What Are the Clinical and Systemic Results of Periodontitis Treatment in Obese Individuals?

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Abstract

Purpose of Review Periodontitis and obesity are characterized by a dysregulated inflammatory state. Obese individuals have a higher chance of presenting periodontitis. Clinical studies in different populations demonstrate that individuals with obesity have worse periodontal conditions. This current review aims to explore recent literature to understand what the impacts of obesity on periodontal treatment outcomes are and to learn whether periodontal treatment can improve systemic biomarkers in obese individuals.

Recent Findings Short- and long-term evaluations demonstrated that non-surgical periodontal treatment could improve clinical parameters in obese individuals, represented as the reduction in mean probing depth, sites with probing depth ≥ 4 mm, and extension of bleeding on probing. However, obese individuals may have less clinical improvement when compared to normal-weight individuals with a similar periodontal profile. Additionally, periodontal treatment may contribute to a reduction in systemic levels of retinol-binding protein 4 and leptin, while promoting an increase in systemic levels of adiponectin.

Summary Overall, obese individuals with periodontitis can significantly benefit from non-surgical periodontal treatment. However, clinical improvements seem to be less prominent in obese individuals with periodontitis compared to non-obese individuals with similar periodontal status. Nevertheless, periodontal treatment may impact significantly on the reduction of several biochemical biomarkers of obesity with or without weight reduction. Further investigations are needed to improve our comprehension of the mechanisms underlying those findings.

Keywords Obesity · Periodontitis · Periodontal disease · Periodontal treatment · Obesity biomarkers · Inflammation

Introduction

Periodontitis is an inflammatory disease associated with a dysbiotic microbiota [1]. As it is a progressive destructive disease, if left untreated, periodontitis may lead to tooth loss [1]. Advances in periodontal research have demonstrated that periodontal microbiota or their products and local inflammatory mediators can impact a significant number of systemic disorders. Inversely, metabolic diseases can modulate periodontal response to microbial challenge [2].

Two main characteristics of periodontitis, chronic low-grade inflammation state and potential hematogenous dissemination of bacteria and their endotoxin, such as lipopolysaccharide, may explain the association between periodontal diseases and systemic conditions [2–4]. Particularly, severe periodontitis cases are at higher risk for cardiovascular disease, acute myocardial infarction, and stroke [5]. Furthermore, the bidirectional relationship between diabetes mellitus and periodontitis is well established, and it is now included in the classification of periodontitis to predict the risk of progression [1]. More recently, the relationship between obesity and periodontitis has been explored, and it also is included in the current classification of periodontal diseases [6, 7].

Hypertrophic or hyperplastic adipose tissue, present in excessive weight gain, can recruit inflammatory cells and induce exacerbated synthesis of pro-inflammatory
adipokines/cytokines [8–10]. As a consequence, the resulting hyper-inflammatory state could impair periodontal response to bacterial challenge [2], leading to a higher chance of periodontitis in obese individuals [11, 12•, 13, 14, 15••]. Thus, this current review aims to explore recent literature, published within the past 5 years, to understand what the impact of obesity on periodontal treatment outcomes are and to find out whether periodontal treatment can improve systemic biomarkers in obese individuals.

**Obesity**

Obesity is characterized by an excessive accumulation of body fat [16]. World Health Organization (WHO) and the National Institutes of Health determine obesity by using the body mass index (BMI), obtained as a ratio given by weight (in kg)/height (in m²) that classifies several categories. Thus, individuals who have a BMI ≥ 30.0 kg/m² are considered obese and categorized into three degrees, according to their level of obesity: I, 30.0–34.9 kg/m²; II, 35.0–39.9 kg/m²; III, ≥ 40.0 kg/m² [17, 18]. However, BMI is only related to total body weight, and it does not indicate fat distribution or weight composition, whether it is muscular or adipose tissue. In this case, some misinterpretations may occur [19]. For these reasons, other clinical parameters may be relevant to complement the diagnosis of obesity, such as waist circumference, hip circumference, and the calculation of the waist/hip ratio [20]. This pattern of distribution of body adiposity can predict a greater or less threat to health [21].

At the cellular level, excessive weight gain is observed in adipose tissue by both hyperplasia and hypertrophy of adipocytes [8, 22], and it is a result of a caloric imbalance and might be originated from a combination of excessive caloric intake and a sedentary lifestyle [23]. Nevertheless, obesity can differ in certain individuals according to their genetic predisposition, as well as environmental changes and epigenetic mechanisms [24].

According to WHO, in 2016, 1.9 billion adults (≥ 18 years of age) were overweight, and more than 650 million exhibited obesity [18]. Prevalence of obesity in the USA ranges from 40 to 45%, according to age group [25], which is relatively high compared to Sweden (16.6%) [26] and China (ranging from from 1.3 to 12.2% depending on the province) [27]. However, obesity is also frequent in developing countries such as Mexico (36.1%) [28] and India (42%) [29]. Additionally, an increase in obesity rates is reported in developing countries as demonstrated in Brazil, which showed a significant increase in the prevalence of obesity from 2006 (11.8%) to 2019 (20.3%) [30]. That report is an example of an anticipated tendency of constant worldwide growth in the prevalence of obesity [18], which is expected to worsen as a consequence of the COVID-19 pandemic [31].

Recognizing obesity as a disease is important to tackle public health issues because it usually is associated with comorbidities, and an increased rate of morbidity and mortality [32, 33]. Indeed, obese adult individuals have a higher relative risk of type 2 diabetes mellitus (T2DM) [34], hypertension [35, 36], dyslipidemia [37, 38], and metabolic syndrome [39]. In addition, the incidence of T2DM increases significantly across tertiles of baseline waist circumference, waist-to-hip ratio, and excess visceral fat mass [40]. Abdominal obesity accentuates the problem by the unusually high influx of portal fatty acids and hormones into the liver from omental adipocytes [41].

