Int. J. Oral Maxillofac. Surg. 2019; 48: 1241–1249
https://doi.org/10.1016/j.ijom.2019.01.015, available online at https://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Systematic Review and Meta-analysis
Dental Implants

Is there an association between overweight/obesity and dental implant complications? A systematic review and meta-analysis

J. L. G. C. Monteiro[1], E. P. Pellizzer[2], C. A. Araújo Lemos[2], S. L. D. de Moraes[3], B. C. do Egito Vasconcelos[1]

[1]Department of Oral and Maxillofacial Surgery, School of Dentistry, University of Pernambuco, Camaragibe, PE, Brazil; [2]Department of Dental Materials and Prosthodontics, Dental School of Araçatuba, Universidade Estadual Paulista, Araçatuba, SP, Brazil; [3]Department of Prosthodontics, School of Dentistry, Universidade de Pernambuco, Camaragibe, PE, Brazil

J. L. G. C. Monteiro, E. P. Pellizzer, C. A. Araújo Lemos, S. L. D. de Moraes, B. C. do Egito Vasconcelos: Is there an association between overweight/obesity and dental implant complications? A systematic review and meta-analysis. Int. J. Oral Maxillofac. Surg. 2019; 48: 1241–1249.

Abstract. The aim of this systematic review was to test the following hypotheses: (1) that there is no difference in implant survival rate between individuals with overweight or obesity and those who are within the ideal weight range; (2) that there are no differences between these groups regarding indicators of peri-implant health. Two independent reviewers performed a literature search of the PubMed/MEDLINE, Scopus, and Cochrane Library databases for studies published up to April 1, 2018. A meta-analysis was performed to determine the risk difference for implant failure and mean difference for marginal bone loss, probing depth, and bleeding on probing. Six studies were selected for review, involving a total of 746 patients with 986 implants: 609 in overweight or obese individuals and 377 in individuals within the ideal weight range. The findings of this systematic review indicate that the first hypothesis should be accepted, since no statistically significant difference in implant survival rate was found between individuals with overweight/obesity and those within the ideal weight range ($P = 0.64$). The second hypothesis was rejected, as the review indicated a difference in marginal bone loss ($P < 0.00001$), probing depth ($P < 0.00001$), and bleeding around dental implants ($P < 0.00001$).

Key words: obesity; dental implants; meta-analysis.

Accepted for publication
Available online 19 February 2019

According to the World Health Organization[1], overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. Recent data indicate that the prevalence of obesity has nearly tripled since 1975. Global estimates show that 2.8 million people die each year due to diseases associated with obesity or overweight, and this is considered an epidemic in high-, middle- and low-income countries[1]. It is predicted that approximately half of the world's population will be obese by the year 2030[2].

Obesity is associated with high rates of mortality and morbidities such as hypertension, type II diabetes, and atherosclerosis[3]. It has recently been suggested that this condition is correlated with a low-grade inflammatory state, characterized by an increase in circulating inflammatory markers[4]. This systemic inflammatory state contributes to an alteration in the immune response and increasing levels of C-reactive protein (CRP), which is an indicator of systemic inflammation[5].

Suvan et al. found that overweight/obese individuals are more likely to have periodontitis compared to normal weight controls[6]. This periodontal tissue destruction is likely related to increased levels of pro-inflammatory cytokines and periodontal pathogens in patients with obesity[7,8]. A recent systematic review concluded that an increased waist circumference, obesity, overweight, and weight gain contribute to a worsening of periodontal measures[9]. The same reasoning may apply to dental implants, but there is no consensus on this issue yet.

Despite the relatively high implant success rate in daily practice, it is important to identify patients who are at greater risk of complications, such as implant failure, which is defined as an osseointegration failure or long-term failure due to peri-implantitis[10]. Considering the growing concerns regarding the high prevalence of overweight and obesity throughout the world and the increasing number of patients seeking dental implant treatment, the aim of this study was to perform a systematic review of the literature on the possible association between overweight/obesity and dental implant complications. The following were the null hypotheses: (1) there is no difference in implant survival rate between individuals with overweight or obesity and those who are within the ideal weight range; (2) there are no differences between these groups regarding indicators of peri-implant health, such as marginal bone loss, probing depth, bleeding on probing, or inflammation mediators around dental implants.

Materials and methods

Protocol and registration

This study was conducted using the PRISMA guidelines[11]. The guiding question was: Is there an association between overweight/obesity and dental implant complications? This systematic review is registered with the International Prospective Register of Systematic Reviews in Health and Social Care (PROSPERO, National Institute for Health Research, UK; CRD42018094848).

Eligibility criteria

The PICO question was used to guide the selection of articles: (1) population: patients undergoing dental implant surgery; (2) intervention: placement of dental implants in individuals with overweight or obesity; (3) comparison: placement of dental implants in individuals within the ideal weight range; (4) outcome: implant survival rate (primary outcome) and marginal bone loss (MBL), probing depth (PD), bleeding on probing, and other complications (secondary outcomes).

The following inclusion criteria were applied: articles published in English, Portuguese or Spanish; randomized controlled trials and retrospective or prospective studies comparing individuals with overweight/obesity to those who are within the ideal weight range. Body mass index (BMI = weight in kilograms divided by height in metres squared, kg/m^2) was categorized as follows: (1) <18.5 kg/m^2 = underweight; (2) 18.5–24.9 kg/m^2 = ideal range; (3) 25–29.9 kg/m^2 = overweight; (4) 30–39.9 kg/m^2 = obesity; and (4) ≥ 40 kg/m^2 = morbid obesity[12]. Narrative review articles and animal studies were excluded.

Sources of information and search criteria

The PubMed/MEDLINE, Cochrane Library, and Scopus databases were searched for pertinent articles published up to April 1, 2018. Medical subject headings (MeSH, PubMed) and terms related to overweight/obesity and dental implants were combined using Boolean operators. The following search was conducted in each database: (dental AND implant) [All fields] AND (obese OR obesity OR weight OR overweight OR body mass index OR BMI OR body fat) [All fields].

