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Review Article

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Surgical treatment of the residual periodontal pocket

Surgery of residual pockets

Graziani et al.

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Abstract

The ultimate goal of periodontal therapy is to prevent further disease progression in order to reduce the risk of tooth loss. This objective can be achieved through a number of therapeutic modalities comprising both the nonsurgical and surgical phases of periodontal therapy. Nonsurgical periodontal treatment has been shown to control periodontal infection and to arrest progression of the disease in a significant number of cases. However, despite completion of nonsurgical treatment, a portion of periodontal pocketsAUTHOR: Would it be possible to clarify in a little more detail (preferably providing a percentage, if possible) what you mean by ‘a portion’ in the phrase ‘a portion of periodontal pockets’, defined as ‘residual’, often remain. The presence of residual pockets may jeopardize tooth survival and be a risk factor of further disease progression, and ultimately tooth loss. Therefore, the aim of this review is to critically evaluateAUTHOR: The phrase ‘to critically evaluate’ is a split infinitive. Please reword the text to remove it, if this can be done in a way in which the correct meaning of the text can be retained. the knowledge available on the indications for and the performance of periodontal surgical treatment of residual pockets in terms of ‘traditional’ (clinical, microbiological), patient-based and systemic health outcomes.

Introduction

The ultimate goal of periodontal therapy is to prevent further disease progression in order to reduce the risk of tooth loss and to restore the tissues that have been lost as a result of periodontitis. These objectives may often be achieved through a number of therapeutic modalities comprising both nonsurgical and surgical phases of periodontal therapyAUTHOR: The term ‘phases of’ is unclear in the phrase ‘comprising both nonsurgical and surgical

phases of periodontal therapy'. Could the phrase be reworded as 'comprising both nonsurgical and surgical periodontal therapy'>. (i.e. the active phase of treatment), which aim to arrest progressive attachment loss, reduce probing pocket depths and control both systemic and local risk factors associated with periodontal disease (1, 40).

Whilst nonsurgical therapy is often successful in controlling periodontal disease, in sites with persistent inflammation and deep pockets, surgical treatment modalities are often considered as the next phase of therapy. The primary aims of periodontal surgery are to create accessibility for proper professional scaling and root planing and to establish a gingival morphology that facilitates efficient patient self-performed infection controlAUTHOR: Please check the wording of the phrase 'that facilitates efficient patient self-performed infection control'. Would something like 'that facilitates efficient infection control self-performed by the patient' be clearer? Please indicate any changes required to the original text to clarify its intended meaning. (96). This is achieved by improved access to the periodontally involved root surface, by correcting the anatomical and morphological sequelae of periodontitis, as well as by reconstructing, and when possible regenerating, the lost (periodontal) tissues. However, the clinical decision-making process and indications for surgical periodontal treatment have not yet been fully clarifiedAUTHOR: For sense, the phrase 'are not entirely clarified' has been reworded as 'have not yet been fully clarified'. Please check/approve the changes..

More than two decades ago, the concept of a 'critical probing depth', defined as a threshold (given in mm) under which treatment may not be beneficialAUTHOR: For clarity, the phrase 'defined as a threshold of mm under which treatment may not be beneficial' has been reworded as 'defined as a threshold (given in mm) under which treatment may not be beneficial'. Please check/approve the changes., was advocated (10, 11, 39, 49). Indeed, whilst nonsurgical periodontal treatment is indicated in the presence of periodontal

pocketsAUTHOR: For clarity, should ‘in the presence of periodontal pockets’ be replaced with ‘for periodontal pockets’? Please indicate any changes required. associated with supra- and subgingival plaque and/or calculus, bleeding on probing and inadequate self-performed plaque control, surgical treatment is often solely recommended in the presence of residual pocketsAUTHOR: For clarity, should ‘in the presence of residual pockets’ be replaced with ‘for residual pockets’? Please indicate any changes required.. The aim of this review was therefore to evaluate the knowledge available on the indications and performance of periodontal surgical treatment of residual pockets in terms of traditional and patient-based periodontal outcomes.

The residual periodontal pocket: effect on disease progression

Nonsurgical periodontal treatment has been proven to reduce a significant amount of periodontal disease (40). Nevertheless, a portionAUTHOR: Would it be possible to clarify in a little more detail (preferably providing a percentage, if possible) what you mean by ‘a portion’. of periodontal pockets, defined as ‘residual’, often remains after nonsurgical treatment. The presence of residual pockets may jeopardize tooth survival and be a determinant of further disease progression and ultimately tooth loss (21, 55). In a review from the 1996 World Workshop in Periodontics, the scientific literature dealing with periodontal diagnostics published from 1989 to 1995 was reviewedAUTHOR: The sentence ‘In a review from the 1996 World Workshop in Periodontics, the scientific literature dealing with periodontal diagnostics published from 1989 to 1995 was reviewed’ jars slightly when read because of the use of ‘review/reviewed’. Would something like ‘In a review from the 1996 World Workshop in Periodontics, scientific literature dealing with periodontal diagnostics, published from 1989 to 1995, was analyzed’ be slightly better here? Please indicate the changes required (if any) to the wording of the original text. (3). Amongst the various aspects related to periodontal diagnostic procedures, the variables that might be of significant

importance in identifying patients that are more susceptible to present with further disease progression following active therapy were investigated. It was concluded that a residual probing pocket depth of ≥ 6 mm had an odds ratio of 10 for periodontal disease progression. In a study by Claffey & Egelberg (10), 16 patients diagnosed with advanced periodontitis underwent initial periodontal treatment. The participants were monitored every 3 months over a 42-month period. Clinical characteristics at baseline and during the 42-month maintenance period were investigated for their association with probing attachment loss. AUTHOR: Is the phrase 'probing attachment loss' correct or do you mean 'probing depth and attachment loss'? Please indicate any changes required., at both patient and site levels (8). The authors reported that the presence of high proportions. AUTHOR: Would it be possible to quantify 'high proportions' (e.g. provide a percentage)? of residual probing pocket depths of ≥ 6 mm after initial nonsurgical periodontal therapy predictably indicated further attachment loss over a 42-month period.

