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PROGRAMA DE PÓS GRADUAÇÃO EM ODONTOLOGIA

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ASSOCIAÇÕES BIDIRECIONAIS ENTRE DOENÇA PERIODONTAL, FADIGA E ATIVIDADE FÍSICA.

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Associações bidirecionais entre doença periodontal, fadiga e atividade física.

Tese apresentada por **João Augusto Peixoto de Oliveira** para obtenção do TÍTULO DE DOUTOR em Clínica Odontológica/Periodontia

Orientador: Prof. Dr. Alex Nogueira Haas

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Sobre o autor:

João Augusto Peixoto de Oliveira é Cirurgião Dentista, especialista em Periodontia e Saúde da Família. Mestre em Periodontia, é docente da Universidade do Vale do Taquari (UNIVATES). Como doutorando, coletou dados para outra pesquisa sobre tratamento das periimplantites e desenvolveu o projeto de pesquisa e análise dos dados do presente trabalho.

“Pastor, não me diga que o paraíso está embaixo da terra

Você não sabe quanto a vida realmente vale

Nem tudo que brilha é ouro

Metade da história nunca foi contada

Agora você vê a luz, lute pelos seus direitos.”

Bob Marley

RESUMO

Introdução e objetivos: As sensações de fadiga podem ser decorrentes de doenças crônicas, como câncer, diabetes e artrite reumatoide, que por sua vez também estão associadas à inexistência de exercício ou inatividade física. Da mesma forma, a doença periodontal vem apresentando associações com várias doenças sistêmicas. O presente trabalho tem como objetivo: 1) Avaliar se a doença periodontal pode agir como preditor de risco para as sensações de fadiga; 2) Avaliar se atividade física auto reportada tem efeito protetor na ocorrência de doença periodontal. **Metodologia:** dois estudos de cunho transversal foram aninhados a um estudo de coorte de base populacional conduzido com adultos de 35 anos ou mais que moram na cidade Porto Alegre, Rio Grande do Sul. Exames periodontais de profundidade de sondagem (PS), sangramento à sondagem (SS), e perda de inserção (PI) foram realizados utilizando um protocolo de exame de 4 sítios por dente, em todos os dentes presentes em 287 indivíduos que foram avaliados no exame de seguimento. A mensuração de fadiga foi realizada através da sub escala de vitalidade do questionário genérico de avaliação de qualidade de vida SF-36 (SF-36 VT). Atividade física foi avaliada através do Questionário de Atividade Física Internacional (IPAQ). Modelos de regressão logística múltiplos foram aplicados para avaliar as associações entre as variáveis periodontais e fadiga, e entre atividade física e periodontite. **Resultados:** com relação à associação entre doença periodontal e fadiga, a porcentagem de indivíduos com fadiga entre os que apresentavam periodontite (20.2%) e aqueles sem periodontite (21.4%) foi muito similar. Modelos ajustados para sexo, fumo e artrite não demonstraram associações significativas entre periodontite e fadiga. No que tange à análise da associação entre atividade física e doença periodontal, indivíduos fisicamente ativos tiveram uma chance significativamente menor de apresentar periodontite severa (OR=0.51; 95%CI: 0.28-0.93) após o ajuste para as variáveis idade, cor da pele, status socioeconômico e fumo. A redução na chance também foi observada para indivíduos que apresentavam PS ≥5mm em 1 dente ou mais (OR=0.41; 95%CI: 0.21-0.79). Quando PI foi considerado o único desfecho periodontal, não foram observadas diferenças significativas, indicando que a atividade física pode agir sobre o componente inflamatório da periodontite. **Conclusão:** nenhuma associação foi encontrada entre os parâmetros periodontais e fadiga neste estudo. A investigação de uma suposta influência da periodontite nas sensações de fadiga em outras populações

deve ser encorajada, pois existem mecanismos plausíveis para esta associação. Por outro lado, a atividade física parece agir como fator protetor para a doença periodontal, reforçando a efetividade de atividades físicas de rotina na prevenção primária e secundária de doenças crônicas devido ao seu efeito anti-inflamatório.

Palavras chave: doenças periodontais; doença crônica; fadiga; exercício; inflamação; estudos transversais.

ABSTRACT

Introduction and aim: Fatigue sensations may arise due to chronic diseases, like as from cancer, diabetes and rheumatoid arthritis. These chronic conditions in turn are associated with lack of exercise or physical inactivity. In the same way, periodontal disease has been associated with several systemic chronic diseases. The present work has the purpose of: 1) to test the hypothesis that periodontal disease may act as an independent risk indicator for fatigue; and 2) to assess the association between physical activity and clinical parameters of periodontitis in a sample of Brazilian adults. **Methods:** two cross-sectional studies were nested to a population-based cohort study conducted with adults 35 years and older living in Porto Alegre, Brazil. Periodontal probing depth (PPD), bleeding on probing (BOP), and clinical attachment loss (CAL) were assessed in four sites/tooth in all present teeth in 287 individuals evaluated at the follow-up examination. Fatigue was assessed by the Short Form-36 vitality subscale (SF-36 VT) and physical activity was assessed by the International Physical Activity Questionnaire (IPAQ). Multiple logistic regression models were applied to assess the associations between periodontal variables and fatigue, and for the associations between physical activity and periodontitis. **Results:** with regard to the association between periodontal disease and fatigue, the percentage of individuals with fatigue among those with (20.2%) and without (21.4%) periodontitis was very similar. Multiple logistic regression models adjusted for sex, smoking and arthritis demonstrated no significant associations between periodontitis and fatigue. With relation to the association between physical activity and periodontitis, after adjusting for age, skin color, socioeconomic status and smoking, physically active individuals had a significantly smaller chance of having severe periodontitis (OR=0.51; 95%CI: 0.28-0.93). The reduction in the odds was also observed for PPD ≥5mm in ≥1 tooth (OR=0.41; 95%CI: 0.21-0.79). When CAL alone was considered the periodontal outcome, no significant associations were found, indicating that PA may act at the inflammatory component of periodontitis. **Conclusion:** No associations between periodontal disease parameters and fatigue were found in this study. The investigation of a supposed burden of periodontitis in fatigue in other populations is still encouraged, since there are plausible mechanisms for this association. On the other hand, physical activity may act as a protective factor for periodontal disease. This

study strengths the effectiveness of routine physical activity in the primary and secondary prevention of chronic diseases throughout improving inflammation.

Key words: periodontal diseases; chronic disease; fatigue; exercise; inflammation; cross sectional studies.

APRESENTAÇÃO:

A presente tese está subdividida em um corpo principal que inclui uma introdução, objetivos, revisão da literatura, considerações finais, referências bibliográficas e anexos. Dois capítulos contendo dois artigos científicos que serão submetidos à revistas científicas internacionais foram redigidos e inseridos no decorrer da presente tese. Cada capítulo apresenta um estudo transversal que está aninhado à segunda fase de um estudo longitudinal de base populacional realizado na cidade de Porto Alegre. Somente os dados do exame de acompanhamento desta segunda fase do estudo longitudinal foram utilizados para a análise dos estudos transversais. A associação entre doença periodontal e fadiga é abordada no primeiro capítulo (Capítulo 1), onde fadiga é trabalhada como o desfecho e a doença periodontal como a principal exposição. O desfecho foi avaliado através de um questionário validado para mensurar fadiga, aplicado na amostra estudada na cidade de Porto Alegre. O segundo capítulo (Capítulo 2) compreende um estudo que avalia a associação entre atividade física e doença periodontal. Nesta relação, a doença periodontal é o principal desfecho em estudo e atividade física a principal exposição. Os indivíduos foram entrevistados com relação à atividades físicas periódicas, objetivando investigar a atividade física como um possível fator protetor para doença periodontal.

SUMÁRIO

1. INTRODUÇÃO

1. INTRODUÇÃO:

Doenças e condições crônicas estão entre os mais comuns, mais onerosos e mais evitáveis de todos os problemas de saúde (Cdc, 2017). As doenças crônicas são de longe a principal causa de mortalidade no mundo, representando 70% de todos os óbitos (WHO, 2017). Em 2012, cerca de metade da população adulta norte-americana (117 milhões de pessoas) possuía uma ou mais condição crônica de saúde, e de cada quatro adultos, um apresentava duas ou mais condições crônicas (Ward *et al.*, 2014). Envolvidos na cadeia causal destas doenças estão os comportamentos de risco à saúde. Inexistência de exercício ou inatividade física, má nutrição, e uso de tabaco e álcool são exemplos de comportamentos responsáveis pela maioria dos adoecimentos, do sofrimento e de mortes prematuras relacionadas às condições e doenças crônicas (CDC, 2017). Estes comportamentos são deletérios, porém modificáveis.

A inatividade física, por exemplo, está em quarto lugar entre os fatores de risco para mortalidade global (6% das mortes em todo mundo), perdendo apenas para hipertensão arterial, uso de tabaco e altos níveis de glicose sanguínea (WHO, 2010). Estima-se que a inatividade física seja a principal causa e colabore para aproximadamente 21–25% de câncer de mama e de cólon, 27% do diabetes e aproximadamente 30% das doenças cardíacas isquêmicas. Tem sido demonstrado que a participação em atividades físicas regulares reduz o risco de doença cardíaca e infarto, diabetes, hipertensão, câncer de cólon, câncer de mama e depressão (WHO, 2010).

Um estilo de vida inativo funciona como um preditor de risco para várias condições crônicas (Pradhan et al., 2001), pois leva à acumulação de gordura visceral, que é acompanhada por infiltração de células pró-inflamatórias do sistema imune no tecido adiposo, aumento da liberação de adipocinas e desenvolvimento de um estado de inflamação sistêmica de baixa intensidade (Ouchi et al., 2011). Este estado tem sido associado com o desenvolvimento de resistência à insulina, aterosclerose, neuro-degeneração e crescimento tumoral (Pradhan et al., 2001; Pedersen e Saltin, 2006; Leonard, 2007), O exercício possui efeitos anti-inflamatórios, e, portanto, a longo prazo, atividade física regular pode proteger contra o desenvolvimento de doenças crônicas (Pedersen e Saltin, 2006; Hardman e Stensel, 2009; Warren et al., 2010; Walsh et al., 2011). Deste modo, é aceito que a inflamação está etiologicamente ligada à patogênese

de várias condições crônicas (Hotamisligil, 2006; Shoelson et al., 2006; Leonard, 2007; Ouchi et al., 2011; Rook e Dalgleish, 2011), e este estado inflamatório é indicado por níveis elevados de marcadores inflamatórios circulantes, como interleucina-6 (IL-6), fator de necrose tumoral (TNF) e proteína C reativa (PCr).

Alguns fatores estão sob investigação para determinação do seu papel em relação à inflamação. Fatores ambientais que podem causar e manter a inflamação incluem vírus, bactérias, xenobióticos, poluição e infecções polimicrobianas, enquanto que fatores ligados ao indivíduo incluem o estresse, a dieta, nutrientes (como a vitamina D), antioxidantes, metabolismo, obesidade, inatividade física, hormônios, tabaco, eventos precoces na vida do indivíduo, idade, comorbidades, injúrias, hipóxia, suscetibilidade/resistência genética, e a epigenética. Tem-se sugerido que o cérebro possa vir a ter um papel na inflamação, o que necessita de mais estudos para colaborar com estas evidências. Isto não inclui apenas o papel do estresse em promover e exacerbar a inflamação na doença crônica, mas também o impacto das respostas psicológicas à doença na resposta inflamatória (i.e. dor e estresse) e o impacto da inflamação na habilidade de enfrentamento do processo (CIHR, 2011).

Ainda há carência de um entendimento básico dos mecanismos moleculares subjacentes à inflamação e sua resolução (CIHR., 2011). Isto inclui a interação entre a vascularização, o estroma e outras células da resposta inflamatória, a biologia do reparo, o impacto longitudinal da inflamação na emergência de doenças secundárias como câncer e fibrose, e os mecanismos moleculares subjacentes ao efeito das mudanças de estilo de vida na resposta inflamatória. Lacunas deste campo de pesquisa ainda incluem as razões para a especificidade tecidual na inflamação crônica versus inflamação aguda, e a influência da inflamação/infecção de um local em outros tecidos, como no caso de infecções periodontais.

Seguindo esta premissa, nos últimos 20 anos foram observadas associações entre doença periodontal e várias doenças sistêmicas (Otomo-Corgel et al., 2012; Linden et al., 2013), como diabetes, doenças cardiovasculares, obesidade, síndrome metabólica, doenças respiratórias, artrite reumatoide, câncer, doença renal crônica, e osteoporose. Especificamente com relação às associações com diabetes e doenças cardiovasculares, os dados sugerem que a doença periodontal pode ser um fator de risco modificador, mesmo que evidências diretas sejam escassas. Mecanismos biologicamente plausíveis suportam

as associações, conjuntamente com modelos animais e evidências sobre efeito sistêmico do tratamento da doença periodontal sobre esses desfechos (Cullinan e Seymour, 2013).

Deste modo, também parece haver um envolvimento da inflamação no desenvolvimento de sintomas de fadiga em pacientes com condições crônicas, incluindo câncer, esclerose múltipla e síndrome da fadiga crônica (Bower et al.,2002; Flachenecker et al., 2004; Fletcher et al., 2009; Heesen et al., 2006; Orre et al., 2009; Raison et al., 2009). Os mecanismos patofisiológicos que levam ao desenvolvimento de fadiga nestes pacientes permanecem desconhecidos. Enquanto vários fatores biológicos e psicológicos podem estar contribuindo, várias linhas de evidência apontam para a possibilidade de fatores inflamatórios também estarem envolvidos (Lasselin, 2012).