To screen for articles in press and not yet indexed in the main databases, a manual search of the following journals was performed: *International Journal of Oral and Maxillofacial Surgery*, *Journal of Oral and Maxillofacial Surgery*, *British Journal of Oral and Maxillofacial Surgery*, *Clinical Oral Implants Research*, and *International Journal of Oral and Maxillofacial Implants*. The reference lists of selected studies were also screened for potential titles that met the inclusion criteria.

Data collection process

Two independent reviewers who had undergone a calibration exercise performed the selection of the articles (J.L.G.C.M. and C.A.A.L.). Inter-examiner kappa scores were calculated to determine the level of agreement in the pre-selection of articles based on titles and abstracts ($\kappa = 0.86$ for PubMed/MEDLINE, $\kappa = 1.0$ for Scopus, and $\kappa = 1.0$ for the Cochrane Library). Titles and abstracts were screened using the inclusion and exclusion criteria. Next, pre-selected studies and those for which insufficient information was found in the title/abstract were submitted to full-text analysis for the determination of eligibility. In cases of a divergence of opinion, a third reviewer (B.C.E.V.) was consulted to make the final decision.

Data extraction

Two reviewers (J.L.G.C.M. and C.A.A.L.) extracted the following data from the articles: author(s) and year of publication, study type, sample characteristics, sample size for each group, measures of obesity employed, and methods of assessing peri-implant health or complications. Given that some obesity-related comorbidities such as diabetes or other implant failure-related factors could influence the results[13], the studies were evaluated with regard to adjustments for confounding factors (yes/no/partial). The following complications were considered: implant loss, peri-implantitis, MBL, PD, and any other complication or factor reported in the studies that may influence peri-implant health.

Summary measures

Review Manager software (RevMan version 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, 2014) was used for the meta-analysis and to construct the forest plots. The Mantel–Haenszel method was used. The risk difference (RD) with a 95% confidence interval (CI) was used to compare the occurrence of implant failure between individuals with overweight/obesity and those within the ideal weight range (dichotomous outcome). A RD value was considered significant when the *P*-value was <0.05. The method described by Hozo et al.[14] was used to calculate the standard deviation (SD) of continuous measures when individual subject data were not available. This method is useful for calculating the SD when only the range of values and mean are available. The mean difference (MD) was used in the meta-analysis for the comparison of continuous measures.

In cases of statistically significant heterogeneity ($P < 0.10$), a random-effects model was used to assess the significance of the treatment effects. When no statistically significant heterogeneity was found, analysis was performed using a fixed-effects model. Heterogeneity was assessed using the Q method (χ^2), with calculation of the I^2 value, which was used to analyze variations in heterogeneity: I^2 above 75% (0–100%) was considered indicative of relevant heterogeneity[15]. Five selected articles were eligible for quantitative analysis (three for implant failure and two for MBL, PD, and bleeding on probing). One article was not included in the quantitative analysis because it only evaluated biomarkers of inflammation around dental implants and the correlation with body fat indices.

Assessment of study quality

Two investigators (J.L.G.C.M. and C.A.A. L.) assessed the methodological quality of the studies using the Methodological Index for Non-Randomized Studies (MINORS) scale, which is a validated 12-item instrument. This is a validated index for the assessment of non-randomized studies. It was developed by a group of surgeons because of the problems faced by clinicians due to the lack of randomized surgical trials and the large number of observational studies in surgery. Each item is scored 0 (not reported), 1 (reported, but inadequate), or 2 (reported and adequate)[16]. A controlled study is considered to be of high quality if it receives a score of ≥16. For non-controlled studies, a score of ≥10 is considered indicative of high quality. Additionally, the articles were classified with regard to the level of scientific evidence based on the classification system proposed by the Oxford Centre for Evidence-Based Medicine (CEBM) in 2009 (Table 1), which is often employed for this purpose. The classification is based on the study design[17].

Results

Details of the search strategy are displayed in Fig. 1. The searches performed in the databases led to the retrieval of 972 articles: 891 from PubMed/MEDLINE, 29 from Scopus, and 52 from the Cochrane Library. After the removal of duplicates,

Table 1. Levels of evidence according to the Oxford Centre for Evidence-Based Medicine (CEBM)[17].

Level of evidence	Meaning
1a	Systematic reviews (with homogeneity) of RCTs
1b	Individual RCTs (with narrow confidence intervals)
1c	'All or nothing'
2a	Systematic reviews (with homogeneity) of cohort studies
2b	Individual cohort studies (including RCTs of low quality)
2c	'Outcome' studies, ecological studies
3a	Systematic reviews (with homogeneity) of case–control studies
3b	Individual case–control studies
4	Case series (as well as cohort and case–control studies of low quality)
5	Expert opinions with no explicit critical considerations or based on physiology or based on studies of low quality

RCT, randomized controlled trial.