The association of residual pockets and other clinical parameters, such as plaque score, bleeding on probing and response to initial nonsurgical periodontal therapy, have been considered to describe more accurately the probability of further attachment loss and tooth loss at subject level (22, 55, 88). Despite the general effectiveness of surgical treatments and meticulous supportive periodontal therapy, some subjects may still present with disease progression and tooth loss over a number of years. Tonetti et al. (88), in a retrospective study on 273 periodontal patients participating in a supportive periodontal therapy program, reported an overall incidence of tooth mortality of 0.23 ± 0.49 teeth per patient per year. Interestingly, a subpopulation of subjects, presenting 10 or more residual pockets with probing pocket depth $\geq 4-5$ mm and bleeding on probing, had an incidence of tooth loss of 0.37 ± 0.81 teeth per patient per year, representing a group of high-risk patients.

In a retrospective cohort of 172 subjects with a mean follow up of 11 years, the significance of residual pockets as a predictive parameter for periodontal disease progression and tooth loss was studied (55). All patients had previously received the active phase of treatment and regular supportive periodontal therapy. The authors observed that the number of residual periodontal pockets increased during supportive periodontal therapy, and as residual probing pocket-depth values incrementally increased, so did the odds ratio for tooth loss. More precisely, a residual probing pocket depth of 5 mm represented a risk factor for tooth loss at site and tooth levels, with odds ratios of 5.8 and 7.7, respectively. The odds ratios for deeper pockets were even higher. The authors concluded that at patient level, heavy smoking, initial diagnosis, duration of supportive periodontal therapy and residual probing pocket depth of ≥ 6 mm were all risk factors for disease progression. Interestingly, it was observed that in subjects receiving supportive periodontal therapy for <10 years, only probing pocket depth of ≥ 7 mm was associated with a significantly higher risk for tooth loss (odds ratio = 18.0; 95% confidence interval: 2.6–125.4); in subjects receiving supportive periodontal therapy for 10 years or longer, an initial probing pocket depth of 5 mm was significantly associated with tooth loss.

Thus, overall there is substantial evidence to state that a residual site with probing pocket depth of ≥ 6 mm represents a true risk factor for both periodontal disease progression and tooth loss. However, the evidence also corroborates that a site with a probing pocket depth of 5 mm is also associated with tooth loss in the long term, therefore, the aim of periodontal treatment should be the closure/elimination of sites with probing pocket depth ≥ 5 mm. AUTHOR: You use 'also' twice in the sentence 'However, the evidence also corroborates that a site with a probing pocket depth of 5 mm is also associated with tooth loss in the long term, therefore, the aim of periodontal treatment should be the closure/elimination of sites with probing pocket depth ≥ 5 mm'. Accordingly, could the sentence be reworded as

something like ‘However, as the evidence corroborates that a site with a probing pocket depth of 5 mm is associated with tooth loss in the long term, the aim of periodontal treatment should be closure/elimination of sites with probing pocket depth ≥ 5 mm’? Please indicate the changes required (if any) to the original text..

Indications for surgical treatment of residual pocketing

Residual pocketing: nonsurgical retreatment or surgery?

Because of the paucity of the literature on residual pocketing, it is difficult to establish which patient/pockets should further be retreated nonsurgically (with or without adjunctive local antibiotics) or surgically. AUTHOR: For clarity, I have reworded the sentence ‘In the case of residual pocketing, it is difficult to establish which patient/pockets should be further re-treated non-surgically, with or without adjunctive local antibiotics, or surgically due to the paucity of the literature on this specific topic’ as ‘Because of the paucity of the literature on residual pocketing, it is difficult to establish which patient/pockets should further be retreated nonsurgically (with or without adjunctive local antibiotics) or surgically’. Please check/approve the changes.. Serino et al. (78), randomly allocated 64 patients whom were already treated nonsurgically. AUTHOR: Please check the wording of the phrase ‘whom were already treated nonsurgically’. Would ‘who had already been treated nonsurgically’ or ‘who were currently undergoing nonsurgical treatment’ be a clearer description of what is meant here? Please indicate any changes required., and presented with deep residual pockets (probing pocket depth >6 mm), to two treatment groups: one surgical and one nonsurgical. All subjects were actively treated. AUTHOR: For consistency with the descriptions given earlier in your article, should the phrase ‘were actively treated’ be replaced with ‘received the active phase of treatment’? Please indicate any changes required. then were meticulously provided with supportive periodontal therapy three to four times per year and followed up for 13 years. Both treatment groups exhibited high standards of self-performed oral hygiene

throughout the entire 13-year follow-up period, maintaining plaque scores at levels below 15%. The data indicate that nonsurgical treatment results in AUTHOR: 'showed a' replaced with 'results in'. Do you agree? a higher percentage of residual periodontal pockets, whilst surgical treatment demonstrates a better performance in terms of pocket closure. The nonsurgical treatment group exhibited 1.6 ± 1.7 (mean \pm standard deviation) AUTHOR: I have added '(mean \pm standard deviation)'. Is this what is meant here? lost teeth, whereas, in contrast, the surgical group exhibited 0.6 ± 1.1 lost teeth.