Em suma, o presente trabalho compreende dois capítulos redigidos na forma de artigos científicos que apresentam resultados de um estudo epidemiológico transversal de base populacional. No primeiro capítulo, se investiga o potencial da doença periodontal em causar sensações de fadiga por meio de determinadas vias sugeridas como conexões entre as duas condições. O segundo capítulo testa-se hipótese de a atividade física funcionar como fator de proteção para a doença periodontal, e da inatividade física como um fator de risco às doenças periodontais, através de mecanismos análogos às vias de associação entre a inatividade física e outras doenças crônicas.

2. OBJETIVOS

2. OBJETIVOS:

2.1. Geral:

- Avaliar as associações entre doença periodontal, atividade física e fadiga.

2.2. Específicos:

- Avaliar se a doença periodontal pode agir como preditor de risco para as sensações de fadiga mensurada através da utilização da subescala de vitalidade do questionário genérico de avaliação de qualidade de vida SF-36.
- Avaliar se atividade física auto reportada reduz as chances de ocorrência de doença periodontal.

3. REVISÃO DA LITERATURA

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3.1 Definição de Fadiga

Fadiga pode ser definida como um declínio na habilidade ou na eficiência em executar atividades físicas ou mentais, causado por atividade mental ou física excessiva, ou por doenças (Ishii *et al.*, 2016). A fadiga é geralmente acompanhada por uma sensação peculiar de desconforto, desejo de descansar, e declínio da motivação, referidos como sensação de fadiga. Mais de 20–30 % da população da Europa e dos Estados Unidos já experimentou fadiga substancialmente (David *et al.*, 1990; Pawlikowska *et al.*, 1994; Loge *et al.*, 1998; Cella *et al.*, 2002; Van't Leven *et al.*, 2010), e mais da metade da população japonesa adulta relata ter experienciado fadiga (Watanabe, 2007). A fadiga é um sintoma comum experimentado em muitas desordens, como diabetes (Fritschi e Quinn, 2010), câncer (Aistars, 1987), doença pulmonar obstrutiva crônica (Small e Lamb, 1999), esclerose múltipla (Hart, 1978) e doenças cardiovasculares (Casillas *et al.*, 2006).

As descrições de fadiga são diversas: uma sensação devastadora de cansaço em repouso, exaustão com a atividade, falta de energia que atrapalha as tarefas diárias, inércia ou falta de condicionamento, e perda de vigor (Zwarts *et al.*, 2008). Na prática médica, fadiga é descrita como uma consequência debilitante de um número de diferentes doenças sistêmicas ou déficits nutricionais (Gibson *et al.*, 2003). Na fisiologia do exercício, fadiga é descrita como uma redução aguda na performance do exercício, que leva a uma eventual incapacidade de produzir força máxima como consequência do acúmulo de metabólitos ou da depleção de substrato (Hagberg, 1981). Em neurofisiologia, fadiga é descrita como uma redução nos comandos eferentes que ativam os músculos, resultando em declínio da força ou tensão como parte do processo de controle central (Gandevia, 2001). Para os patologistas, a fadiga está associada com déficits mental e físico, indicadores de desordens metabólicas ou neuromusculares (Hart e Freel, 1982).

Estas definições, tomadas paralelamente em conjunto com as definições encontradas em dicionários, concentram-se na fraqueza física e mental que caracteriza a fadiga. Entretanto, estas definições se concentram mais em selecionar aspectos do fenômeno do que considerar todos os impactos da fadiga no indivíduo fatigado. Definições que oferecem um conceito de fadiga como uma experiência holística, e não apenas um fenômeno que afeta a performance física ou mental, parecem ser mais válidas

e reflexivas do que aquelas que descrevem a fadiga vivenciada por indivíduos doentes (Ream e Richardson, 1996). Outras definições de fadiga, como as encontradas na especialidade de enfermagem, possuem uma visão mais ampla e holística. Em estudo sobre fadiga auto reportada em pacientes com artrite reumatoide, Tack (1990) definiu fadiga como "uma sensação subjetiva de cansaço generalizado ou exaustão". O termo "generalizado" faz alusão ao indivíduo como um todo sendo acometido pela sensação de fadiga, mais do que a sensação restrita a estruturas anatômicas, regiões ou funções específicas. Hubsky e Sears (1992) definiram a fadiga generalizada experimentada por pacientes com esclerose múltipla como uma "sensação e experiência corporal total". Appels e Mulder (1988) descreveram a fadiga que antecede infarto do miocárdio como "uma sensação de fadiga excessiva e energia diminuída que é acompanhada por sensações de desânimo e derrota". Estas definições se refletem na definição de Piper (1986), onde a fadiga é definida como "a percepção da complexa interação de fatores somáticos e psicológicos". Estes sentimentos podem ser ilustrados através do estudo de Schaefer (1990), no qual um indivíduo descreveu a fadiga da seguinte forma:

"Fadiga significa que todo o meu ser está cansado. O cansaço penetra toda a estrutura óssea; você pode senti-lo na medula de seus ossos. É um cansaço totalmente físico, liderado por um cansaço mental. É como uma corrente subterrânea que enfraquece seus pensamentos. Seu corpo está desgastado".

A sensação de fadiga é um fenômeno complexo. Está associado com uma percepção consciente de mudanças nas funções do corpo, como falta de ar oriunda do aumento da ventilação, aperto no coração pelo aumento do débito cardíaco, sensação de calor e desconforto devido ao aumento da temperatura e transpiração, e a sensação de aumento da atividade muscular associada com o aumento da geração de força causada pelo aumento do nível de atividade física (Hampson *et al.*, 2001). Também há funções mentais cognitivas associadas com a sensação de fadiga. Estas incluem o nível de motivação no momento da atividade, memória de sessões prévias de exercícios e um componente de tomada de decisão associado baseado na relação entre a capacidade motora e sensorial atual e a memória de eventos passados (Ulmer, 1996).

A sensação de fadiga trabalha como um alarme biológico a pedir descanso para evitar romper a homeostase (Ishii *et al.*, 2016). Por outro lado, tem sido hipotetizado que as sensações de fadiga persistentes diminuem a habilidade e a eficiência para desempenhar certas atividades, levando à Síndrome da Fadiga Crônica (Tanaka e

Watanabe, 2010). Essa desordem é diagnosticada quando a fadiga perdura durante seis meses sem estar subordinada a alguma desordem somática, conjuntamente com a presença de outros critérios adicionais (Fukuda *et al.*, 1994).

Fadiga é um conceito determinado por duas dimensões, uma psicológica e outra fisiológica (i.e. fenômeno corporal que contribui para a percepção de fadiga). Assim, fatores psicológicos como bem-estar, problemas de concentração, atividade física e funcionamento social podem todos afetar a maneira que a fadiga é experienciada (Vercoulen *et al.*, 1994).

Até o presente momento, conforme o melhor conhecimento disponível, não existem estudos que se propuseram a estudar a associação entre doença periodontal e fadiga. Alguns estudos investigaram o impacto da doença periodontal na qualidade de vida relacionada à saúde oral especificamente, utilizando a ferramenta Oral Health Impact Profile (OHIP-14) (Bernabé e Marcenes, 2010; Brauchle *et al.*, 2013; Jansson *et al.*, 2014). Como foi relatado anteriormente, existem evidências da influência da doença periodontal na saúde geral, como um dos fatores impactantes em desordens crônicas. Como efeito cascata, a doença periodontal acaba por impactar em eventos negativos ou fatores psicológicos, componentes do domínio da saúde mental. Milanesi *et al* (2015) aferiram qualidade de vida relacionada à saúde oral e geral, utilizando os instrumentos OHIP-14 e o instrumento desenvolvido pela Organização Mundial da Saúde-WHO Qol-bref, respectivamente. Os autores avaliaram o impacto do tratamento periodontal em indivíduos portadores da síndrome metabólica, e constataram que domínios como limitação funcional, desconforto psicológico, incapacidade física e incapacidade psicológica foram estatisticamente significantes com relação à saúde oral. Entretanto, não houve diferenças significativas com relação à avaliação da saúde geral. Neste sentido, enfatiza-se a utilidade de ferramentas para mensurar constructos teóricos multidimensionais, como qualidade de vida e saúde física e mental.

A fadiga por privação de sono mostrou ser um fator modificador para a doença periodontal em ratos (Nakada *et al.*, 2015), pois influencia o eixo hipotálamo-hipófise-adrenal, relacionado com resistência sistêmica. Apesar da relação entre doença periodontal e fadiga se encontrar em fase de construção de hipótese, é possível que haja reciprocidade entre as duas condições.

3.2. A hipótese da doença periodontal como preditor de risco para fadiga: Mecanismos que embasam a plausibilidade biológica para a associação

A doença periodontal é uma doença imuno-infecto-inflamatória, caracterizada pela perda progressiva das estruturas que fornecem suporte ao dente, mais especificamente fibras colágenas e osso alveolar. A doença periodontal está associada a uma microbiota complexa, com a presença de bactérias anaeróbicas gram-negativas (Socransky et al., 1998), resultando na elevação dos níveis de citocinas inflamatórias, observados pelo aumento da concentração de mediadores inflamatórios no fluido crevicular gengival (Gamonal et al., 2000). Mediadores pró inflamatórios que são produzidos localmente, como interleucinas 1 (IL-1) e 6 (IL-6), e o fator de necrose tumoral alfa (TNF α), podem extravasar para a corrente sanguínea (Cairo et al., 2010), supostamente exercendo efeitos distantes ou sistêmicos em outros sistemas do organismo. Componentes bacterianos como proteínas de membrana externa e endotoxinas (lipopolissacarideo / LPS) podem ser disseminados através da corrente sanguínea (Pizzo et al., 2010). Em resposta à bacteremia e aos antígenos bacterianos que se dispersam sistemicamente, os eritrócitos, leucócitos e células teciduais dos locais onde os antígenos são relocados, como células endoteliais e hepatócitos, podem produzir mediadores pró-inflamatórios e uma consequente inflamação sistêmica. Nesta perspectiva, pode-se supor que as doenças periodontais possam influenciar os níveis de marcadores inflamatórios sanguíneos conhecidos como fatores de risco para condições sistêmicas (Slade et al., 2000; Wu et al., 2000; Paraskevas et al., 2008).

Em termos gerais, o mecanismo pelo qual a doença periodontal exerce influência sobre a fadiga consiste ainda em um vasto campo de investigação. Apesar de haver elementos plausíveis para a doença periodontal atuar como fator modificador, são necessários estudos de associação como primeiro nível de geração de evidência. A hipótese que suporta a associação entre doença periodontal e fadiga parece residir em mecanismos e fenômenos centrais, ao nível do sistema nervoso central.

3.2.1 Citocinas pró inflamatórias e a fadiga central

Linhas de evidência levam à possibilidade de que fatores inflamatórios estão também envolvidos no mecanismo de fadiga. Suportando essa premissa, dados indicam que o bloqueio da citocina inflamatória IL-1β com o anticorpo monoclonal XOMA052, melhora parcialmente a fadiga motor em pacientes com diabetes tipo 2 (Cavelti-Weder *et*

al., 2011). A habilidade de citocinas pró-inflamatórias para agir no cérebro e induzir sintomas comportamentais, incluindo fadiga, está bem documentada tanto em estudos experimentais como estudos clínicos (Kelley *et al.*, 2003; Dantzer, Robert *et al.*, 2008; Majer *et al.*, 2008; Capuron e Miller, 2011). No nível clínico, o envolvimento da inflamação no desenvolvimento de sintomas de fadiga tem sido mostrado em pacientes com condições médicas crônicas, incluindo o câncer, esclerose múltipla e síndrome da fadiga crônica (Bower *et al.*, 2002; Flachenecker *et al.*, 2004; Heesen *et al.*, 2006; Fletcher *et al.*, 2009; Orre *et al.*, 2009; Raison *et al.*, 2009).

A inflamação desempenha um papel principal no desenvolvimento de sintomas de fadiga em pacientes doentes tratados com citocinas, notavelmente com interferon-α (Capuron *et al.*, 2002; Capuron *et al.*, 2007). Resultados similares foram achados em idosos (Capuron *et al.*, 2011). Todas estas condições compartilham a ativação de processos imune/inflamatórios crônicos. Similarmente a estas condições, a doença periodontal é caracterizada por um estado inflamatório crônico de baixa intensidade. Dado o bem documentado papel da inflamação no desenvolvimento da fadiga em condições crônicas ou imunológicas (Bower, 2007; Miller *et al.*, 2008; Capuron e Miller, 2011), especula-se que a inflamação sistêmica também poderia contribuir para os sintomas de fadiga em pacientes afetados por doença periodontal.

Oliveira *et al*, (2015) evidenciaram uma associação entre doença periodontal e aptidão física em policiais militares. Segundo os autores deste trabalho, a elevação de citocinas pró-inflamatórias observadas na doença periodontal poderia modificar o metabolismo muscular localmente, levando a uma pobre aptidão física. Adicionalmente, a doença periodontal poderia estar associada à aptidão física dos indivíduos influenciando as sensações de fadiga originadas de mecanismos localizados no sistema nervoso central (fadiga central). Neste mecanismo de fadiga central, a tarefa em execução seria interrompida precocemente, justamente para prevenir o colapso total (Baron *et al.*, 2008; Ament e Verkerke, 2009). Estudos têm demonstrado que músculos fadigados, a princípio, mantém sua capacidade de produção de força quando submetidos, por exemplo, à estimulação elétrica (Baron *et al.*, 2008; Taylor e Gandevia, 2008). Esses resultados sugerem que a interrupção de uma tarefa ou gesto motor não está restrita aos fenômenos locais que acontecem no músculo.

Em situações fisiológicas, citocinas, como IL-1β e TNF-α, não conseguem ultrapassar a barreira hemato-encefálica (BHE). Entretanto, podem alcançar o cérebro em

locais nos quais este isolamento está comprometido, ou ausente, como nos órgãos circunventriculares. Várias células, dentro do SNC, podem produzir IL-1β e/ou TNF-α em certas condições inflamatórias. Sendo assim, a BHE é modificada e afetada por substâncias circulantes e, mais ainda, por células, substâncias, e eventos circundantes ao SNC. Os macrófagos localizados no sistema nervoso central são hábeis em produzirem IL-1β e TNF-α, que por sua vez provocam sensações de fadiga muscular (Carmichael *et al.*, 2010).