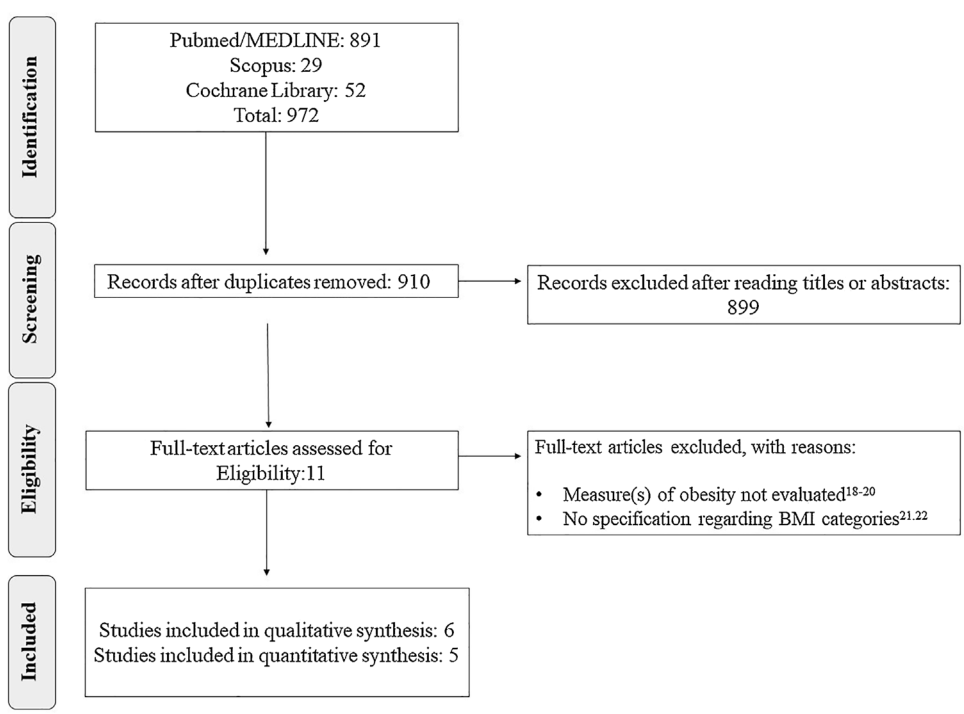

Fig. 1. PRISMA flow diagram of the study selection process.

910 studies remained. Following the analysis of the titles and/or abstracts, 11 studies were submitted to full-text analysis, five of which were excluded due to the absence of an obesity measure[18–20] or failure to specify BMI categories[22,21]. Thus, six studies were included in the present review[23–28].

The studies were evaluated for feasibility regarding data synthesis and one study was not included in the meta-analysis due to missing data. Thus, six studies were submitted to qualitative analysis and five studies were submitted to quantitative analysis. All studies were categorized as level 2b according to the CEBM levels of evidence. Four were retrospective, one was prospective, and one was a cross-sectional study. The studies involved a total of 746 patients and the placement of 986 implants: 609 in individuals considered overweight/obese and 377 in individuals within the ideal weight range. Most studies considered a BMI $\geq$30 kg/m^2 as indicating obesity. One study included an overweight category (BMI 25–29.9 kg/m^2) and another considered a BMI of 27 kg/m^2 as indicating class I obesity. Table 2 displays the characteristics of the studies included in this review.

Implant failure

Implant failure was reported in three studies[23–25]. In the study by Knabe et al.[23], no implant failure was detected in either group (obese and non-obese) after follow-up ranging from 2 to 3 years. BMI had no impact on implant survival in the study by Otzel et al.[24], in which seven out of 65 implants failed in patients without obesity (BMI <30 kg/m^2; 10.8% failure rate) and eight out of 244 failed in obese individuals (BMI $\geq$30 kg/m^2; 3.2% failure rate). Hazem et al.[25] also found no impact of BMI on implant survival. The meta-analysis using a random-effects model (Fig. 2) indicated no statistically significant difference in the implant survival rate between obese and non-obese individuals ($P = 0.64$; RD −0.02, 95% CI −0.09 to 0.06). The total number of implants installed in each group was considered in this analysis.

Marginal bone loss, probing depth, and bleeding on probing around dental implants

Two studies involved measures of MBL, PD, and bleeding on probing around dental implants[26,27]. The mean values for these measures were higher in obese individuals than in the controls (ideal weight range) in both studies.

Vohra et al.[27] stratified the participants into different levels of obesity and found that the highest mean values for these measures occurred among individuals with a BMI $\geq$40 kg/m^2 (class III obesity); they also demonstrated a statistically significant difference between individuals

Table 2. Characteristics of the studies included in this review.

First author, publication year	Type of study/ CEBM category	Measures of obesity employed	Adjustment for confounders: Systemic	Adjustment for confounders: Local[a]	Number of individuals (*n*)	Methods of assessment of peri-implant health/complications
Knabe et al.[23], 2017	Prospective/2b	BMI	Yes	Partial	120	Failure rate[b]
Otzel et al.[24], 2017	Retrospective/2b	BMI	Yes	Partial	177	Failure rate[c]
Vohra et al.[27], 2018	Retrospective/2b	BMI	Yes	Partial	84	Plaque index[d] Bleeding on probing[d] Probing depth[d] MBL levels[e]
Hazem et al.[25], 2016	Retrospective/2b	BMI	Yes	Partial	220	Failure rate[f] Signs of infection (fistula tracks, pus) MBL (present/absent)[g]
Abduljabbar et al.[26], 2016	Retrospective/2b	BMI	Yes	Partial	72	Non-stimulated whole saliva analysis[h] Probing depth Bleeding on probing MBL levels[i]
Elangovan et al.[28], 2014	Cross-sectional/2b	BMI, WC, % total body fat	Yes	Partial	73	PISF analysis[j] Plaque levels[k] Probing depth Bleeding on probing Presence of suppuration Mobility Pain on percussion or palpation

BMI, body mass index; CEBM, Centre for Evidence-Based Medicine; MBL, marginal bone loss; PISF, peri-implant sulcular fluid; WC, waist circumference.

[a] Smoking was considered a local factor.

[b] No description of the method used to determine implant failure.

[c] Defined as an implant requiring replacement.

[d] According to the Seventh European Workshop on Periodontology.

[e] Defined as the distance from the widest supracrestal part of the implant to the alveolar crest.

[f] The implant was considered a failure if it was removed from the patient's mouth.

[g] No measurements of bone levels were made, but bone loss was recorded as present or absent based on whether it was noted in the treatment record.

[h] Measurement of levels of interleukins IL-6 and IL-1β through enzyme-linked immunosorbent assay.

[i] Defined as the linear distance from the implant–abutment junction to the most coronal part of the alveolar crest.

