potential situations that could lead to confusion. The disagreement at any stage was resolved by discussion and mutual decision with a third reviewer (MCMB). The final decision was always based on the full text reading—for more details on reasons for exclusion, see Figure 1.

Data collection process

Data were independently extracted by the two reviewers using a standardized form in order to facilitate the critical appraisal performance. The qualitative results were described in the article in a consensus meeting, in the order of the PECO contents: Table 2 – Author/year, country, study design, population (sample size/gender, mean age, correlated conditions), periodontal assessment (diagnosis criteria, periodontal diagnosis), PF (method, measure or category), and OCEBM 2011 levels of evidence; and Table 4 – Author/year, dependent variable, sample size and exposition group, sample size and comparator group, *p*-value, and statistical inference.

Study risk of bias assessment

Two reviewers independently evaluated the quality of the included studies using "JBI Critical Appraisal Tools for Analytical Cross-Sectional Studies". This standard appraisal is a set of checklists regarding the criteria for inclusion, study participants and setting, measurement of exposure, measurement of the condition, confounding factors and the strategies to deal with them, measurement of outcomes, and statistical analysis. The overall appraisal was classified as "Include", "Exclude", and "Seek further info". In case of disagreement, agreement was reached in a consensus meeting with a third reviewer (MCMB).

Synthesis methods and effect measures

The study selection process, study characteristics, risk of bias in studies, impact of periodontitis on PF and certainty of evidence are described in the form of text, figure, and tables. Methodological differences among studies restricted the synthesis methods. The synthesis of qualitative results followed the SWiM reporting guideline[25]. The question addressed in this review followed the direction of effect and vote counting as standardized metrics. In addition, the robustness of the synthesized results and the potential impact of confounders considered the results of the adjusted multivariate analyses.

Certainty assessment

The Classification of Assessment, Development and Assessment Recommendations (GRADE) was used to assess the quality of responses in this systematic review, based on five factors: serious risk of bias, serious inconsistence between studies, serious indirectness, serious imprecision, and likely publication bias[26, 27]. Thus, the evidence quality index was defined in four categories: high, moderate, low, and very low applied to the primary outcomes[28–30]. For each of risk of GRADE domains, authors have the option of decreasing their level of certainty one or two levels. Observational studies starting at low can be upgraded based on three criteria: large effect, dose-response effect and "Effect of all plausible confounding factors would be to reduce the effect (where an effect is observed) or suggest a spurious effect (when no effect is observed)".

RESULTS

Study selection

There were identified 5389 records from the electronic databases and registers. After removing 2690 duplicates, we screened the remaining papers through titles and abstracts (Phase 1), followed by full text reading (Phase 2). Ninety-five studies were excluded by publication type, 22 by study design, and 2577 by participant. The full text reading confirmed the inclusion of seven studies, enrolling 10478 patients (Fig. 1 and Table 2)[31–37] – the inter-reviewer reliability in the study selection process was $\kappa \geq 0.8$ for all databases.

Study characteristics

The studies included in this review were from four different countries: Japan[31], Germany[32, 35, 37] USA [33], and Brazil[34, 36]. The year of publication ranged from 2010 to 2021. The average number of participants per study was 1497 with a minimum of 72 [32] and a maximum of 4078 [37], and age ranged between 20 and 77 years old. Periodontal diagnostic criteria varied across studies including mild, moderate, and severe periodontitis [35–37]. Three other studies reported the effect of periodontal parameters (e.g., PD [probing depth], CAL [clinical attachment loss], and BOP [bleeding on probing]), not periodontal diagnosis, on PF[35–37]. In addition, PF assessment included maximum oxygen consumption[31-33], PFT (physical fitness test)[34, 36], handgrip strength[35], and CPET (cardiopulmonary exercise testing)[37].

Most of the studies had also been concerned about the potential confounding factors that might affect the result of the studies. These confounding factors included age[31–37], gender[31, 33, 37], socioeconomic factors[37], number of teeth[31], smoking status[31, 33, 37], alcohol consumption [37], anthropometric parameters[31–37], physical activity[32–34, 36, 37], diabetes[31, 33, 35, 37] and cardiovascular diseases[31, 33], oral inflammatory burden[36], CRP (C-reactive protein)[33] and hsCRP (high-sensitive C-reactive protein)[35]. The statistical result of these studies had been adjusted for confounding factors and Eremenko et al.[35] also stratified the results based on gender. Additionally, four studies included smoking history in the exclusion criteria[32, 34–36].

The level of evidence based on study design (OCEBM, 2011) ranged between 2[35, 37] and 3[31–34, 36]. For more details on the methods, see Table 2.

Risk of bias within studies

Overall, the methodological quality of the included studies was high. All studies clearly defined the eligibility criteria of the participants and described them as well as the study settings in detail. The measurement of oral health conditions as the exposure was reliably performed by trained and calibrated examiners. The assessment of periodontal conditions including diagnostic criteria, PD, CAL, and BOP was carried out objectively, showing valid and reliable measurements. In addition, the outcomes were measured using a broad range of standardized tests, such as maximum oxygen consumption[31-33], physical fitness test (PFT)[34, 36], handgrip strength (GS)[35], and cardiopulmonary exercise testing[37]. Due to the limited number of studies included, publication bias cannot be completely ruled out.

Impact of periodontitis on physical fitness

Participants in the lowest quintile in BMI and highest quintile in VO_{2max} (maximum oxygen consumption during exercise) showed a lower risk of severe periodontitis compared to participants with other combined quintiles in BMI and in VO_{2max} (OR = 0.17 [95% CI: 0.05–0.55])[31]. According to Shimazaki et al., obesity and PF had some interactive effect on periodontal health status[31]. In addition, high BMI (body mass index) score, increased hsCRP, low level of physical activity and severe periodontitis were significantly associated with low VO_{2peak} (maximum oxygen consumption over a period of 30 seconds during the test) levels. In contrast, age and moderate periodontitis were not significantly associated with low VO_{2peak}[32].

