UNIVERSIDADE FEDERAL DE SERGIPE
PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

IMPACTO DO TABAGISMO NA PERI-IMPLANTITE E FALHA DE IMPLANTES DENTAIS: AVALIAÇÃO DA QUALIDADE DA EVIDÊNCIA DE META-ANÁLISES DE ESTUDOS OBSERVACIONAIS

Aracaju/SE

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GUSTAVO MARQUES SOBRAL DOS SANTOS

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1. Prof. Dr. Wilton Mitsunari Takeshita _____

2. Prof. Dr. Julio Leornado Oliveira Lima _____

Dedico este trabalho à minha família, em especial
aos meus pais, esposa, irmãos e sobrinhos.

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“Que os vossos esforços desafiem as impossibilidades, lembrai-vos de que as grandes coisas do homem foram conquistadas do que parecia impossível.”

(Charles Chaplin)

RESUMO

Introdução: diversas revisões sistemáticas e meta-análises têm avaliado a relação entre o tabagismo, peri-implantite e falha dos implantes. Com o aumento do número de publicações nos últimos anos e a sua importância no processo de tomada de decisão em saúde, é fundamental avaliar o grau de evidência desses estudos. **Objetivos**: avaliar a qualidade da evidência de meta-análises de estudos observacionais que avaliaram a relação entre o tabagismo, peri-implantite e falha dos implantes. **Metodologia:** uma busca foi realizada nas bases de dados PUBMED, Web of Science, Scopus, Lilacs, Cochrane Library e literatura cinza para identificar meta-análises que avaliaram os efeitos do tabagismo na peri-implantite e/ou falha dos implantes. Buscou-se estudos publicados em inglês, espanhol e portugues publicados a partir de fevereiro de 2011, período correspondente à criação do PROSPERO. Não foram incluídos no estudo meta-análises de estudos pré-clínicos. A avaliação da qualidade metodológica, do risco geral de viés e do grau de evidência dos estudos incluídos foram realizadas pelas ferramentas AMSTAR 2, ROBIS e GRADE, respectivamente. **Resultados:** um total de 7 meta-análises foram incluídas. A avaliação pelo AMSTAR 2 indicou que 4 meta-análises apresentaram qualidade metodológica moderada e 3 criticamente baixa (kappa = 0.659; concordância substancial). O ROBIS mostrou que 4 meta-análises apresentaram baixo risco de viés e 3 alto risco (kappa = 0.589; concordância moderada). O GRADE concluiu que 5 meta-análises apresentaram evidência muito baixa, 1 baixa e outra moderada. **Conclusão:** embora as meta-análises que avaliaram a relação entre o tabagismo, peri-implantite e falha dos implantes apresentaram desfechos desfavoráveis aos fumantes, a qualidade da evidência é baixa. Portanto, as informações disponíveis nessas meta-análises devem ser interpretadas com cautela para a prática clínica.

Palavras-chave: implantes dentários; fumo; revisão sistemática; meta-análise; odontologia baseada em evidências.

ABSTRACT

Introduction: Several systematic reviews and meta-analyses have evaluated the relation between smoking, peri-implantitis, and implant failure. With the increasing number of publications in recent years and its importance in the health decision-making process, it is essential to assess the degree of evidence of these studies. **Objectives**: To evaluate the quality of evidence of meta-analyses of observational studies that assessed the relationship between smoking, peri-implantitis and dental implant failure. **Materials and methods**: A search was conducted in the PUBMED, Web of Science, Scopus, Lilacs, Cochrane Library databases and grey literature to identify meta-analyses that assessed smoking and its effects on peri-implantitis and/or implant failure. Studies in English, Spanish and Portuguese published from February 2011 period corresponding to the creation of PROSPERO were searched. Meta-analyses of preclinical studies were not included in the study. The evaluation of the methodological quality, general risk of bias and degree of evidence of the included studies was performed by the AMSTAR 2, ROBIS and GRADE tools, respectively. **Results**: A total of 7 meta-analyses were included. The AMSTAR 2 evaluation indicated that 4 presented moderate methodological quality and 3 were critically low (kappa = 0.659; substantial agreement). ROBIS showed that 4 presented low risk of bias and 3 presented high risk (kappa = 0.589; moderate agreement). GRADE concluded that 5 meta-analyses showed very low evidence, 1 showed low and the other showed moderate evidence. **Conclusion**: Although meta-analyses evaluating the relationship between smoking, peri-implantitis and failure implants present unfavourable outcomes for smokers, the quality of evidence is low. Therefore, the information available in these meta-analyses should be interpreted with caution to clinical practice.

Key-words: Dental implants; smoking; review; meta-analysis; evidence-based dentistry.

SUMÁRIO

1. INTRODUÇÃO

O sucesso dos implantes dentais pode ser avaliado pela mobilidade dos implantes, perda óssea marginal e condições dos tecidos em torno dele[1]. Apesar de apresentarem altas taxas de sucesso[2], muitos fatores de risco podem influenciar negativamente a sobrevida dos implantes[3–5]. Dentre os diversos fatores de risco, o tabagismo tem sido associado, em revisões sistemáticas e meta-análises, à perda óssea periodontal, peri-implantar e falha dos implantes[6–11].

A fumaça do tabaco contém mais de 4000 substâncias potencialmente tóxicas, incluindo monóxido de carbono, nitrosaminas, benzenos, aldeídos, cianeto de hidrogênio e nicotina[12], considerado o principal componente químico[13]. O mecanismo que envolve a ação do tabaco no organismo ainda não está totalmente elucidado, mas sabe-se que a nível celular ele reduz a proliferação de glóbulos vermelhos, macrófagos, fibroblastos, colágenos e pode aumentar a adesividade plaquetária, fator que dificulta a cicatrização e perfusão do tecido devido a microformação de coágulos nos vasos sanguíneos[14,15]. Além disso, o tabaco pode exercer efeito negativo na imunidade, interferindo na quimiotaxia e nos mecanismos de fagocitose dos neutrófilos, diminuindo a produção de imunoglobulinas e a função dos linfócitos[16–18]. Considerando esses efeitos, tem sido sugerido que o consumo do tabaco prejudique a cicatrização da interface osso-implante[19]

Com o aumento do número de publicações nos últimos anos e a sua importância no processo de tomada de decisão em saúde, é fundamental avaliar o grau de evidência dos resultados das revisões sistemáticas e meta-análises. A qualidade da evidência desses estudos inclui avaliação da qualidade metodológica, o risco geral de viés e uma série de indicadores que refletem como a confiança em uma estimativa de efeito é adequada para suportar uma recomendação específica. Estes indicadores incluem o risco de viés dos estudos individuais, inconsistência entre os estudos, evidência indireta, imprecisão e tamanho de efeito, viés de

publicação e sensibilidade, controle dos confundidores e avaliação de um gradiente dose-resposta[20].