[j] Peri-implant sulcular fluid analysis was performed by measuring levels of interleukins (IL-1α, 1β, 6, 8, 10, 12, 17), tumour necrosis factor alpha (TNF-α), C-reactive protein (CRP), osteoprotegerin, leptin, and adiponectin. Measurements were performed using a multiplexed fluorescent bead-based immunoassay.

[k] Measured using the modified Quigley–Hein plaque index.

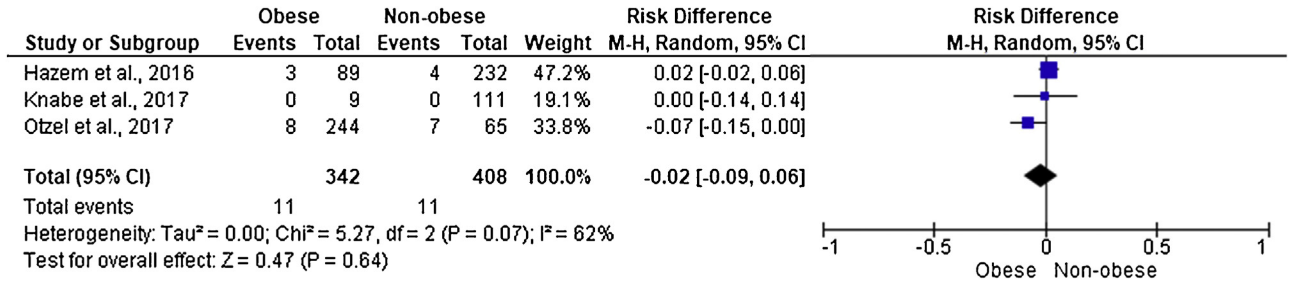

Fig. 2. Meta-analysis through a random-effects model indicating no statistically significant difference in implant survival rate between obese and non-obese individuals.

with a BMI 27.5–34.9 kg/m^2 and those with a BMI within the ideal range (BMI 18.5–22.9 kg/m^2). Values were also higher among individuals with class II and class III obesity compared to the controls (ideal range). Table 3 shows the results of the studies regarding the implant failure rate, as well as MBL, PD, and bleeding on probing around dental implants, when available.

The meta-analysis demonstrated a statistically significant increase in MBL, PD, and bleeding around dental implants in obese individuals compared to those within the ideal weight range (Fig. 3). The mean difference was 2.04 mm (95% CI 1.46 to 2.61, $P < 0.00001$) for MBL, 2.19 mm (95% CI 1.85 to 2.53, $P < 0.00001$) for PD, and 15.98% (95% CI 13.72 to 18.23, $P < 0.00001$) for bleeding around dental implants.

Inflammation measures

Three studies provided information on inflammation measures[26–28]. One study assessed the concentration of interleukins (IL-1β and IL-6) in saliva[26]. One study measured the levels of inflammatory mediators in the peri-implant sulcular fluid (PISF)[28] and one study correlated CRP levels in blood samples with clinical and radiographic peri-implant variables. The results of these studies are found in Table 4.

Overall, inflammatory mediators were increased in obese individuals compared to non-obese individuals. Elangovan et al.[28] found a modest, but statistically significant association between waist circumference and levels of IL-1β in the PISF around dental implants. Vohra et al.[27] found a significant positive correlation between serum CRP levels and bleeding on probing, and a significant negative correlation between serum CRP levels and MBL in class III obesity (BMI ≥40 kg/m^2). Abduljabbar et al.[26] found that whole salivary levels of IL-1β and IL-6 were significantly higher among obese individuals compared to normal weight controls. Since these inflammatory mediators were measured in different manners (non-stimulated whole saliva, PISF analysis, and serum levels), a meta-analysis was not viable.

Quality analysis of studies

Overall, the studies analyzed were of high level quality. The MINORS score ranged from 15 to 20 (Table 5). A common deficiency was the lack of a sample size calculation in most studies. The follow-up period varied among the studies. The participants in the retrospective studies also had different follow-up periods. A major limitation was that some studies included patients with implants functioning for different periods[26–28]. One study stated that only early failures (prior to crown placement) occurred[25]. In one study, it was not clear whether the implants were functioning after the last follow-up[23].

Discussion

The rapid increase in the global prevalence of obesity has led to increased concerns regarding the health-related complications of this condition. High levels of body fat are related to various inflammatory reactions, which result in a chronic low-grade inflammatory state7.

Table 3. Results of studies on failure rate, marginal bone loss, probing depth, and peri-implant bleeding.

First author, publication year	BMI categories (kg/m^2) for each study	Number of implants	Implant failure rate (%)	MBL (mm), mean (SD)	Probing depth (mm), mean (SD)	Peri-implant bleeding on probing (%), mean (SD)
Knabe et al.[23], 2017	Obese (≥30)	9	0	NR	NR	NR
	Non-obese (< 30)	111	0	NR	NR	NR
Otzel et al.[24], 2017	Obese (≥30)	244	3.2	NR	NR	NR
	Non-obese (< 30)	65	10.8	NR	NR	NR
Vohra et al.[27], 2018	Class I obesity (27.5–34.9)	39	NR	1.8 (0.35)[b]	2.4 (0.22)[b]	19.1 (2.25)[b]
	Class II obesity (35–39.9)	35	NR	2.6 (0.52)[c]	3.1 (0.27)[c]	25.4 (3.95)[c]
	Class III obesity (≥40)	26	NR	2.7 (0.45)[c]	3.6 (0.45)[c]	27.8 (2.12)[b]
	Normal weight (18.5–22.9)	43	NR	0.9 (0.62)	1.2 (0.35)	11.7 (2.37)
Hazem et al.[25], 2016	Obese (≥30)	89	3.37	NR	NR	NR
	Overweight (25–29.9)	122	2.45	NR	NR	NR
	Normal weight (18.5–24.9)	110	0.9	NR	NR	NR
Abduljabbar et al.[26], 2016	Obese (≥30)	45	NR	3.4 (0.55)[d]	4.4 (0.8)[d]	28.2 (4.22)[d]
	Normal weight (18.5–24.9)	48	NR	0.8 (0.6)	2.1 (0.17)	10.1 (2.65)

BMI, body mass index; MBL, marginal bone loss; NR, not reported; SD, standard deviation.