Evidence suggests that the dysfunction of adipose tissue leads to aberrant production of inflammatory molecules, known as adipokines [9, 42]. In obesity, hypertrophic or hyperplastic white adipocytes recruit several types of inflammatory cells, such as macrophages, T lymphocytes, and mast cells. This inflammatory cell influx leads to an enhancement of pro-inflammatory adipokines/cytokines synthesized in adipose tissue [10, 43, 44]. These adipocytokines act in an endocrine and/or paracrine manner to trigger insulin resistance, endothelial dysfunction, and vascular inflammation [45]. In summary, obesity holds a complex and multifactorial etiology and represents a relevant risk factor for the development of numerous chronic inflammatory pathologies, such as T2DM [34, 46, 47], cardiovascular diseases [48–51], breast cancer [10, 43–52], nonalcoholic fatty liver disease [53, 54], Alzheimer’s disease [55–57], and periodontitis [58].

**Obesity and Periodontitis Association**

Periodontitis is not only associated with periodontal tissue breakdown but also associated with systemic diseases, such as cardiovascular disease and other metabolic diseases [3, 4]. Additionally, individuals with obesity have been identified as having worse periodontal conditions in different populations [11, 12•, 13, 14, 15••]. Women may present greater prevalence of periodontitis and poorer periodontal parameters compared to non-obese women [14, 15••]. However, the association between periodontitis and obesity may not be influenced by gender [59].

Obese patients with periodontitis compared to non-obese with periodontitis may present significantly higher mean periodontal probing depth (PD), probably indicating worse inflammatory clinical aspects and greater challenge for treatment [15••]. Furthermore, the link between obesity and periodontitis may start early in life, as demonstrated in a
Individuals with obesity present a constant inflammatory state; consequently, it is plausible to imagine that it impacts on the subgingival environment and influences local microbiota. Data from young adults with overweight or obesity without destructive periodontal disease demonstrated higher levels of the pathogenic species Tannella forsythia and Porphyromonas gingivalis compared to normal-weight individuals with similar periodontal status [60]. Additional analysis of that study demonstrated that obesity parameters, such as waist circumference, hip circumference, and waist-hip ratio, had a significant positive association with bleeding on probing (BOP) and clinical attachment level (CAL). Moreover, experimental studies demonstrated that obesity status [64]. Lourenço et al. [64] demonstrated that different oral species, such as Porphyromonas gingivalis and Treponema denticola. Similar findings were reported in other studies, in which a positive correlation was found between T. forsythia and P. gingivalis and obesity measurements, such as BMI, waist circumference, and waist-hip ratio [61, 62]. Another study, targeting obese women, demonstrated that subgingival microbiota had only a few species differing between obese and non-obese with or without periodontitis [14]. It is worth stressing that those species, in particular P. gingivalis, are considered keystone pathogens in the context of the initiation of a dysbiosis in the periodontium [63]. A higher prevalence of P. gingivalis in obese individuals compared to non-obese individuals may be indicating an initial dysbiotic state [14]. Potentially, it would indicate an increase in the chances of future destructive disease in susceptible individuals [63].

Periodontal bacteria or their endotoxins and inflammatory products can directly or indirectly lead to systemic complications [2]. Frequent bacteremia and systemic spreading of local inflammation, known as metastatic inflammation, occur in patients with periodontitis, potentially impacting pre-existing or causing metabolic disorders [2]. Besides hemotogenic dissemination of bacteria, endotoxins, and inflammatory mediators, periodontal bacteria can disseminate through aspiration, i.e., hospitalized patients under artificial ventilation, or ingestion, which can cause inflammatory exacerbation in the lung or gut, respectively [2]. It has been demonstrated that ingested oral bacteria may colonize and persist in the gut [64], which can alter intestinal immune response, mainly through the accumulation of Th1 cells [65]. Gut microbiota diversity may be impacted by periodontal status [64]. Lourenço et al. [64] demonstrated that different oral species, such as Selenomonas, Leptotrichia, Tannerella, and Campylobacter, in stool samples from healthy or gingivitis/periodontitis patients, presented a positive significant association with bleeding on probing (BOP) and clinical attachment level (CAL). Moreover, experimental studies have demonstrated that animals fed with a high-fat diet and colonized with P. gingivalis may develop glucose intolerance because of the induced inflammation [66].

Periodontitis may also be associated with an impaired incretin axis in obese individuals [67••]. Solini et al. demonstrated that, while insulin levels were similar between obese individuals with and without periodontitis, significantly higher levels of glucoregulatory hormones, glucagon, and glucose-dependent insulintropic polypeptide (GIP) were found in obese individuals with periodontitis [67••]. Furthermore, individuals with periodontitis and obesity express higher levels of chemerin, an immune-modulatory adipokine molecule, in gingival crevicular fluid compared to non-obese periodontitis patients [68]. Moreover, other pro-inflammatory cytokines, such as interleukin-6 (IL-6), are as well highly expressed in periodontitis sites from obese compared to non-obese individuals with periodontitis [68].

Other adipokines, such as retinol-binding protein 4 (RBP4) and leptin, have been investigated in gingival crevicular fluid and serum of individuals with obesity and periodontitis [69, 70••, 71••, 72••, 73]. RBP4 induces the production of mediators that regulate the recruitment and adherence of leukocytes; while leptin is a proinflammatory cytokine that can be induced by lipopolysaccharide [69]. Higher levels of RBP4 in gingival crevicular fluid and serum can be found in obese compared to non-obese individuals with periodontal health. However, obese individuals with periodontitis present higher levels of RBP4 compared to non-obese individuals with periodontitis. Interestingly, the same study demonstrated that levels of leptin were higher in the gingival crevicular fluid of periodontally healthy obese and non-obese individuals compared to obese and non-obese individuals with periodontitis [69].