Tomasi et al. (85), in a multilevel analysis, indicated the sites that may not respond to a second session of nonsurgical treatment and therefore require a surgical intervention (86). Thirty-two patients with residual pockets (of probing pocket depth ≥ 5 mm) 3 months after nonsurgical treatment were randomly assigned to one of two retreatment protocols: ultrasonic instrumentation alone; or ultrasonic instrumentation plus application of an 8.8% doxycycline gel. The authors concluded that the probability of pocket closure was not improved by the adjunctive antibiotic therapy. Interestingly, the multilevel regression analysis revealed that none of the selected subject-related variables of age, gender or smoking had a significant impact on the outcome. Conversely, the presence of plaque at a single site had a significant, negative impact on the outcome. Furthermore, the presence of furcation involvement (degree 2 or 3) at molar sites, and any sites associated with the presence of an angular bony defect, showed significantly poorer treatment results (85). Regarding the molars presenting with furcation involvement, the multilevel analysis revealed that adjunctive application of doxycycline had no significant effect on the outcome variable and nor did plaque, age or sex. The results of this study show that initial vertical probing pocket depth and degree of initial furcation involvement were factors significant at site level, and current smoking was a significant factor at patient level (86). In those aforementioned conditions, a second session of

nonsurgical treatment did not lead to further improvement and therefore a surgical approach may be necessary.

Conclusion/treatment suggestions

There is significant evidence to support the idea that residual pockets of ≥ 5 mm after nonsurgical periodontal treatment represent a risk factor for further disease progression and tooth loss and therefore constitute a clear indication for periodontal surgery (Fig. 1). Residual pockets of 4, 5 or 6 mm or deeper have been suggested as a clear indication for a surgical intervention (10, 11, 49, 55, 88). Nonsurgical retreatment may be attempted if moderate residual pockets are associated with nonmolar, nonfurcated teeth possibly showing a suprabony pattern of bone loss (85).

More specifically:

- Probing pocket depth ≤ 4 mm. Numerous studies have evaluated the effect of surgery on shallow sites (probing pocket depth < 4 mm) and have concluded that a surgical approach created a loss of mean clinical attachment and importantly, gingival recession (44, 45, 60). Therefore, a probing pocket depth of ≤ 4 mm does not represent an indication for surgery. A nonsurgical periodontal treatment approach appears to be more appropriate.
- Probing pocket depth ≥ 5 mm. A number of studies have suggested that a probing pocket depth of ≥ 5 mm is a clear indication for a surgical intervention (44, 47, 85, 86),(), ()AUTHOR: Are references missing here or should ‘,(), ()’ be deleted?.
- Probing pocket depth ≥ 6 mm. A systematic review indicated probing pocket depth ≥ 6 mm as the threshold for surgical treatment of periodontal pockets (40). Numerous authors agree that surgical intervention of deep lesions would permit gaining more in terms of probing pocket depth when compared with a nonsurgical approach. This is in agreement with other studies of deeper pockets (78).

Performance of surgical intervention on residual pockets

Effect of conservative periodontal surgery on residual pockets

‘Pocket elimination’, defined as pocket-depth reduction to gingival sulcus levels, has been considered. AUTHOR: Please check the tense of the phrase ‘has been considered’. Would ‘is considered’ be more accurate? Please indicate any changes required. one of the main goals of periodontal therapy. This procedure is indeed essential because of the need to improve accessibility to root surfaces for the therapist during treatment and for the patient during periodontal maintenance and self-performed oral hygiene (96). Pocket elimination is usually associated with all periodontal surgical approaches utilizing a ‘respective’ surgical approach. In contrast, the term, ‘pocket closure’ is usually associated with more conservative approaches, when no attempt of a physical reduction of the gingival tissue is performed but the treatment strategy focuses on enhancing the cleaning of the colonized root surface in order to trigger wound healing with minimal tooth loss (46, 70, 81).

Surgical treatment of pockets remaining. AUTHOR: ‘residing’ replaced with ‘remaining’. Do you agree? after successful cause-related therapy aims to re-establish periodontal anatomy and create an oral ambient compatible with periodontal health. Periodontal osseous defects are differentiated into suprabony, intrabony and inter-radicular or furcation. According to the classification by Goldman & Cohen (30), suprabony defects are those in which the base of the pocket is located coronal to the alveolar crest. Intrabony defects, on the other hand, are defined by the apical location of the base of the pocket with respect to the residual alveolar crest. Inter-radicular or furcation defects are the result of conditions entailing pathological resorption of bone within the furcation of a multirrooted tooth. Different surgical approaches, varying from access flaps to resective or regenerative techniques, have been suggested to treat residual periodontal defects.

Conservative surgery (i.e. access flaps) encompasses a range of surgical procedures aimed at gaining access to the root surface in order to remove residual plaque/calculus. There is no

active removal of alveolar bone and minimal resection of soft tissues. Graziani et al. (32) classified these procedures into open flap debridement (46), minimally resective flaps (e.g. the modified Widman flap) (70) and flaps aimed at conserving interdental soft tissues (Fig. 2). Among these, the preservation flaps utilized as access flaps are the modified papilla preservation technique (12), simplified papilla preservation flap (13), papilla preservation flap (81), microsurgical periosteal flap variation of papilla preservation flaps (80, 95) and modified minimally invasive surgical technique (14).

The performance of the different flaps included within the conservative periodontal surgery classification regarding intrabony defects has been thoroughly studied in a recent systematic review and meta-analysis (34). This review included 27 trials with 12 months of follow up reporting on 647 subjects and 734 intrabony defects. At baseline, the defects were characterized by an average intrabony component of 4.53 mm, clinical attachment level of 8.75 mm and pocket depth of 6.74 mm. The data demonstrate that after surgical treatment (after ‘pooling’ of all types of flaps), probing pocket-depth reduction at 12 months was 2.85 mm (95% confidence interval: 2.47–3.22) ($P < 0.0001$) and, for those studies with a longer follow up, probing pocket-depth reduction was 2.77 mm (95% confidence interval: 1.59–3.94) ($P < 0.0001$). The percentage of probing pocket-depth reduction after surgery was 41.63% (QIAUTHOR: Please replace ‘QI’ with the full term.: 32.91–50.33%). Residual probing pocket depth was 4.18 mm (95% confidence interval: 3.71–4.64) after 12 months. The results of this review suggest that in intrabony defects, the use of access flap surgery represents a valid surgical approach for the reduction and, in some cases, the complete elimination of residual periodontal pockets.