[a]This study used different values of BMI to classify different levels of obesity.

[b]Statistically significant difference ($P < 0.05$) in comparison to class II obesity, class III obesity, and individuals within the ideal weight range.

[c]Statistically significant difference ($P < 0.05$) in comparison to class I obesity and individuals within the ideal weight range.

[d]Statistically significant difference ($P < 0.05$) in comparison to individuals within the ideal weight range.

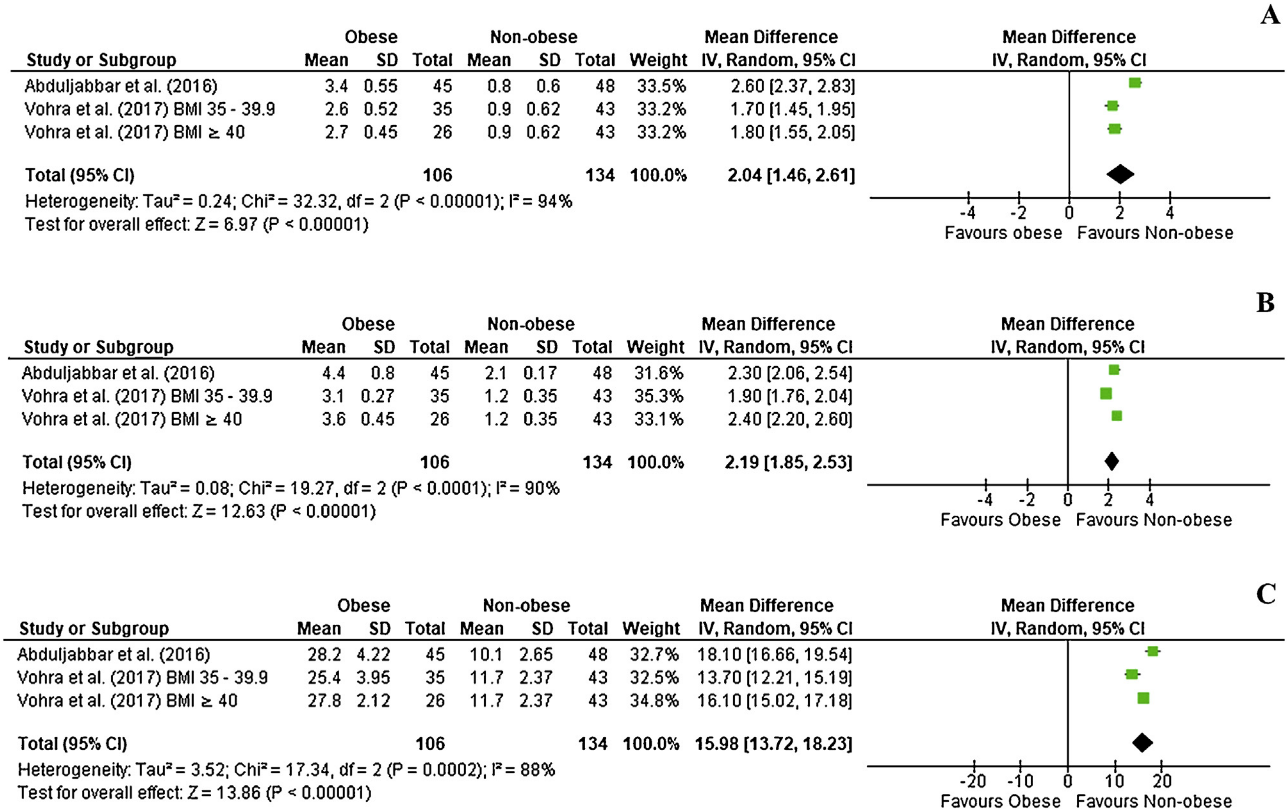

Fig. 3. Meta-analysis demonstrating a statistically significant increase in (A) marginal bone loss, (B) probing depth, and (C) bleeding around dental implants in obese patients compared to normal-weight individuals.

Table 4. Results of studies on measures of inflammation.

First author, publication year	Measures of inflammation	Results
Abduljabbar et al.[26], 2016	Non-stimulated whole salivary IL-1β and IL-6[a]	Non-stimulated whole salivary IL-1β and IL-6 were significantly higher among obese individuals than among those within the ideal weight range ($P < 0.0001$) Mean (SD) IL-1β (pg/ml) in obese individuals: 2462.7 (254.2)[b] Mean (SD) IL-6 (pg/ml) in obese individuals: 361.3 (26.4)[b] Mean (SD) IL-1β (pg/ml) in individuals in ideal weight range: 1088.3 (103.2)[b] Mean (SD) IL-6 (pg/ml) in individuals in ideal weight range: 133.2 (9)[b]
Elangovan et al.[28], 2014	Concentrations of IL (1α, 1β, 6, 8, 10, 12, 17), TNF-α, CRP, OPG, leptin, and adiponectin were measured[c] Individual measures for each BMI category were not available	A modest, but statistically significant association was found between WC and levels of IL-1β in PISF
Vohra et al.[27], 2018	Blood samples were collected and CRP was assessed	A significant positive correlation was found between CRP levels and BOP ($P = 0.0148$) and a significant negative correlation ($P = 0.0212$) was found for MBL in the class III obesity group (BMI ≥40)

BMI, body mass index; BOP, bleeding on probing; CRP, C-reactive protein; IL, interleukin; MBL, marginal bone loss; OPG, osteoprotegerin; PISF, peri-implant sulcular fluid; SD, standard deviation; TNF-α, tumour necrosis factor alpha; WC, waist circumference.

[a] Measurement of levels of IL-6 and IL-β through enzyme-linked immunosorbent assay.

[b] The SD was calculated using the method described by Hozo et al.[14].