Insulin resistance, commonly observed feature in obese patients, is an initial step and key factor for T2DM and the development of metabolic syndrome [74]. Total circulating adiponecint and high molecular weight adiponectin inversely correlated with adiposity, BMI, glucose, insulin, and triglyceride levels, and visceral fat accumulation; as a consequence, they are decreased in obesity [75]. In this context, a close correlation between hypoadiponectinemia with a decrease in insulin sensitivity and T2DM has also been described in population-based studies [76, 77]. Thus, there is an inverse association between total plasma adiponectin levels and the incidence of T2DM [78, 79]. This correlation is corroborated by the intracellular crosstalk with insulin pathways since adiponectin directly interacts with insulin receptor substrates 1 and 2 (IRS1/2). This binding evokes downstream activation of PI3K, a major component of the insulin pathway [16], ameliorating the insulin response and triggering anti-inflammatory pathways in peripheral tissues (Fig. 1a). In individuals with normal insulin sensitivity, insulin activates two different paths. The first one is an anti-inflammatory, anti-apoptotic, and anti-oxidative path mediated by IRS activation. In this case, adiponectin acts as a co-activator of IRS response enhancing insulin sensitivity and a
strong anti-inflammatory molecule by inhibiting nuclear factor kappa-B (NFκ-B) response [80]. The secondary branch of the insulin pathway is MAPK/ERK activation related to cellular proliferation and growth that evokes a pro-inflammatory phenotype. However, in non-obese individuals, these two pathways are balanced (Fig. 1a) [81].
On the other hand, in insulin and adiponectin-resistant patients, the inflammatory status of adipose tissue disrupts the IRS arm of insulin pathways, favoring a pro-inflammatory phenotype. Initially, low circulating adiponectin results in a downregulation of the metabolic arm (IRS path) and nuclear translocation of unphosphorylated FOXO1, which, in turn, reduces adiponectin receptor synthesis and membrane translocation [82]. The downregulation of the adiponectin pathway results in oxidative stress and activation of NFκ-B (Fig. 1b) [16]. In addition, the low-grade inflammation observed in obese individuals is a result of augmented expression of inflammatory cytokines, by visceral adipose tissue [9]. Among those molecules expressed and synthesized by this dysfunctional tissue are tumor necrosis factor-alpha (TNF-α) and IL-6. In obese individuals, these pro-inflammatory adipokines act in an endocrine and/or paracrine manner to trigger insulin resistance, endothelial dysfunction, and vascular inflammation by inhibiting the IRS branch of the insulin pathway in peripheral tissues (Fig. 1b), favoring a pro-inflammatory response [10, 45]. Taken together, these molecular responses might be responsible for enhancing local inflammation, such as periodontitis, by inducing an insulin and adiponectin resistant status and elevating systemic inflammation.

Impact of Obesity on Periodontal Treatment

Interventional studies have investigated whether obesity may impair the outcomes of periodontitis treatment. A systematic review, which included eight studies, investigated the impact of obesity in the reduction of PD after non-surgical periodontal treatment [83]. Three reports included in that review demonstrated that obesity may not interfere with the clinical outcomes, while other five studies found obesity negatively influencing the reduction of PD after periodontal treatment, especially when moderate and severe PD were present before treatment. One of those studies found that the negative impact of obesity on clinical periodontal parameters can be compared to those of the smoking habit. However, another systematic review demonstrated that obesity does not impact periodontitis treatment [59].

More recently, other studies with obese and non-obese individuals demonstrated that obesity status does not impact clinical periodontal outcomes after non-surgical therapy [68, 71••, 72••, 73, 84••, 85]. Those studies demonstrated that periodontal treatment led to a significant improvement in periodontal conditions in both groups in a short term [68, 71••, 72••, 85], 6-month [73], and 9-month [84••] follow-up.
### Table 1  Intervention studies showing the impact of obesity on periodontal treatment results

| Study | Methods | Results |
|-------|---------|---------|
| Balli et al. [68] | **Aim:** - to investigate how the obesity/periodontitis and non-surgical periodontal treatment affect GCF chemerin levels in periodontitis and to understand how chemerin may be utilized as a potential diagnostic/prognostic biological indicator for periodontal disease - to discern the relation between chemerin and IL-6, a highly functional, proinflammatory adipocytokine | **Follow up:** 6 weeks  
**N** non-obese group: 20  
**N** obese group: 20  
Age: 30–49 years  
Periodontal status: generalized chronic periodontitis  
Treatment: non-surgical periodontal treatment in 2–3 visits  
Smoking: smokers were excluded | **PD (mm)**  
**Baseline**  
Non-obese: 4.1 ± 0.4  
Obese: 4.1 ± 0.2  
**6 weeks**  
Non-obese: 2.7 ± 0.4  
Obese: 2.8 ± 0.3 |
| Martinez-Herrera et al. [71••] | **Aim to:** - explore the effect of non-surgical periodontal treatment on parameters of oxidative stress in leukocytes and leukocyte-endothelial cell interactions in an obese population with periodontitis - determine whether adjunctive dietary therapy can modulate these responses | **Follow up:** 12 weeks  
**N** obese without diet group: 23  
**N** obese with diet group: 26  
Age: 30–60 years  
Periodontal status: stages I, II, and III periodontitis  
Treatment: non-surgical periodontal treatment in one session and adjunctive use of 0.12% chlorhexidine mouthwash for 14 days  
Smoking: percent of smoker similar between groups | **Absolute change**  
**Obese without diet**  
Mean PD (mm): −0.18 ± 0.22  
Mean CAL (mm): −0.18 ± 0.20  
Sites PD 4–5 mm (%): −9.22 ± 12.53  
BOP (%): −12.3 ± 13.6  
**Obese with diet**  
Mean PD (mm): −0.17 ± 0.16  
Mean CAL (mm): −0.13 ± 0.22  
Sites PD 4–5 mm (%): −8.11 ± 8.09  
BOP (%): −10.3 ± 10.9  
No significant differences were found between groups regarding absolute change at 12 weeks after periodontal therapy |
Martinez-Herrera et al. [72••]

**Aim to:**
- evaluate whether dietary weight loss intervention improves the response of obese subjects to non-surgical periodontal treatment
- explore whether the reduction in the levels of inflammatory parameters after weight loss correlates with the response to periodontal treatment

**Follow up:** 12 weeks

*Mean PD (mm)*

|                      | Baseline | 12 weeks |
|----------------------|----------|----------|
| Obese without diet  | 3.04 ± 0.49 | 2.92 ± 0.42 |
| Obese with diet     | 3.04 ± 0.46 | 2.81 ± 0.32 |