Overweight/obese individuals demonstrated significantly lower PFT scores than eutrophic individuals. In addition, ≥ 1 tooth with CAL ≥ 4 mm was significantly associated with lower PFT scores compared to those without periodontitis—1-mm increment in PD or CAL significantly decreased the odds of reaching the highest PFT score by 69% or 75%, respectively[34]. Furthermore, each millimeter of diminished CAL was associated with reduction in GS by 1.47 kg (95% CI: -2.29– -0.65) and 0.38 kg (-0.89– -0.14) in men and women respectively. The impact of periodontitis on reducing GS was modified by anthropometric measures related to adiposity and inflammation[35].

Mean PD and mean CAL were consistently associated with $\dot{V}O_{2peak}$ and exercise duration in the study by Holtfreter et al. Statistically significant associations with $\dot{V}$O2@AT (oxygen uptake at anaerobic threshold), VÉ/$\dot{V}CO_2$ slope (slope of the minute ventilation changes as a function of the pulmonary carbon dioxide output) also occurred. Further, mainly older individuals with higher levels of periodontitis severity were associated with lower $\dot{V}O_{2peak}$. In addition, only mean PD reflecting current disease severity was consistently linked to cardiorespiratory fitness in two cross-sectional samples of the general population[27].

Hoppe et al. evaluated the association between OIB (oral inflammatory burden)—as the combination of periodontal and endodontic disease load—and PF. There was no significant association between AP (apical periodontitis), RCT (root canal treatment) and EB (endodontic burden) with PF. Whereas, PD, CAL and OIB were significantly associated with low PF—low BE compromised the association between unfavorable periodontal parameters and PF. The OIB was independently associated with poor PF in males[36].

In contrast, in the study by Thai et al.[33], clinical measures of periodontitis were not related to cardiorespiratory fitness. Multivariable adjusted mean e$\dot{V}O_{2max}$ (estimated maximum amount of oxygen consumption during exercise) values were similar between healthy participants and those with moderate/severe periodontitis. Participants in the highest quartile of PD and CAL had lower odds of reduced e$\dot{V}O_{2max}$. For more details on results of individual studies, see Table 2.

Quality of evidence

According to GRADE approach, there is still low evidence to recommend the association between periodontitis and PF reported in the studies (Figure 2). The inconsistency and imprecision domains limited the certainty of the evidence by heterogeneity or variability in results and including relatively few events, respectively.

DISCUSSION

This study evaluated the current literature with respect to the evidence on the impact of periodontitis on PF reported in observational (analytical) studies. Recognizing the limitations of this study, our results suggest that periodontitis and unfavorable periodontal parameters may affect PF. Importantly, the certainty of evidence for this cross-sectional association was considered low.

Many epidemiologic[35, 37] and cross-sectional studies[31, 32, 34, 36] have reported a significant relationship between periodontitis or mean PD/CAL and PF. In contrast, a population-based study (NHANES [1999–2004]) found no significant relationship between periodontitis and VO_{2max} among healthy adults. The chance of reduced eVO_{2max} was halved among patients with moderate/severe periodontitis compared to healthy participants, and there was no significant association between eVO_{2max} and mean PD and CAL[33]. Although partial-mouth periodontal examination protocols frequently used in epidemiological periodontal surveys pose a risk of classification bias and of estimated effects potentially biased toward the null[38], all studies included in this systematic review showed consistent cross-sectional associations of periodontitis or mean PD/CAL with PF[31, 32, 34–37], except for Thai et al.[33].

The severity of periodontal disease and some clinical parameters such as PD and CAL is associated and therefore may influence PF. Increased CAL was associated with decreased GS and the chance to reach the highest PFT score[34–36]. The increased mean PD also decreased the chance to reach the highest PFT score[34]. In three of the seven studies, PD and CAL were significantly associated with PF[34, 36, 37] – it was not possible to distinguish between actual periodontal symptoms and the long-term consequences of the inflammatory episodes that add up to lifetime CAL. The negative effect of EB on PF became more obvious when both endodontic and periodontal diseases were present. The OIB variable arising from merging EB and CAL may represent a cumulative experience of both periodontal and endodontic diseases load[36].

Participants who had a higher VO_{2max} level tended to have a lower risk of severe periodontitis, and participants who had the combined highest VO_{2max} and lowest BMI category had a conspicuously lower risk of severe periodontitis[31]. In the study by Holtfreter et al.[37], associations with mean PD were most convincing for VO_{2peak} and exercise duration. According to the authors, this might be explained by the fact that assessments of VO_{2peak} and exercise duration are observer independent, resulting in high measurement accuracy and validity. In addition, inconsistent results for remaining CPET parameters might be explained by high observer variabilities, the fact that they were derived from other parameters, and the fact that all of them are affected by multiple risk factors[37, 39–41].

Physical fitness denotes a multidimensional system that is difficult to assess. Medical history, physical examination, body composition, cardiorespiratory endurance, and potential confounders should be considered in association studies. Physical fitness and periodontitis share common risk factors including smoking[42–46] and those associated with inflammation such as obesity, diabetes and chronic inflammatory conditions[47, 48]. Therefore, these risk factors should be considered confounders in correlation/causal studies. It is important to emphasize that all included studies considered them as exclusion criteria or adjusted variables in multivariate regression analysis, thereby (theoretically) increasing homogeneity and validity.

The question addressed in this systematic review highlights an issue of clinical relevance that needs to be investigated. For Eremenko et al.[35], an association between physical strength and periodontal measures was to be expected even in the absence of causative pathological processes. The decline in physical power and periodontal deteriorations could occur in parallel without any causal relationship. It is possible that the biological mechanism involved in the relationship between periodontitis and PF have similarities to those previously described in periodontal medicine for cardiometabolic conditions. Furthermore, aging (i.e., immunosenescence) and anthropometric measurements related to adiposity and inflammation could potentiate these mechanism[35, 49–52].

The fatigue sensation during exercise may be magnified by periodontitis due to increasing levels of pro-inflammatory cytokines in the bloodstream[34, 52]. Jae et al.[50] reported an inverse association between resting inflammatory status and cardiorespiratory fitness. Alongside, systemic inflammation has been linked to spirometric lung volumes[53], which are in turn associated with decreased exercise capacity[54]. Although periodontal treatment improves systemic inflammation[55], biomarkers of vascular health, and surrogate measures of cardiovascular diseases[56], it remains unclear whether it would have clinically meaningful effects on cardiopulmonary function. Chronic low-grade inflammation, characterized by persistent elevated concentrations of circulating pro-inflammatory cytokines across the life span has been associated with the development of noncommunicable diseases. Obesity and metabolic disorders interact with local inflammation in periodontitis and the development of muscle weakness, particularly with increasing age[57, 58]. It's important to consider that, if these factors attenuate the association between periodontitis and PF, we can speculate that they are associated with inflammation, mediating this relationship [31, 32].