Citocinas são potentes executores de funções do SNC e IL-1β é reconhecida por estar envolvida em respostas de defesa do corpo. A meia-vida da IL-1β é de 2,5 - 3 horas (Moors e Mizel, 2000) e do TNF-α em torno de uma hora (Waage *et al.*, 1989), sendo uma estratégia interessante a fim de manter o organismo/região imóvel, objetivando uma economia energética, ou seja, uma estratégia altamente organizada que pode ser crítica para a sobrevivência do organismo (Dantzer, 2004). Interessantemente, numa situação experimental cujos macrófagos foram removidos do SNC, observou-se uma diminuição na concentração de IL-1β, o que provocou uma redução da fadiga e melhora na recuperação pós-exercício físico (Carmichael *et al.*, 2006; Carmichael *et al.*, 2010), portanto, claramente demonstrando o papel desta citocina, produzida tanto perifericamente como centralmente, em induzir fadiga central (Sheng *et al.*, 1996). Para confirmar esta hipótese, injeção desta citocina de forma intracerebroventricular, em modelos animais, resultou nos chamados "sintomas de doença" como fadiga, mal-estar, anorexia e outros (Carmichael *et al.*, 2006; Dantzer, 2006).

3.2.2. Estresse oxidativo

Evidências também têm sugerido um papel crucial de espécies reativas de oxigênio (ERO) na destruição periodontal (Chapple e Matthews, 2007). Levando em consideração que os indivíduos que sofrem de periodontite têm maior risco de desenvolver outras doenças inflamatórias sistêmicas crônicas, há um potencial papel de ERO como um dos mecanismos desta associação. O estresse oxidativo tem sido associado tanto com o início da destruição periodontal (Chapple e Matthews, 2007) quanto com a inflamação sistêmica (Basu *et al.*, 2009). D'aiuto e colaboradores (2010) demonstraram existir uma associação linear direta, porém discreta, entre os parâmetros clínicos periodontais, a inflamação sistêmica e o estresse oxidativo sistêmico.

Kennedy *et al.,* (2005) mensuraram estresse oxidativo em pacientes com a Síndrome da Fadiga Crônica, utilizando o padrão ouro de mensuração de estresse oxidativo in vivo, os isoprostanos. Foi demonstrado que estes pacientes possuem níveis significativamente elevados de estresse oxidativo, os quais estavam correlacionados com vários sintomas da Síndrome da Fadiga Crônica.

O exercício vigoroso aumenta os índices bioquímicos de estresse oxidativo mensurado tanto sistemicamente quanto localmente no músculo que está trabalhando (Alessio, 1993; Sen, 1995). Khawli & Reid (1994) avaliaram fibras musculares como sítio dos eventos de oxirredução testando os efeitos da N-acetilcisteína (NAC), um antioxidante não específico, em feixes de fibras curarizadas isoladas de diafragma de ratos e estudadas in vitro, uma abordagem que elimina influências não musculares. Feixes de fibras experimentais imersos em solução de NAC foram comparados com feixes de fibras controle em solução tamponada. Utilizando protocolos estandardizados os autores mostraram que NAC diminuiu a fadiga de feixes de fibras em comparações de força e frequência combinadas. Estes achados somados a dados de outros estudos in vitro que utilizaram NAC e outras sondas (Reid *et al.*, 1992; Diaz *et al.*, 1994) estabeleceram que antioxidantes podem agir diretamente nas fibras musculares para retardar a fadiga. Oxidantes derivados do próprio músculo devem promover fadiga via efeitos autócrinos ou parácrinos nas fibras contraídas.

3.3. Atividade física

Atividade física (AF) é definida como qualquer movimento corporal produzido pelos músculos esqueléticos que resulta em gasto de energia (Caspersen *et al.*, 1985). AF na vida diária pode ser categorizada como esportiva, ocupacional, condicionante, doméstica e outros. O gasto calórico advindo da AF é expressado como uma taxa (quilocalorias por unidade de tempo), e a quantidade de energia gasta por cada indivíduo é uma variável contínua, que varia de baixa a alta. A quantidade total de gasto calórico associada com AF é determinada pela quantidade de massa muscular produzindo movimentos corporais e pela intensidade, duração e frequência das contrações musculares (Taylor *et al.*, 1978). Todas as pessoas realizam AF no sentido de manutenção da vida. Entretanto, a quantidade de atividade está largamente sujeita às escolhas pessoais, as quais podem variar consideravelmente de um indivíduo para outro durante o tempo.

AF é um constructo multidimensional, e não há uma medida que mensure todas as facetas deste constructo. A pesquisa é geralmente dificultada pelo desafio de se empregar uma medida válida e confiável que satisfaça adequadamente a pergunta de pesquisa (Dishman, 1994; Lee *et al.*, 1995; Welk, 2002; Macfarlane *et al.*, 2006; Reilly *et al.*, 2008). O método da água duplamente marcada é uma forma de calorimetria indireta onde a produção total de gás carbônico pode ser mensurada pelas diferentes eliminações da água marcada com as formas isotópicas de hidrogênio e oxigênio ou, respectivamente, ^{18}O e ^{2}H (deutério). O deutério é eliminado como água, enquanto que o ^{18}O é eliminado como água e gás carbônico. Assim, a diferença entre tais taxas de eliminação, corrigidas pelo conjunto de água corporal, corresponderia à produção de gás carbônico, que, por equações de calorimetria indireta, é convertida ao gasto energético total. Este método permanece como o padrão ouro para mensurar gasto total de energia, entretanto, ele não é sempre utilizado nas pesquisas pois é caro, necessita de sobrecarga do indivíduo, é demorado e não consegue registrar dados qualitativos (Melanson Jr *et al.*, 1996; Westerterp, 2009). Questionários são o método mais comum para mensurar AF (Castillo-Retamal e Hinckson, 2011) e baseiam-se na habilidade de memória dos participantes. Estudos de validação comparando questionários auto reportados ao método de água duplamente marcada são inconsistentes (Westerterp, 2009); entretanto, incluem vantagens de serem custo-efetivos, facilidade de administração, e acurácia em medir atividade intensa (Ishikawa-Takata *et al.*, 2008; Besson *et al.*, 2010), determinando categorias discretas de nível de atividade (i.e., baixa, moderada e alta), ranqueando indivíduos e ou grupos em sua atividade física (Corder *et al.*, 2009), provendo detalhes sobre AF e mostrando melhorias em grupos ou indivíduos. (Jacobs Jr *et al.*, 1993; Shephard, 1999; Shephard, 2003).

Com relação à associação entre atividade física e doença periodontal, alguns estudos se propuseram a investigar esta relação (Tabela 1). Merchant *et al*. (2003), realizaram estudo prospectivo de base populacional, mensurando atividade física através de questionários e também utilizando tabelas de gasto energético por unidade para estimar equivalentes metabólicos (METs), encontrando uma associação linear inversa entre atividade física contínua e periodontite auto-reportada, independentemente de fatores de risco conhecidos. É possível que os benefícios de um estilo de vida fisicamente ativo possam se estender à saúde periodontal. A atividade física auto reportada e a adesão a níveis recomendados de atividade física têm mostrado associação significativa com baixa

prevalência de periodontite (Al-Zahrani *et al.*, 2005a; b). Bawadi *et al*. (2011), aplicando o Questionário Internacional de Atividade Física (IPAQ), demonstrou que indivíduos altamente ativos apresentavam menores índices de sangramento, menor perda de inserção e porcentagem de sítios com perda de inserção periodontal ≥ 3mm, quando comparados com indivíduos com baixos ou moderados níveis de atividade física. Sanders *et al.* (2009) examinaram as associações de atividade física com interleucina 1-β (IL-1β), proteína C reativa (CRP) e periodontite, concluindo que a atividade física associada ao lazer pode ser um fator de proteção contra uma resposta inflamatória exacerbada na periodontite.

Tabela 1. Resumo dos estudos que se propuseram a estudar a associação entre AF e doença periodontal.

Autor	**Ano**	**Desenho**	**n**	**Local de realização**	**Constructo**	**Mensuração constructo**	**Mensuração DP**	**Resultado**
Wakai et al.	1999	Transversal	630	Japão	Condicio-namento físico	Capacidade aeróbica, testes de força, equilíbrio, etc.	CPITN	Pobre condicionamento físico associado a maior CPITN
Merchant et al.	2003	Longitudinal prospectivo (12 anos)	39.461	EUA	Atividade física	Cálculo de MET/questionário	DP auto reportada	Risco de DP diminuiu 3% para cada incremento de 10 MET.
Al-Zahrani et al.	2005 [a]	Transversal	2521	EUA	Atividade física	Questionário	Exame de dois quadrantes aleatórios PS e PI faces V e MV	Associação significativa entre nível aumentado de AF e baixa prevalência de periodontite entre não fumantes e ex fumantes.
Al-Zahrani et al.	2005 [b]	Transversal	12110	EUA	Exercício físico	Questionário	Exame de dois quadrantes aleatórios PS e PI faces V e MV	Exercício diminuiu em 40% a chance de periodontite
Shimazaki et al.	2010	Transversal	1160	Japão	Condicio-namento físico	VO_{2max}	CPITN	Baixo BMI e alto VO_{2max} tiveram menor risco de peridontite severa (OR=0.17).
Bawadi, et al.	2011	Transversal	340	Jordânia	Atividade física	IPAQ	Protocolo de seis sítios NIC e PS	Maior chance de periodontite em indivíduos com baixos níveis de AF

4. CAPÍTULO 1

Lack of association between periodontal disease and fatigue: a cross-sectional observational study

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Abstract

***Background**:* Several chronic diseases are associated with pathologic fatigue, including diabetes, cancer, and cardiovascular diseases. As periodontal disease is an immune-mediated inflammatory disease and a potential source of low-grade systemic inflammation, it may be speculated a possible role of periodontitis in fatigue symptoms. The aim of the present study was test the hypothesis that periodontal disease may act as an independent risk indicator for fatigue

Materials and methods: This cross-sectional study was nested to a population-based cohort study conducted with adults 35 years and older living in Porto Alegre, Brazil. Periodontal probing depth (PPD) and clinical attachment loss (CAL) were assessed in four sites/tooth in all present teeth in 287 individuals evaluated at the follow-up examination. Fatigue was assessed by the Short Form-36 vitality subscale (SF-36 VT). Multiple logistic regression models were applied to assess the associations between periodontal variables and fatigue.

Results: Overall, women (27.2%) presented more fatigue than men (9.9%) ($p<0.001$). Individuals with arthritis also presented more fatigue ($p=0.02$). The percentage of individuals with fatigue among those with (20.2%) and without (21.4%) periodontitis according to the AAP-CDC criteria was very similar. Similar distributions were observed for periodontitis defined by CAL ≥5mm and BOP ≥40%. Multiple logistic regression models adjusted for sex, smoking and arthritis demonstrated no significant associations between periodontitis (AAP-CDC), CAL≥5mm and BOP ≥40% with fatigue.

Conclusion: No associations between periodontal disease parameters and fatigue were found in this study. The investigation of a supposed burden of periodontitis in fatigue in other populations is still encouraged, since there are plausible mechanisms for this association.

Keywords: periodontal diseases; chronic disease; fatigue; inflammation; cross sectional studies.

Introduction

Periodontal disease may be linked to a number of systemic diseases and conditions, including nutritional and metabolic diseases, cardiovascular diseases, musculoskeletal diseases, respiratory tract diseases, pregnancy complications, among others (Chapple e Genco, 2013; Sanz e Kornman, 2013; Tonetti e Dyke, 2013; Monsarrat *et al.*, 2016). Certain pathophysiological mechanisms have been suggested to support these relationships, such as bacteremia, endotoxemia, and release of inflammatory mediators and acute-phase reactants (Dyke e Winkelhoff, 2013; Schenkein e Loos, 2013; Hajishengallis, 2015). In addition, severe periodontitis has been associated with increased systemic oxidative stress and reduced anti-oxidant capacity (D'aiuto *et al.*, 2010), which suggests a synergistic interaction between periodontal disease and diabetes (Allen *et al.*, 2009; Patil *et al.*, 2016) and metabolic syndrome (Bullon *et al.*, 2009).

Fatigue is broadly defined as a subjective sensation of generalized tiredness or exhaustion (Tack, 1990). The symptom of fatigue is a multidimensional concept covering both physiological and psychological aspects (Flechtner e Bottomley, 2003). Clinical fatigue may be manifested as (1) generalized weakness, resulting in inability to initiate certain activities, (2) easy fatigability and reduced capacity to maintain performance, and (3) mental fatigue resulting in impaired concentration, loss of memory, and emotional lability (Markowitz e Rabow, 2007). According to studies conducted in general clinical practice, 25–30% of the patients complained about fatigue, while in population-based studies 30–50% of the individuals reported symptoms of fatigue (Van't Leven *et al.*, 2010). Furthermore, several chronic diseases are associated with pathologic fatigue, including diabetes (Fritschi e Quinn, 2010), cancer (Bower, 2014), and cardiovascular diseases (Casillas *et al.*, 2006). Nonetheless, there is a group of severely fatigued patients that do not have a somatically demonstrable disease (Zwarts *et al.*, 2008) and no etiology can be identified in one third of cases of fatigue (Rosenthal *et al.*, 2008).