**Absolute change**

|                      | −0.12 ± 0.22 | −0.23 ± 0.23 |
|----------------------|--------------|--------------|
| Obese without diet  |              | *p < 0.05*   |
| Obese with diet     |              |              |

*No longer significant when adjusted by complement component 3 as a covariate*  

**Sites PD 4–5 mm (%)**

|                      | Baseline | 12 weeks |
|----------------------|----------|----------|
| Obese without diet  | 26.2 ± 14.7 | 20.3 ± 14.9 |
| Obese with diet     | 27.8 ± 14.7 | 17.5 ± 10.5 |

**Absolute change**

|                      | −5.89 ± 10.1 | −10.4 ± 9.86 |
|----------------------|--------------|--------------|
| Obese without diet  |              | *p < 0.05*   |
| Obese with diet     |              |              |

*No longer significant when adjusted by tumor necrosis factor-α as a covariate*

Martinez-Herrera et al. [70••]

**Aim to:**
- determine serum retinol-binding protein 4 (RBP4) levels in obese and lean subjects with and without chronic periodontitis and evaluate the effect of non-surgical periodontal treatment on serum RBP4 levels
- explore the relationship between RBP4 levels and other clinical and periodontal parameters

**Follow up:** 3 months

*Reduction in number of teeth with PD ≥ 4 mm*

|                      | Non-obese: 34.5% | Obese: 20.0% (*p* = 0.02 between groups) |

**Multivariate model analysis (dependent variable: n teeth with PD ≥ 4 mm)**

| Independent variables | β  | *p* |
|-----------------------|----|-----|
| PD                    | 0.785 | <0.001 |
| RBP4                  | 0.192 | 0.02 |

**Mean reduction in PD (mm; 95% CI)**

|                  | Non-obese: 0.6 (0.5, 0.8) | Obese: 0.4 (0.2, 0.6) |

**Mean reduction in CAL (mm; 95% CI)**

|                  | Non-obese: 0.6 (0.4, 0.7) | Obese: 0.5 (0.3, 0.7) |

**Mean reduction in BOP (%)**

|                  | Non-obese: 14.9 (9.0, 20.7) | Obese: 58.8 (45.6, 72.0) |

Md Tahir et al. [86]

**Aim to:**
- evaluate the impact of non-surgical periodontal therapy on clinical parameters, serum resistin level, and periodontal pathogen count in periodontitis patients with obesity and with normal weight

**Follow up:** 12 weeks

|                  | Non-obese group: 30 | Obese group: 18 |
|------------------|---------------------|-----------------|
| Age              | ≥30 years           |                 |

**Periodontal status:** chronic periodontitis

**Treatment:** non-surgical periodontal treatment and adjunctive use of 0.12% chlorhexidine mouthwash for 14 days

**Smoking:** 53% of non-obese were smokers; 17% of obese were smokers

**Mean reduction in PD (mm; 95% CI)**

|                  | Non-obese: 0.6 (0.5, 0.8) | Obese: 0.4 (0.2, 0.6) |

**Mean reduction in CAL (mm; 95% CI)**

|                  | Non-obese: 0.6 (0.4, 0.7) | Obese: 0.5 (0.3, 0.7) |

**Mean reduction in BOP (%)**

|                  | Non-obese: 14.9 (9.0, 20.7) | Obese: 58.8 (45.6, 72.0) |

Significant difference between groups for BOP
| Study                          | Methods                                                                 | Results                                                                                           |
|-------------------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| Peralta et al. [84••]        | Follow up: 9 months                                                     |                                                                                                  |
| Aim to:                       | N non-obese group: 39                                                   |                                                                                                  |
|                               | N obese group: 55                                                       |                                                                                                  |
|                               | Age: ≥45 years                                                          |                                                                                                  |
|                               | Periodontal status: periodontitis stages II, III, and IV                |                                                                                                  |
|                               | Treatment: one-stage full-mouth disinfection protocol                   |                                                                                                  |
|                               | Smoking: percent of smoker similar between groups                       |                                                                                                  |
|                               | Mean PD (mm)                                                            |                                                                                                  |
|                               | Baseline                                                               |                                                                                                  |
|                               | Non-obese: 2.98 ± 0.5                                                   |                                                                                                  |
|                               | Obese: 2.90 ± 0.3                                                       |                                                                                                  |
|                               | 9 months                                                               |                                                                                                  |
|                               | Non-obese: 2.27 ± 0.5                                                   |                                                                                                  |
|                               | Obese: 2.22 ± 0.4                                                       |                                                                                                  |
|                               | Mean CAL (mm)                                                           |                                                                                                  |
|                               | Baseline                                                               |                                                                                                  |
|                               | Non-obese: 4.23 ± 1.2                                                   |                                                                                                  |
|                               | Obese: 4.03 ± 0.9                                                       |                                                                                                  |
|                               | 9 months                                                               |                                                                                                  |
|                               | Non-obese: 3.67 ± 1.1                                                   |                                                                                                  |
|                               | Obese: 3.53 ± 1.0                                                       |                                                                                                  |
|                               | Gingival index                                                         |                                                                                                  |
|                               | Baseline                                                               |                                                                                                  |
|                               | Non-obese: 0.32 ± 0.3                                                   |                                                                                                  |
|                               | Obese: 0.37 ± 0.2                                                       |                                                                                                  |
|                               | 9 months                                                               |                                                                                                  |
|                               | Non-obese: 0.27 ± 0.1                                                   |                                                                                                  |
|                               | Obese: 0.23 ± 0.2                                                       |                                                                                                  |
|                               | No significant differences were found between groups for periodontal    |                                                                                                  |
|                               | clinical parameters evaluated after therapy                            |                                                                                                  |
|                               | Mean PD (mm)                                                            |                                                                                                  |
|                               | Baseline                                                               |                                                                                                  |
|                               | Non-obese: 3.37 ± 0.6                                                   |                                                                                                  |
|                               | Obese: 3.69 ± 0.7 (p < 0.05 between groups)                             |                                                                                                  |
|                               | 6 months                                                               |                                                                                                  |
|                               | Non-obese: 2.66 ± 0.4                                                   |                                                                                                  |
|                               | Obese: 2.86 ± 0.5 (p < 0.01 between groups)                             |                                                                                                  |
|                               | Mean CAL (mm)                                                           |                                                                                                  |
|                               | Baseline                                                               |                                                                                                  |
|                               | Non-obese: 3.91 ± 0.8                                                   |                                                                                                  |
|                               | Obese: 4.16 ± 0.9                                                       |                                                                                                  |
|                               | 6 months                                                               |                                                                                                  |
|                               | Non-obese: 3.26 ± 0.8                                                   |                                                                                                  |
|                               | Obese: 3.26 ± 0.8                                                       |                                                                                                  |
|                               | BOP (%)                                                                |                                                                                                  |
|                               | Baseline                                                               |                                                                                                  |
|                               | Non-obese: 47.34 ± 2.1                                                  |                                                                                                  |
|                               | Obese: 52.61 ± 19.4                                                    |                                                                                                  |
|                               | 6 months                                                               |                                                                                                  |
|                               | Non-obese: 21.73 ± 10.1                                                |                                                                                                  |
|                               | Obese: 31.2 ± 11.8 (p < 0.001 between groups)                          |                                                                                                  |