Suprabony defects, because of their horizontal pattern of tissue destruction and relative paucity of cellular sources for wound healing, are a less-predictable type of periodontal defect to manage in comparison with intrabony defects. In a recent systematic review comparing the

performance of enamel matrix derivatives and open flap debridement in the treatment of suprabony defects 6 months after surgery, the conservative approach showed significant changes between preoperative and postoperative values (35). More precisely, in suprabony defects presenting at baseline with probing pocket depth of 5.19 ± 1.84 mm, the open flap debridement resulted in a probing pocket-depth reduction of 1.41 ± 1.35 mm. Residual probing pocket depth was 3.83 mm (95% confidence interval: 3.47–4.19) ($P < 0.01$).

Although these results are inferior to the performance of the access flap in intrabony defects, a probing pocket-depth reduction of approximately 2 mm is not clinically negligible (Fig. 3). Inter-radicular or furcation defects represent a clinical challenge for daily practice as a result of their particular anatomical features and posterior location in the mouth. These defects have been classified by Hamp et al. (36) as: class I when horizontal loss of periodontal tissue support is <3 mm; class II when horizontal loss is >3 mm without encompassing the total width of the furcation; and class III when a horizontal through-and-through destruction of the periodontal tissue is present. The performance of open flap debridement in the surgical treatment of class II mandibular furcation defects is the subject of another systematic review from our group (36). Eleven randomized clinical trials with a minimum of 6 months of follow up were assessed. A total of 199 patients and 251 class II furcation defects were included in the study. Probing pocket-depth reduction at 6 months was reported to be 1.38 mm (95% confidence interval: 0.91–1.85) ($P < 0.001$). This clinical result highlights the stabilization of periodontal attachment after access flap surgery, and may be of great clinical significance for the maintenance and survival of multirooted teeth. AUTHOR: For sense, ‘This clinical result highlights the stabilization of the periodontal attachment after an access flap, and may be of great clinical significance for the maintainability and survival of the involved multi-rooted teeth’ has been reworded as ‘This clinical result highlights the stabilization of periodontal

attachment after access flap surgery, and may be of great clinical significance for the maintenance and survival of multirrooted teeth'. Please check/approve the changes..

Effect of periodontal surgery on periodontal microbiota

Ideally, periodontal therapy should be capable of decreasing the number of periodontal pathogens whilst maintaining or re-establishing host-compatible species conducive with health (84). Nonsurgical treatment and its effect on the subgingival biofilm has been thoroughly studied. Several authors agree that nonsurgical treatment drastically reduces the total mass/burden of the subgingival biofilm; however, the proportion of subgingival sites colonized by periodontal pathogens is only transiently affected by scaling and root planing, and no eradication of bacteria is to be expected in deep residual pockets (6, 17, 82).

Microbiological burden indeed has an impact on surgical healing. Heitz-Mayfield et al. (36) assessed, using DNA–DNA checkerboard analysis, microbial colonization in deep periodontal defects of 122 patients with advanced chronic periodontitis scheduled for surgical treatment. Total bacterial load and the counts of red-complex bacteria were negatively associated with clinical attachment level gains, 1 year following treatment. The probability of achieving clinical attachment level gains above the median (i.e. >3 mm) was significantly decreased by higher total bacterial counts, higher counts of red-complex bacteria AUTHOR: Please check/approve the wording added (underlined) to the phrase 'higher counts of red-complex bacteria' and higher AUTHOR: 'higher' added. Is this correct? *Tannerella forsythia* counts immediately before surgery. Therefore, the presence of high bacterial load and specific periodontal pathogen complexes in deep periodontal pockets associated with intrabony defects had a significant negative impact on the 1-year outcome of surgical/regenerative treatment.

Levy et al. (48) investigated 29 subgingival taxa in plaque samples obtained from the mesiobuccal aspect of every tooth, in 11 adult periodontitis patients, using checkerboard

DNA–DNA hybridization. The 3-month postsurgical data were compared with values obtained before surgery, which corresponded to the outcome of nonsurgical debridement. Surgery resulted in further reduction (beyond nonsurgical therapy) in the levels of *T. forsythia* and *Porphyromonas gingivalis*. Furthermore, *Prevotella nigrescens* was affected more by surgery than by scaling and root planing. Sites with residual pocket depths >2.4 mm had higher levels of *Treponema denticola*, *T. forsythia* and *P. nigrescens* than did sites with pocket depth less than 2.5 mm after surgery.

Rawlinson et al. (71) used culture methods to investigate the effects of modified Widman flap surgery on the microbial flora remaining in residual periodontal pockets (probing pocket depth ≥ 5 mm) after nonsurgical treatment. Six patients with adult periodontitis were enrolled in the study and were assessed clinically and microbiologically at baseline and 3, 6 and 12 months after therapy. All patients initially underwent nonsurgical periodontal treatment that resulted in little clinical improvement and had minimal effect on the total microbial count. Subsequent modified Widman flap surgery resulted in clinical improvements accompanied by a reduction in the total mean colony-forming units and a reduction in the frequency of detection and proportion of important species such as *Prevotella intermedia*, *Porphyromonas asaccharolytica* and *Bacteroides ureolyticus*.

Mombelli et al. (57) analyzed 852 subgingival samples from 17 patients previously treated for periodontitis. AUTHOR: For sense, ‘from 17 previously treated periodontitis patients’ has been reworded as ‘from 17 patients previously treated for periodontitis’. Please check/approve the changes.. This study was carried out to assess the persistence patterns of *P. gingivalis*, *P. intermedia*/*P. nigrescens* and *Aggregatibacter actinomycetemcomitans* after mechanical therapy, including surgery. The authors reported a significant, positive correlation between the number of residual deep sites (probing pocket depth >4 mm) and the prevalence of *P. gingivalis*-positive sites. Sites positive for *P. intermedia*/*P. nigrescens* correlated with the

mean bleeding on probingAUTHOR: Please check the wording of the sentence ‘Sites positive for *P. intermedia*/*P. nigrescens* correlated with the mean bleeding on probing’. Would something like ‘The number of sites positive for *P. intermedia*/*P. nigrescens* was found to correlate with the mean bleeding on probing value’ be a more accurate description of what is meant here? Also, please specify if the correlation is negative or positive..