Embora não exista uma ferramenta universal, o AMSTAR (**A** **M**ea**S**urement **T**ool to **A**ssess systematic **R**eviews)[21], o ROBIS (**R**isk **o**f **B**ias in **S**ystematic **R**eviews)[22] e o GRADE (**G**rading of **R**ecommendations **A**ssessment, **D**evelopment and **E**valuation)[20] são instrumentos que tem sido utilizados para avaliação da qualidade metodológica, risco de viés e qualidade da evidência, respectivamente. Recentemente foi lançado o AMSTAR 2[23], o qual sofreu um processo de desenvolvimento em relação à ferramenta original para permitir a inclusão de avaliação de revisões sistemáticas de estudos randomizados e não randomizados de intervenções em saúde.

Apesar de diversas revisões sistemáticas e meta-análises terem associado o tabagismo à peri-implantite e falha dos implantes, a qualidade da evidência é pobremente analisada nesses estudos. O presente trabalho tem a finalidade de analisar a qualidade metodológica, risco de viés e o grau de evidência das revisões sistemáticas e meta-análises que avaliaram a relação entre o tabagismo, peri-implantite e falha dos implantes.

2. OBJETIVO

2.1 Geral

Analisar a qualidade da evidência das revisões sistemáticas e meta-análises que avaliaram a relação entre o tabagismo, peri-implantite e falha dos implantes dentais.

3. METODOLOGIA

3.1 Questão de pesquisa

O presente estudo enfocou a seguinte questão: qual a qualidade da evidência das revisões sistemáticas e meta-análises sobre o impacto do tabagismo na falha de implantes e peri-implantite?

3.2 Desenho de estudo e critérios de elegibilidade

Este estudo foi desenhado como um overview de revisões sistemáticas com meta-análises de estudos observacionais que avaliaram a relação entre o tabagismo, peri-implantite e falha dos implantes dentais. Buscou-se estudos publicados em português, espanhol ou inglês, desde o lançamento do banco de dados PROSPERO (fevereiro de 2011) até fevereiro de 2018. Meta-análises de estudos pré-clínicos foram excluídas.

O PROSPERO é um banco de dados internacional de registro de revisões sistemáticas em saúde e assistência social cuja finalidade é ajudar a reduzir a duplicação não planejada de revisões, aumentar a transparência e minimizar o risco de viés[24]. *Overview* e revisões de questões metodológicas com pelo menos um desfecho direto do paciente ou relevância clínica são aceitas e o presente estudo foi registrado no banco de dados PROSPERO sob o protocolo CRD42018097078.

3.3 Estratégia de busca

Uma busca nas bases de dados PUBMED, Web of Science, Scopus, Lilacs (via Bireme) e Cochrane Library foi realizada para identificar revisões sistemáticas e meta-análises que obedeceram aos critérios de elegibilidade. Literatura cinza foi explorada através do Google Scholar e OpenThesis. Além disso, uma busca manual nas referências de artigos incluídos também foi realizada. A combinação dos termos utilizados para todas as bases de dados foi a seguinte: ((smoke OR smoker OR smoking OR nicotine OR cigarette OR tobacco OR risk factors) AND (oral implant

OR dental implant OR osseointegration OR peri implantitis OR peri-implant)) AND meta-analysis. Esses termos foram adaptados de acordo com as regras de cada base de dados.

3.4 Rastreio da literatura e seleção do estudo

Dois investigadores independentes (G.M.S.S. e M.L.T.M) selecionaram os estudos pesquisados com base no título e no resumo do trabalho. Os estudos relevantes foram lidos em texto completo e selecionados de acordo com os critérios de elegibilidade. Desacordos entre os dois revisores foram resolvidos por consenso ou por um terceiro revisor (PRSM-F).

3.5 Extração dos dados

Dois investigadores independentes (G.M.S.S. e M.L.T.M) extraíram os dados das meta-análises usando um protocolo pré-definido. Informações sobre sobrenome do autor, país, título do estudo, ano e periódico de publicação, fator de impacto (baseado em periódicos listados no JCR dentro do ano de publicação do estudo)[25], objetivo do estudo, características dos estudos incluídos, desfechos de interesse, registro no banco de dados do PROSPERO, o uso da declaração de MOOSE (**M**eta-Analysis **o**f **O**bservational **S**tudies in **E**pidemiology)[26] e os fatores que determinam a certeza da evidência foram verificados.

3.6 Avaliação da qualidade metodológica e do risco geral de viés

A qualidade metodológica e risco de viés das meta-análises foram avaliados usando AMSTAR 2[23] e ROBIS[22], respectivamente, por dois pesquisadores independentes (G.M.S.S. e M.L.T.M). O AMSTAR 2 é uma ferramenta de avaliação crítica para revisões sistemáticas de estudos randomizados ou não randomizados de intervenções de saúde que consistem em questões destinadas a avaliar a adequação dos métodos usados na revisão e incluiu 16 itens relacionados a (1) estratégia PICO; (2) estabelecimento de um protocolo prévio; (3) seleção de desenhos de estudo para inclusão; (4) estratégia de busca; (5) seleção do estudo em duplicata; (6) extração de dados em duplicata; (7) lista de estudos excluídos; (8) estudos incluídos; (9) avaliação do risco de viés de estudos individuais; (10) fontes

de financiamento; (11) métodos para meta-análise; (12) impacto do risco de viés nos resultados da meta-análises; (13) impacto do risco de viés ao discutir a validade do estudo; (14) possíveis fontes de heterogeneidade; (15) viés de publicação; e (16) potenciais fontes de conflito de interesses. Esses itens foram respondidos para cada meta-análise no site https://amstar.ca/ e avaliados como “sim”, “sim parcial” ou “não”. As classificações de itens individuais não foram combinadas para criar uma pontuação geral, mas a qualidade das meta-análises foi classificada como alta, moderada, baixa ou criticamente baixa de acordo com a diretriz AMSTAR 2.

O ROBIS é uma ferramenta lançada recente para avaliar o risco de viés durante o processo de delineamento, condução e análise de revisões sistemáticas e consiste em três fases diferentes: (1) avaliar a relevância (opcional), (2) identificar preocupações em torno de quatro domínios (critérios de elegibilidade do estudo, identificação e seleção de estudos, coleta de dados e avaliação do estudo, síntese e achados) e (3) julgamento do risco de viés. As respostas às perguntas no ROBIS podem ser categorizadas como “sim”, “provavelmente sim”, “não”, “provavelmente não” ou “nenhuma informação”. O risco de viés pode ser julgado como baixo, alto ou incerto.

A estatística kappa (k) foi calculada para entender a extensão da concordância inter-observador em termos dos itens AMSTAR 2 e ROBIS. Kappa menor que 0,2 foi definido como “baixa concordância”, 0,2 a 0,4 como “concordância justa”, 0,4 a 0,6 como “concordância moderada”, 0,6 a 0,8 como “concordância substancial” e kappa = 0,8 a 1,0 como “concordância quase perfeita”. Também foi calculado o teste de confiabilidade com o coeficiente alfa de Cronbach para as ferramentas AMSTAR 2 e ROBIS. Para fins de pesquisa, o alfa deve ser maior que 0,7 a 0,8, mas, para fins clínicos, alfa deve ser pelo menos 0,90.