Suvan et al. [15••]           
Aim to:                        
- investigate the potential influence of intensive periodontal treatment on the association of periodontal inflammation with GIP and GLP-1 levels in obese and nonobese individuals

Follow up: 6 months
N non-obese group: 57
N obese group: 58
Age: ≥35 years
Periodontal status: generalized moderate to severe chronic periodontitis
Treatment: non-surgical periodontal treatment in a single-stage
Smoking: smokers not included

Mean PD (mm)
Baseline
Non-obese: 3.37 ± 0.6
Obese: 3.69 ± 0.7 (p < 0.05 between groups)

6 months
Non-obese: 2.66 ± 0.4
Obese: 2.86 ± 0.5 (p < 0.01 between groups)

Mean CAL (mm)
Baseline
Non-obese: 3.91 ± 0.8
Obese: 4.16 ± 0.9

6 months
Non-obese: 3.26 ± 0.8
Obese: 3.26 ± 0.8

BOP (%)
Baseline
Non-obese: 47.34 ± 2.1
Obese: 52.61 ± 19.4

6 months
Non-obese: 21.73 ± 10.1
Obese: 31.2 ± 11.8 (p < 0.001 between groups)
| Study                      | Methods                                                                 | Results                                                                 |
|---------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|
| Suvan et al. [87••]       | Follow up: 6 months                                                    | Percent of PD > 4 mm                                                   |
| Aim to:                   | N normal weight group: 58                                              | **Baseline**                                                          |
|                           | N obese group: 57                                                      | Normal: 26.68 (13.70)                                                  |
|                           | Age: ≥ 35 years                                                       | Obese: 32.01 (14.77) (p <0.05 between groups)                           |
|                           | Periodontal status: generalized moderate to severe chronic periodontitis | 6 months                                                               |
|                           | Treatment: non-surgical periodontal treatment in a single-stage        | Normal: 9.06 (6.75)                                                   |
|                           | Smoking: smokers were excluded                                         | Obese: 14.53 (10.09) (p =0.001 between groups)                         |
|                           |                                                                        | Percent of PD > 5 mm                                                  |
|                           |                                                                        | **Baseline**                                                          |
|                           |                                                                        | Normal: 13.79 (10.43)                                                 |
|                           |                                                                        | Obese: 17.87 (13.04)                                                  |
|                           |                                                                        | 6 months                                                               |
|                           |                                                                        | Normal: 3.31 (3.65)                                                   |
|                           |                                                                        | Obese: 6.92 (6.75) (p =0.001 between groups)                           |
|                           |                                                                        | **BOP (%)**                                                           |
|                           |                                                                        | **Baseline**                                                          |
|                           |                                                                        | Normal: 47.34 (20.10)                                                 |
|                           |                                                                        | Obese: 52.61 (19.47)                                                  |
|                           |                                                                        | 6 months                                                               |
|                           |                                                                        | Normal: 21.73 (10.14)                                                 |
|                           |                                                                        | Obese: 31.21 (11.82) (p <0.001 between groups)                         |
| Study | Methods | Results |
|-------|---------|---------|
| Wanichkittikul et al. [73] | Follow up: 6 months | Median PD (mm; Q1, Q3) |
| **Aim to:** | N NW with SP: 5 | **Baseline** |
| - investigate changes in serum leptin, adiponectin, and CRP levels after non-surgical periodontal treatment in Thai patients with overweight or obesity who did or did not exhibit severe periodontitis | N NW without SP: 7 | NW with SP: 5.91 (4.93, 6.38) |
| | N Owt/Ob with SP: 6 | NW without SP: 2.79 (2.63, 3.04) |
| | N Owt/Ob without SP: 11 | Owt/Ob with SP: 4.88 (4.07, 5.96) |
| | Age: ≥ 35 years | Owt/Ob without SP: 3.29 (2.85, 3.50) |
| | Periodontal status: severe and non-severe periodontitis | **6 months** |
| | Periodontal treatment: non-surgical periodontal treatment in 2–6 visits | NW with SP: 3.96 (3.28, 4.17) |
| | Smoking: smokers were excluded | NW without SP: 1.29 (1.11, 1.70) |
| | Median CAL (mm; Q1, Q3) | Owt/Ob with SP: 3.41 (2.81, 4.30) |
| | Baseline | Owt/Ob without SP: 1.26 (1.19, 1.67) |
| | 6 months | (significant reduction after treatment in all groups) |
| | NW with SP: 6.36 (5.12, 7.37) | Median BOP (%; Q1, Q3) |
| | NW without SP: 1.46 (1.18, 2.96) | **Baseline** |
| | Owt/Ob with SP: 6.04 (5.16, 8.48) | NW with SP: 85.33 (83.95, 100.00) |
| | Owt/Ob without SP: 1.30 (0.67, 3.00) | NW without SP: 62.96 (36.90, 66.67) |
| | 6 months | Owt/Ob with SP: 81.64 (68.24, 99.31) |
| | NW with SP: 5.05 (4.18, 5.96) | Owt/Ob without SP: 81.25 (74.40, 91.23) |
| | NW without SP: 1.33 (0.89, 1.79) | **6 months** |
| | Owt/Ob with SP: 5.02 (4.42, 7.19) | NW with SP: 23.46 (21.03, 32.59) |
| | Owt/Ob without SP: 1.50 (0.26, 2.39) | NW without SP: 20.24 (14.88, 24.07) |
| | (significant reduction after treatment, except for NW without SP group) | Owt/Ob with SP: 25.37 (23.07, 33.08) |
| | Median BOP (%; Q1, Q3) | Owt/Ob without SP: 21.43 (17.90, 23.21) |
| | Baseline | (significant reduction after treatment in all groups) |
| Study | Methods | Results |
|-------|---------|---------|
| Zuza et al. [85] | Follow up: 3 months  
N non-obese group: 26  
N obese group: 28  
Age: 35–55 years  
Periodontal status: generalized moderate to severe chronic periodontitis  
Treatment: non-surgical periodontal treatment in a single stage  
Smoking: smokers were excluded | Percent of PD 4–6 mm  
Baseline  
Non-obese: 37.5 ± 4.1  
Obese: 39.9 ± 6.2  
3 months  
Non-obese: 7.7 ± 1.8 (p < 0.05 within group)  
Obese: 8.7 ± 3.3 (p < 0.05 within group)  
Percent of PD ≥ 7 mm  
Baseline  
Non-obese: 6.6 ± 3.9  
Obese: 5.3 ± 4.1  
3 months  
Non-obese: 1.7 ± 0.6 (p < 0.05 within group)  
Obese: 2.1 ± 1.9 (p < 0.05 within group)  
Percent of CAL 4–6 mm  
Baseline  
Non-obese: 44.3 ± 4.4  
Obese: 39.5 ± 5.4  
3 months  
Non-obese: 21.8 ± 3.9 (p < 0.05 within group)  
Obese: 23.8 ± 4.4 (p < 0.05 within group)  
Percent of CAL ≥ 7 mm  
Baseline  
Non-obese: 9.7 ± 3.6  
Obese: 8.3 ± 2.9  
3 months  
Non-obese: 2.6 ± 2.1 (p < 0.05 within group)  
Obese: 3.0 ± 2.6 (p < 0.05 within group)  
BOP (%)  
Baseline  
Non-obese: 45.6 ± 3.1  
Obese: 48.5 ± 2.6  
3 months  
Non-obese: 7.9 ± 2.1 (p < 0.05 within group)  
Obese: 7.1 ± 1.9 (p < 0.05 within group) |