Farazi et al.[59] examined the joint association of inflammation-related lifestyle behaviors with cardiorespitatory fitness and reported a strong inverse association between pro-inflammatory lifestyle and cardiorespitatory fitness. The term "P4 medicine" has been hailed as the future of medicine[60–63] in which medicine should move from a reactive to a proactive clinical approach for patient care incorporating the four pillars of prediction, prevention, personalization, and participation for patient management. Under this concept—new paradigm––the focus should be on the overall patient well-being rather than merely treat a disease and its symptoms. Regarding P4 periodontics, personalized periodontics[64] represents an innovative approach that considers individual differences in clinical decisions, including people's lifestyle and behavior.

The intersection between inflammation and infection leading to considerable disease-related tissue destruction has been discussed in recent years. More recently, host modulation and the personalized approach in health seek to resolve inflammation and return to tissue homeostasis in chronic inflammatory conditions such as periodontitis[63, 65, 66]. Periodontitis is a multifactorial chronic inflammatory disease associated with dysbiotic biofilm and characterized by the progressive destruction of the tooth support apparatus[67]. In this scenario, a new paradigm for managing periodontitis based on controlling the inflammation has been presented[63, 65, 66]. The principle of this treatment involves the medical model of "treat to target", in which the disease course is altered from activity to remission focused on treatment target[68]. These principles are aligned with changing the trajectory of the periodontitis disease course, as proposed by Bartold and Ivanovski[63]. Modulating inflammation through anti-infective treatment does not disregard the important role of dental plaque but refocuses attention in the central role of inflammation in critical nexus between infection and inflammation[69]. Thus, modifiable traditional markers, modifiable inflammatory markers, and modifiable systemic risk factors must be taken into account when considering an individual's disease status, including periodontitis and PF. Reducing oral infection and inflammation must be the main goals of periodontal care in the context of personalized periodontics and systemic inflammatory conditions.

The following strengths of our study merit special consideration: i) three of the seven studies were population-based setting with a large number of individuals in both genders and a wide age range; ii) all examination methods are well standardized, and examiners were thoroughly trained/calibrated; and iii) high methodological quality of the articles (the main strength of the included studies). Nonetheless, it is important to mention that four[31, 32, 34, 36] of the seven studies used convenience samples. In these cases, selection bias and the selection of specific groups of people with different characteristics from the general population may compromise the external validity of the study. The following limitations deserve consideration: i) cross-sectional observation is not able to give more detail information about the causal relationship between periodontitis and PF—any inferences about causality cannot be made; and ii) meta-analyses were unfeasible due to the number of studies and methodological heterogeneity. The limitations of the literature made it quite challenging to conclude on the impact of periodontitis on PF. Lastly, it must be emphasized that results should be cautiously interpreted, and definitive conclusions in favor of an association between periodontitis and PF cannot be made. According to the authors, well-designed randomized controlled trials are demanded and should be encouraged.

CONCLUSION

Implications for clinical practice: The current findings suggest, with low certainty of evidence, that periodontitis and unfavorable periodontal parameters may affect PF. Even with some limitations, this systematic review provides information on the interaction between periodontitis and PF and highlights the need for further studies on this topic.

Implications for research: Notwithstanding, the current evidence supports the notion that it would be useful to perform randomized controlled trials investigating the effect of periodontal treatment on PF, given the effect sizes of individual studies, cross-sectional associations, and methodological issues such as number of studies and dissimilarities in periodontal assessment and PF measurement.

Data Availability Statement The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

CONFLICTS OF INTEREST

None of the authors disclose any financial, consulting or personal relationships with other people or organizations that could influence the authors' work.

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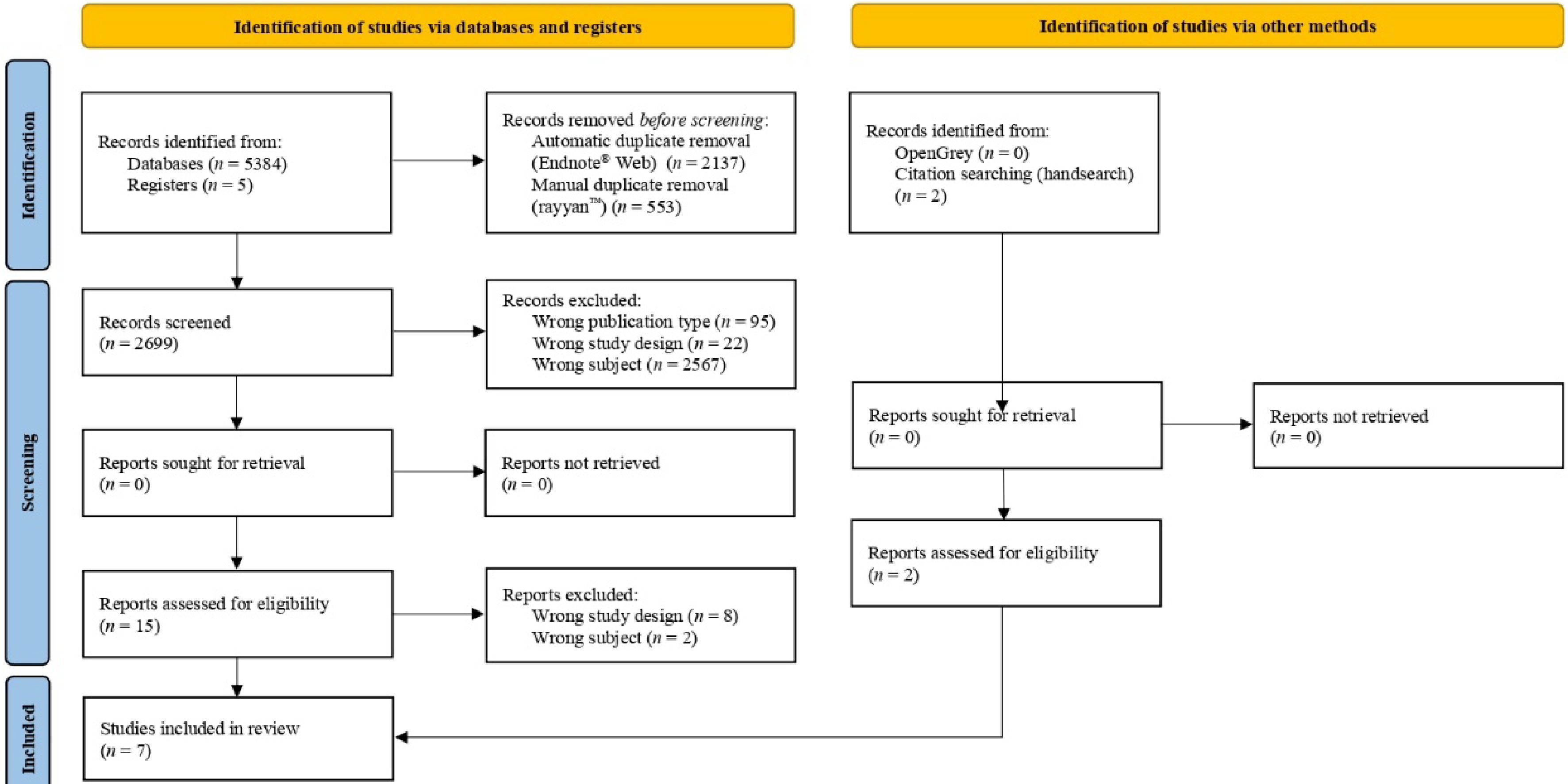