3.7 Avaliação da qualidade de evidência

A qualidade das evidências das meta-análises incluídas foi determinada usando o sistema GRADE. Dois autores (G.M.S.S. e M.L.T.M) avaliaram independentemente as evidências relativas à falha dos implantes e peri-implantite, e os fatores que aumentam ou diminuam a qualidade das evidências foram detalhados

para garantir a transparência e a confiabilidade dos resultados. Os fatores que determinam a certeza da evidência incluíram o risco de viés de estudos individuais, evidência indireta, inconsistência, imprecisão, viés de publicação, tamanho do efeito, gradiente dose-resposta e direção de confundimento plausível.

No risco de avaliação de viés, observamos o uso da escala de Newcastle-Ottawa (NOS) para estudos observacionais. A NOS contém oito itens, categorizados em três dimensões, incluindo seleção, comparabilidade e - dependendo do tipo de estudo - Outcome (estudos de coorte) ou Exposição (estudos caso-controle). Um sistema estrelar é usado para permitir uma avaliação semi-quantitativa da qualidade do estudo. Um estudo pode receber um máximo de uma estrela para cada item numerado nas categorias Seleção e Outome/Exposição e um máximo de duas estrelas pode ser dado para comparabilidade. A NOS varia entre zero e nove estrelas e estudos com aproximadamente 70% ou mais dos domínios satisfatoriamente preenchidos foram classificados como tendo baixo risco de viés.

A presença de inconsistência ou heterogeneidade para dados meta-analisados foi avaliada com base na variação das estimativas de efeito entre os estudos, sobreposição de intervalos de confiança e estatística I^2. Valores de I^2 superiores a 75% indicaram considerável heterogeneidade. As evidências foram indiretas se uma metanálise incluísse desfechos substitutos ou se dois ou mais corpos de evidências fossem necessários para analisar a relação entre o tabagismo e os desfechos de interesse. A imprecisão foi analisada com base nos intervalos de confiança (ICs) em torno das estimativas de efeito e a magnitude do efeito do tabagismo na falha do implante foi considerada grande se OR (odds ratio)/RR (razão de risco)> 2 ou <0,5 na presença de evidência direta de pelo menos dois estudos, sem confundidores plausíveis. Meta-análises incluídas nesta *overview* também foram avaliadas em relação à presença de viés de publicação, confudidor residual plausível e um gradiente dose-resposta de relação entre tabagismo e desfechos de interesse. Se os estudos não analisaram a avaliação do risco de viés para estudos individuais, o potencial viés de publicação, as estimativas ajustadas e um gradiente dose-resposta, a qualidade das evidências foi rebaixada.

3.8 Análise dos dados

O resumo narrativo das características das meta-análises incluídas foi exibido em tabelas. Os dados dicotômicos foram resumidos como OR ou RR e os resultados contínuos foram sintetizados como diferença de média ponderada ou padrão, com ICs de 95%. Para responder à questão de pesquisa, a qualidade geral da evidência foi julgada como alta, moderada, baixa ou muito baixa de acordo com as recomendações GRADE.

4. RESULTADOS

IMPACT OF SMOKING ON PERI-IMPLANTITIS AND DENTAL IMPLANT FAILURE: EVALUATING THE QUALITY OF EVIDENCE OF META-ANALYSES OF OBSERVATIONAL STUDIES

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ABSTRACT

The aim of this study was to evaluate the degree of evidence in meta-analyses of observational studies of relationship between smoking, peri-implantitis and dental implant failure. A search was conducted in 5 databases and grey literature. Studies in English, Spanish and Portuguese published from February 2011, period corresponding to the creation of PROSPERO, were searched. Meta-analyses of preclinical studies were not included. The evaluation of methodological quality, risk of bias and degree of evidence were performed by AMSTAR 2, ROBIS and GRADE tools, respectively. A total of 7 meta-analyses were included. The AMSTAR 2 indicated that 4 meta-analyses presented moderate methodological quality and 3 were critically low (kappa=0.659; substantial agreement). ROBIS showed that 4 meta-analyses presented low risk of bias and 3 presented high risk (kappa=0.589; moderate agreement). GRADE concluded that 5 meta-analyses showed very low evidence, 1 showed low and the other moderate evidence. Although meta-analyses evaluating the relationship between smoking, peri-implantitis and failure implants present unfavourable outcomes for smokers, the quality of evidence is low. Therefore, the information available in these meta-analyses should be interpreted with caution to clinical practice.

Key-words: Dental implants; smoking; meta-analysis; evidence-based dentistry.

INTRODUCTION

The success of dental implants can be assessed by implant mobility, marginal bone loss and tissue conditions(1). Although high success rates(2), many risk factors may negatively influence implant survival(3–5). Among the several risk factors, smoking has been associated in systematic reviews and meta-analyses with periodontal bone loss, peri-implantitis and implant failure(6–11).

Tobacco smoke contains more than 4000 potentially toxic substances, including carbon monoxide, nitrosamines, benzenes, aldehydes, hydrogen cyanide and nicotine(12), which is considered the main chemical component(13). The mechanism that involves the action of tobacco in the body is not fully elucidated, but it is known that at the cellular level it reduces the proliferation of red blood cells, macrophages, fibroblasts, collagens and can increase platelet adhesiveness, a factor that hinders tissue healing and perfusion due to the micro-formation of clots in the vessels(14,15). In addition, tobacco may exert a negative effect on immunity, interfering with chemotaxis and neutrophil phagocytic mechanisms, reducing the production of immunoglobulins and the function of lymphocytes(16–18). Considering these effects, it has been suggested that tobacco consumption impairs the healing of the bone-implant interface(19).

With the increase in the number of publications in recent years and its importance in the health decision-making process, it is essential to assess the degree of evidence of the results of systematic reviews and meta-analyses. The quality of evidence of these studies includes the assessment of methodological quality, the overall risk of bias and a series of indicators that reflect how the confidence in an estimate of effect is adequate to support a specific recommendation. These indicators include the risk of bias in individual studies, inconsistency in studies, indirectness, imprecision and effect size, publication bias and sensitivity, control of confounders and evaluation of a dose-response gradient(20).

Although there is no universal tool, AMSTAR (**A** **M**ea**S**urement **T**ool to **A**ssess systematic **R**eviews)(21), ROBIS (**R**isk **o**f **B**ias in **S**ystematic **R**eviews)(22) and GRADE (**G**rading of **R**ecommendations **A**ssessment, **D**evelopment and **E**valuation)(20) are instruments that have been used to evaluate methodological

quality, risk of bias and quality of evidence, respectively. AMSTAR 2(23) has been released recently and it has undergone a development process over the original tool to allow the inclusion of evaluation of systematic reviews of randomized and nonrandomized studies of health interventions.

Although several systematic reviews and meta-analyses have associated smoking with peri-implantitis and implant failure, the quality of evidence is poorly analysed in these studies. The present study has the purpose of evaluating the methodological quality, the overall risk of bias and the degree of evidence of systematic reviews and meta-analyses that evaluated the relationship between smoking, implant failure and peri-implantitis.