Collectively, these studies suggest that surgical management of deep residual pockets is capable of influencing a shift in the microbiological composition, which is more compatible with periodontal health.

Factors affecting the degree of pocket elimination/closure/reduction

Despite the general effectiveness of the different therapeutic approaches outlined above, there is substantial variation in clinical response, especially in more severely involved sites. This variance suggests that different factors contribute to and affect the clinical outcome of surgical treatment.

Based on data currently available, the factors that influence the surgical management of residual periodontal pockets may be classified as patient-related, defect-related and therapist-related.

Patient-related factors

Factors inherent in the patient’s lifestyle and oral-hygiene habits represent risk factors associated with periodontal breakdown (27). Therefore, if suchAUTHOR: ‘the above’ replaced with ‘such’. Do you agree? factors are not properly controlled during the cause-related phase of the therapy they may interfere with, or even compromise, the outcome obtainedAUTHOR: For sense, the phrase ‘the obtainable outcome’ has been replaced with ‘the outcome obtained’. OK?.

Plaque control

It has been well established that postoperative plaque control is a critical determinant of the success or failure of both nonsurgical and surgical periodontal therapy (59, 74). A study by Rosling et al. (74) investigated the importance of optimal standards of oral hygiene in the long-term maintenance of the surgical outcome. Twenty-four patients with advanced periodontitis were included. After an initial examination, patients were randomly distributed into one test group and one control group. All patients were given oral-hygiene instructions and then subjected to periodontal surgery using the modified Widman flap procedure. Following treatment, during a 2-year period, the patients of the test group were recalled once every second week for professional tooth cleaning. The control patients were recalled once every 12 months for prophylaxis. The results in the test group showed a clinical attachment level gain of 3.5 ± 0.3 mm and a radiographic bone fill of 2.5 ± 0.3 mm. The control patients, on the other hand, could not maintain a high standard of oral hygiene, and exhibited progressive deterioration of the periodontal tissues during the postsurgical observation period. More precisely, loss of clinical attachment of 2.1 ± 0.4 mm and bone loss of 0.9 ± 0.3 mm were observed. These results were further reinforced in a study investigating the outcome of periodontal treatment following different modes of periodontal surgery in patients not recalled for maintenance care (59). The authors concluded that different surgical techniques were effective in obtaining a short-term periodontal amelioration but the lack of adequate plaque control following periodontal surgery resulted in reoccurrence of periodontal pocketing and significant further attachment loss (59).

Smoking

Smoking is a major risk factor for periodontal disease progression. The literature supports the fact that smokers have an increased risk (odds ratio of 2–8) for developing periodontal disease

compared with nonsmokers (43). Tobacco smoking is responsible for some immune-response alterations, causing impairment of the viability and functions of polymorphonuclear cells, reduced levels of IgG and inhibition and proliferation of B- and T-cells (61). In addition, smokers have characteristics that may compromise wound healing, such as increased local vasoconstriction (7), a higher proportion of neutrophil-released reactive oxygen species (54) and a higher incidence of bacteria from the red complex (35). Enhanced healing after surgical treatment has been shown in nonsmokers compared with smokers. Preber et al. (67) investigated the influence of cigarette smoking on the outcome of surgical therapy in 54 patients, 24 of whom were smokers. Patients presented moderate to severe periodontitis and were surgically treated with the modified Widman flap operation. The probing pocket-depth reduction at the 12-month follow-up was 0.76 ± 0.36 mm in smokers compared with 1.27 ± 0.43 mm in nonsmokers. The difference was statistically significant ($P < 0.001$) and persisted after accounting for plaque control, suggesting that smoking may impair the outcome of surgical therapy. A recent systematic review by Patel et al. (64), demonstrated that smoking negatively influences bone formation following periodontal-regenerative procedures. A meta-analysis of three out of the 10 included studies revealed that smoking resulted in a statistically significant smaller bone gain, as measured by a change in probing bone level after the treatment of intrabony defects. The meta-analysis showed a standardized mean difference of -2.05 mm (95% confidence interval: -2.64 to -1.47) using the random-effects model. Although a standardized mean difference was used to test the difference, a less secure weighted mean difference was calculated as -2.1 mm (standard deviation = 0.55 mm). This difference was statistically significant, and it was concluded that smoking has a clinically significant negative effect on bone regeneration after periodontal treatment.

Defect-related factors

Intrabony defects have been classified according to their morphology in terms of residual bony walls, width of the defect (or radiographic angle) and topographic extension around the tooth. Three-wall, two-wall and one-wall defects have been defined as those that describe defects based on AUTHOR: For clarity, 'on the basis of' has been replaced with 'defects based on'. Is this interpretation of the text correct? the number of residual alveolar bony walls. This represents the primary classification system. However, frequently, intrabony defects present a complex anatomy consisting of a three-walled component in the most apical portion of the defect, and two- and/or one-walled components in the more superficial portions. Such defects are frequently referred to as combination defects (62). This wide range of osseous defect characteristics has long been related to the success of regenerative therapy (25), particularly the number of residual bony walls (30, 69, 89, 90) and overall defect depth. A series of studies focused on factors that affect healing of intraosseous defects treated by guided tissue regeneration (87, 88), also identified increased total depth of the intraosseous component of the defect, absence of hypermobility, as well as decreased radiographic width of the defect angle as important positive correlates of regeneration. It was suggested that with an increased radiographic defect angle between the root surface and defect wall, there was a reduced amount of regeneration. This may reflect space loss and clot disturbance caused by postoperative collapse of the membrane, the greater distances required for cellular repopulation of the wound or an enhanced susceptibility to oral environmental factors leading to incomplete bone fill. Oral environmental factors, such as mechanical trauma and infection, are also proposed as primary reasons for incomplete bone fill of the most superficial portion of the defect.