[c] Peri-implant sulcular fluid analysis was performed. Measurements of mediators of inflammation were performed using a multiplexed fluorescent bead-based immunoassay.

Fat accumulated in hepatocytes and adipocytes secretes inflammatory cytokines, such as tumour necrosis factor alpha (TNF-α) and IL-6[29]. Indeed, adipose tissue acts as an endocrine organ and mainly consists of subcutaneous and internal adipose tissue, the latter of which constitutes approximately 20% of body fat and consists mainly of visceral adipose tissue. Moreover, evidence from animal studies has indicated that macrophage infiltration in adipose tissue is associated with the chronic inflammatory state found in obesity[30,31]. In the present review study, it was found that measures of MBL, PD, and

Table 5. MINORS scale assessment for each study included.

Component	Knabe et al.[23]	Otzel et al.[24]	Vohra et al.[27]	Hazem et al.[25]	Abduljabbar et al.[26]	Elangovan et al.[28]
A clearly stated aim[a]	2	2	2	2	2	2
Inclusion of consecutive patients[b]	2	2	2	2	2	2
Prospective collection of data[c]	2	2	2	2	2	2
Endpoint appropriate to the aim of the study[d]	1	1	1	1	1	1
Unbiased assessment of the study endpoint[e]	1	0	2	1	1	1
Follow-up period appropriate to the aim of the study[f]	2	2	2	1	2	2
Loss to follow-up less than 5%[g]	2	0	1	0	1	1
Prospective calculation of the study size[h]	0	0	0	0	2	0
An adequate control group[i]	2	2	2	2	2	2
Contemporary groups[j]	2	1	1	1	1	1
Baseline equivalence of groups[k]	2	2	2	2	2	2
Adequate statistical analyses[l]	2	1	2	2	2	2
Total score	20	15	19	16	20	18

MINORS (Methodological Index for Non-Randomized Studies): the items are scored 0 (not reported), 1 (reported, but inadequate), or 2 (reported and adequate). The global ideal score is 16 for non-comparative studies and 24 for comparative studies.

[a] The question addressed should be precise and relevant in light of the available literature.

[b] All patients potentially suitable for inclusion (satisfying the criteria for inclusion) have been included in the study during the study period (no exclusion, or details about the reasons for exclusion).

[c] Data were collected according to a protocol established before the beginning of the study.

[d] Unambiguous explanation of the criteria used to evaluate the main outcome, which should be in accordance with the question addressed by the study. The endpoints should also be assessed on an intention-to-treat basis.

[e] Blind evaluation of objective endpoints and double-blind evaluation of subjective endpoints. Otherwise, the reasons for not blinding should be stated.

[f] The follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events.

[g] All patients should be included in the follow-up. Otherwise, the proportion lost to follow-up should not exceed the proportion experiencing the major endpoint.

[h] Information on the size of the detectable difference of interest with calculation of the 95% confidence interval according to the expected incidence of the outcome event and information about the level for statistical significance and estimates of power when comparing the outcomes.

[i] Having a gold standard diagnostic test or therapeutic intervention recognized as the optimal intervention according to the available published data.

[j] The control and study group should be managed during the same time period (no historical comparison).

[k] The groups should be similar regarding the criteria other than the studied endpoints. There should be an absence of confounding factors that could bias the interpretation of the results.

[l] Whether the statistical analyses were in accordance with the type of study, with calculation of confidence intervals or relative risk.

inflammation around dental implants were higher in individuals with overweight or obesity. The reason for these elevated measures may be correlated with the elevated presence of these inflammatory mediators in the oral environment. Moreover, increased susceptibility to infection is correlated with the obesity-related chronic inflammatory state, which disturbs protective immunity[32].

PISF analysis, which was used in one study included in this review[28], has a stronger correlation with clinical parameters. Since it may be difficult to diagnose peri-implant disease only on a clinical basis, this method is a reasonable way to assess disease activity[33].

The findings of this review should be interpreted with caution, since the studies did not consider other important factors that may exert a long-term influence on peri-implant health. For instance, a recent meta-analysis showed that cement-retained prostheses exhibited less MBL than screw-retained prostheses[34]. Another meta-analysis found that short implants (length less than 8 mm) have a higher risk of failure[35]. The studies also varied regarding the period in which the implants were functioning. In one study, there was mention that only early failures were considered[23]. The evaluation of early failures represents a more ideal scenario for the assessment of the isolated influence of obesity or overweight on the osseointegration of dental implants, since these failures occur prior to the introduction of masticatory forces.

All studies used the BMI to categorize patients and one study also used waist circumference[28]. The BMI is a widely accepted measure to classify medical risk according to weight status. However, the BMI does not distinguish between fat-free mass and fat-mass, which have opposing associations with health risks. Studies have reported that waist circumference is a more reliable indicator of visceral fat than BMI[36,37] and that both indicators independently contribute to the prediction of non-abdominal, abdominal subcutaneous, and visceral fat[38].

The findings of this systematic review indicate that the first hypothesis should be accepted, since no statistically significant difference in implant survival rate was found between individuals with overweight/obesity and those within the ideal weight range. In contrast, the second hypothesis was rejected, as the review indicated a difference in peri-implant health indicators between the groups. Due to the inclusion of retrospective cohort studies in this review, interpretation of the meta-analysis results should be done with caution, since these studies are not appropriate to determine causation. Furthermore, the results of a meta-analysis that combines the results of observational studies of heterogeneous quality can be highly biased. It is also difficult to control for confounding factors in non-randomized studies. Moreover, retrospective studies are prone to missing data and need large sample sizes if outcomes (such as implant failure) are rare.

In conclusion, within the limitations of this review, dental implants are feasible for obese or overweight individuals. However, there is some evidence that these patients may be at greater risk of clinical complications in comparison to those who are within the ideal weight range, as well as increased concentrations of inflammatory markers around implants and in the oral environment. This indicates that these patients should be submitted to more regular follow-up evaluations and that health professionals should warn these patients of a possible association between overweight/obesity and peri-implant health. Randomized clinical trials with well-established inclusion criteria and the control of local and systemic factors are needed to gain a better understanding of this issue.