The understanding of the underlying biological mechanisms of fatigue has increased in the last years. Inflammation has arisen as a key biological pathway for chronic illness-related fatigue (Cavelti-Weder *et al.*, 2011; Lasselin *et al.*, 2012; Bower, 2014). For instance, higher levels of circulating C-reactive protein (CRP) and interleukin 6 (IL-6) predicted the onset of fatigue approximately 3 years later (Cho *et al.*, 2013). Peripheral inflammatory cytokines can signal the central nervous system to generate symptoms of fatigue and other behavioral changes via alterations in neural processes

(Dantzer, R. *et al.*, 2008; Capuron e Miller, 2011; Harrington, 2012). Moreover, oxidative stress also might lead to cognitive and behavioral deficits (Salim, 2017), and key markers of oxidative stress are correlated with various symptoms of Chronic Fatigue Syndrome (CFS) (Kennedy *et al.*, 2005).

As periodontal disease is an immune-mediated inflammatory disease and a potential source of low-grade systemic inflammation (Moutsopoulos e Madianos, 2006), a possible role of periodontitis in fatigue symptoms may be speculated. A supposed association is supported by plausible biological mechanisms, along with analogy with other fatigue related chronic conditions. Therefore, the aim of the present study was to assess the association between periodontal disease and fatigue, testing the hypothesis that periodontal disease may act as an independent risk indicator for fatigue.

Materials and methods

Study design and sample

This study is a cross-sectional study nested to a population-based prospective cohort study. In 2011, the Caries-Perio Collaboration Group from the Federal University of Rio Grande do Sul designed a survey by drawing a representative sample of adults living in Porto Alegre, Brazil. Gingival recession (GR) and other oral outcomes were assessed in 1023 individuals aged 35 years and older. After 4 years, 414 (40.5%) individuals were re-examined (Figure 1) by recording periodontal probing depth (PPD) and GR, which allowed the diagnosis of periodontitis using various definition criteria. Thus, this study was conducted with data collected in the follow-up examination of the cohort, which was conducted between January 2016 to March 2017. Individuals with less than 3 teeth and elderly (60 years and older) were excluded from this study, with a final sample of 285 individuals 35 to 59 years of age.

Detailed information regarding the sampling strategy at baseline was previously published (Costa *et al.*, 2014; Rios *et al.*, 2014; Wagner, T. P. *et al.*, 2016). In brief, a multistage probability sampling strategy was applied. The city was divided in 86 neighborhoods comprising the primary sampling units that were stratified in low and high income. The second stage consisted on a random selection of sectors proportional to the total number of sectors in each PSU. The third stage consisted of selecting households

consecutively according to the sector starting point until the sector sample size was reached. The number of individuals to be selected within each sector was estimated based on the proportional distribution of the sample size.

One researcher visited each selected sector one day before the start of data collection to invite residents to participate. Residents were not included only after the third attempt of invitation. Interviews and clinical examinations were conducted inside the household. Examinations were conducted using three portable devices: a medical headlight, a portable compressor and a bendable chair.

Ethical aspects

The study protocol was reviewed and obtained ethical approval from the Research Ethics Committee, Federal University of Rio Grande do Sul, Porto Alegre, Brazil. Prior to the participation, all patients read and signed a consent form.

Interview

Participants were interviewed using a structured questionnaire containing questions regarding socio-demographic variables, oral hygiene habits, self-perceived oral health, access to dental services, medical history and behavioral factors. The SF-36 vitality subscale was applied during the interview. Three trained and calibrated interviewers conducted applied the questionnaire.

Periodontal examination

All permanent fully erupted teeth were examined by four periodontists using a manual periodontal probe. A protocol of four sites per tooth (disto-buccal, mid-buccal, mesio-buccal, and lingual/palatal) was used. GR, PPD and bleeding on probing (BOP) were recorded. PPD was defined as the distance between the free gingival margin to the bottom of the pocket/sulcus. GR was defined as the distance from the cement-enamel junction (CEJ) to the free gingival margin. If the CEJ was located apical to the gingival margin, this assessment was given a negative sign. Clinical attachment loss (CAL) was obtained by the sum of GR and PPD.

Reproducibility

Intra and inter-examiner reproducibility was assessed with duplicate measures conducted in a total of 16 patients (1,231 sites). During the fieldwork, 42 participants (2896 sites) allowed to perform the duplicate measurements. Weighted Kappa values for the four examiners range between 0.87 and 0.92.

Outcome

Fatigue was assessed through a self-administered questionnaire called the Short Form-36 vitality subscale (SF-36 VT), version 1.0. The Short Form-36 (SF-36®) is a general health questionnaire (Ware Jr e Sherbourne, 1992), which has been employed to compare the relative burden of diseases, and to differentiate the health benefits produced by a wide range of different treatments. The SF-36 was translated into Brazilian Portuguese and was cross-cultural validated (Ciconelli *et al.*, 1999).

The SF-36 VT was developed to measure vitality, conceptualized as a single continuum from energy to fatigue, and has 4 questions (2 on energy and 2 on fatigue) about sensations and feelings during the last month, as follows: (1) Did you feel full of pep? (2) Did you have a lot of energy? (3) Did you feel worn out? (4) Did you feel tired?

Individuals answered in a six-point Likert scale ranging from none of the time (1 point) to all of the time (6 points). The two fatigue items are scored in a reverse manner. The scores are summed to produce a total raw score, which ranges from 4 (minimum) to 24 (maximum). Lower scores indicate greater fatigue and higher scores represent less fatigue (Ware *et al.*, 1993).

Individuals were dichotomized into exhausted and non-exhausted using a cut-off of 12 points for the SF-36 VT (Lindeberg *et al.*, 2010). Then, individuals scoring below 12 were defined as exhausted.

Exposure variables

The following exposure variables were associated with fatigue: age, sex, skin color, socioeconomic status, educational status, smoking, diabetes, heart disease and arthritis. Three periodontal variables were explored in association with fatigue: severe

periodontitis defined according to the AAP-CDC criteria, periodontitis defined as the presence of at least 30% of teeth with CAL ≥5mm, and presence of BOP in ≥40% of sites.

Age was categorized into two categories (35-49, 50-59). Skin color was dichotomized into non-white and white. Educational level was defined according to years of education into low (≤8 years), middle (9-11 years) and high (≥12 years). Socioeconomic status was categorized using cut-off points adapted from the CCEB classification (Abep, 2013) that considers the amount of consumer goods and the educational level of the head of the family as follows: low (≤20 points), middle (21-26 points) and high (≥27 points).

The total number of packs of cigarettes consumed in a lifetime (packyears) was calculated for each individual by multiplying the number of cigarettes consumed per day by the years of habit, and dividing by 20. Smoking exposure was categorized into never-smokers (0 packyears), light-moderate smokers (<20 packyears) and heavy smokers (≥20 packyears).

Body mass index (BMI) was calculated by dividing the individuals' body weight to the square of height. The height of the participants was obtained by self-reporting in centimeters, whereas the weight was assessed in kilograms using a mechanical scale. BMI was categorized into: underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5 – 24.9 kg/m^2), overweight (BMI 25 – 29.9 kg/m^2), and obese (BMI ≥ 30 kg/m^2). Only 3 individuals were classified as underweight and were aggregated to the normal weight group.

Statistical analyses

The individual was the unit of analysis. The significance level was set at 5%. Data analyses were performed using a statistical package (Stata 14 for Macintosh, STATA Corp., College Station, USA).

Cross-tabulation of independent variables with fatigue was performed and p-values were calculated with chi-square or Fisher's exact tests when appropriate. Simple and multiple logistic regression models were fitted to assess the associations between exposure variables and fatigue. Univariable models were fitted for each independent variable, and those presenting p values <0.25 were entered in a multivariable model. Maintenance of variables in the final model was determine by a combination of p values <0.05 and analyses of effect modification (Hosmer e Lemeshow, 2000). These steps were

conducted to identify among all independent variables, excluding periodontal parameters, which were associated with fatigue in the studied sample. Finally, three separate models were reported, one for each periodontal definition, adjusted for other independent variables significantly associated with fatigue.

Results

Table 1 shows the distribution of individuals with and without fatigue according to independent variables. A significantly higher percentage of women (27.2%) presented fatigue than men (9.9%) ($p<0.001$). Additionally, the percentage of fatigue was significantly higher among individuals with arthritis ($p=0.02$). No other variable was associated with fatigue at the 5% level of significance. This was also true for periodontal variables. The percentage of individuals with fatigue among those with (20.2%) and without (21.4%) periodontitis according to the AAP-CDC criteria was very similar. Similar distributions were observed for periodontitis defined by CAL ≥5mm and BOP ≥40%.

In the univariable logistic regression models (Table 2), sex and arthritis were also significantly associated with fatigue. Additionally, education, smoking and heart disease were further included in a multiple model. Among them, sex, smoking and arthritis remained in the final multiple model in which the three periodontal variables were included each in one final model (Table 3). With the inclusion of other variables to the periodontal models, there were no significant associations between periodontal disease parameters and fatigue.

Discussion

The present study assessed the relationship between periodontal clinical parameters and sensations of fatigue in a southern Brazilian sample of adults. To the best of the authors' knowledge, this is the first study investigating this relationship. However, the results showed no association between periodontal disease and fatigue. Many factors supposed to be involved and may be contributing for these results, taking into account that this is an incipient research field.

There is robust evidence showing the association of periodontal diseases with cardiovascular disease, diabetes, and adverse pregnancy outcomes (Chapple e Genco, 2013; Sanz e Kornman, 2013; Tonetti e Dyke, 2013; Nazir, 2017). Experimental, mechanistic, in vitro and in vivo studies have established the plausibility of a link between periodontal diseases and systemic conditions, and they have identified biological pathways by which these effects may be mediated (Mani Ameet *et al.*, 2013). Furthermore, there is emerging evidence for periodontal therapy having significant clinical effects on systemic diseases and conditions (Jeffcoat *et al.*, 2014), such as glycemic control in type 2 diabetes and rheumatoid arthritis (Borgnakke, 2015).

Nevertheless, the evidence for a systemic effect of periodontal diseases has also been questioned in the literature (El-Shinnawi e Soory, 2013) (Otomo-Corgel *et al.*, 2012). It has been also suggested that periodontitis may have a less decisive importance on systemic inflammation and, in consequence, in the development of systemic chronic conditions than other exposures (Papapanou, 2015). The etiology of a complex disease encompasses the aggregate effects of multiple exposures, external and host-derived, detrimental and protective, each of which can account for only a fraction of the variance in the outcome in the population (Rothman e Greenland, 2005). In this regard, fatigue is generally acknowledged to be complex and/or multifaceted condition (Aistars, 1987; Ream e Richardson, 1996), encompassing physiological, psychological, and situational components, such as life or work events (Fritschi e Quinn, 2010). It is possible that too many confounders may contribute to fatigue, influencing the lack of association found in this study between periodontal status and fatigue.

Another important issue is relative to the concept of fatigue, which is difficult to define. Within the scientific literature, definitions of fatigue vary greatly, and defining fatigue becomes more challenging because there is poor differentiation among causes, indicators, and effects (Winningham *et al.*, 1994). Terms including fatigue, sleepiness, tiredness, lacking energy, and exhaustion are used interchangeably (Fritschi e Quinn, 2010). Furthermore, although fatigue is a widely experienced symptom, it is also difficult to measure (Ream e Richardson, 1996). In this regard, a range of fatigue measures is currently available; yet, reviews of their psychometric properties have focused on a small number of fatigue scales tested most frequently in individuals with cancer (Whitehead, 2009). Hence, cancer, diabetes and arthritis-related fatigue are difficult to distinguish from fatigue experienced by the general population, strengthening the adversities for the

measurement of fatigue in a population basis. This was corroborated in the present study, where fatigue was associated with arthritis, but not with other already known risk factors such as diabetes.

Reflecting these limitations, there is also great heterogeneity in the structure of the scales that measure fatigue, some of them focusing on the multidimensional facets of fatigue while others following a domain-specific approach (Dittner *et al.*, 2004). Only a few scales have undergone validation, and even in those that have, the documented validation procedures did not fulfill accepted methodological criteria (Lienert e Raatz, 1998) in terms of appropriate sample size and inclusion of external criteria (Krupp *et al.*, 1989; Schwartz *et al.*, 1993). In a systematic review, Whitehead (2009) concluded that specific comparisons between scales to explore their ability to measure explicit aspects of fatigue are needed. Additionally, the capacity of existing scales to represent differences in the fatigue experience by age, gender, and cultural and social factors is largely unknown. Specifically related to the SF-36 VT, the construct validity was supported by factor analysis (Mchorney *et al.*, 1993) and had a relative validity of 0.67 in discriminating between patients with minor versus serious medical conditions. For SF-36 VT internal-consistency reliability, Cronbach's alpha coefficient was 0.87 (n= 3445) (Mchorney *et al.*, 1994). In relation to sensitivity/responsiveness to change, SF-36 VT scores increased following treatment of anemia of chronic disease in patients with rheumatoid arthritis (Kaltwasser *et al.*, 2001). SF-36 VT scores improved in osteoarthritis patients after hip replacement surgery (Bachmeier *et al.*, 2001) and following treatment of early rheumatoid arthritis (Kosinski *et al.*, 2002). On the other hand, there are conceptual concerns over the assumption of fatigue and energy as opposite ends of a single continuum, as energy is a positive health state, rather than an absence of fatigue, which is supported by data demonstrating the 2 energy and 2 fatigue items load on 2 separate factors (Hewlett *et al.*, 2011). Therefore, the subjective nature of the symptom fatigue (Dittner *et al.*, 2004) and the fact that it is challenging to actually quantify its severity (Manzullo e Escalante, 2002) are possible explanations for the results found in the present study.

The specific mechanisms of fatigue are essentially unknown. Some believe that fatigue is psychological in origin (Tavel, 2017). However, psychological fatigue has also not been adequately defined in the literature. Psychological fatigue symptoms may originate from emotional phenomena or may arise from alterations in neurotransmitter

release such as is seen in clinical depression (Dantzer, R. *et al.*, 2008). A study of fatigue in primary care patients suggested that psychological disorders were more predictive of fatigue than were physical illnesses (Wijeratne *et al.*, 2007). Psychological phenomena not usually treated clinically, including stress and burnout phenomena, have also been associated with increased levels of fatigue (Neckel *et al.*, 2017). Systemic inflammatory challenge in periodontal disease is a physiological episode derived from clinical events and probably it is not enough to collaborate for the onset of psychological events of fatigue.