Therapist-related factors

When it comes to surgical procedures, some component of the variability in outcomes may be attributed to the therapist. Although these individual operator differences are difficult to

define from literature reports, careful analysis of the actions of a specific practitioner may reveal aspects of procedures that are capable of influencing both the surgical outcome and a patient's perception of that intervention and sometimes of the whole treatment plan. Also, the operative technique itself is always considered a critical determinant of the clinical outcomes. Surgeons who are experienced in a procedure may be expected to achieve a higher clinical response than those who are less experienced in the procedure. The influence of the clinician's capability or of his/her degree of experience appears evident in multicenter studies. One such multicenter study investigated the added benefits of guided tissue regeneration in deep intrabony defects, and found that a difference of 1.2 mm in clinical attachment level gain was observed between different centers, where the participant presented the same defect and lifestyle characteristics (88). Another multicenter study, by Sanz et al. (76), confirmed this finding and reported a highly significant center effect in terms of clinical attachment level gain following application of enamel matrix derivatives or guided tissue regeneration; more precisely, the difference in clinical attachment level gain between the center in which the largest gain was obtained and that which obtained the smallest gain, was 2.6 mm. For clarity, the sentence 'more precisely the difference between the center that obtained the largest clinical attachment level gains and the one with the smallest was 2.6 mm' has been reworded as 'more precisely, the difference in clinical attachment level gain between the center in which the largest gain was obtained and that which obtained the smallest gain, was 2.6 mm'. Please check/approve the changes..

Moreover, it is reasonable to assume that, with new surgical procedures, critical details of the surgical technique must be determined as one way of improving surgical outcomes and reducing variability. Tu et al. (93) highlighted the fact that the advent of new improved flap designs, such as modified or simplified papilla-preservation procedures (12, 13), has

contributed to better performance of conservative surgery. However, the surgical technique often implicitly includes case selection, which may vary greatly among surgeons.

One of the reasons for the higher performance of these conservative flaps may be wound healing. Successful wound healing is strongly influenced by preservation of the microvasculature of soft tissues as well as by revascularization rates (16). A study evaluating gingival blood flow following periodontal surgery affirmed that the gingival blood flow presented an overall increase at 7, 15, 30 and 60 days after surgery, compared with baseline.

The values at the palatal and alveolar mucosa sites were very similar to those at baseline.

Interestingly, increased blood flow changesAUTHOR: Is the phrase 'increased blood flow changes' correct, or would 'increased blood flow' be more accurate here? Please indicate the changes required (if any) to the original text. were observed 30 and 60 days following surgery at the buccal interdental sites, suggesting the combination of increased vascular trauma of the area and possible blood flow contamination from deeper tissue layersAUTHOR: Please check the wording of the phrase 'and possible blood flow contamination from deeper tissue layers'.

Would 'and possible contamination of blood from deeper tissue layers' be more accurate here? Please indicate the changes required (if any) to the original text. such as the periodontal ligament vascular plexus. These topographic differences in the patterns of microvascular blood-flow alterations during the wound-healing period were further confirmed in a follow-up study by the same group (73). The clinical trial compared gingival blood flow during the healing period following simplified papilla preservation and modified Widman flap surgery (72). It was confirmed that periodontal access flaps represent an ischemia–reperfusion flap model and it was observed that the simplified papilla preservation flap may be associated with faster recovery of the gingival blood flow postoperatively compared with the modified Widman flap.

Effect of periodontal surgery on patient-based outcomes

Patient-based outcomes are subjective measures that capture patients' perspectives of disease or therapy and complement conventional clinical measures (42, 91). Patient-based outcomes were identified as a research priority at the 2003 World Workshop on Emerging Science in Periodontology (87); their assessment should be considered of primal importance. AUTHOR: The meaning of the phrase 'primal importance' is unclear. Would 'prime importance' or 'primary importance' be better here? Please indicate the changes required. in periodontal therapy as patients' opinions may differ from traditional clinical end points (58). Several studies have confirmed that periodontal disease impacts negatively on oral health-related quality of life (4, 65, 75). In a recent study, Bernabé & Marcenes (8) demonstrated the existence of a correlation between extent and/or severity of periodontal disease and poorer oral health-related quality of life. Furthermore, Gerritsen et al. (28) reported that tooth loss, which is the probable end point of an untreated periodontitis or of a nonregular supportive periodontal therapy following successful periodontal therapy, impairs oral health-related quality of life.

In a recent systematic review, Shanbhag et al. (79) studied the impact of periodontal therapy on oral health-related quality of life in adults. The authors included 11 studies of 'medium' methodological quality. All studies reported impaired oral health-related quality of life before therapy. Nine studies reported a statistically significant improvement in oral health-related quality of life after nonsurgical treatment ($P < 0.05$). Surgical therapy had a positive impact on oral health-related quality of life; however, this was less evident with respect to nonsurgical treatment. The authors concluded that surgical periodontal therapy could moderately improve the oral health-related quality of life of adults in the immediate (1 week)

and long (12 months) term. Therefore, the perceived benefit of surgical therapy may be relatively less than the benefit of nonsurgical treatment and should be correlated with other clinical indicators of periodontal health.

Effect of periodontal surgery on systemic health

The relationship between periodontitis and systemic health has yet to be elucidated (52). A number of studies have investigated severe chronic periodontitis and systemic inflammation, concluding that, compared with healthy subjects, patients with periodontitis tend to have increased circulating systemic inflammatory markers (63, 83). Furthermore, it is expected that both nonsurgical and surgical treatment of periodontitis may reduce the overall inflammatory burden; however, the results are not always consistent. Whilst there is some evidence supporting the impact of nonsurgical therapy on systemic biomarkers (15), there is a clear lack of evidence regarding surgical interventions.