MATERIALS AND METHODS

Research question

The present study focused on the following question: what is the quality of evidence in meta-analyses on the impact of smoking in implant failure and peri-implantitis?

Study design and eligibility criteria

This study was designed as an overview of systematic reviews with meta-analyses of observational studies analysing the relationship between smoking, implant failure and peri-implantitis. Studies published in Portuguese, Spanish or English have been searched since the launch of the PROSPERO database (February 2011) until February 2018. Meta-analyses of preclinical studies were excluded.

PROSPERO is an international registry database of systematic reviews on health and social care used to support the reduction of unplanned duplication of reviews, the enhancement of transparency and the decrease in the risk of bias(24). Overviews and reviews of methodological issues with at least one direct outcome of the patient or clinical relevance are accepted and the present study was registered on the PROSPERO database under protocol CRD42018097078.

Search strategy

The search was conducted using PubMed, SCOPUS, Lilacs, Web of Science, and Cochrane Library. Google Scholar and OpenThesis were used to find grey literature. The reference lists of all eligible studies were also manually screened to identify additional studies for inclusion. For the articles not available in the electronic databases, or for the data not available in the articles included in this overview, the authors were contacted to obtain the necessary information. The search strategy structure used the following terms: ((smoke OR smoker OR smoking OR nicotine OR cigarette OR tobacco OR risk factors) AND (oral implant OR dental implant OR osseointegration OR peri-implantitis OR peri-implant)) AND meta-analysis. These terms have been adapted according to the rules of each database.

Literature screening and study selection

Two independent investigators (G.M.S.S. and M.L.T.M) screened the searched studies based on the paper's title and abstract. Relevant studies were read in full-text and selected according to the eligibility criteria. Disagreements between the two reviewers were resolved by consensus or by a third reviewer (PRSM-F).

Data extraction

Two independent investigators (G.M.S.S. and M.L.T.M) extracted data from the meta-analyses using a predefined protocol. Information about the author's last name, country, study title, year and journal of publication, impact factor (based on journals listed in the JCR in the year of the study publication)(25), aim of the study, characteristics of included studies, outcomes of interest, register in the PROSPERO database, use of MOOSE (**M**eta-Analysis **o**f **O**bservational **S**tudies in **E**pidemiology)(26) statement and the factors determining the certainty of evidence were checked.

The results data included crude and adjusted estimates in terms of *odds ratio* (OR) or relative risk (RR). For adjusted data, estimates with 95% of confidence intervals (CIs) that had been adjusted for one or more potential confounders were extracted. For studies that applied regression or multilevel modelling, the adjusted data from the most fully identified model was extracted.

Assessment of the methodological quality and the risk of bias of meta-analyses

The methodological quality and the risk of bias of meta-analyses were evaluated using AMSTAR 2(23) and ROBIS(22), respectively, by two independent investigators (G.M.S.S. and M.L.T.M). AMSTAR 2 is a critical appraisal tool for systematic reviews of randomized or non-randomized studies of healthcare interventions that consists of questions designed to assess the appropriateness of the methods used in the review and it included 16 items related to (1) PICO strategy; (2) establishment of protocol *a priori*; (3) selection of study designs for inclusion; (4) search strategy; (5) study selection in duplicate; (6) data extraction in duplicate; (7) the list of excluded studies; (8) included studies; (9) assessment of risk of bias of individual studies; (10) funding sources; (11) methods for meta-analysis; (12) impact of risk of bias on the results of meta-analysis; (13) impact of risk of bias when discussing the validity of the study; (14) possible sources of heterogeneity; (15) publication bias; and (16) potential sources of conflict of interest. These items were answered for each meta-analysis on the website https://amstar.ca/ and were rated as “yes”, “partial yes”, “no” or “not applicable”. Individual item ratings were not combined to create an overall score, but the quality of meta-analyses was classified as high, moderate, low, or critically low according to the AMSTAR 2 guideline.

ROBIS is a recent tool used to assess the risk of bias during the delineation process, conduction and analysis of systematic reviews and it consists of three different phases: (1) to assess the relevance (optional), (2) to identify concerns across four domains (study eligibility criteria, identification and selection of studies, data collection and study appraisal, and synthesis and findings), and (3) to judge risk of bias. Answers to the questions in ROBIS can be categorized as “yes”, “probably yes”, “no”, “probably no”, or “no information”. The risk of bias can be judged as low, high, or unclear. The kappa statistics (k) was calculated to understand the extent of interobserver agreement in terms of the AMSTAR 2 and ROBIS items. A kappa less than 0.2 is defined as ‟poor agreement”, 0.2 to 0.4 as ‟fair agreement”, 0.4 to 0.6 as ‟moderate agreement”, 0.6 to 0.8 as ‟substantial agreement”, and a kappa = 0.8 to 1.0 as ‟almost perfect agreement”. The reliability test with the Cronbach alpha coefficient for the AMSTAR 2 and ROBIS tools was also calculated. For research

purposes, the alpha should be greater than 0.7 to 0.8, but for clinical purposes, alpha should be at least 0.90.

Assessment of the quality of evidence

The quality of evidence of the included meta-analyses was determined using the GRADE (**G**rading of **R**ecommendations **A**ssessment, **D**evelopment and **E**valuation) system. Two authors (G.M.S.S. and M.L.T.M) independently assessed the evidence related to the implant failure and peri-implantitis, and the upgraded or downgraded factors affecting the quality of evidence were depicted in detail to guarantee the transparency and reliability of the results. The factors determining the certainty of evidence included the risk of bias of individual studies, indirectness, inconsistency, imprecision, publication bias, effect size, dose-response gradient and direction of plausible confounding.

In the risk of bias assessment, we observed the use of Newcastle-Ottawa scale (NOS) for observational studies. The NOS contains eight items, categorized into three dimensions including Selection, Comparability, and -depending on the study type - Outcome (cohort studies) or Exposure (case-control studies). A star system is used to allow a semi-quantitative assessment of the study quality. A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome/Exposure categories and a maximum of two stars can be given for Comparability. The NOS ranges between zero up to nine stars and studies with approximately 70% or more of the satisfactorily fulfilled domains were classified as having a low risk of bias.

The presence of inconsistency or heterogeneity for meta-analysed data was evaluated based on the variation in the effect estimates across studies, CIs overlapping and I^2 statistic. I^2 values higher than 75% indicated considerable heterogeneity. The evidence was indirect if a meta-analysis included surrogate outcomes or if two or more bodies of evidence were required to analyse the relationship between smoking and the outcomes of interest. The imprecision was analysed based on CIs around the effect estimates and the magnitude of the smoking effect on implant failure was considered large if OR/RR >2 or <0.5 in the presence of

direct evidence from at least two studies, with no plausible confounders. Meta-analyses included in this overview were also evaluated regarding the presence of publication bias, plausible residual confounder, and a dose-response gradient of relationship between smoking and the outcomes of interest. If the assessment of risk of bias for individual studies, the publication bias potential, the adjusted estimates, and a dose-response gradient were not analysed, the quality of evidence was downgraded.