Despite the unexpected results and issues related to instruments measuring fatigue, the present study employed recommended methodology for the assessment of periodontitis. Application of periodontitis definition according AAP-CDC criteria met a suggested stringent threshold (Linden *et al.*, 2013). Furthermore, avoidance of surrogate endpoints for periodontitis also strengthened the present data. This enables future comparisons by other studies in the same research field.

It may be concluded that there were no associations between periodontal descriptors and fatigue in this Brazilian sample. Periodontal disease in particular represents a significant inflammatory and infectious burden and contributes to the total burden of inflammation and infection. However, the extent of this contribution will vary from patient to patient. Taking into account that research into the condition of fatigue is in its infancy; more research is needed in this direction to allow the establishment or not of a causal relationship with periodontitis. The investigation of a supposed burden of periodontitis over fatigue must be tested in other populations, since there are plausible mechanisms for this association. Employment of different instruments to measure fatigue must be encouraged.

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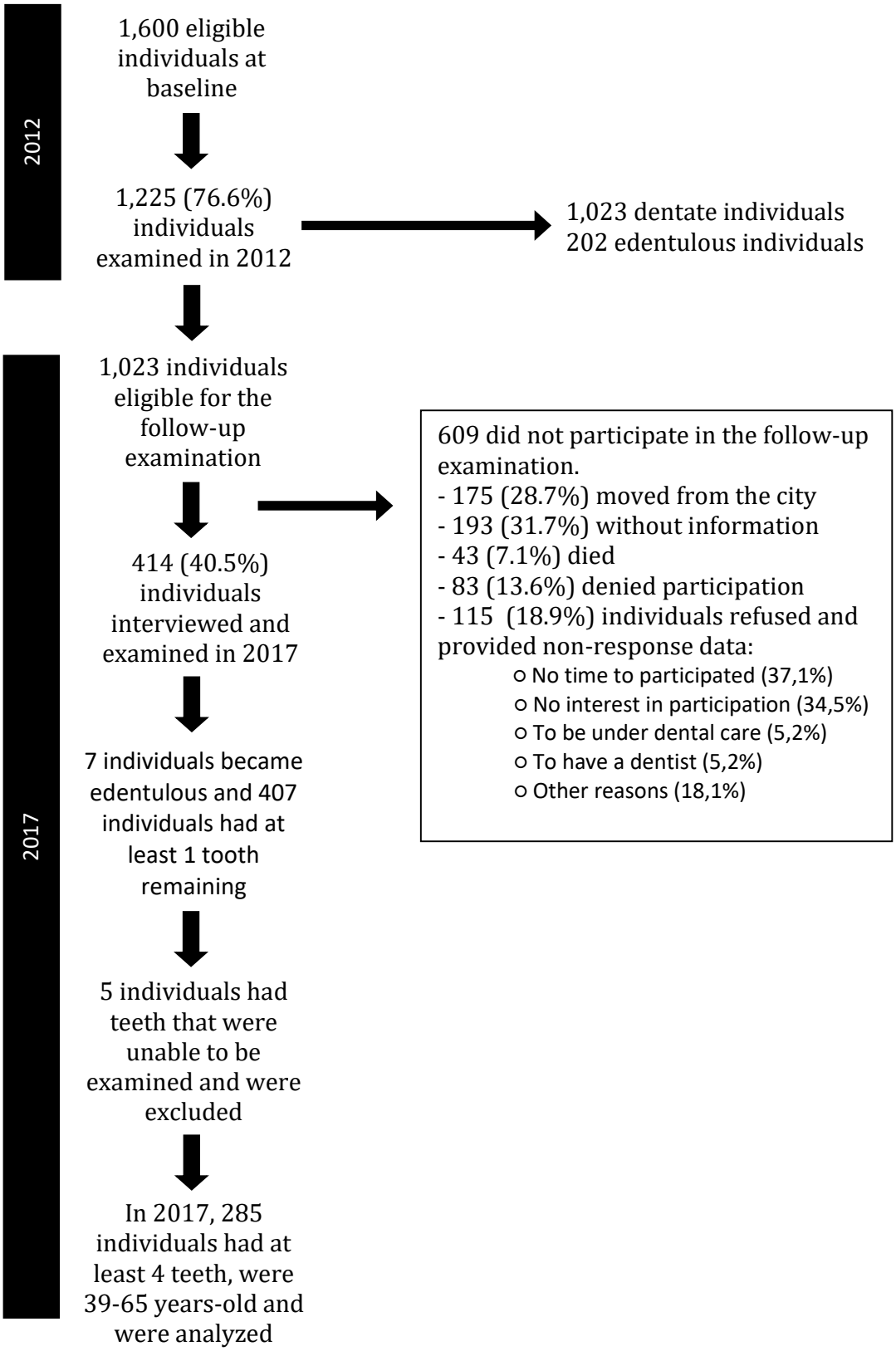

Figure 1. Flowchart of the study.

Table 1. Sample characteristics according to fatigue status.

	Whole sample n (%)	Fatigue		
		No n (%)	Yes n (%)	p*
Age				
39-49 years	84 (29.5)	64 (76.2)	20 (23.8)	
50-65 years	201 (70.5)	161 (80.1)	40 (19.9)	0.52
Sex				
Females	184 (64.6)	134 (72.8)	50 (27.2)	
Males	101 (35.4)	91 (90.1)	10 (9.9)	<0.001
Skin color				
Non-Whites	95 (33.3)	147 (77.4)	43 (22.6)	
Whites	190 (66.7)	78 (82.1)	17 (17.9)	0.44
Socioeconomic status				
Low	108 (37.9)	83 (76.9)	25 (23.2)	
Middle	101 (35.4)	79 (78.2)	22 (21.8)	
High	76 (26.7)	63 (82.9)	13 (17.1)	0.60
Education				
Low	132 (46.3)	100 (75.8)	32 (24.2)	
Middle	103 (36.1)	86 (83.5)	17 (16.5)	
High	50 (17.5)	39 (78.0)	11 (22.0)	0.35
Smoking exposure				
Never smokers	128 (44.9)	104 (81.3)	24 (18.7)	
Moderate	90 (31.6)	73 (81.1)	17 (18.9)	
Heavy	67 (23.5)	48 (71.5)	19 (28.4)	0.25
Diabetes				
No	245 (86.3)	192 (78.4)	53 (21.6)	
Yes	39 (13.7)	32 (82.1)	7 (17.9)	0.68
Heart disease				
No	155 (54.6)	127 (81.9)	28 (18.1)	
Yes	130 (45.6)	98 (75.4)	32 (24.6)	0.19
Arthritis				
No	250 (87.7)	203 (81.2)	47 (18.8)	
Yes	35 (12.3)	22 (62.9)	13 (37.1)	0.02
Periodontitis AAP-CDC				
No	196 (68.8)	154 (78.6)	42 (21.4)	
Yes	89 (31.2)	71 (79.8)	18 (20.2)	0.88
Periodontitis 30% CAL≥5mm				
No	205 (71.9)	159 (77.6)	46 (22.4)	
Yes	80 (28.1)	66 (82.5)	14 (17.5)	0.42
BOP ≥40%				
No	208 (73.0)	164 (78.9)	44 (21.1)	
Yes	77 (27.0)	61 (79.2)	16 (20.8)	1.00
Total	**285 (100.0)**	**225 (79.0)**	**60 (21.0)**	

*P-values from Fisher's exact test or chi-square.

Table 2. Simple logistic regression models of the association between independent variables and fatigue.

Independent variables	OR	95%CI	p
Age			
35-49 years	1		
50-65 years	0.79	0.43 – 1.46	0.46
Sex			
Males	1		
Females	3.39	1.63 – 7.02	0.001
Skin color			
Non-Whites	1		
Whites	1.34	0.71 – 2.50	0.35
Socioeconomic status			
Low	1		
Middle	0.92	0.48 – 1.77	0.81
High	0.68	0.31 – 1.44	0.32
Education			
Low	1		
Middle	0.62	0.32 – 1.19	0.15
High	0.88	0.40 – 1.92	0.75
Smoking exposure			
Never smokers	1		
Moderate	1.01	0.50 – 2.01	0.98
Heavy	1.71	0.85 – 3.42	0.12
Diabetes			
No	1		
Yes	0.79	0.33 – 1.89	0.60
Heart disease			
No	1		
Yes	1.48	0.84 – 2.62	0.18
Arthritis			
No	1		
Yes	2.55	1.19 – 5.43	0.01
Periodontitis AAP-CDC			
No	1		
Yes	0.93	0.50 – 1.72	0.82
Periodontitis 30% CAL≥5mm			
No	1		
Yes	0.73	0.37 – 1.42	0.36
BOP ≥40%			
No	1		
Yes	0.97	0.51 – 1.86	0.95

Table 3. Multiple logistic regression final models of the association between periodontal variables and fatigue.

Independent variables*	OR	95%CI	p*
Model 1			
Periodontitis AAP-CDC			
No	1		
Yes	0.98	0.52 – 1.86	0.95
Model 2			
Periodontitis 30% CAL≥5mm			
No	1		
Yes	0.40	0.36 – 1.51	0.41
Model 3			
BOP ≥40%			
No	1		
Yes	0.97	0.50 – 1.90	0.94

*Models are adjusted for sex, smoking and arthritis.

5. CAPÍTULO 2

Association between physical activity assessed by IPAQ and periodontitis in Brazilian adults: a cross-sectional study.

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Running title: Physical activity and periodontal disease

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Aim: Few studies have focused on investigating the benefits of physical activity (PA) in the prevention of periodontal diseases. Moreover, PA has been measured with non-validated questionnaires limiting the validity of the associations. The aim of this study was to assess the association between PA and parameters of periodontitis in a sample of Brazilian adults.

Methods: This cross-sectional study was nested to a population-based cohort study conducted between 2011-12 and 2016-17 with adults 35 years and older living in Porto Alegre, Brazil. Probing depth (PPD) and clinical attachment loss (CAL) were recorded in four sites/tooth in all present teeth in 285 individuals evaluated at the follow-up examination. A structured questionnaire gathered demographics and behavioral variables. PA was assessed by the International Physical Activity Questionnaire (IPAQ), and individuals were dichotomized into physically inactive and active according to validated cut-off points. Male and female individuals with 4 or more teeth, and between 35-59 years of age were included. Multiple logistic regression models were applied to estimate odds ratios (OR) for the associations between PA and periodontitis defined by the AAP-CDC criteria.

Results: After adjusting for age, skin color, socioeconomic status and smoking, physically active individuals had a significantly smaller chance of having severe periodontitis (OR=0.51; 95%CI: 0.28-0.93). The reduction in the odds was also observed for PPD ≥5mm in ≥1 tooth (OR=0.41; 95%CI: 0.21-0.79). When CAL alone was considered the periodontal outcome, no significant associations were found, indicating that PA may act at the inflammatory component of periodontitis.

Conclusion: PA may act as a protective factor for periodontal disease. This study strengths the effectiveness of routine physical activity in the primary and secondary prevention of chronic diseases throughout improving inflammation.

Key words: periodontal diseases; chronic disease; exercise; inflammation; cross sectional studies.

Introduction

Physical activity (PA) is conceptualized as any bodily movement produced by skeletal muscles that results in energy expenditure above a basal level (CDC, 2015). Physiologic benefits of regular PA include energy balance, increase of lean body mass, cardiovascular effects, favorable changes in plasma lipids and lipoproteins, enhancement of insulin sensitivity, effects on the immune response, and neurological and psychological effects (Miles, 2007). In contrast, an inactive lifestyle leads to the accumulation of visceral fat, accompanied by adipose tissue infiltration by pro-inflammatory immune cells, increased release of adipokines and the development of a low-grade systemic inflammatory state (Ouchi *et al.*, 2011). Therefore, a prolonged inflammatory state resulting from lack of PA has detrimental health effects and predisposes to a number of chronic diseases and health conditions, and has been associated with the development of insulin resistance, atherosclerosis, neurodegeneration and tumor growth (Pradhan *et al.*, 2001; Pedersen e Saltin, 2006; Leonard, 2007).

Indeed, there is irrefutable evidence of the effectiveness of routine PA in the primary and secondary prevention of several chronic diseases (Reiner *et al.*, 2013; Warburton e Bredin, 2017). Regular PA is considered a major independent modifiable risk factor which has a protective effect on cardiovascular disease, stroke, type 2 diabetes, colon and breast cancers (Warburton *et al.*, 2006). Lifestyle behavioral interventions, including changes in food/dietary intake and PA, have clinically significant benefits for improving inflammation over the long-term (Nicklas *et al.*, 2005).

Contrarily, a few studies have focused on investigating the benefits of PA in the occurrence of periodontal diseases. There are some cross-sectional studies investigating this association (Wakai *et al.*, 1999; Al-Zahrani *et al.*, 2005a; b; Shimazaki *et al.*, 2010; Bawadi *et al.*, 2011), and all of them have found that PA may act as a protective factor for periodontal disease. Only one prospective study (Merchant *et al.*, 2003) was conducted and observed that physically active adults had lower risk of self-reported periodontitis. Moreover, Australian individuals who met public health recommendations for PA presented lower levels of the proinflammatory biomarkers interleukin 1 beta (IL-1b) and c-reactive protein (CRP) in gingival crevicular fluid (GCF) (Sanders *et al.*, 2009). Nevertheless, PA has been assessed with different methods and tools, with the great

majority of the studies applying non-validated methodologies to measure PA, which may lead to biased associations. Additionally, this association was evaluated in very few populations, specifically only in the United States using data from NHANES III, in Japan and Jordan. Noteworthy, partial periodontal recording protocols were used in all studies, except one (Bawadi *et al.*, 2011).