Only one study has investigated the impact of both nonsurgical and surgical periodontal treatment on peripheral blood markers of inflammation (31). This prospective cohort trial looked at the acute body response and included 14 patients with generalized advanced chronic periodontitis. The participants received both nonsurgical and surgical therapy and were followed over a 12-month period. Peripheral blood markers (C-reactive protein, serum amyloid A, D-dimers, cystatin C and leukocyte counts) were analyzed after nonsurgical therapy at 1, 7, 30, 90 and 180 days. Following this, two surgical interventions were carried out per subject, and serum samples were collected and analyzed at days 1 and 7 after each surgery. A final blood sample was collected 90 days after the second surgical intervention. The results showed that after the first periodontal surgery, there was a marked and statistically significant increase in both serum C-reactive protein [$237 \pm 67\%$ (mean \pm standard deviation)] and serum amyloid A ($56 \pm 150\%$; 95% confidence interval 88–387%; $P = 0.033$).

95% confidence interval: 269–832%; $P = 0.003$) concentrations. Following the second periodontal surgery, both C-reactive protein and serum amyloid A showed more modest, yet statistically significant, increases ($P < 0.05$). At 12 months, the levels of a serum marker of kidney function, cystatin C, were significantly reduced compared with baseline (mean \pm standard deviation difference of 0.18 ± 0.03 mg/ml; 95% confidence interval 0.12–0.24; $P < 0.001$). The authors thus concluded that both nonsurgical and surgical periodontal therapy are associated with systemic inflammation. In turn, this systemic inflammation contributes to the overall inflammatory burden of an individual, potentially leading to an increased risk of vascular events. Although this study had a small sample size and noAUTHOR: ‘lack of’ replaced with ‘no’. Do you agree? control group, it is the only clinical trial, to date, that has assessed periodontal surgery and systemic markers of inflammation. Undoubtedly, further studies are required to confirm the above findings.

Economic evaluation of periodontal surgery

Active periodontal treatment, when supplemented by supportive periodontal therapy, is successful both in reducing tooth loss (19, 41, 55) and in promoting an individual’s quality of life (5, 92). Ideally, periodontal health should be achieved in the least invasive and most cost-effective manner possibleAUTHOR: For sense, ‘possible’ has been added. OK?, particularly when considering that a patient should ideally commit to lifelong regular visits for maintenance of therapeutic outcomes (50). Therefore, an economic evaluation of various periodontal treatment modalities to ascertain which therapy provides the greatest ‘value for money’ is of major public interest (94). To be specific, an economic evaluation of periodontal surgery should try to answer the following questions: ‘Is it less expensive to wait for a tooth to be lost or provide treatment with periodontal surgery?’ and ‘Does the improvement in treatment outcomes (for example, pocket depth reduction or number of residual pockets)

following periodontal surgery, justify its higher cost in comparison with nonsurgical alternative treatments?’

It would be useful to elucidate the relative economic value of treating residual periodontal pockets with periodontal surgery compared with less-invasive and time-consuming procedures, or even tooth extraction and/or restoration. A variety of economic evaluation methodologies could be used to identify any differences, including cost–benefit, cost-effectiveness and cost utility analyses (9, 18, 66, 94). The differences between these methodologies concern AUTHOR: For sense, ‘have to do with’ has been replaced with ‘concern’. Do you agree? the outcome measure used to value the potential benefit of the periodontal surgery when it is weighted against cost. For example, cost–benefit analysis assigns a monetary value to the benefits of periodontal surgery (94). Cost-effectiveness measures the benefits in natural units, such as tooth survival or days free of periodontal disease, maintaining a functional and esthetically acceptable dentition (24). However, because of the chronic nature of the disease, this may not be feasible in the context of a prospective trial; therefore, surrogate treatment outcomes, such as probing pocket-depth reduction, clinical attachment level gain, radiographic bone fill or frequency distribution of residual pockets >5 mm could be considered (51). Finally, cost utility analysis utilizes a quality-of-life measure based on an individual’s preferences, such as the quality adjusted life year (2). Currently, economic evaluations of periodontal treatment have mainly used the cost-effectiveness or cost utility methodologies, emphasizing nonsurgical active or supportive therapy and the use of adjunctive antimicrobials (29, 37, 50). Cost-effectiveness studies have shown that the cost of supportive periodontal therapy is relatively lower when compared with the cost of implants or crown/bridgework (68), and the patients will benefit from greater periodontal stability and higher tooth-survival rates (26). Fardal et al. (23) reported that periodontal treatment (including periodontal surgery) and supportive periodontal therapy is

cost-effective when compared with tooth extraction and replacement with fixed restorations. They reported that in a 16.5-year period, patients who completed baseline periodontal treatment but were not compliant during supportive periodontal therapy could restore only two to three of their missing teeth with bridgework or implants, respectively, before the cost of replacing any additional tooth would exceed the cost of lifetime periodontal treatment. Patients who did not have any supportive periodontal therapy at all, could replace three to four teeth with bridgework or implants, respectively, before the cost of restoration exceeded that of periodontal treatment and maintenance. The same group also determined the cost-effectiveness of periodontal treatment, including periodontal surgery, in patients with chronic periodontitis of different levels of severity and risk (53). Considering the benefit of tooth preservation, they reported that the cost of periodontal treatment is justifiable in high- or moderate-risk patients regardless of disease severity but may not be considered worthwhile. AUTHOR: For clarity, I have added 'worthwhile'. Do you agree? in low-risk patients with mild periodontal disease. Similarly, nonsurgical and surgical periodontal treatment of molars with furcation involvement, including open flap debridement, root resection, guided-tissue regeneration and tunneling, was more cost-effective than replacing them with implant-supported restorations (77).