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Fig. 1 Screening and enrolment

Quality criteria	**Rating**	**Quality of the evidence**
Risk of bias	No	
Inconsistency	Serious (-1)	
Indirectness	No	
Imprecision	Serious (-1)	
Publication Bias	Unlikely	
Large effect	Large (+1)	⊕⊕◯◯ Low (GRADE C)
Dose-response gradient	No	
All plausible confounding would reduce the demonstrated effect or increase the effect if no effect was observed	Yes (+1)	
Overall quality of evidence across all critical outcomes: Our confidence in the effect is limited: The true effect may be substantially different from the estimate of the effect		

Fig. 2 Assessing the quality of evidence across studies for main outcome (PF)

Table 1 Search strategies

Search Strategy	Electronic databases
(Periodontal Diseases[MeSH] OR Periodontitis[MeSH] OR Chronic Periodontitis[MeSH] OR Aggressive Periodontitis[MeSH] OR Periodontitis, Aggressive, 2[Supplementary Concept] OR Periodont*[Tiab]) AND (Exercise[MeSH] OR Exercise Test[MeSH] OR Physical Fitness[MeSH] OR Physical Functional Performance[MeSH] OR Physical Endurance[MeSH] OR Exercise[Tiab] OR Physical Fitness[Tiab] OR Exercises[Tiab] OR Physical Activity[Tiab] OR Physical Activities[Tiab] OR Stress Test[Tiab] OR Treadmill Test[Tiab] OR Functional Performance[Tiab] OR Physical Performance[Tiab] OR Physical Frailty[Tiab])	**MEDLINE|PubMed** (N = 495 results)
(TS=(Periodont*)) AND TS=(Exercise OR "Exercise Test" OR "Physical Fitness" OR "Physical Functional Performance" OR "Physical Endurance" OR Exercises OR "Physical Activity" OR "Physical Activities" OR "Stress Test" OR "Treadmill Test" OR "Functional Performance" OR "Physical Performance" OR "Physical Frailty")	**Web of Science** (N = 567 results)
ID Search Hits #1 MeSH descriptor: [Periodontal Diseases] explode all trees #2 MeSH descriptor: [Periodontitis] explode all trees #3 MeSH descriptor: [Chronic Periodontitis] explode all trees #4 MeSH descriptor: [Aggressive Periodontitis] explode all trees #5 (Periodont*):ti,ab,kw #6 #1 OR #2 OR #3 OR #4 OR #5 #7 MeSH descriptor: [Exercise] explode all trees #8 MeSH descriptor: [Exercise Test] explode all trees #9 MeSH descriptor: [Physical Fitness] explode all trees #10 MeSH descriptor: [Physical Functional Performance] explode all trees #11 MeSH descriptor: [Physical Endurance] explode all trees #12 (Exercise OR Physical Fitness OR Exercises OR Physical Activity OR Physical Activities OR Stress Test OR Treadmill Test OR Functional Performance OR Physical Performance OR Physical Frailty):ti,ab,kw #13 #7 OR #8 OR #9 OR #10 OR #11 OR #12 #14 #6 AND #13	**Cochrane CENTRAL** (N = 261 results)
(INDEXTERMS ('periodontal AND disease') OR INDEXTERMS (periodontitis) OR INDEXTERMS ('chronic AND periodontitis') OR INDEXTERMS ('aggressive AND periodontitis') OR TITLE-ABS-KEY (periodont*)) AND (INDEXTERMS (exercise) OR INDEXTERMS ('exercise AND test') OR INDEXTERMS (fitness) OR INDEXTERMS ('physical AND performance') OR INDEXTERMS (endurance) OR TITLE-ABS-KEY (exercise) OR TITLE-ABS-KEY ('physical AND fitness') OR TITLE-ABS-KEY (exercises) OR TITLE-ABS-KEY ('physical AND activity') OR TITLE-ABS-KEY ('physical AND activities') OR TITLE-ABS-KEY ('stress AND test')	**Scopus** (N = 2846 results)