CAL clinical attachment level, BOP bleeding on probing, GCF gingival crevicular fluid, IL interleukin, NW normal weight, Owt/Ob overweight/obese, PD probing depth, Q1 first quartile, Q3 third quartile, SP severe periodontitis
post-therapy (Table 1). Conversely, Martinez-Herrera et al. [70••] found a significant difference in the extension of teeth with PD ≥ 4 mm after treatment in 3 months post-therapy when obese was compared to non-obese individuals. In that study, lean individuals had a 34.5% reduction in the number of teeth with PD ≥ 4 mm, while obese individuals had only 20% as displayed in Table 1. Another short period evaluation also demonstrated a lesser improvement in the extension of BOP in obese compared to non-obese individuals with periodontitis [86]. In a 6-month evaluation after treatment, Suvan et al. [87••] were also able to demonstrate that obese patients had significantly less improvement in periodontal parameters after therapy compared to lean individuals. Those differences were detected in the final percent of PD > 4 mm, percent of PD > 5 mm, and percent of pulp involved (Table 1). Another study by Suvan et al. [15••] demonstrated at 6 months that, although a significant reduction was detected in mean PD and percent of BOP is detected in comparison with baseline, those parameters were significantly higher in obese compared to non-obese with similar mean CAL and percent of BOP in the baseline (Table 1).

The impact of weight loss has also been evaluated concerning periodontal status after bariatric surgery or dietary therapy [71••, 72••, 88•]. Dos Santos et al. [88•] performed a systematic review to assess whether bariatric surgery would have any influence on the clinical periodontal conditions in obese patients with periodontitis. Four out of 6 included studies showed that patients had worst periodontal conditions after bariatric procedures up to 12 months of observation.

Treatment of periodontitis associated with dietary therapy was investigated by Martinez-Herrera et al. [72••] who demonstrated that obese individuals that lose weight along with periodontal treatment have a significantly higher reduction in mean PD and percentage of sites with moderate PD (4 to 5 mm) than obese individuals with periodontitis without weight loss (Table 1). However, when researchers adjusted their data for complement 4 and TNF-α, respectively, those differences were no longer significant. Another study by Martinez-Herrera et al. [71••] confirmed that, demonstrating that obese individuals on low-calorie diet compared to a group without diet had similar clinical periodontal outcomes after non-surgical periodontal treatment (Table 1).

Impact of Periodontal Treatment on Systemic Health of Obese Individuals

Another question investigated is whether periodontal treatment can impact obesity biomarkers, which could result in an improvement in systemic health. Balli et al. [68] demonstrated that non-surgical periodontal treatment can lead to a decrease in the expression of chemerin in gingival crevicular fluid in obese individuals with periodontitis. Even though it was tested locally, it is potentially indicating that systemic levels of that adipokine might be reduced after periodontal therapy. However, other investigations showed that periodontal treatment was not efficient in reducing serum levels of resistin in obese and non-obese individuals [86]. On the other hand, Suvan et al. [15••] demonstrated that obese individuals can significantly reduce their systemic levels of glucagon after periodontal treatment, becoming similar to the ones of non-obese individuals (Table 2). Periodontitis treatment can also lead to a reduction in systemic levels of leptin, and C-reactive protein, especially in patients with severe periodontitis [73, 85]. Periodontal therapy can also contribute to a significant increase in systemic levels of adiponectin [73]. Moreover, an improvement in the lipid profile of obese individuals may also be a consequence of the treatment of periodontitis [85] (Table 2).