Periodontitis is an immune-inflammatory disease in which bacteria induce a series of host responses that mediate destructive events in the periodontium. It is plausible that PA may protect the periodontium by attenuating an excessive host inflammatory response. Therefore, an association between PA and periodontitis may be expected. The aim of the present study was to investigate the association between PA and periodontal diseases, testing the research hypothesis that PA may be a protective factor for periodontitis.

Material and Methods

Study design and sample

This study is a cross-sectional study nested to a population-based prospective cohort study. In 2011, the Caries-Perio Collaboration Group from the Federal University of Rio Grande do Sul designed a survey by drawing a representative sample of adults living in Porto Alegre, Brazil. Gingival recession (GR) and other oral outcomes were assessed in 1023 individuals aged 35 years and older. After 4 years, 414 (40.5%) individuals were re-examined (Figure 1) by recording periodontal probing depth (PPD) and GR, which allowed the diagnosis of periodontitis using various definition criteria. Thus, this study was conducted with data collected in the follow-up examination of the cohort, which was conducted between January 2016 and March 2017. Individuals with less than 3 teeth and elderly (60 years and older) were excluded from this study, with a final sample comprised by 285 individuals 35 to 59 years of age.

Detailed information regarding the sampling strategy at baseline was previously published (Costa *et al.*, 2014; Rios *et al.*, 2014; Wagner *et al.*, 2016). In brief, a multistage probability sampling strategy was applied. The city was divided in 86 neighborhoods comprising the primary sampling units that were stratified in low and high income. The second stage consisted on a random selection of sectors proportional to the total number

of sectors in each PSU. The third stage consisted of selecting households consecutively according to the sector starting point until the sector sample size was reached. The number of individuals to be selected within each sector was estimated based on the proportional distribution of the sample size.

One researcher visited each selected sector one day before the start of data collection to invite residents to participate. Residents were not included only after the third attempt of invitation. Interviews and clinical examinations were conducted inside the household. Examinations were conducted using three portable devices: a medical headlight, a portable compressor and a bendable chair.

Ethical aspects

The study protocol was reviewed and obtained ethical approval from the Research Ethics Committee, Federal University of Rio Grande do Sul, Porto Alegre, Brazil. Prior to the interview, all patients read and signed a consent form.

Interview

Participants were interviewed using a structured questionnaire containing questions regarding socio-demographic variables, oral hygiene habits, self-perceived oral health, access to dental services, medical history and behavioral factors. Three trained and calibrated interviewers conducted applied the questionnaire.

International Physical Activity Questionnaire (IPAQ)

IPAQ assesses physical activity undertaken across a comprehensive set of domains including leisure time, domestic activities, work-related and transport-related activities. IPAQ comprises a set of four questions that can be used to obtain internationally comparable data on health–related physical activity. The short version employed in this study is suitable for use in national and regional surveillance systems. Cross-cultural validation for Brazilian Portuguese was applied by Matsudo et al. (2012).

Both categorical and continuous indicators of physical activity are possible from the IPAQ short form. In summary, energy expenditure rate in PA is computed by weighting each type of activity by its energy requirements defined in METS (multiples of the resting metabolic rate) to yield a score in MET–minutes. An average MET score is derived for each type of activity (Ainsworth *et al.*, 2000): Walking = 3.3 METs, Moderate PA = 4.0 METs and Vigorous PA = 8.0 METs. A continuous score is expressed as MET-min per week: MET level x minutes of activity x events per week. Individuals are classified into "highly active" when perform vigorous-intensity activity on at least 3 days and accumulating at least 1500 METminutes/week OR 7 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 3000 MET-minutes/week. Individuals are classified into "minimally active" if perform 3 or more days of vigorous activity of at least 20 minutes per day OR 5 or more days of moderate-intensity activity or walking of at least 30 minutes per day OR 5 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 600 MET-min/week. Inactive individuals are those who reported no activity OR some activity is reported but not enough to meet categories "minimally active" or "highly active". Full access to the questionnaire and scoring protocol is available at the official web page of IPAQ (http://www.ipaq.ki.se/ipaq.htm). For the purpose of comparisons, IPAQ categorization was dichotomized into physically inactive individuals (IPAQ inactive category) and physically active individuals (aggregation of IPAQ minimally and highly active categories) in the present study.

Periodontal examination

All permanent fully erupted teeth were examined by four periodontists using a manual periodontal probe. A protocol of four sites per tooth (disto-buccal, mid-buccal, mesio-buccal, and disto-lingual/palatal) was used. Gingival recession (GR), periodontal probing depth (PPD) and bleeding on probing (BOP) were recorded. PPD was defined as the distance between the free gingival margin to the bottom of the pocket/sulcus. GR was defined as the distance from the cement-enamel junction (CEJ) to the free gingival margin. If the CEJ was located apical to the gingival margin, this assessment was given a negative sign. Clinical attachment loss (CAL) was obtained by the sum of GR and PPD.

Reproducibility

Intra and inter-examiner reproducibility was assessed with duplicate measures conducted in a total of 16 patients (1,231 sites). During the fieldwork, 42 participants (2896 sites) allowed to perform the duplicate measurements. Weighted Kappa values for the four examiners range between 0.87 and 0.92.

Outcome variables

The periodontal status of the individuals was defined using three different criteria. Individuals were dichotomized into those having or not severe periodontitis according to the AAP-CDC criteria (Eke *et al.*, 2012). Moreover, two additional definitions were used considering CAL and PPD separately: individuals were considered to have periodontal disease if they presented at least 1 tooth with (1) CAL ≥5mm and (2) PPD ≥5mm in a proximal site.

Exposure variables

Added to IPAQ, the following traditional risk indicators/factors were associated with each of the three periodontal outcomes: age, sex, skin color, socioeconomic status, educational status, smoking, diabetes and dental visits.

Age was categorized into two categories (35-49, 50-59). Skin color was dichotomized into non-white and white. Educational level was defined according to years of education into low (≤8 years), middle (9-11 years) and high (≥12 years). Socioeconomic status was categorized using cut-off points adapted from the CCEB classification (Abep, 2013) that considers the amount of consumer goods and the educational level of the head of the family as follows: low (≤20 points), middle (21-26 points) and high (≥27 points).

The total number of packs of cigarettes consumed in a lifetime (packyears) was calculated for each individual by multiplying the number of cigarettes consumed per day by the years of habit, and dividing by 20. Smoking exposure was categorized into never-

smokers (0 packyears), light-moderate smokers (<20 packyears) and heavy smokers (≥20 packyears).

Statistical analyses

Fisher's exact or chi-square tests were applied to compare the distribution of individuals with or without periodontal disease according to each exposure variable. Multiple logistic regression models were fitted to estimate odds ratios (OR) and 95% confidence intervals for the associations between IPAQ and periodontal disease. Model fitting followed the purposeful approach (Hosmer e Lemeshow, 2000). Modeling started by fitting simple models for each exposure variable, and those presenting p values <0.25 were entered in a multiple model. Maintenance of variables in the final model was determine by a combination of p values <0.05 and analyses of effect modification. Three different models were fitted for each periodontal outcome considering the traditional risk factors. Thereafter, IPAQ was included in each final model.

The individual was the unit of analysis. The significance level was set at 5%. Data analyses were performed using a statistical package (Stata 14 for Macintosh, STATA Corp., College Station, USA).

Results

The percentage of individuals with severe periodontitis, CAL ≥5mm in ≥1 tooth and PPD ≥5mm in ≥1 tooth according to traditional risk indicators for periodontal disease and PA are shown in Table 1. The percentage of individuals with severe periodontitis was significantly higher among whites and individuals with diabetes. Variables associated with CAL ≥5mm were age and education. Whites, low socioeconomic status and diabetes were associated with higher percentages of individuals with PPD ≥5mm. In regards to PA, 20.1% of the active individuals had severe periodontitis compared to 32.1% among those inactive (p=0.04). This finding was similar when PPD ≥5mm was evaluated, whereas no significant difference was observed for CAL ≥5mm.

In the univariable logistic regression models, skin color, socioeconomic status, education, smoking, diabetes and PA were associated with severe periodontitis (Table 2). Age, socioeconomic status, education and smoking were associated with CAL ≥5mm.

Skin color, socioeconomic status, education, diabetes and PA were associated with PPD ≥5mm.

Multiple logistic regression models of physical activity as a protective factor for periodontal disease are shown in Table 3. The chance of having severe periodontitis was 49% significantly lower in active compared to inactive individuals (OR=0.51; 95%CI=0.28 – 0.93). This reduction in the chance of disease was also observed for PPD ≥5mm (OR=0.41; 95%CI=0.21 – 0.79). No significant association was found for the CAL ≥5mm in ≥1 tooth (p=0.37).

Discussion

This cross-sectional study aimed to investigate the association between PA and periodontal diseases in a Brazilian sample. Physically active individuals had significantly smaller chances to present severe periodontitis and PPD ≥5mm in ≥1 tooth, independently of other variables. Take into account that prospective studies are necessary to confirm the hypothesis, the authors suggest that PA may act as a protective factor for periodontal disease. This study strengths the effectiveness of routine physical activity in the primary and secondary prevention of chronic diseases throughout improving inflammation.

The results of the present study corroborate the findings from other previous cross-sectional studies. Poor physical fitness affecting aerobic capacity, foot balance and reaction was associated with a higher Community Periodontal Index (CPI) in Japanese subjects aged 23 to 83 years (Wakai *et al.*, 1999). In another sample of Japanese subjects, Shimazaki *et al*., (2010) observed that individuals with lower BMI and higher maximum oxygen uptake (VO2max) had a significantly lower risk of severe periodontitis. Furthermore, Al-Zahrani *et al*. (2005a) found a significant association between increased level of physical activity and lower periodontitis prevalence among never and former smokers in a subset of the third national health and nutrition examination survey (NHANES III). Moreover, another study that analyzed data from the NHANES III revealed that individuals who maintained normal weight, had a high-quality diet and engaged in the recommended level of exercise (≥5 episodes of moderate or ≥3 episodes of vigorous-intensity physical activity per week), were 40% less likely to have periodontitis compared to individuals who maintained none of these health-enhancing behaviors (Al-Zahrani *et al.*, 2005b). In addition, Jordanian individuals who were highly

physically active had a significantly lower average plaque index, average gingival index, average CAL and percentage of sites with CAL≥3 mm compared to individuals with a low level of physical activity and individuals with a moderate level of physical activity (Bawadi *et al.*, 2011). One prospective longitudinal study (Merchant *et al.*, 2003) assessed the association of self-reported physical activity, walking and periodontitis in 39.461 male, US based, health professionals ageing 40–75 years old. These individuals were followed up for 12 years and an inverse, linear association between sustained physical activity and periodontitis was found.

Reviews on the anti-inflammatory effects of exercise (Petersen e Pedersen, 2005; Flynn e Mcfarlin, 2006; Mathur e Pedersen, 2008) have focused on three possible mechanisms: the reduction in visceral fat mass; increased production and release of anti-inflammatory cytokines from contracting skeletal muscle such molecules are termed myokines (Pedersen e Febbraio, 2008); and reduced expression of Toll-like receptors (TLRs) on monocytes and macrophages with subsequent inhibition of downstream responses, such as the production of pro-inflammatory cytokines and the expression of major histocompatibility complex (MHC) and co-stimulatory molecules (Gleeson *et al.*, 2006). Furthermore, mouse studies have revealed that the anti-inflammatory effects of exercise also rely on other mechanisms, such as the inhibition of monocyte and macrophage infiltration into adipose tissue and the phenotypic switching of macrophages within adipose tissue (Kawanishi *et al.*, 2010). Analysis of human peripheral blood following exercise has revealed a reduction in the circulating numbers of pro-inflammatory monocytes (Timmerman *et al.*, 2008) and an increase in the circulating numbers of regulatory T cells (TReg cells) (Yeh *et al.*, 2006; Wang *et al.*, 2012). This suggests that such mechanisms may also be involved in the anti-inflammatory effects of exercise in humans. In this regard, Sanders *et al*., (2009) observed a dose–response relation of decreasing probability of detectable inflammatory marker CRP in GCF at increasing levels of PA among cases of periodontitis. Thus, anti-inflammatory effects of PA probably impacted in periodontal inflammation in our sample, whereas physically active individuals had lower levels of PPD. Additionally, PA was associated with lower severity of periodontal disease in the present study, which reinforces the protective role of PA.

In a study of a large, multiethnic population-based cohort from multiple sites across the United States (Vella *et al.*, 2017), higher levels of moderate-to-vigorous

physical activity were associated with significantly higher levels of adiponectin and lower levels of leptin, IL-6, and resistin. These results also suggested that physical activity may positively influence levels of selected adiposity associated inflammatory markers, irrespective of total and/or central adiposity. Furthermore, evidence from studies with animals showed that physical activity or acute exercise can modulate the response to lipopolysaccharide (LPS)-induced inflammation in mouse adipose tissue (Peppler *et al.*, 2017). Additionally, non-exhaustive physical exercise reduces the formation of reactive oxygen species (ROS) and other oxidants, improves antioxidant defense system and enhances the resistance of tissues against the toxic action of ROS (Kruk, 2011).

Another possible benefit from PA over periodontal diseases was suggested by Anderson (2016), which evaluated the association between physical activity and serum IgG antibodies. His findings showed that in unadjusted and minimally adjusted models, physical activity was significantly, positively associated with a cluster of antibodies associated with healthy periodontal states. These findings indicated that physical activity may also improve the periodontal microbiota.