Table 1 Search strategies

OR TITLE-ABS-KEY ('treadmill AND test') OR TITLE-ABS-KEY ('functional AND performance') OR TITLE-ABS-KEY ('physical AND performance') OR TITLE-ABS-KEY ('physical AND frailty'))	
#3 – #1 AND #2 #2 – 'exercise'/exp OR exercise OR 'exercise test'/exp OR 'exercise test' OR 'fitness'/exp OR fitness OR 'physical performance'/exp OR 'physical performance' OR 'endurance'/exp OR endurance OR exercise:ti,ab,kw OR 'physical fitness':ti,ab,kw OR exercises:ti,ab,kw OR 'physical activity':ti,ab,kw OR 'physical activities':ti,ab,kw OR 'stress test':ti,ab,kw OR 'treadmill test':ti,ab,kw OR 'functional performance':ti,ab,kw OR 'physical performance':ti,ab,kw OR 'physical frailty':ti,ab,kw 151,017 #1 – 'periodontal disease'/exp OR 'periodontal disease' OR 'periodontitis'/exp OR periodontitis OR 'chronic periodontitis'/exp OR 'chronic periodontitis' OR 'aggressive periodontitis'/exp OR 'aggressive periodontitis' OR periodont*:ti,ab,kw	**Embase** (N = 1213 results)
(mh:("periodontal diseases" OR periodontitis OR "chronic periodontitis" OR "aggressive periodontitis") OR tw:(periodont*)) AND (mh:(exercise OR "exercise test" OR "physical fitness" OR "physical functional performance" OR "physical endurance") OR tw:(exercise OR "physical fitness" OR exercises OR "physical activity" OR "physical activities" OR "stress test" OR "treadmill test" OR "functional performance" OR "physical performance" OR "physical frailty")) AND (db:("LILACS"))	**LILACS|VHL** (N = 2 result)
(periodont*) AND (exercise* OR physical fitness OR physical functional performance OR physical endurance OR physical activity OR physical activities OR stress test OR treadmill test OR functional performance OR physical performance OR physical frailty)	**Protocol registries and other sources** (N = 2 result)

Table 2 Characteristics of included studies										
		Population			**Periodontal assessment**		**Physical fitness**		**OCEBM (2011) levels of evidence**
Author, year Country	**Study design**	**Sample size | Gender**	**Mean age**	**Confounding factors**	**Diagnosis criteria**	**Periodontal diagnosis**	**Parameter**	**Method**	
Shimazaki et al., 2010[31] Japan	Cross-sectional study (retrospective data)	1160	20–77y	Age, gender, number of teeth, smoking status, fasting plasma glucose, and systolic blood pressure	Partial-mouth recording protocol Two groups based on the number of sextants with CPI code 3 or 4 No or mild periodontitis: zero to two sextants (*n* = 936; 80.7%) Severe periodontitis: ≥ 3 sextants (*n* = 224; 19.3%)	No or slight periodontitis, and severe periodontitis	Maximum amount of oxygen your body can utilize during exercise – VO_{2max}	Heart rate measurement at three different submaximal workloads, using an electric-bicycle ergometer	3
Eberhard et al., 2014[32] Germany	Cross-sectional study	72 healthy men	45–65y Mean age: 52.7 ± 5.4y	Age, BMI, and physical activity	Full-mouth recording protocol Moderate periodontitis: ≥ 2 interproximal sides with CAL ≥ 4 mm, or by ≥ 2 interproximal sides with PD ≥ 5 mm (not at the same tooth) Severe periodontitis: ≥ 2 interproximal sides with CAL ≥ 6 mm and ≥ 1 interproximal side with PD ≥ 5 mm (not at the same tooth) No or mild periodontitis was specified if neither moderate nor severe periodontitis was diagnosed	No or mild periodontitis, moderate periodontitis, and severe periodontitis	Maximum oxygen consumption was defined as the maximum mean value over a period of 30 seconds during the test – VO_{2peak}	Cardiorespiratory fitness was measured directly from respiratory gas exchange during a standardized cardiopulmonary stepwise exercise testing on a cycle ergometer (Ergoline, Bitz, Germany). All tests have been stopped with the onset of dyspnoea and/or peripheral muscle fatigue. The resulting VO_{2peak} value in ml O_2 per kg body weight per minute allowed a direct comparison of individuals regardless of body weight.	3

Table 2 Characteristics of included studies

Thai et al., 2014[33] USA	Cross-sectional study (retrospective data)	2856 (NHANES 1999–2004)	20–49y	Age, gender, education level, race/ethnicity, smoking status, hypertension, pulse, BMI, MET minutes per week ({[(number of times engaged in the activity in past 30 days x average duration of activity x MET score for activity)/30 days] x 7 days}), physical activity, diabetes (HbA1c ≥ 6.5% or self-report of physician diagnosed diabetes), cholesterol, CRP, and wight blood cell count	Partial-mouth recording protocol Moderate periodontitis: ≥ 2 interproximal sides with CAL ≥ 4 mm, or by ≥ 2 interproximal sides with PD ≥ 5 mm (not at the same tooth) Severe periodontitis: ≥ 2 interproximal sides with CAL ≥ 6 mm and ≥ 1 interproximal side with PD ≥ 5 mm (not at the same tooth) No or mild periodontitis was specified if neither moderate nor severe periodontitis was diagnosed	No or mild periodontitis, moderate periodontitis, and severe periodontitis	Estimated maximum amount of oxygen your body can utilize during exercise – eVO_{2max}	Cardiorespiratory fitness assessment: 2-minute warm-up, two 3-minute exercise stages and a 2-minute cool down with the goal of reaching approximately 75% of the age predicted maximum heart rate by the end of the test. Heart rate was monitored continuously, and blood pressure was measured at the end of each stage eVO_{2max} was determined based on heart rate measured during the two 3-minute exercise states	3
Oliveira et al., 2015[34] Brazil	Cross-sectional study	111 male military police officers	≥ 20y	Age, BMI, and physical activity	Full-mouth recording protocol Participants were categorized according to the number of teeth with PD ≥ 5 mm and AL ≥ 4 mm (no teeth and ≥1 tooth) BOP categories (median value [15% of sites])	Moderate periodontitis	Physical fitness test (PFT score range: 0–300)	Four physical fitness exercises: 1) Push-up exercises begin with the participant lying on his stomach on the floor. With his palms flat on the floor and using his arms as leverage, the participant pushes his body up and lowers his	3

Table 2 Characteristics of included studies

			Moderate periodontitis (≥ 2 interproximal sites with CAL ≥ 4 mm and ≥ 1 interproximal site with PD ≥ 5 mm in nonadjacent teeth)			body down to the floor. The maximum number of repetitions is recorded; 2) Pull-up exercises are conducted with the body suspended by the hands from a bar. Using his arms, the participant lifts and lowers his body until his chin was leveled with the bar. The maximum number of repetitions is recorded; 3) Sit-up exercises begin with the person lying with his back on the floor. The participant lifts his upper and lower vertebrae from the floor until his upper body (above the buttocks) does not touch the ground. The maximum number of repetitions in one minute is recorded; and 4) For the running exercise, the participant is asked to run for 12 minutes in an athletics track. This fitness test is similar to those performed in national armies and police departments from other countries Individuals were classified according to whether the highest PFT	