Data analysis

The narrative summary of the characteristics of the included meta-analyses is displayed in tables. The dichotomous data were summarized as OR or RR, and continuous results were synthesized as weighted or standard mean difference with 95% CIs. To answer the research question, the overall quality of evidence was judged as high, moderate, low, or very low according to the GRADE guideline.

RESULTS

Search and selection of articles

The initial search found 5,147 reports, of which 87 were collected from PubMed, 74 from Web of Science, 103 from SCOPUS, 11 from Lilacs, 4870 from Google Scholar and 2 from Cochrane Library. No study was found in OpenThesis database. Nineteen studies were considered as potentially relevant and were fully analysed. After a thorough reading, 12 studies were excluded: 2 due to the study design(19,27), 3 due to the outcomes of interest(28–30), 1 due to the language of publication(31), 3 because they did not perform meta-analysis(32–34) and 3 because they were small comments(6,35,36). Finally, seven studies(37–43) met the eligibility criteria and were included in the overview. A flowchart of the study selection process and the specific reasons for exclusion is detailed in Figure 1.

Characteristics of included meta-analyses

The main characteristics of the 7 meta-analyses are detailed in Table 1. Only one study was recorded in the PROSPERO database. All studies were published in English and the journal's impact factor ranged from 1.107(38) to 3.624(42). The 7

meta-analyses covered 172 observational studies that assessed the relationship between smoking and implant failure or peri-implantitis. Five meta-analyses(38–40,42,43) included failure of the implant as an outcome of interest and 2(37,41) included peri-implantitis. A meta-analysis used marginal bone loss as a surrogate outcome(37).

Although only one meta-analysis(42) has reported the use of the MOOSE statement, we have checked the 35 items of all meta-analyses included. The compliance with MOOSE checklist items ranged from 60%(37) to 91.4%(42) (Appendix A). Information on problem definition, description of study outcomes, exposure, study design, study population, researchers, keywords used in search strategy, list of citations, justification for exclusion, heterogeneity assessment, description of statistical methods, descriptive data for each study, individual and overall estimates and the statistical uncertainty of the findings were reported in all meta-analyses.

Assessment of the methodological quality and risk of bias

The quality of the meta-analyses included was critically low(37,38,43) or moderate(39–42), as determined using the AMSTAR 2 tool (Table 2). The quality was strongly influenced by the lack of protocol registration(37–41,43) (6/7, 85.7%), the non-inclusion of PICO elements in the research question and inclusion criteria(37,38,41–43) (5/7, 71.4%), the lack of duplicate data extraction report(37–41) (5/7, 71.4%), the poor investigation of publication bias and its impact on the results of meta-analysis(37,38,41–43) (5/7, 71.4%) and the inadequate assessment of risk of bias in the individual studies and its impact on the results of meta-analysis(37,38,43) (3/7, 42.9%).

The risk of bias of included meta-analyses was evaluated by ROBIS, as described in Table 3. The evaluations for phase 2 showed that 42.85% of all evaluations presented a high risk of bias, 53.57% showed low risk bias and 3.57% showed uncertain risk. The domains 1 (eligibility criteria), 2 (identification and selection of studies) and 3 (data collection and study evaluation) had high bias risk judgments in 42.85% of the evaluations, low bias risk in 57.14% and no uncertain

risk. Domain 4 (syntheses and findings) presented a high bias risk judgement in 42.85%, low bias risk in 42.85% and uncertain risk in 14.28%. Three meta-analyses(39–41) showed low risk of bias in all domains of phase 2. According to phase 3, corresponding to the bias judgment, 3 meta-analyses(37,38,43) were classified as having a high risk of bias and 4 studies(39–42) were classified as low risk of bias. The kappa values showed that the consistency of the subjective evaluation of two reviewers (G.M.S.S. and M.L.T.M) in terms of the AMSTAR 2 (0.659) and ROBIS (0.589) items were substantial and moderate, respectively. The reliability test with Cronbach's alpha coefficient for the tools showed a score of 0.730 for the first tool and 0.902 for the second tool.

Quality of evidence

In all meta-analyses, an association between smoking and outcomes of interest was found. The relationship between smoking and implant failure was reported as OR in 2 meta-analyses(38,39) and pooled estimates ranged from OR 1.72 (95% CI, 1.32-2.25) to OR 1.96 (95% CI, 68-2,30). In three meta-analyses(40,42,43), the RR was used as an effect measure and the estimates ranged from RR 1.87 (95% CI, 1.35-2.58) to RR 2.23 (95% CI, 96-2,53). Four meta-analyses(38,40,42,43) were graded as having a very low quality or low quality of evidence, and only one meta-analysis(39) showed a moderate quality of evidence. The quality of evidence was limited by the risk of bias of individual studies, the magnitude of the smoking effect on implant failure, the potential influence of confounding factors, and the lack of assessment of a dose-response gradient.

The relationship between smoking and peri-implantitis was described in 2 meta-analyses(37,41). A meta-analysis(37) used marginal bone loss as a surrogate outcome and estimates were reported as mean difference. The other study(41) reported the association between smoking and peri-implantitis as RR and the pooled estimate was 1.49 (95% CI, 1.09-2.04). Both meta-analyses were graded as having a very low quality of evidence. Table 4 summarizes the quality of the evidence from the meta-analyses included.

DISCUSSION

Studies have indicated an association between smoking and early and late adverse outcomes in patients with dental implants. The mechanism involving the action of tobacco has not yet been fully elucidated, but it is likely that the action of the toxins in tobacco release catecholamines that result in vasoconstriction, decreased tissue perfusion, and immune system alterations that interfere with the healing of the bone-implant interface(14–19,29,30). Since the available evidence is crucial for decision-making in clinical practice(44,45), we evaluated the quality of the evidence in meta-analyses on the impact of smoking on peri-implantitis and implant failure. Although meta-analyses of observational studies suggest an association between smoking, peri-implantitis and implant failure, the current quality of evidence is low.

The evaluation of methodological quality by AMSTAR 2 indicated that the included meta-analyses presented limitations regarding protocol registration, use of the PICO strategy, data extraction, publication bias and assessment of risk of bias in individual studies. The protocol register is important because it reduces unplanned duplication of reviews, increases transparency, and minimizes the risk of bias. Studies have shown that the rate of this registry is still low in Dentistry and that its absence can have serious implications in the transparency of the procedures of synthesis of the evidence(46,47). The use of PICO strategy(48), acronym for the terms **p**opulation, **i**ntervention, **c**omparison and **o**utcome, is essential to define the research question in a structured manner. The combination of these terms makes it possible to investigate the research question, seek the best evidence and perform a better quality review(49,50). Data extraction is also a fundamental process for the quality of a review. The extraction should be standardized, elaborated prior to the survey of the study and performed by two independent reviewers to ensure that the data were not defined in a *post hoc* manner, because the search for a favourable outcome to the hypothesis of the authors can generate false positives(51). The assessment of risk of bias in individual studies is one of the most important aspects of a systematic review since the inclusion of poor quality studies may compromise the reliability of the review results(52,53). The recommendation is to include all studies and evaluate the influence of each one on the results. The NOS instrument has been widely used to assess the risk of bias in observational studies(54), however it has been criticized and therefore has been progressively replaced by other

alternatives, such as ACROBAT-NRSI (A Cochrane Risk Of Bias Assessment Tool Non-Randomized Studies), which is better aligned with GRADE(55). The selection of studies included with appropriate designs, selection of studies in duplicate, list and justification of excluded studies, description of the studies included with appropriate details and statistical combination of results in the appropriate way were present in all meta-analyses.