The relationship between physical activity and the the immune system is not fully understood, but it is known that moderate intensity exercise can improve immune defenses, while the extreme effort can reduce them. Most of the research shows that intensive, repetitive exercise causes a decrease in the salivary IgA levels and an increased susceptibility to upper respiratory tract infection in athletes (Peters, 1997). This means that both too little and too much physical activity may increase the risk of infections (Nieman, 1994). Indeed, poor oral health of elite athletes is a consistent finding in published studies (Needleman *et al.*, 2014). A cross-sectional study with Olympic athletes revealed rare periodontal health (Needleman *et al.*, 2013). Gingivitis was present in more than three quarters of athletes and there was irreversible periodontitis in more than 15% of athletes. In terms of extent, at least half of the mouth was affected by gingivitis or periodontitis in 76% and 8.3% of athletes, respectively. Nevertheless, a possible bidirectional relationship between periodontal disease and PA was proposed by Oliveira *et al*. (2015). In this work, authors found that males who presented periodontal disease had increased odds for poor physical fitness.

Limitations of the present study are many and inferences must be drawn with caution. This cross-sectional design does not allow establishment of a cause-effect

relationship between PA and periodontal disease. Furthermore, PA and periodontal diseases share many common risk factors, like as lifestyle. In this way, behavioral factors may act as mediators in the relationship of PA and periodontitis. Both moderate- and vigorous-intensity PAs are important for physical and mental health (Biddle *et al.*, 2015). Moreover, increased reported PA may have a positive and direct influence on self-esteem (Sani *et al.*, 2016). In the same way, there is some evidence showing associations of instability of self-esteem and perfectionism with oral health behaviors and oral health status (Dumitrescu *et al.*, 2012). A healthy lifestyle assembles a set of attributes and consequently may concur for the results of the present study. On the other hand, employment of a full mouth examination protocol of four sites per tooth and application of a reliable and valid questionnaire to measure PA (IPAQ) strengths the findings of the present study.

The benefits from PA for prevention of a number of chronic diseases are well known and were extensively investigated. Longitudinal prospective studies with population based samples, as well as interventional studies must be encouraged to enable a possible classification for PA as a protective factor for periodontal diseases. Moreover, effective tools and protocols of assessment of both PA and periodontal disease must be employed to ensure accuracy of measurements. In addition, knowledge about the effect of PA in primary and secondary prevention of periodontal diseases is paramount. If there is real effectiveness of PA to prevent periodontal diseases, counselling from oral health practitioners and public health policies must be stimulated for people awareness.

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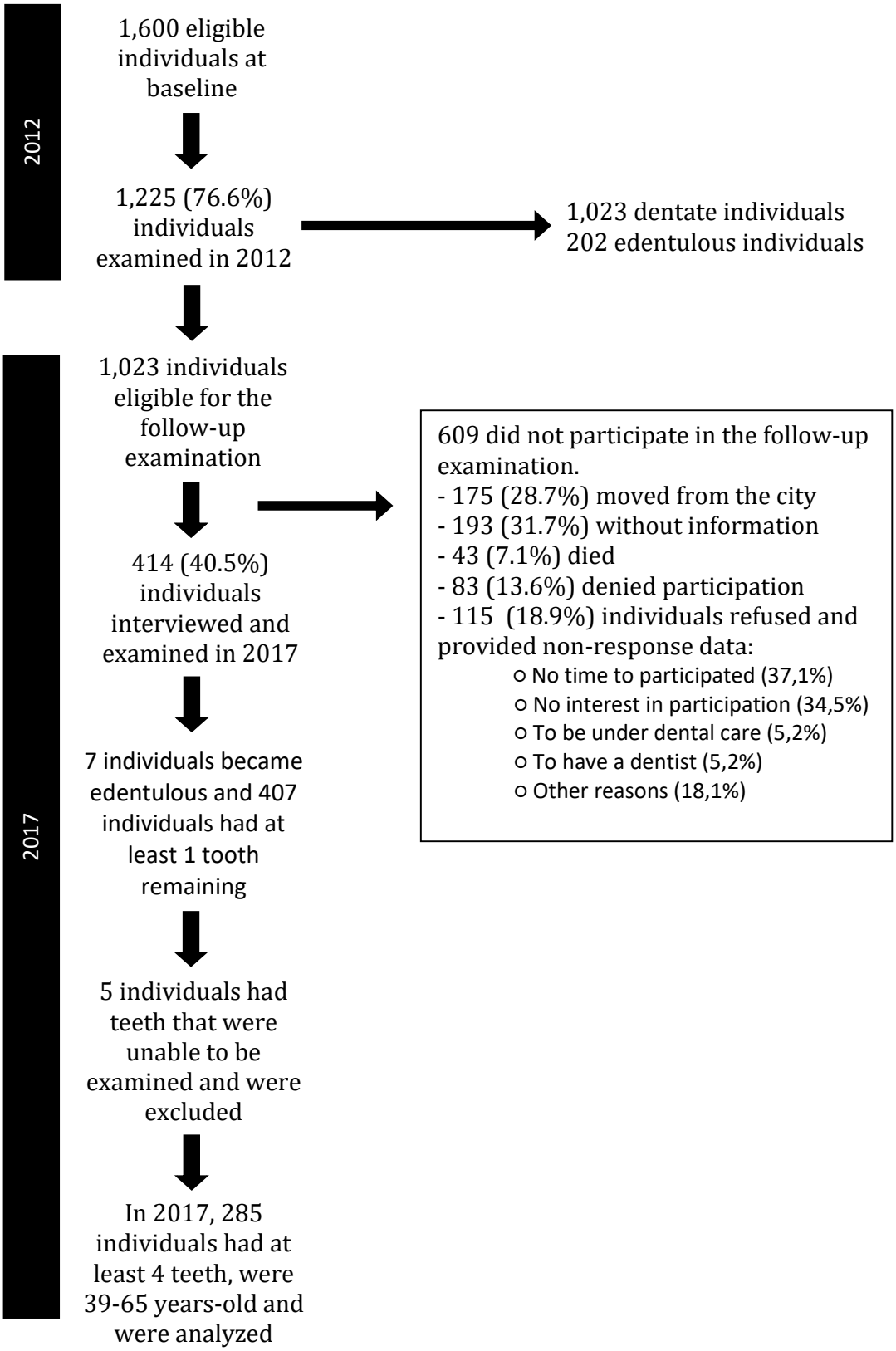

Figure 1. Flowchart of the study.

Table 1. Percentage of individuals with severe periodontitis, CAL ≥5mm in ≥1 tooth and PPD ≥5mm in ≥1 tooth according to traditional risk indicators and physical activity.

	Whole sample	Severe periodontitis AAP-CDC		CAL ≥5mm in ≥1 tooth		PPD ≥5mm in ≥1 tooth	
	n=285	n (%)	p	n (%)	p	n (%)	p
Age (years)							
35-49 years	84	16 (19.1)		58 (69.0)		16 (19.0)	
50-65 years	201	51 (25.4)	0.29	165 (82.1)	0.02	39 (19.4)	1.00
Sex							
Females	101	27 (26.7)		85 (84.1)		21 (20.8)	
Males	184	40 (21.7)	0.38	138 (75.0)	0.10	34 (18.5)	0.64
Skin color							
Non-Whites	190	35 (18.4)		145 (76.3)		26 (13.7)	
Whites	95	32 (33.7)	0.01	78 (82.1)	0.30	29 (30.5)	0.001
Socioeconomic status							
Low	108	30 (27.8)		91 (84.3)		28 (25.9)	
Middle	101	26 (25.7)		79 (78.2)		21 (20.8)	
High	76	11 (14.5)	0.09	53 (69.7)	0.06	6 (7.9)	0.01
Education							
Low	132	37 (28.0)		112 (84.8)		33 (25.0)	
Middle	103	24 (23.3)		78 (75.7)		19 (18.4)	
High	50	6 (12.0)	0.08	33 (66.0)	0.02	3 (6.0)	0.01
Smoking exposure							
Never smokers	128	22 (17.2)		97 (75.8)		18 (14.1)	
Moderate	90	25 (27.8)		67 (74.4)		20 (22.2)	
Heavy	67	20 (29.8)	0.07	59 (88.1)	0.08	17 (25.4)	0.11
Dental visits							
Irregular	113	26 (23.0)		82 (72.6)		23 (20.3)	
Regular	172	41 (23.8)	0.88	141 (82.0)	0.08	32 (18.6)	0.76
Diabetes							
Yes	39	15 (38.6)		34 (87.1)		13 (33.3)	
No	245	52 (21.2)	0.02	189 (77.1)	0.21	42 (17.1)	0.03
Physical activity (IPAQ)							
Inactive	81	26 (32.1)		66 (81.5)		23 (28.4)	
Active	204	41 (20.1)	0.04	157 (77.0)	0.43	32 (15.7)	0.02

Table 2. Simple logistic regression models of traditional risk indicators and physical activity for severe periodontitis, CAL ≥5mm in ≥1 tooth and PPD ≥5mm in ≥1 tooth.

	Severe periodontitis AAP-CDC		CAL ≥5mm in ≥1 tooth		PPD ≥5mm in ≥1 tooth	
	OR (95%CI)	p	OR (95%CI)	P	OR (95%CI)	p
Age (years)						
35-49 years	1		1		1	
50-59 years	1.44 (0.77-2.71)	0.25	2.05 (1.14-3.69)	0.02	1.02 (0.53-1.95)	0.94
Sex						
Females	1		1		1	
Males	0.76 (0.43-1.34)	0.34	0.56 (0.30-1.06)	0.07	0.86 (0.47-1.58)	0.63
Skin color						
Non-Whites	1		1		1	
White	2.24 (1.28-3.94)	0.005	1.42 (0.76-2.65)	0.26	2.77 (1.51-5.05)	0.001
Socioeconomic status						
Low	1		1		1	
Middle	0.90 (0.48-1.66)	0.74	0.67 (0.33-1.35)	0.26	0.75 (0.39-1.42)	0.38
High	0.44 (0.2-0.94)	0.03	0.43 (0.21-0.87)	0.02	0.24 (0.09-0.62)	0.003
Education						
Low	1		1		1	
Middle	0.78 (0.43-1.41)	0.41	0.55 (0.29-1.07)	0.08	0.67 (0.35-1.28)	0.23
High	0.35 (0.13-0.89)	0.03	0.34 (0.16-0.73)	0.006	0.19 (0.05-0.65)	0.009
Smoking exposure						
Never smokers	1		1		1	
Moderate	1.85 (0.96-3.55)	0.06	0.93 (0.50-1.73)	0.82	1.74 (0.86-3.52)	0.12
Heavy	2.05 (1.02-4.11)	0.04	2.35 (1.01-5.47)	0.04	2.07 (0.99-4.36)	0.05
Dental visits						
Irregular	1		1		1	
Regular	1.04 (0.59-1.83)	0.87	1.71 (0.97-3.03)	0.06	0.89 (0.49-1.62)	0.71
Diabetes						
No	1		1		1	
Yes	2.31 (1.13-4.73)	0.02	2.04 (0.75-5.39)	0.16	2.41 (1.14-5.08)	0.02
Physical activity (IPAQ)						
Inactive	1		1		1	
Active	0.53 (0.29-0.94)	0.03	0.75 (0.39-1.45)	0.40	0.47 (0.25-0.86)	0.02

Table 3. Multiple logistic regression of physical activity as a protective factor for severe periodontitis, CAL ≥5mm in ≥1 tooth and PPD ≥5mm in ≥1 tooth.

	Severe periodontitis AAP-CDC*		CAL ≥5mm in ≥1 tooth**		PPD ≥5mm in ≥1 tooth***	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Physical activity (IPAQ)						
Inactive	1		1		1	
Active	0.51 (0.28 – 0.93)	0.03	0.74 (0.38 – 1.43)	0.37	0.41 (0.21 – 0.79)	0.01

*Model adjusted for skin color and smoking.

**Model adjusted for age, dental visits and smoking.

***Model adjusted for skin color, socioeconomic status and smoking.

6. CONSIDERAÇÕES FINAIS

O presente trabalho avaliou a relação entre os parâmetros clínicos periodontais e sensações de fadiga, e também investigou a associação entre atividade física e doença periodontal em um estudo transversal aninhado a um estudo de coorte de base populacional.

Com relação à associação entre fadiga e doença periodontal, este foi o primeiro trabalho que se propôs a investigar esta relação. Entretanto, os resultados não mostraram associação entre doença periodontal e fadiga. Não há como negar a robusta evidência acerca da relação da doença periodontal com algumas doenças e condições sistêmicas. Porém, levando em consideração que a associação entre periodontite e as sensações de fadiga ainda consiste em um campo de pesquisa incipiente, alguns fatores determinantes podem estar influenciando esta relação: 1) um efeito decisivo menos importante da periodontite na inflamação sistêmica e no desenvolvimento de condições sistêmicas crônicas do que outras exposições relacionadas a fadiga; 2) a complexidade do fenômeno fadiga que engloba componentes psicológicos, fisiológicos e situacionais; 3) a dificuldade para definir fadiga e o consequente desafio para mensurá-la e quantificar sua severidade em nível populacional.

Por outro lado, indivíduos fisicamente ativos tiveram menores chances de apresentar periodontite severa e profundidade de sondagem ≥5mm em um ou mais dentes, independentemente de outras variáveis. Estes resultados corroboraram os achados de outros estudos transversais que investigaram essa relação ao redor do mundo. Levando em consideração que são necessários estudos prospectivos para confirmar a hipótese, os autores do presente trabalho sugerem que a atividade física poderia agir como um fator protetor para a doença periodontal. O presente estudo reforça a efetividade da atividade física rotineira na prevenção primária e secundária de doenças crônicas, através do seu efeito anti-inflamatório.

Dada a multifatorialidade das doenças e condições crônicas, há necessidade de cautela na interpretação destas ligações, e também de um incremento de mais estudos para investigar a relação de atividade física, doença periodontal, e fadiga. No caso particular da atividade física, é imperativo que mais estudos prospectivos observacionais e intervencionais sejam delineados com o objetivo de elucidar esta associação. Em relação à fadiga, avaliações psicométricas são necessárias para refinar e comparar os instrumentos destinados a mensurar este constructo, além de um consenso sobre o conceito fadiga. A execução de mais estudos de associação das doenças periodontais e fadiga deve ser

encorajada, levando em consideração que existe plausibilidade biológica para justificar tal relação.