Further analysis of Martinez-Herrera et al. [71••] investigated oxidative stress in leukocytes and leukocyte-endothelial cell interactions after treatment of periodontitis in obese individuals with or without dietary treatment. It was interesting to observe that both groups, with or without low calories diet, had their serum levels of RBP4 and TNF-α significantly decreased after periodontal treatment. Moreover, another striking piece of data is that periodontal treatment alone was able to reduce total superoxide and intracellular calcium as found in without diet group. It is important to highlight that finding because it may be indicating that periodontal treatment may help improve the systemic conditions of obese individuals under weight-loss therapy. Another study by Martinez-Herrera et al. [70••] compared non-obese and obese individuals regarding serum levels of many biochemical parameters after treatment of periodontitis (Table 2). Once again, the authors were able to demonstrate that periodontal treatment alone can significantly reduce serum levels of RBP4 and TNF-α in 12 weeks of observation. The effect of dietary therapy and periodontal treatment was also investigated by the same group on systemic parameters of inflammation [72••]. It was observed that levels of RBP4 reduce after therapy in both, regardless of the diet. However, a significant decrease in levels of TNF-α and C3 was observed after periodontal therapy only for the obese individuals going on a low calory diet (Table 2).

Conclusions

Recent literature demonstrated that obese individuals with periodontitis benefit from non-surgical periodontal treatment. However, periodontal therapy can result in inferior clinical improvements in obese individuals compared to non-obese ones. Nevertheless, available evidence demonstrated that periodontal treatment significantly reduces...
### Table 2 Impact of periodontal treatment on obesity biomarkers