Table 2 Characteristics of included studies

								score (300) was "achieved" (better physical fitness) or "not achieved"	
Eremenko et al., 2016[35] Germany	Cross-sectional study (retrospective data)	2089 (SHIP-2) 982 male and 1107 female	Male: 56.7 ± 13.3y Female: 55.0 ± 13.0y	Age, mean CAL, interaction CAL x age (50–69), interaction CAL x age (≥ 70), BMI, WHR, HbA1c, and hsCRP	Full-mouth recording protocol PD and CAL were assessed at four sites per tooth (midbuccal, mesiobuccal, distobuccal, and midlingual/palatal)	NA	Handgrip strength	Measured by handheld Smedley type dynamometer used for diagnostic purposes (Scandidact, Denmark) Strength was also expressed as handgrip strength in relation to BMI (GS_{BMI}) Handgrip strength measured grip strength left- and right-handed – maximum strength of either hand was used as dependent variable	2
Hoppe et al., 2017[36] Brazil	Cross-sectional study	112 male military police officers	≥ 20y	Age, BMI, and physical activity Radiographic assessment of AP and RCT variables. EB was calculated as the sum of the total number of teeth with AP and/or RCT for each individual. EB was categorized as zero, 1–2 or ≥3 teeth. The OIB was calculated combining EB and AL and was	Partial-mouth recording protocol Three sites per tooth (midbuccal, mesiobuccal, and distolingual/palatal), including: PD, CAL, and BOP	NA	Physical fitness test (PFT score range: 0–300)	Combination of physical strength and cardiorespiratory fitness	3

Table 2 Characteristics of included studies

				defined according to 4 categories: EB < 3 and no CAL ≥ 4 mm; EB ≥ 3 and no CAL ≥ 4 mm; EB < 3 and CAL ≥ 4 mm; and EB ≥ 3 and CAL ≥ 4 mm					
Holtfreter et al., 2021[37] Germany	Two independent cross-sectional studies of the SHIP-1 (retrospective data)	1639 SHIP-1 participants, and 2439 SHIP-Trend-0 participants	≥ 4y	Age, gender, equivalent income, smoking status, alcohol consumption, physical activity, self-reported general health, BMI, type 2 diabetes mellitus, and time between basic and spiroergometry examinations	Partial-mouth recording protocol Mean PD and CAL	NA	Cardiopulmonary exercise testing – CPET	Measured using a calibrated electromagnetically braked cycle ergometer. The following parameters were assessed: peak oxygen uptake (VO_{2peak}), oxygen uptake at anaerobic threshold (VO_2@AT), the minute ventilation changes as a function of the pulmonary carbon dioxide output (VÉ/VCO_2 slope), peak oxygen pulse (O_2HR_{max}), and exercise duration	2

Footnote: AP, apical periodontitis; BF, percentage (%) body fat; BMI, body mass index; BOP, bleeding on probing; CAL, clinical attachment loss; CPET, cardiopulmonary exercise testing; CRP, C-reactive protein; EB, endodontic burden; eVO_{2max}, estimated maximum amount of oxygen consumption during exercise; HbA1c, glycated haemoglobin A1c; hsCRP, high-sensitive C-reactive protein; MET, metabolic equivalent; NHANES, national health and nutrition examination survey; O_2HR_{max}, peak oxygen pulse; OIB, oral inflammatory burden; PD, probing depth; RCT, root canal treatment; SD, standard deviation; SHIP-1, 5-y follow-up (2002–2006) of the Study of Health in Pomerania; SHIP-Trend-0, second Study of Health in Pomerania; SHIP-2, 10-y follow-up (launched in 2008) of the Study of Health in Pomerania; VÉ/VCO_2 slope, slope of the minute ventilation changes as a function of the pulmonary carbon dioxide output; VO_{2max}, maximum oxygen consumption during exercise; VO_{2peak}, maximum oxygen consumption over a period of 30 seconds during the test; VO_2@AT, oxygen uptake at anaerobic threshold; WHO, World Health Organization; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; y, years old; β, regression coefficient; 95% CI, confidence interval; and NA, not applicable. Regarding periodontal examinations, all permanent teeth were assessed, excluding the third molars. Reference: OCEBM Levels of Evidence Working Group*. "The Oxford Levels of Evidence 2". Oxford Centre for Evidence-Based Medicine. https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebm-levels-of-evidence. * OCEBM Levels of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson.

Table 3 JBI critical appraisal checklist for analytical cross-sectional studies

	Questions								
Studies	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Overall appraisal**
Shimazaki et al., 2010[31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Eberhard et al., 2014[32]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Thai et al., 2014[33]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Oliveira et al., 2015[34]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Eremenko et al., 2016[35]	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Include
Hoppe et al., 2017[36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Holtfreter et al., 2021[37]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include

Footnote: 1, Were the criteria for inclusion in the sample clearly defined?; 2, Were the study participants and the setting described in detail?; 3, Was the exposure measured in a valid and reliable way?; 4, Were objective, standard criteria used for measurement of the condition?; 5, Were confounding factors identified?; 6, Were strategies to deal with confounding factors stated?; 7, Were the outcomes measured in a valid and reliable way?; and 8, Was appropriate statistical analysis used?