According to the ROBIS tool, the meta-analyses presented a high risk of bias because they did not have concerns about the 4 domains. In domain 1, the main problems encountered were the lack of a prior registration of a protocol containing pre-defined objectives and eligibility criteria(37–41,43) and the restriction on eligibility criteria, mainly in relation to language(37,38,43). If only published studies with language restriction, such as English, are used from certain electronic databases, a large number of eligible studies may be lost, resulting in a substantial selection bias(56). In domain 2 the biggest problem was the limitation in the use of electronic databases to identify published and unpublished studies(37,38,43). One of the most difficult tasks of a review is to certify that all eligible studies will be found to synthesize all the available evidence(57). In addition to the largest possible number of electronic databases, a comprehensive survey should include a search for the grey literature, including annals of scientific events pertinent to the researched subject and a search on international theses and dissertations databases(58). In domain 3, the non-extraction of data by at least 2 evaluators(37–40) and the inadequate assessment of the risk of bias in the individual studies(37,38,43) were the main problems. Domain 4 had the worst result. In this domain, the main difficulties were the lack of robust results(37,38,41,42), the non-reporting or non-explanation of the pre-defined analyses, since only one study was pre-registered(42), and the lack of reporting if the biases found in the studies were minimally addressed in the synthesis(37,38,42,43). This tool showed that the main positive points of the meta-analyses were the use of appropriate terms and structures in the search strategy, selection of studies in duplicate, presence of sufficient characteristics of included studies for interpretation of the results, inclusion of all studies in the synthesis of results, synthesis of the results and the approach of heterogeneity in the synthesis.

GRADE has been widely used to assess the quality of evidence from meta-analyses of clinical trials and observational studies(20). The starting point of the evaluation of the evidence is the appreciation of the research design. Outcomes from randomized clinical trials begin the evaluation with high quality scores, while those generated by observational studies begin with poor quality. From the initial classification, the criteria are defined, and the judgment of these aspects allows to reduce or raise the level of evidence. Factors that may decrease the quality of evidence are the methodological limitation (risk of bias), inconsistency, indirectness, inaccuracy and publication bias. Particularly for observational studies, the factors that may increase the quality of evidence are the great magnitude effects, the presence of a dose/response gradient and residual confounding factors that increase confidence in the estimate. If the meta-analyses show results of a high quality outcome, it is understood that future research will hardly modify the observed effect, whereas a very low quality outcome will probably have its estimates changed with the publication of new studies(59).

In the present overview, we observed that the quality of evidence for the evaluated outcomes was low. It was mainly influenced by the risk of bias in the individual studies, magnitude of the effect of smoking on implant failure, potential influence of confounding factors and lack of evaluation of a dose-response gradient. Of the 7 meta-analyses, only 2(39,40) evaluated the risk of bias of the individual studies using NOS, satisfactorily filling 70% or more of the domains of the tool. The magnitude of the effect of smoking on implant failure was not considered large in none of the meta-analyses. When the magnitude of effect is large in observational studies, it is likely that the intervention has an important effect, even in the presence of confounding factors(60). One of the main limitations observed in the meta-analyses was the fact that they were subject to confounding factors such as the use or non-use of bone grafting, implant structure, implant insertion in different sites, insertion of implants in fresh alveolus, different periods of healing, different prosthetic configurations, type of antagonistic dentition, splinting or not of implants, presence of bruxism, presence of other risk factors. The presence of a dose-response gradient is a finding that reinforces the probability of a cause-and-effect relationship occurrence, thus increasing confidence in estimation(60). There is evidence in the literature to

suggest that smoking may have a dose-effect relationship with osseointegration(61) but no meta-analysis has taken into account the dose-response gradient, such as the ratio between the number of cigarettes smoked per day or smoking period and the incidence of peri-implantitis or implant failure.

The explicit report of a systematic review or meta-analysis is extremely important and makes it possible to use the published evidence adequately. There are some tools available, including MOOSE, that contain specifications for writing the introduction, search strategy, methods, results, discussion and conclusion. This checklist aims to improve the usefulness and the reporting of systematic reviews and meta-analyses of observational studies for authors, reviewers, editors, readers and clinical decision makers(26). In our study, the compliance with the MOOSE checklist items showed from 60% to 91.4%. Some MOOSE items are fundamental requirements in the bias risk assessment tools and methodological quality and this may explain the fact that studies with poor reports have a poor quality of evidence.

In our knowledge, this study is the first overview that systematically and critically reviewed meta-analyses on smoking and its relationship with peri-implantitis and dental implant failure. We evaluated the methodological quality, the overall risk of bias as well as the quality of evidence using the AMSTAR, ROBIS and GRADE tools, respectively. However, the present study presented some limitations. The first limitation was the restriction to the language of eligibility limited to English, Spanish or Portuguese. The second was the restriction to the period of search for studies that was limited from 2011, despite having a plausible justification (PROSPERO establishment). These two factors can generate a sampling bias. The third was that our assessment was based on what the meta-analyses provided us. The authors have possibly projected and conducted their meta-analyses more fully but may have hidden important information of our interest. In this case, our results may have been influenced by the quality of the meta-analysis reports. Finally, the fourth, because although two reviewers in our study have been used independently in the AMSTAR and ROBIS tools, we must emphasize that some subjectivity may exist. However, we recorded each evaluation basis and made a frequent discussion among all authors regarding any questions to keep the process transparent. As a suggestion for future

research, in view of the results presented in this study, we suggest that future meta-analyses should be well planned and conducted, following the tool recommendations appropriately for each study design to achieve the highest level of evidence.

CONCLUSION

Although meta-analyses evaluating the relationship between smoking, peri-implantitis and failure implants present unfavourable outcomes for smokers, the quality of evidence is low. Therefore, the information available in these meta-analyses should be interpreted with caution to the clinical practice.