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8. **ANEXOS**

ANEXO 1

REGISTRO Nº ☐☐☐

Data ☐☐ / ☐☐ / ☐☐☐☐ **Setor censitário** ☐☐

Entrevistador ☐ Maurício ☐ Ricardo ☐ Fernando ☐ Outro .....

DADOS PESSOAIS

1.1. Nome ..... **1.2. Endereço** .....

1.3. Telefone res. ( ) ..... **1.4. Telefone cel.** ( ) ..... **1.5. E-mail** .....

1.6. Contato familiar ..... **1.7. Telefone res.** ( ) ..... **1.8. Telefone cel.** ( ) .....

1.9. Sexo [1] Masculino [2] Feminino **1.10. Data de nascimento** ☐☐ / ☐☐ / ☐☐☐☐

1.11. Idade ☐☐ anos **1.12. Raça** [1] Branca [2] Negra/Preta [3] Parda/Mulata [4] Amarela [5] Indígena

1.13. Estado civil [1] Solteiro [2] Casado ou em união estável [3] Divorciado [4] Viúvo [5] Outro .....

CARACTERIZAÇÃO SOCIOECONÔMICA

2.1. Você é alfabetizado? [1] Sim [2] Não

2.2. Você estudou até: [1] Nunca estudou [2] 1ª a 4ª série do 1º grau [3] 5ª a 8ª série do 1º grau [4] 2º grau incompleto [5] 2º grau completo [6] 3º grau incompleto [7] 3º grau completo [8] Pós - graduação

2.3. Quantas pessoas, incluindo você, residem nessa casa? ☐☐ — **2.4. Acima de 35 anos?** ☐☐

2.5. Quantos cômodos estão servindo permanentemente de dormitório para os moradores desse domicílio? ☐☐

Quantos...você possui? (Não possui = 0 / 1 / 2 / 3 / 4 ou mais = 4)

2.6. Aspiradores de pó		**2.12. Máquinas de lavar roupas**	
2.7. Automóveis		**2.13. Microondas**	
2.8. Banheiros		**2.14. Rádios**	
2.9. Computadores		**2.15. Refrigeradores**	
2.10. Empregadas (pagamento mensal)		**2.16. Televisões coloridas**	
2.11. Freezer (considerar um refrigerador duplex)		**2.17. Videocassetes / DVDs**	

2.18. No mês passado, quanto receberam, em reais, juntas, todas as pessoas que moram na sua casa?

[1] Até 250 [2] 251 a 480 [3] 481 a 1.500 [4] 1.501 a 2.500 [5] 2.501 a 4.500 [6] 4.501 a 9.500 [7] Mais de 9.500

[8] Não sabe [9] Não respondeu

HISTÓRIA MÉDICA

Você apresenta algumas das seguintes doenças? (Sim = 1 / Não = 2 / Não sabe = 3)

3.1. Artrite reumatóide		**3.4. Osteoporose**	
3.2. Diabetes		**3.5. Refluxo gástrico**	
3.3. Doença cardíaca ou arterial			

3.6. Você está usando alguma medicação? [1] Sim [2] Não

3.7. Qual? .....

3.8. Você tem amigdalite? [1] Nunca [2] Menos de uma vez por ano [3] Uma vez por ano [4] Mais de uma vez por ano

FATORES COMPORTAMENTAIS

4.1. Você fuma atualmente? [1] Sim **4.2. Quantos cigarros por dia?** ☐☐ **4.3. Há quantos anos?** ☐☐

[2] Não **4.4. Você fumou anteriormente?** [1] Sim [2] Não

4.5. Quantos cigarros por dia? ☐☐ **4.6. Por quantos anos?** ☐☐ **4.7. Há quantos anos parou de fumar?** ☐☐

4.8. Você toma chimarrão: [1] Nunca [2] Raramente [3] Às vezes [4] Freqüentemente

4.9. Você ingere bebidas alcoólicas: [1] Nunca [2] Raramente [3] Às vezes [4] Freqüentemente

4.10. Qual tipo? [1] Nenhum [2] Cerveja [3] Cachaça [4] Vinho [5] Outro.....

4.11. Quantas doses/copo você geralmente ingere por semana? ☐☐

4.12. Você costuma apertar ou ranger os dentes? [1] Sim [2] Não [3] Não sabe

HÁBITOS DE HIGIENE BUCAL

5.1. Com que freqüência você escova seus dentes?

[1] Nunca escova [2] Menos de uma vez por dia [3] Uma vez por dia [4] Duas vezes por dia [5] Três vezes ou mais por dia

5.2. Qual tipo de escova você usa?

[1] Não usa escova [2] Macia [3] Média [4] Dura [5] Não sabe

5.3. Você divide a escova com alguém? [1] Sim [2] Não

5.4. O que você usa para limpar entre seus dentes?

[1] Nada [2] Palito de dentes [3] Fio dental [4] Outro .....

5.5. Com que freqüência?

[1] Nunca usa [2] Menos de uma vez por dia [3] Uma vez por dia [4] Duas vezes por dia [5] Três vezes ou mais por dia

5.6. Você limpa a língua?

[1] Nunca escova [2] Menos de uma vez por dia [3] Uma vez por dia [4] Duas vezes por dia [5] Três vezes ou mais por dia

5.7. O que você usa para limpar a língua?

[1] Nada [2] Cerdas da escova [3] Dorso da escova [4] Limpador de língua [5] Outros.....

5.8. Você usa algum produto para bochecho?

[1] Nenhum [2] Cepacol [3] Listerine [4] Plax [5] Oral-B [6] Malva [7] Outros.....

5.9. Com que freqüência?

[1] Nunca usa [2] Menos de uma vez por dia [3] Uma vez por dia [4] Duas vezes por dia [5] Três vezes ou mais por dia

5.10. Você usa bochecho para?

[1] Não usa [2] Manter dentes limpos [3] Reduzir sangramento gengival [4] Clarear dentes [5] Manter hálito fresco

O produto para bochecho apresenta álcool? [1] Sim [2] Não [3] Não sabe

HALITOSE

6.1. Você sente mau hálito, mau cheiro ou gosto ruim na boca? [1] Nunca [2] Raramente [3] Algumas vezes [4] Sempre

6.2. Em que momento do dia você sente mau hálito? [1] Não sente [2] Manhã [3] Tarde [4] Noite [5] Todo o dia

6.3. Você foi avisado por alguma pessoa que tem mau hálito? [1] Sim [2] Não

6.4. Por quem? [1] Ninguém [2] Companheiro (a) [3] Familiar [4] Amigo (a) [5] Dentista

6.5. Das pessoas que vivem na sua casa, quantas você diria que usualmente possuem mau hálito? ☐☐

ANEXO 2

Versão Brasileira do Questionário de Qualidade de Vida -SF-36

Nome:_____

Idade: _____ Sexo: _____

ESCALA VITALIDADE

Essas questões são sobre como você se sente e como tudo tem acontecido com você durante as últimas 4 semanas. Para cada questão, por favor dê uma resposta que mais se aproxime da maneira que você se sente, em relação às últimas 4 semanas.

	Todo tempo	A maior parte do tempo	Uma boa parte do tempo	Alguma parte do tempo	Uma pequena parte do tempo	Nunca
a) Quanto tempo você tem se sentido cheio de vigor, de vontade, de força?	6	5	4	3	2	1
b) Quanto tempo você tem se sentido com muita energia?	6	5	4	3	2	1
c) Quanto tempo você tem se sentido esgotado?	1	2	3	4	5	6
d) Quanto tempo você tem se sentido cansado?	1	2	3	4	5	6

ANEXO 3

FICHA CLÍNICA

PROFUNDIDADE DE SONDAGEM

17			16			15			14			13			12			11			21			22			23			24			25			26			27		
DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV
DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL
47			46			45			44			43			42			41			31			32			33			34			35			36			37		
DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV
DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL

PERDA DE INSERÇÃO

17			16			15			14			13			12			11			21			22			23			24			25			26			27		
DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV
DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL
47			46			45			44			43			42			41			31			32			33			34			35			36			37		
DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV
DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL

SANGRAMENTO À SONDAGEM (0=ausente; 1=sangramento)

17			16			15			14			13			12			11			21			22			23			24			25			26			27		
DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV
DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL
47			46			45			44			43			42			41			31			32			33			34			35			36			37		
DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	DV	VV	MV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV	MV	VV	DV
DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	DL	LL	ML	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL	ML	LL	DL

ANEXO 4

QUESTIONÁRIO INTERNACIONAL DE ATIVIDADE FISICA (IPAQ) – VERSÃO CURTA

Nome:_____
Data: ___/___/___ Idade: ___ Sexo: F( ) M( )

As perguntas incluem as atividades que você faz no trabalho, para ir de um lugar a outro, por lazer, por esporte, por exercício ou como parte das suas atividades em casa ou no jardim. Suas respostas são **MUITO IMPORTANTES**. Por favor, responda cada questão mesmo que considere que não seja ativo. Obrigado por sua participação!

Para responder as questões lembre que:

→Atividades físicas **VIGOROSAS** são aquelas que precisam de um grande esforço fisico e que fazem respirar **MUITO** mais forte que o normal.

→Atividades físicas **MODERADAS** são aquelas que precisam de um grande esforço fisico e que fazem respirar **UM POUCO** mais forte que o normal.

Para responder as perguntas pense somente nas atividades que você realiza **por pelo menos 10 minutos contínuos** de cada vez.

1a Em quantos dias da última semana você **CAMINHOU** por pelo menos 10 minutos contínuos em casa ou no trabalho, como forma de transporte para ir de um lugar para outro, por lazer, por prazer ou como forma de exercício?
dias _____ por **SEMANA** ( ) Nenhum

1b. Nos dias em que você caminhou por pelo menos 10 minutos contínuos quanto tempo no total você gastou caminhando **por dia**?
horas: _____ Minutos: _____

2a. Em quantos dias da última semana, você realizou atividades **MODERADAS** por pelo menos 10 minutos contínuos, como por exemplo pedalar leve na bicicleta, nadar, dançar, fazer ginástica aeróbica leve, jogar vôlei recreativo, carregar pesos leves, fazer serviços domésticos na casa, no quintal ou no jardim como varrer, aspirar, cuidar do jardim, ou qualquer atividade que fez aumentar **moderadamente** sua respiração ou batimentos do coração **(POR FAVOR NÃO INCLUA CAMINHADA)**
dias _____ por **SEMANA** ( ) Nenhum

2b. Nos dias em que você fez essas atividades moderadas por pelo menos 10 minutos contínuos, quanto tempo no total você gastou fazendo essas atividades **por dia**?
horas: _____ Minutos: _____

3a Em quantos dias da última semana, você realizou atividades **VIGOROSAS** por pelo menos 10 minutos contínuos, como por exemplo correr, fazer ginástica aeróbica, jogar

futebol, pedalar rápido na bicicleta, jogar basquete, fazer serviços domésticos pesados em casa, no quintal ou cavoucar no jardim, carregar pesos elevados ou qualquer atividade que fez aumentar **MUITO** sua respiração ou batimentos do coração.
dias _____ por **SEMANA** ( ) Nenhum

3b. Nos dias em que você fez essas atividades vigorosas por pelo menos 10 minutos contínuos quanto tempo no total você gastou fazendo essas atividades **por dia**?
horas: _____ Minutos: _____

Estas últimas questões são sobre o tempo que você permanece sentado todo dia, no trabalho, na escola ou faculdade, em casa e durante seu tempo livre. Isto inclui o tempo sentado estudando, sentado enquanto descansa, fazendo lição de casa visitando um amigo, lendo, sentado ou deitado assistindo TV. Não inclua o tempo gasto sentando durante o transporte em ônibus, trem, metrô ou carro.

4a. Quanto tempo no total você gasta sentado durante um **dia de semana**?
_____horas ____minutos

4b. Quanto tempo no total você gasta sentado durante em um **dia de final de semana**?
_____horas ____minutos

ANEXO 5

UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

FACULDADE DE ODONTOLOGIA

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO:

Sr.(a).....

Nos últimos anos, a cárie dentária também tem sido mais comumente observada na raiz dos dentes. Esse tipo de cárie acontece com maior freqüência em adultos e em idosos. Assim como a cárie que ocorre na coroa do dente, a cárie radicular também precisa ser prevenida, diagnosticada e tratada.

Este estudo objetiva determinar a ocorrência de cárie radicular na população adulta de Porto Alegre, assim como os fatores que possam aumentar o risco de estabelecimento desta doença.

O senhor será submetido a um exame bucal, no qual seus dentes serão examinados. Também realizaremos uma coleta de sua saliva para verificar se não há problema de secura bucal. Uma entrevista sobre dados pessoais e hábitos também será realizada.Todos os materiais utilizados para o exame e para a coleta de saliva são descartáveis e esterilizados. O exame bucal será repetido duas vezes com intervalo de um ano.

Desconfortos que possam ser associados a sua participação no estudo são os mesmos de um exame odontológico comum.

Como benefícios de sua participação, destacamos o diagnóstico de sua condição de saúde bucal e a contribuição para que medidas de prevenção e tratamento da doença cárie sejam estabelecidos direcionados à população adulta e idosa.

A participação no estudo é totalmente voluntária. A decisão de não participar mais do estudo pode ser tomada a qualquer momento, sem nenhum prejuízo.

Atenciosamente,

Pesquisador responsável

Nome: **Telefone:**

Assinatura:.....

Eu confirmo que entendi a natureza da pesquisa e aceito participar da mesma.

Nome: Telefone:

Assinatura:.....

Data:...../...../.....