Acknowledgements. Richard Boike provided English editing of the manuscript. All authors have read and approved the manuscript.

Funding. This work received financial support from the Brazilian fostering agencies Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES; Coordination for the Improvement of Higher Education Personnel) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq; National Council for Scientific and Technological Development). The first author was granted a master's degree scholarship from CAPES.

Competing interests. The authors declare no conflicts of interest.

Ethical approval. Not applicable.

Patient consent. Not applicable.

References

1. World Health Organization. *10 facts on obesity*. Geneva: World Health Organization; 2017 . https://www.who.int/features/factfiles/obesity/en/ [Accessibility verified July 18, 2018].
2. Finkelstein EA, Khavjou OA, Thompson H, Trogdon JG, Pan L, Sherry B, Dietz W. Obesity and severe obesity forecaststhrough 2030. *Am J Prev Med* 2016;**42**:563–70. http://dx.doi.org/10.1016/j.amepre.2011.10.026.
3. Ding C, Chan Z, Magkos F. Lean, but not healthy: the 'metabolically obese, normal-weight' phenotype. *Curr Opin Clin Nutr Metab* 2016;**19**:408–17. http://dx.doi.org/10.1097/MCO0000000000000317.
4. Freitas WR, Oliveira LVF, Perez EA, Ilias EJ, Lottenberg CP, Silva AS, Urbano JJ, Oliveira MC, Vieira RP, Ribeiro-Alves M, Alves VLS, Kassab P, Thuler FR, Malheiros CA. Systemic inflammation in severe obese patients undergoing surgery for obesity and weight-related diseases. *Obes Surg* 2018;**28**:1931–42. http://dx.doi.org/10.1007/s11695-017-3104-9.
5. Akram Z, Abduljabbar T, Abu Hassan MI, Javed F, Vohra F. Cytokine profile in chronic periodontitis patients with and without obesity: a systematic review and meta-analysis. *Dis Markers* 2016;**2016**: 4801418. http://dx.doi.org/10.1155/2016/4801418.
6. Suvan JE, Petrie A, Nibali L, Darbar U, Rakmanee T, Donos N, D'Aiuto F. Association between overweight/obesity and increased risk of periodontitis. *J Clin Periodontol* 2015;**42**:733–9. http://dx.doi.org/10.1111/jcpe.12421.
7. Pradeep AR, Nagpal K, Karvekar S, Patnaik K. Levels of lipocalin-2 in crevicular fluid and tear fluid in chronic periodontitis and obesity subjects. *J Investig Clin Dent* 2016;**7**:376–82. http://dx.doi.org/10.1111/jicd.12165.
8. Maciel SS, Feres M, Gonçalves TED, Zimmermann GS, Silva HDP, Figueiredo LC, Duarte PM. Does obesity influence the subgingival microbiota composition in periodontal health and disease? *J Clin Periodontol* 2016;**43**:1003–12. http://dx.doi.org/10.1111/jcpe.12634.
9. Keller A, Rohde JF, Raymond K, Heitmann BL. Association between periodontal disease and overweight and obesity: a systematic review. *J Periodontol* 2016;**86**:766–76. http://dx.doi.org/10.1902/jop.2015.140589.
10. Vissink A, Spijkervet F, Raghoebar GM. The medically compromised patient: are dental implants a feasible option? *Oral Dis* 2018;**24**:253–60. http://dx.doi.org/10.1111/odi.12762.
11. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009;**151**:264–9. http://dx.doi.org/10.7326/0003-4819-151-4-200908180-00135.
12. Centers for Disease Control and Prevention. *Defining adult overweight and obesity*. Atlanta, GA: Centers for Disease Control and Prevention; 2016 . https://www.cdc.gov/obesity/adult/defining.html [Accessibility verified July 18, 2018].
13. Moy PK, Medina D, Shetty V, Aghaloo TL. Dental implant failure rates and associated risk factors. *Int J Oral Maxillofac Implants* 2005;**20**:569–77.
14. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005;**5**:13. http://dx.doi.org/10.1186/1471-2288-5-13.
15. Egger M, Davey Smith G. Principles of and procedures for systematic reviews. In: Egger M, Davy Smith G, Altman DG, editors. *Systematic reviews in health care. Evidence-Based Health Care*. 2017:23–42.
16. Slim K, Nine E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. *ANZ J Surg* 2003;**73**:712–6. http://dx.doi.org/10.1046/j.1445-2197.2003.0278.x.
17. *Oxford Centre for Evidence-Based Medicine—Levels of evidence (March 2009)*. [Accessibility verified November 3, 2018] https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/.
18. Turri A, Rossetti PHO, Canullo L, Grusovin MG, Dahlin C. Prevalence of peri-implantitis in medically compromised patients and smokers: a systematic review. *Int J Oral Maxillofac Implants* 2016;**31**:111–8.
19. Vercruyssen M, Marcellis K, Coucke W, Naert I, Quirynen M. Long-term, retrospective evaluation (implant and patient-centred outcome) of two-implants-supported overdenture in the mandible. Part 1: survival rate. *Clin Oral Implants Res* 2010;**21**:357–65.
20. Alsaadi G, Quirynen M, Komárek A, Steenberghe DV. Impact of local and systemic factors on the incidence of oral implant failures, up to abutment connection. *J Clin Periodontol* 2007;**34**:610–7. http://dx.doi.org/10.1111/j.1600-051X.2007.01077.x.
21. Maniewicz S, Buser R, Duvernay E, Vazquez L, Loup A, Perneger TV, Schimmel M, Müller F. Short dental implants retaining two-implant mandibular overdentures in very old, dependent patients: radiologic and clinical observation up to 5 years. *Int J Oral Maxillofac Implants* 2017;**32**:415–22. http://dx.doi.org/10.11607/jomi.5361.
22. Müller F, Duvernay E, Loup A, Vazquez L, Herrmann FR, Schimmel M. Implant-supported mandibular overdentures in very old adults: a randomized controlled trial. *J Dent Res* 2013;**92**:154S–60S. http://dx.doi.org/10.1177/0022034513509630.
23. Knabe C, Mele A, Kann PH, Peleska B, Adel-Khattab D, Renz H, Reuss A, Bohner M, Stiller M. Effect of sex-hormone levels, sex, body mass index and other host factors on human craniofacial bone regeneration with bioactive tricalcium phosphate grafts. *Biomaterials* 2017;**123**:48–62. http://dx.doi.org/10.1016/j.biomaterials.2017.01.035.
24. Otzel M, Bilski WM, Bilski A. Risk factors associated with dental implant failure: a study of 302 implants placed in a regional center. *J Contemp Dent Pract* 2017;**18**:705–9. http://dx.doi.org/10.5005/jp-journals-10024-2111.
25. Hazem A, Bissada NF, Demko C, Paes A, Lang LA. Comparison of preprosthetic implant complications and failures between obese and nonobese patients. *Int J Oral Maxillofac Implants* 2016;**31**:1093–9. http://dx.doi.org/10.11607/jomi.4438.
26. Abduljabbar T, Al-Sahaly F, Kellesarian SV, Kellesarian TV, Al-Anazi M, Al-Khathami M, Javed F, Vohra F. Comparison of