DISCLOSURES

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Figure 1 – Flowchart summarizing the selection of studies

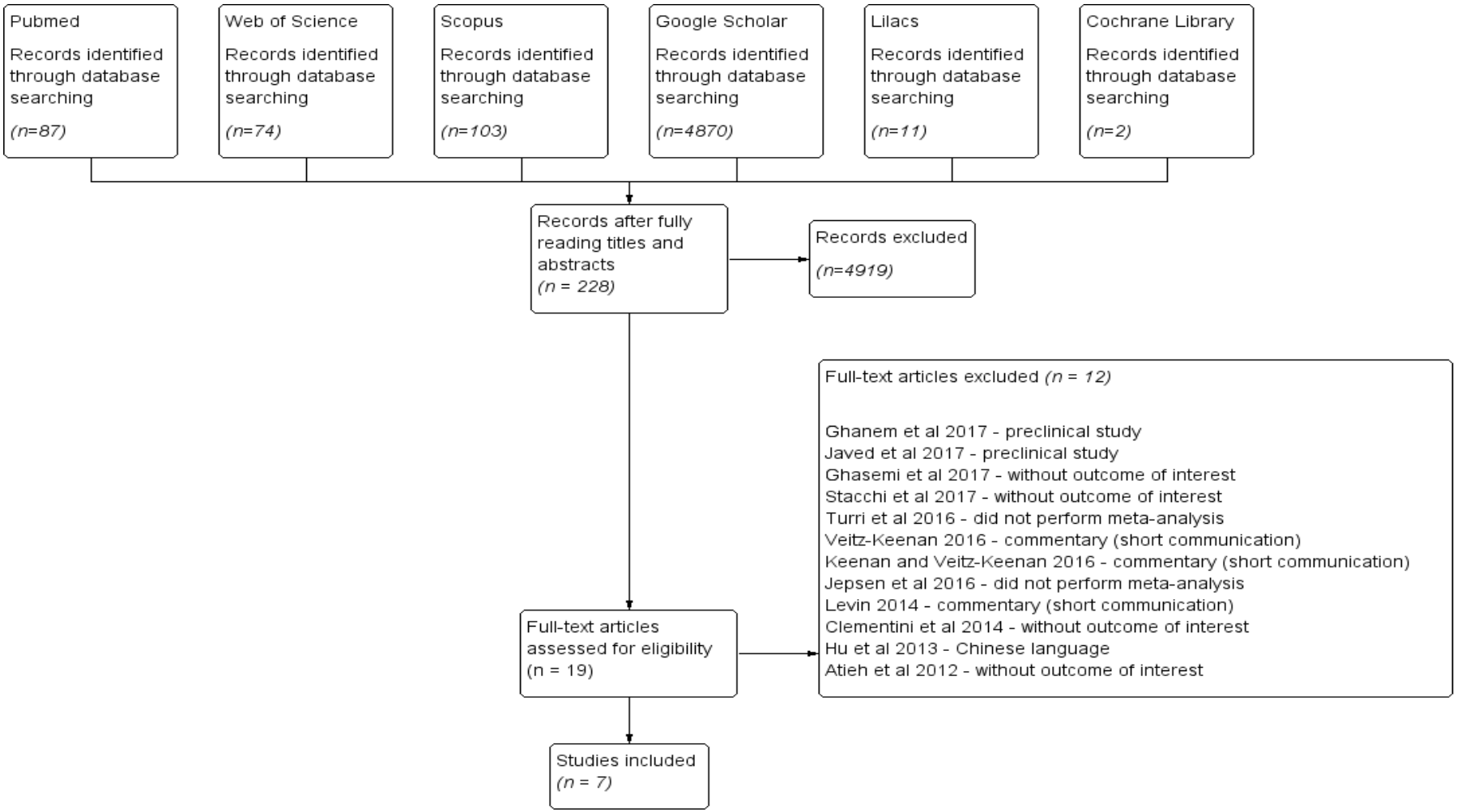

Table 1 **-** Summary of the characteristics of meta-analyses included

Author	Year	Journal	IF	Prior Register	MOOSE	Bias risk	Publication bias	Outcomes	N° studies	Design study
Doornewaard	2017	Clin Implant Dent Relat Res	2.939	No	No	No	No	Peri-implant bone loss	87	48 prospectives 39 retrospectives
Manzano	2016	Implant Dent	1.107	No	No	Undefined	No	Implant failure	9	Prospective and retrospectives
Moraschini	2016	Int J Oral Maxillofac Surg	1.918	No	No	NOS	Yes	Marginal bone loss Implant failure	15	5 prospectives cohort 10 retrospectives cohort
Sgolastra	2015	Clin Oral Implants Res	3.464	No	No	NOS	Yes	Peri-implantitis	7	Prospectives cohort
Chrcanovic	2015	J Dent	3.109	No	No	NOS	Yes	Marginal bone loss Implant failure Postoperative infections	107	4 RCT 16 CCT 16 prospectives 71 retrospectives
Chambrone	2014	Clin Oral Implants Res	3.624	Yes	Yes	NOS	No	Implant failure	7	4 retrospectives 2 prospectives 1 RCT
Chen	2013	PLoS One	3.534	No	No	McHarm	Yes	Implant failure	51	51 observationals

IF, Impact Factor; NOS, Scale Newcastle-Ottawa; McHarm, McMaster Quality Assessment Scale of Harms; RCT, Clinical trials randomized; CCT, Clinical trials controlled; MOOSE, Meta-analysis of observational studies in epidemiology.

Table 2. Assessment of methodological quality using AMSTAR 2 tool.

	Appraisal criteria	Doornewaard	Manzano	Moraschini	Sgolastra	Chrcanovic	Chambrone	Chen
1	Did the research questions and inclusion criteria for the review include the components of PICO?	No	No	Yes	No	Yes	No	No
2	Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	No	No	No	No	No	Yes	No
3	Did the review authors explain their selection of the study designs for inclusion in the review?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4	Did the review authors use a comprehensive literature search strategy?	No	No	Yes	Yes	Yes	Yes	Yes
5	Did the review authors perform study selection in duplicate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Did the review authors perform data extraction in duplicate?	No	No	No	N	N	Yes	Yes
7	Did the review authors provide a list of excluded studies and justify the exclusions?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8	Did the review authors describe the included studies in adequate detail?	Yes	Partial yes	Yes	Yes	Yes	Yes	Yes
9	Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	No	No	Yes	Yes	Yes	Yes	No
10	Did the review authors report on the sources of funding for the studies included in the review?	No	Yes	Yes	No	No	Yes	Yes
11	If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12	If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	No	No	Yes	Yes	Yes	Yes	No
13	Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	No	No	Yes	Yes	Yes	Yes	No
14	Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes	Yes	Yes	Yes	Yes	Yes	No
15	If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	No	No	Yes	No	Yes	No	No
16	Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	No	Yes	Yes	Yes	Yes	Yes	Yes
	Methodological quality	Critically low	Critically low	Moderate	Moderate	Moderate	Moderate	Critically low

Table 3. Assessment of risk of bias of meta-analyses using ROBIS tool.

Study	Phase 2				Phase 3
	Eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias
Doornewaard	☹	☹	☹	☹	☹
Manzano	☹	☹	☹	☹	☹
Moraschini	☺	☺	☺	☺	☺
Sgolastra	☺	☺	☺	☺	☺
Chrcanovic	☺	☺	☺	☺	☺
Chambrone	☺	☺	☺	☹	☺
Chen	☹	☹	☹	?	☹

☺=low risk; ☹=high risk; ?=unclear risk

Table 4. GRADE evidence profile for the relationship between smoking, implant failure and peri-implantitis.