Table 4 Results of individual studies

Author, year	Dependent variable	Sample size	Exposition group	Sample size	Comparator group	*p*-value	Statistical inference
Shimazaki et al., 2010[31]	VO_{2max} (ml/kg/minute; median [quartile, third quartile])	224	Severe periodontitis VO_{2max}: 31.6 (27.4, 36.0)	936	No or mild periodontitis VO_{2max}: 28.6 (25.6, 32.5)	< 0.001	OR and 95% CI for severe periodontitis by quintile of BMI, BF, and VO_{2max}: Crude OR (95% CI): BMI, OR ≤ 3.90 (2.24–6.78), $p < 0.001$; BF, OR ≤ 2.51 (1.55–4.06), $p = 0.002$; and VO_{2max}, OR ≤ 6.88 (3.74–12.64), $p < 0.001$ Multivariate OR (95% CI), adjusted for age, gender, number of teeth, smoking status, fasting plasma glucose, and systolic blood pressure: BMI, OR = 2.42 (1.33–4.42), $p = 0.07$; BF, OR = 1.30 (0.75–2.23), $p = 0.34$; and VO_{2max}, OR = 2.42 (1.23–4.78), $p = 0.02$
Eberhard et al., 2014[32]	VO_{2peak} (ml/kg/minute; mean ± SD [95% CI])	30* 12**	Moderate periodontitis* VO_{2peak}: 27.9 ± 4.9 (26.1–29.7) Severe periodontitis** VO_{2peak}: 25.8 ± 6.6 (21.6–30)	30	No or mild periodontitis VO_{2peak}: 30.5 ± 5.3 (28.6–32.5)	0.026	Multivariate regression analysis with VO_{2peak} as the dependent variable: Age: β = -0.173 (95% CI: -0.374–0.027), $p = 0.09$ BMI: β = -0.702 (95% CI: -0.981– -0.323), $p < 0.001$ Physical activity: β = 0.062 (95% CI: 0.006–0.119), $p = 0.031$ Moderate periodontitis: β = -2.008 (95% CI: -4.313–0.297), $p = 0.087$ Severe periodontitis: β = -3.431 (95% CI: -6.568– -0.294), $p = 0.033$
Thai et al., 2014[33]	eVO_{2max} (ml/kg/minute; mean ± SD) Mean: 39.73 ± 9.29	116 (4.05%)† 9 (0.31%)‡	Moderate periodontitis† Severe periodontitis‡ Multivariable adjusted mean eVO_{2max} (moderate/severe): 39.7 ± 60.9	2,738 (95.63%)	No or mild periodontitis Multivariable adjusted mean eVO_{2max}: 39.7 ± 60.21	1.00	Multivariable adjusted mean eVO_{2max} for PD ± (SE): ≤ 40.37 ± 0.53, $p = 0.28$ Multivariable adjusted mean eVO_{2max} for CAL ± (SE): ≤ 39.85 ± 0.39, $p = 0.99$ Participants in the highest quartile of CAL had lower odds of reduced eVO_{2max}: OR = 0.89 (95% CI: 0.64–1.24) Individuals in the fourth quartile of PD versus the first had lower odds of reduced eVO_{2max}: OR = 0.77 (95% CI: 0.51–1.15)

Table 4 Results of individual studies

Oliveira et al., 2015[34]	PFT score (mean ± SD)	40 (36%)	Moderate periodontitis PD ≥ 5 mm: 24 (21.6%) teeth CAL ≥ 4 mm: 54 (48.7%) teeth BOP categories (> 15% of sites): mean 17.7 ± 10.1% PFT score PD ≥ 5 mm (≥ 1 tooth): 276.8 ± 24.7[A] PFT score PD ≥ 4 mm (≥ 1 tooth): 277.8 ± 23.6[B] PFT score BOP (> 15% of sites): 283.4 ± 19.3[C]	71 (64%)	No periodontitis PFT score PD ≥ 5 mm (0 teeth): 293.4 ± 21.4[A] PFT score PD ≥ 4 mm (≥ 1 tooth): 285.9 ± 20.2[B] PFT score BOP (≤ 15% of sites): 280.3 ± 25.2[C]	0.15[A] 0.03[B] 0.94[C]	Participants with moderate/severe periodontitis had a statistically significant lower odds of reduced eVO_{2max}: OR = 0.48 (95% CI: 0.23–0.98) Periodontal parameters according to the PFT category (PFT maximum score): Mean PD (mm): Yes = 2.06 ± 0.33, No = 2.23 ± 0.48, $p = 0.03$ Mean CAL (mm): Yes = 2.17 ± 0.36, No = 2.56 ± 0.89, $p = 0.01$ Number of teeth with PD ≥ 5 mm: Yes = 0.26 ± 0.73, No = 0.72 ± 2.05, $p = 0.15$ Number of teeth with CAL ≥ 4 mm: Yes = 1.33 ± 2.23, No = 3.05 ± 5.1, $p = 0.04$ BOP (% of sites): Yes = 15.35 ± 8.02, No = 19.16 ± 10.93, $p = 0.04$ Logistic regression (multivariable model adjusted for confounding factors) of the association between maximum PFT score and periodontal status: Mean PD (mm), OR = 0.31 (95% CI: 0.1–0.95 [$p = 0.04$]); mean CAL (mm), OR = 0.25 (95% CI: 0.09–0.69 [$p = 0.01$]); BOP (%), OR = 0.01 (95% CI: 0.001–0.46 [$p = 0.02$]); PD ≥ 5 mm, OR = 0.32 (95% CI: 0.10–0.99 [$p = 0.04$]); CAL ≥ 4 mm, OR = 0.33 (95% CI: 0.13–0.84 [$p = 0.02$]); and moderate periodontitis, OR = 0.47 (95% CI: 0.18–1.08 [$p = 0.07$])
Eremenko et al., 2016[35]	GS (kg)	2,089	Mean CAL (mm)	NA	NA	NA	Multiple regression of GS on mean CAL (adjusted for confounding factors after stratification according to gender): male participants, β = -1.47 (95% CI: -2.29– -0.65 [$p < 0.001$]); and female participants, β = -0.38 (95% CI: -0.89– -0.14 [$p = 0.15$]) – for each additional millimeter of mean CAL, GS decreased by 1.47 and 0.38 kg in men and women respectively Multiple regression of relative GS (10 x GS_{BMI}) as dependent variable on mean CAL (adjusted for confounding factors after stratification according to gender): male participants, β = -0.65