| Study                          | Methods                                                                 | Results                                                                 |
|-------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Martinez-Herrera et al. [71••] | Additional information on Table 1                                       | **Levels of RBP4**                                                      |
|                               | Studied parameters:                                                     | **Baseline**                                                           |
|                               | - Systemic levels of RBP4                                               | Obese without diet: 4.4 ± 0.9                                           |
|                               | - Systemic levels of TNF-α                                               | Obese with diet: 3.7 ± 1.1                                             |
|                               | - Oxidative stress of leucocytes (total ROS production, super-oxygen production, levels of cytosolic Ca²⁺, mitochondrial membrane potential) | **12 weeks**                                                           |
|                               | - Antioxidant status                                                    | Obese without diet: 3.9 ± 1.1*                                          |
|                               | - Leucocytes and endothelial cells interaction                          | Obese with diet: 3.3 ± 0.9*                                            |
|                               |                                                                         | **Levels of TNF-α**                                                    |
|                               |                                                                         | **Baseline**                                                           |
|                               |                                                                         | Obese without diet: 17.8 ± 3.1                                         |
|                               |                                                                         | Obese with diet: 17.1 ± 6.2                                           |
|                               |                                                                         | **12 weeks**                                                           |
|                               |                                                                         | Obese without diet: 16.5 ± 4.1                                         |
|                               |                                                                         | Obese with diet: 13.0 ± 1.8*                                           |
|                               |                                                                         | * intragroup analysis, a significant difference compared to baseline   |
|                               |                                                                         | After treatment, both groups had a significant reduction in:           |
|                               |                                                                         | - Total superoxide                                                    |
|                               |                                                                         | - Intracellular calcium                                                |
| Martinez-Herrera et al. [72••] | Additional information on Table 1                                       | **Levels of RBP4**                                                    |
|                               | Studied parameters:                                                     | **Baseline**                                                           |
|                               | - glucose                                                               | Obese without diet: 3.78 ± 1.11                                        |
|                               | - insulin                                                               | Obese with diet: 3.79 ± 1.11                                           |
|                               | - HOMA-IR                                                               | **12 weeks**                                                           |
|                               | - TC                                                                    | Obese without diet: 3.44 ± 1.05 (p < 0.05 within group)                |
|                               | - HDL-C                                                                 | Obese with diet: 3.36 ± 0.97 (p < 0.05 within group)                   |
|                               | - LDL-C                                                                 | **Levels of TNF-α**                                                    |
|                               | - TG                                                                    | **Baseline**                                                           |
|                               | - TNF-α                                                                 | Obese without diet: 19.0 ± 11.7                                        |
|                               | - IL-6                                                                  | Obese with diet: 16.3 ± 9.6                                           |
|                               | - hs-CRP                                                                | **12 weeks**                                                           |
|                               | - C3                                                                    | Obese without diet: 14.4 ± 4.7                                         |
|                               | - RBP4                                                                  | Obese with diet: 11.9 ± 4.2 (p < 0.05 within group)                    |
|                               |                                                                         | **Levels of C3**                                                       |
|                               |                                                                         | **Baseline**                                                           |
|                               |                                                                         | Obese without diet: 128 ± 18                                          |
|                               |                                                                         | Obese with diet: 137 ± 30                                             |
|                               |                                                                         | **12 weeks**                                                           |
|                               |                                                                         | Obese without diet: 129 ± 28                                          |
|                               |                                                                         | Obese with diet: 124 ± 32 (p < 0.05 within group)                      |
| Martinez-Herrera et al. [70••] | Additional information on Table 1                                       | **Levels of RBP4**                                                    |
|                               | Studied parameters:                                                     | **Baseline**                                                           |
|                               | - glucose                                                               | Non-obese: 3.2 ± 0.6                                                  |
|                               | - insulin                                                               | Obese: 3.8 ± 1.0                                                      |
|                               | - HOMA-IR                                                               | **12 weeks**                                                           |
|                               | - TC                                                                    | Non-obese: 3.0 ± 0.7*                                                 |
|                               | - HDL-C                                                                 | Obese: 3.4 ± 1.0*                                                    |
|                               | - LDL-C                                                                 | **Levels of TNF-α**                                                    |
|                               | - TG                                                                    | **Baseline**                                                           |
|                               | - TNF-α                                                                 | Non-obese: 10.8 ± 3.8                                                 |
|                               | - IL-6                                                                  | Obese: 17.2 ± 9.8                                                     |
|                               | - hs-CRP                                                                | **12 weeks**                                                           |
|                               | - RBP4                                                                  | Non-obese: 9.6 ± 4.9*                                                |
|                               |                                                                         | Obese: 13.9 ± 5.3*                                                   |
|                               |                                                                         | * intragroup analysis, a significant difference compared to baseline   |
|                               |                                                                         | No other parameter showed a significant difference after periodontal treatment in both groups |
| Study                          | Method                          | Results                                                                 |
|-------------------------------|---------------------------------|-------------------------------------------------------------------------|
| Md Tahir et al. [86]          | Additional information on Table 1 | *Levels of resistin* (95% CI)                                           |
| Parameter:                    |                                 | Baseline                                                               |
| - Serum resistin              |                                 | Non-obese: 6.9 (4.3, 9.6)                                              |
|                               |                                 | Obese: 14.7 (10.8, 18.5)                                               |
|                               |                                 | **12 weeks**                                                            |
|                               |                                 | Non-obese: 9.5 (6.9, 12.0)                                              |
|                               |                                 | Obese: 17.6 (12.4, 22.7)                                               |
|                               |                                 | **Mean change**                                                         |
|                               |                                 | Non-obese: 2.5 (0.9, 4.1)                                              |
|                               |                                 | Obese: 2.9 (−3.4, 9.3)                                                 |
| Suvan et al. [15••]           | Additional information on Table 1 | *Levels of insulin*                                                    |
| Studied parameters:           |                                 | Baseline: higher in obese (*p* < 0.001)                                |
| - TC                          |                                 | **6 months**: higher in obese (*p* < 0.001)                            |
| - HDL-C                       |                                 | *Levels of glucagon*                                                   |
| - LDL-C                       |                                 | Baseline: higher in obese (*p* < 0.006)                                |
| - TG                          |                                 | **6 months**: similar between groups                                   |
| - glucose                     |                                 | *Levels of GLP-1*                                                      |
| - insulin                     |                                 | Baseline: similar between groups                                       |
| - HOMA-IR                     |                                 | **6 months**: similar increase in both groups (*p* < 0.05 compared to baseline) |
| - HOMAXB                      |                                 | *Levels of GIP*                                                        |
| - hs-CRP                      |                                 | Baseline: similar between groups                                       |
| - MDA                         |                                 | **6 months**: similar increase in both groups                           |
| - glucagon                    |                                 |                                                                         |
| - GLP-1                       |                                 |                                                                         |
| - GIP                         |                                 |                                                                         |
| Wanichkittikul et al. [73]    | Additional information on Table 1 | *Levels of leptin* (median Q1, Q3)                                     |
| Studied parameters:           |                                 | Baseline                                                               |
| - Leptin                      |                                 | NW with SP: 12.13 (9.93, 20.70)                                        |
| - Adiponectin                 |                                 | NW without SP: 6.69 (5.99, 11.29)                                      |
| - CRP                         |                                 | Owt/Ob with SP: 16.17 (8.32, 28.93)                                    |
|                               |                                 | Owt/Ob without SP: 15.76 (11.40, 23.35)                                |
|                               |                                 | **6 months**                                                           |
|                               |                                 | NW with SP: 10.10 (6.16, 17.25)                                        |
|                               |                                 | NW without SP: 6.70 (4.72, 7.75)                                       |
|                               |                                 | Owt/Ob with SP: 12.80 (7.18, 21.81)                                    |
|                               |                                 | Owt/Ob without SP: 13.61 (9.90, 20.42)                                 |
|                               |                                 | (**significant reduction after treatment, except for NW without SP group**) |
|                               |                                 | *Levels of adiponectin* (median Q1, Q3)                                |
|                               |                                 | Baseline                                                               |
|                               |                                 | NW with SP: 4.23 (2.69, 6.44)                                          |
|                               |                                 | NW without SP: 3.22 (2.70, 5.02)                                       |
|                               |                                 | Owt/Ob with SP: 4.57 (2.90, 6.45)                                      |
|                               |                                 | Owt/Ob without SP: 3.29 (2.00, 4.82)                                   |
|                               |                                 | **6 months**                                                           |
|                               |                                 | NW with SP: 5.85 (3.65, 9.08)                                          |
|                               |                                 | NW without SP: 5.48 (4.86, 7.92)                                       |
|                               |                                 | Owt/Ob with SP: 6.81 (5.35, 7.96)                                      |
|                               |                                 | Owt/Ob without SP: 4.18 (3.25, 7.68)                                   |
|                               |                                 | (**significant increase after treatment in all groups**)              |
|                               |                                 | *Levels of CRP* (median Q1, Q3)                                        |
|                               |                                 | Baseline                                                               |
|                               |                                 | NW with SP: 1.58 (0.66, 3.97)                                          |
|                               |                                 | NW without SP: 0.56 (0.41, 4.36)                                       |
|                               |                                 | Owt/Ob with SP: 3.17 (2.08, 8.04)                                      |
|                               |                                 | Owt/Ob without SP: 3.35 (1.41, 5.64)                                   |
|                               |                                 | **6 months**                                                           |
|                               |                                 | NW with SP: 0.84 (0.44, 2.71)                                          |
|                               |                                 | NW without SP: 0.50 (0.20, 6.33)                                       |
|                               |                                 | Owt/Ob with SP: 2.10 (0.72, 5.29)                                      |
|                               |                                 | Owt/Ob without SP: 2.47 (0.88, 3.26)                                   |
|                               |                                 | (**significant reduction after treatment in all groups**)             |
several biochemical biomarkers of obesity with or without weight reduction. Further investigations are needed to improve our comprehension of mechanisms that can explain that mechanism.

Despite controversies in clinical findings after periodontal therapy in obese individuals, dental professionals should be aware that obesity is a chronic metabolic disease, and that periodontal treatment should be a part of a comprehensive treatment of obesity. It is reasonable to propose that the management of periodontitis in obese individuals should require the interaction between dental professionals and other health care providers, as physicians, nutritionists, and physical educators. On the other hand, obese individuals should be referred for periodontal prevention and treatment not only to promote improvement in systemic inflammatory status but also in the quality of life.

### Compliance with Ethical Standards

#### Conflict of Interest

The authors declare no competing interests.

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- Of major importance

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