peri-implant clinical and radiographic inflammatory parameters and whole salivary destructive inflammatory cytokine profile among obese and non-obese men. *Cytokine* 2016;**88**:51–6. http://dx.doi.org/10.1016/j.cyto.2016.08.017.

27. Vohra F, Alkhudhairy F, Al-Kheraif AA, Akram Z, Javed F. Peri-implant parameters and C-reactive protein levels among patients with different obesity levels. *Clin Implant Dent Relat Res* 2018;**20**:130–6. http://dx.doi.org/10.1111/cid.12556.
28. Elangovan S, Brogden KA, Dawson DV, Blanchette D, Pagan-Rivera K, Stanford CM, Avila-Ortiz G. Body fat indices and biomarkers of inflammation: a cross-sectional study with implications for obesity and peri-implant oral health. *Int J Oral Maxillofac Implants* 2014;**29**:1429–34. http://dx.doi.org/10.11607/jomi.3758.
29. Kim HM, Kim YM, Huh JH, Lee ES, Kwon MH, Lee BR, Chung CH, Ko HJ. α-Mangostin ameliorates hepatic steatosis and insulin resistance by inhibition CC chemokine receptor 2. *PLoS One* 2017;**12**:e0179204. http://dx.doi.org/10.1371/journal.pone.0179204.
30. Ding S, Jiang J, Wang Z, Zhang G, Yin J, Wang X, Yu Z. Resveratrol reduces the inflammatory response in adipose tissue and improves adipose insulin signaling in high-fat diet-fed mice. *PeerJ* 2018;**6**:e5173. http://dx.doi.org/10.7717/peerj.5173.
31. Kang M, Jeong J, Lee J, Park S, Sung Y, Choi M, Kwon W, Jang S, Choi KS, Choo YS, Yoon D, Kim MO, Ryoo ZY. Placental growth factor (PlGF) is linked to inflammation and metabolic disorders in mice with diet-induced obesity. *Endocr J* 2018;**65**:437–47. http://dx.doi.org/10.1507/endocrj.EJ17-0363.
32. Alwarawrah Y, Kiernan K, MacIver NJ. Changes in nutritional status impact immune cell metabolism and function. *Front Immunol* 2018;**9**:1055. http://dx.doi.org/10.3389/fimmu.2018.01055.
33. Kajale AM, Mehta DS. Interleukin-1β level in peri-implant crevicular fluid and its correlation with the clinical and radiographic parameters. *J Indian Soc Periodontol* 2014;**18**:220–5. http://dx.doi.org/10.4103/0972-124X.131331.
34. Lemos CA, de Souza Batista VE, Almeida DA, Santiago Júnior JF, Verri FR, Pellizzer EP. Evaluation of cement-retained versus screw-retained implant supported restorations for marginal bone loss: a systematic review and meta-analysis. *J Prosthet Dent* 2016;**115**:419–27. http://dx.doi.org/10.1016/j.prosdent.2015.08.026.
35. Lemos CA, Ferro-Alves ML, Okamoto R, Mendonça MR, Pellizzer EP. Short dental implants versus standard dental implants placed in the posterior jaws: a systematic review and meta-analysis. *J Dent* 2016;**47**:8–17. http://dx.doi.org/10.1016/j.jdent.2016.01.005.
36. Leitzmann MF, Moore SC, Koster A, Harris TB, Park Y, Hollenbeck A, Schatzkin A. Waist circumference as compared with body-mass index in predicting mortality from specific causes. *PLoS One* 2011;**6**: e18582. http://dx.doi.org/10.1371/journal.pone.0018582.
37. Jia WP, Lu JX, Xiang KS, Bao YQ, Lu HJ, Chen L. Prediction of abdominal visceral obesity from body mass index, waist circumference and waist–hip ratio in Chinese adults: receiver operating characteristic curves analysis. *Biomed Environ Sci* 2003;**16**:206–11.
38. Janssen I, Heymsfield SB, Allison DB, Kotler DP, Ross R. Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat. *Am J Clin Nutr* 2002;**75**. 683–638.

Address:
Belmiro Cavalcanti do Egito Vasconcelos
Faculdade de Odontologia de Pernambuco
Universidade de Pernambuco
Av. Gen. Newton Cavalcanti
1650
Tabatinga
Camaragibe
PE
CEP 54.753-220
Brazil
Tel.: +55 (81) 98886 8677
E-mail: belmiro.vasconcelos@upe.br