Table 4 Results of individual studies

							(95% CI: -0.96– -0.34 [$p < 0.001$]); and female participants, β = -0.24 (95% CI: -0.48– -0.01 [$p = 0.038$]) The association between GS and periodontal measures was attenuated in both, women and men, by introducing visceral obesity indicated by WHR or CRP as covariate
Hoppe et al., 2017[36]	PFT score (mean ± SD)	NA	PD ≥ 5 mm (≥ 1 tooth): 6 (24%)[D] CAL ≥ 4 mm (≥ 1 tooth): 15 (27.3%)[E] AP (≥ 1 tooth): 10 (37%)[F] Endodontic treatment (≥ 1 tooth): 16 (39%)[G] EB (AP and/or RCT in 1-2 teeth): 17 (44%)[H] EB (AP and/or RCT in ≥ 3 teeth): 2 (22.2%)[I] OIB (EB < 3 and CAL ≥ 4 mm): 12 (30.8%)[J] OIB (EB ≥ 3 and CAL ≥ 4 mm): 3 (18.8%)[K]	NA	PD ≥ 5 mm (0 tooth): 36 (41.4%)[D] CAL ≥ 4 mm (0 tooth): 27 (47.4%)[E] AP (0 tooth): 32 (37.7%)[F] Endodontic treatment (0 tooth): 26 (36.6%)[G] EB (no AP and/or RCT): 23 (35.9%)[H, I] OIB (EB < 3 and no CAL): 26 (46.4%)[J, K]	0.16[D] 0.03[E] 1[F] 0.84[G] 0.45[H] 0.39[I] 0.12[J] 0.02[K]	Logistic regression (multivariable model adjusted for confounding factors) of the association between maximum PFT score and periodontal status: PD ≥ 5 mm, OR = 0.3 (95% CI: 0.09–0.96 [$p = 0.04$]); CAL ≥ 4 mm, OR = 0.31 (95% CI: 0.11–0.89 [$p = 0.03$]); EB (AP and/or RCT in 1-2 teeth), OR ≤ 1.79 (95% CI: 0.60–6.16 [$p = 0.27$]); EB (AP and/or RCT in ≥ 3 teeth), OR ≤ 0.79 (95% CI: 0.7–4.52 [$p = 0.22$]); OIB (EB < 3 and CAL ≥ 4 mm), OR = 0.44 (95% CI: 0.16–1.2 [$p = 0.11$]); and OIB (EB ≥ 3 and CAL ≥ 4 mm), OR = 0.19 (95% CI: 0.04–0.87 [$p = 0.03$])
Holtfreter et al., 2021[37]	CPET test (median [25th, 75th quartile]): VO_{2peak} (ml/minute, and ml/kg/minute), VO_2@AT (ml/minute), VÉ/VCO_2 slope,	NA	Mean PD (mm) and CAL (mm)	NA	NA	NA	Multiple linear regression of CPET as dependent variable on mean PD (adjusted for confounding factors after stratification according to two cross-sectional study populations {mean [95% CI]}): VO_{2peak} (ml/minute): SHIP-1 ≤ 2052 (2016–2087 [$p < 0.001$]), and SHIP-Trend-0 ≤ 2031 (2002–2060 [$p < 0.001$]) VO_{2peak} (ml/kg/minute): SHIP-1 ≤ 26.4 (25.9–26.9 [$p < 0.001$]), and SHIP-Trend-0 ≤ 25.6 (25.2–26 [$p < 0.001$]) VO_2@AT: SHIP-1 ≤ 1124 (1106–1141 [$p = 0.02$]), and SHIP-Trend-0 ≤ 1015 (1000–1031 [$p = 0.02$])

Table 4 Results of individual studies

O_2HR_{max} (ml/beat), and exercise duration (minute)	VÉ/VCO_2 slope: SHIP-1 ≤ 25.69 (25.25–26.13 [$p = 0.2$]), and SHIP-Trend-0 ≤ 27.53 (27.24–27.81 [$p = 0.006$]) O_2HR_{max}: SHIP-1 ≤ 13.41 (13.22–13.60 [$p = 0.07$]), and SHIP-Trend-0 ≤ 13.16 (12.97–13.34 [$p = 0.009$]) Exercise duration: SHIP-1 ≤ 9.4 (9.2–9.5 [$p < 0.001$]), and SHIP-Trend-0 ≤ 9.9 (9.7–10 [$p < 0.001$]) Multiple linear regression of CPET as dependent variable on mean CAL (adjusted for confounding factors after stratification according to two cross-sectional study populations {mean [95% CI]}): VO_{2peak} (ml/minute): SHIP-1 ≤ 2045 (2010–2080 [$p < 0.001$]), and SHIP-Trend-0 ≤ 2033 (2012–2055 [$p < 0.001$]) VO_{2peak} (ml/kg/minute): SHIP-1 ≤ 26.1 (25.6–26.5 [$p < 0.001$]), and SHIP-Trend-0 ≤ 25.6 (25.2–26.1 [$p = 0.018$]) VO_2@AT: SHIP-1 ≤ 1115 (1111–1159 [$p = 0.049$]), and SHIP-Trend-0 ≤ 1013 (994–1032 [$p = 0.64$]) VÉ/VCO_2 slope: SHIP-1 ≤ 25.76 (25.24–26.29 [$p = 0.07$]), and SHIP-Trend-0 ≤ 27.37 (27.01–27.73 [$p = 0.07$]) O_2HR_{max}: SHIP-1 ≤ 13.52 (13.28–13.77 [$p = 0.02$]), and SHIP-Trend-0 ≤ 13.14 (12.92–13.37 [$p = 0.2$]) Exercise duration: SHIP-1 ≤ 9.3 (9.2–9.5 [$p < 0.001$]), and SHIP-Trend-0 ≤ 10.1 (9.9–10.2 [$p < 0.001$]) While in participants younger than 50y, no statistically significant associations of mean PD or mean CAL with VO_{2peak} were observed, participants older than 50y had lower VO_{2peak} values with increasing mean PD

Footnote: AP, apical periodontitis; BF, percentage (%) body fat; BMI, body mass index; BOP, bleeding on probing; CAL, clinical attachment loss; CPET, cardiopulmonary exercise testing; EB, endodontic burden; eVO_{2max}, estimated maximum amount of oxygen consumption during exercise; OIB, oral inflammatory burden; O_2HR_{max}, peak oxygen pulse; OR, odds ratio; PD, probing depth; RCT, root canal treatment; SD, standard deviation; SE, standard error; SHIP-2, study of health in Pomerania; VÉ/VCO_2 slope, slope of the minute ventilation changes as a function of the pulmonary carbon dioxide output; VO_{2max}, maximum oxygen consumption during exercise; VO_{2peak}, maximum oxygen consumption over a period of 30 seconds during the test; VO_2@AT, oxygen uptake at anaerobic threshold; y, years old; β, regression coefficient; 95% CI, 95% confidence interval; and NA, not applicable.