Author	Number of observational studies	Pooled estimates (95CI%)	Methodological quality (AMSTAR 2)	RoB of meta-analysis (ROBIS)	Certainty								Evidence
					RoB of individual studies (NOS)	Inconsistency	Indirectness	Imprecision	Publication bias	Magnitude of effect	Confounders	Dose-response	
Implant failure													
Manzano	6	OR 1.72 (1.32-2.25)	Critically low	High risk	NA	Not serious	Not serious	Not serious	NA	No	NA	NA	⊕◯◯◯ VERY LOW
Moraschini	11	OR 1.96 (1.68-2.30)	Moderate	Low risk	Not serious	Not serious	Not serious	Not serious	Undetected	No	NA	NA	⊕⊕⊕◯ MODERATE
Chambrone	7	RR 1.87 (1.35-2.58)	Moderate	Low risk	Serious	Not serious	Not serious	Not serious	NA	No	NA	NA	⊕◯◯◯ VERY LOW
Chen	33	RR 1.92 (1.67-2.21)	Critically low	High risk	Serious	Serious	Not serious	Not serious	Undetected	No	NA	NA	⊕◯◯◯ VERY LOW
Chrcanovic	104	RR 2.23 (1.96-2.53)	Moderate	Low risk	Not serious	Serious	Not serious	Not serious	Undetected	No	NA	NA	⊕⊕◯◯ LOW
Peri-implantitis													
Doornewaard	4	MD 0.63 (0.14-1.12)	Critically low	High risk	NA	Very serious	Serious	Serious	NA	No	NA	NA	⊕◯◯◯ VERY LOW
Sgolastra	7	RR 1.49 (1.09-2.04)	Moderate	Low risk	Serious	Not serious	Not serious	Not serious	NA	No	NA	NA	⊕◯◯◯ VERY LOW

OR, odds ratio; RR, relative risk; MD, mean difference; CI, confidence interval; RoB, risk of bias; NA, not analyzed; AMSTAR 2, A measurement tool to assess systematic reviews; ROBIS, risk of bias in systematic reviews; NOS, Newcastle-Ottawa.

Appendix A – MOOSE checklist of the meta-analyses

	ITEM	Doornewaard	Manzano	Moraschini	Sgolastra	Chrcanovic	Chambrone	Chen
1	Problem definition	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Hypothesis statement	Yes	Yes	Yes	No	Yes	Yes	No
3	Description of study outcome(s)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4	Type of exposure or intervention used	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5	Type of study designs used	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Study population	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7	Qualifications of searchers (eg, librarians and investigators)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8	Search strategy, including time period included in the synthesis and key words	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9	Effort to include all available studies, including contact with authors	No	No	Yes	Yes	Yes	Yes	Yes
10	Databases and registries searched	No	No	Yes	Yes	Yes	Yes	Yes
11	Search software used, name and version, including special features used (eg, explosion)	No	No	No	Yes	No	No	No
12	Use of hand searching (eg, reference lists of obtained articles)	No	Yes	Yes	Yes	Yes	Yes	Yes
13	List of citations located and those excluded, including justification	Yes	Yes	Yes	Yes	Yes	Yes	Yes
14	Method of addressing articles published in languages other than English	No	No	No	Yes	Yes	No	No
15	Method of handling abstracts and unpublished studies	No	No	No	Yes	Yes	Yes	No
16	Description of any contact with authors	No	No	Yes	Yes	Yes	Yes	Yes
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Yes	Yes	Yes	Yes	Yes	Yes	No
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	No	Yes	Yes	Yes	Yes	Yes	No
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	No	Yes	No	Yes	No	Yes	No

Continua

Appendix A – MOOSE checklist of the meta-analyses

20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	No	No	No	No	No	No	Yes
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	No	Yes	Yes	Yes	Yes	Yes	No
22	Assessment of heterogeneity	Yes	Yes	Yes	Yes	Yes	Yes	Yes
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Yes	Yes	Yes	Yes	Yes	Yes	Yes
24	Provision of appropriate tables and graphics	Yes	Yes	Yes	Yes	Yes	Yes	Yes
25	Graphic summarizing individual study estimates and overall estimate	Yes	Yes	Yes	Yes	Yes	Yes	Yes
26	Table giving descriptive information for each study included	Yes	Yes	Yes	Yes	Yes	Yes	Yes
27	Results of sensitivity testing (eg, subgroup analysis)	Yes	No	Yes	Yes	Yes	Yes	Yes
28	Indication of statistical uncertainty of findings	Yes	Yes	Yes	Yes	Yes	Yes	Yes
29	Quantitative assessment of bias (eg, publication bias)	No	No	Yes	Yes	Yes	Yes	Yes
30	Justification for exclusion (eg, exclusion of non-English language citations)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
31	Assessment of quality of included studies	No	Yes	Yes	Yes	Yes	Yes	Yes
32	Consideration of alternative explanations for observed results	Yes	No	Yes	Yes	Yes	Yes	Yes
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	Yes	No	Yes	Yes	Yes	Yes	Yes
34	Guidelines for future research	Yes	Yes	No	Yes	No	Yes	Yes
35	Disclosure of funding source	No	Yes	Yes	Yes	Yes	Yes	Yes
	Present items	**21/35**	**24/35**	**29/35**	**32/35**	**31/35**	**32/35**	**27/35**
	%	**60**	**65,71**	**82,85**	**91,43**	**88,57**	**91,43**	**77,14**

Conclusão

5. CONSIDERAÇÕES FINAIS

Apesar das meta-análises que avaliaram a relação entre o tabagismo, falha dos implantes e peri-implantite apresentarem resultados desfavoráveis aos fumantes, a qualidade da evidência é baixa. Portanto, as informações disponíveis nessas meta-análises devem ser interpretadas com cautela para a prática clínica. Além disso, futuros estudos devem ser conduzidos de forma rigorosa para evitar potenciais vieses.

6. COMUNICADO DE IMPRENSA

A fumaça do cigarro contém mais de 4000 substâncias potencialmente tóxicas que interferam no metabolismo ósseo e consequentemente na cicatrização óssea ao redor dos implantes. Diversos estudos têm avaliado a relação entre o tabagismo, perda dos implantes e peri-implantite. Porém, com o aumento do número de publicações nos últimos anos de revisões sistemáticas e meta-análises, e devido a sua importância no processo de tomada de decisão em saúde e aplicabilidade clínica, é fundamental avaliar a qualidade da evidência desses estudos.

Apesar dos estudos mostrarem resultados desfavoráveis aos fumantes, a qualidade da evidência dos estudos que avaliaram a relação entre o tabagismo, peri-implatite e/ou falha dos implantes é considerada baixa. Portanto, as informações disponíveis neste estudo devem ser interpretadas com cautela para a prática clínica odontológica. Além disso, futuros estudos devem ser conduzidos de forma rigorosa para evitar falhas metodológicas.

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