It is still unknown whether periodontal surgery provides the greatest value for money in terms of additional clinical benefit for additional money spent, in comparison with nonsurgical alternative treatments. A cost utility analysis by Antczak-Bouckoms & Weinstein (2) concluded that nonsurgical debridement presented with a lower cost and increased QATYs. AUTHOR: Please replace 'QATYs' with the full term, here, and elsewhere in the text. when contrasted with a surgical approach, taking into consideration the increased prevalence of side effects following surgical treatment. However, the costs of the maintenance phase, retreatment or possible prosthetic rehabilitation (in the case of tooth loss) were not taken into

account. This may have influenced the total incremental costs, assuming that nonsurgical treatment would result in more residual pockets and lost teeth. Furthermore, the side effects of surgical treatment were heavily weighted in the calculation of QATYs, underestimating the clinical effectiveness of surgery. Miremedi et al. (56), in a cost-effectiveness analysis, reported that €700 could be saved, on average, by performing nonsurgical debridement instead of immediate surgical debridement because of the increased chair time for the surgical procedure. However, periodontal surgery may reduce the need for, and consequently the cost of, any additional treatment in the future, as it would probably result in fewer residual pockets. AUTHOR: For clarity, 'most likely result in less' has been reworded as 'probably result in fewer'. Please check/approve the changes.

One of the main challenges in interpreting the results of the above studies and conducting an economic evaluation in periodontology, is choosing clinical outcome measures that can be clearly related to cost and benefit (50, 94). Future studies on financial evaluation of periodontal surgery should consider the following points:

- Cost estimation should be based on the incremental cost of evaluated treatment compared with the alternatives (18). AUTHOR: The meaning of 'of evaluated treatment' is unclear. Would something like 'of the treatment evaluated' be a clearer description? Please indicate the changes required to clarify the intended meaning of the text. For example, in a cost-effectiveness analysis of periodontal surgery, the estimation should be based on costs arising from periodontal surgery and the subsequent supportive periodontal therapy for a number of years minus all the costs arising from the alternative intervention [e.g. extraction and replacement with a dental implant, or a bridge, including the cost of implant maintenance (20) or against nonsurgical alternatives]. When surrogate measurements, such as probing pocket-depth reduction or the prevalence of residual pockets, are used to evaluate the benefit of surgical treatment against, for example, nonsurgical alternatives, the calculated cost for each treatment should include a possible additional cost for retreatment of residual pockets that are

expected to appear in higher frequency when only nonsurgical treatment is provided. If the total incremental cost is negative then periodontal surgery is clearly cost-effective and there is no need to value the benefits, as far as they are positive. AUTHOR: The meaning of the phrase 'as far as they are positive' is unclear. Do you mean something like 'as they are positive'? Please indicate the changes required to the original text to clarify its intended meaning. If the incremental cost is positive, then this needs to be weighed against the value of these incremental benefits.

- The most appropriate clinical outcome for financial evaluation of periodontal surgery is tooth loss. It is clear that tooth loss has a negative effect on quality-of-life measures, and the resultant cost of alternative treatments to restore this missing tooth would be easier to calculate (94). However, long-term studies that follow patients for many years through the supportive periodontal therapy phase are necessary. On the other hand, widely accepted short-term surrogate clinical measurements, such as probing pocket-depth reduction and/or clinical attachment level gain, may not have a precise and reproducible impact on patients and are also difficult to reconcile with a specific cost.
- Although cost utility analysis allows comparison between various procedures whose outcomes are also different (e.g. tooth preservation vs. tooth restoration with an implant), the currently used quality adjusted life year may not capture some secondary clinical, functional or esthetic benefits of periodontal surgery. Furthermore, universally accepted and preference-based outcome criteria (utility measurements) have yet to be established. Therefore, future financial evaluation studies for periodontal surgery should consider using a combination of clinical outcomes and utility measurements.

Therefore, in high-risk patients, periodontal surgery, as part of a comprehensive periodontal treatment that includes supportive periodontal therapy, could be more cost effective than extensive prosthetic rehabilitation with fixed prostheses. The various types of periodontal surgery should be evaluated financially in comparison with other less-invasive, time-consuming and costly periodontal therapies. Future studies should be long term, calculate

incremental costs for the evaluated treatments based mainly on tooth loss and use universally accepted utility measurements.

Discussion

Pocket elimination/closure has undoubtedly been a major goal of periodontal therapy and has been rendered possible through nonsurgical and surgical treatments. Nevertheless, residual pockets are often present and represent a clinical condition with the ability to compromise both the conquered therapeutic results AUTHOR: Please check the wording of the phrase 'the conquered therapeutic results'. Would something like 'the therapeutic results achieved' be more accurate? Please indicate any changes required.and the remaining, periodontally healthy sites. As previously mentioned:

- A residual site with probing pocket depth ≥ 6 mm represents a true risk factor for both periodontal disease progression and tooth loss. However, a site presenting a probing pocket depth of 5 mm is also associated with tooth loss in the long term. The aim of periodontal treatment therefore should be the closure/elimination of sites with probing pocket depth ≥ 5 mm.
- Surgical treatment shows a higher performance, in terms of probing pocket-depth reduction and elimination of microbiota noncompatible with periodontal health, than does nonsurgical retreatment of residual pockets. In particular, residual pockets associated with the presence of angular bony defects, molar sites and furcation sites, especially in smokers, should be treated with surgery as any attempt of retreatment has proved not to be effective.
- The use of different surgical approaches has been suggested to treat residual periodontal defects; these vary from conservative access flap surgery to more 'respective' techniques.

- From a microbiological point of view, deep residual pockets harbor bacterial species correlated with periodontal disease and capable of driving AUTHOR: ‘determining’ replaced with ‘driving’. Please check/approve the change. a new periodontal breakdown. The current evidence suggests that only surgical management of deep residual pockets can influence a shift in the microbiological composition that is more compatible with periodontal health.
- From a patient’s point of view, residual pockets represent a reason for impairment of the oral health-related quality of life. Nevertheless, patient outcomes are only minimally changed by surgical treatments; nonsurgical therapy is the treatment phase associated with the majority of changes perceived by the patients AUTHOR: For clarity, ‘being the non-surgical therapy the treatment phase associated with the majority of changes perceived by the patients’ has been reworded as ‘; nonsurgical therapy is the treatment phase associated with the majority of changes perceived by the patients’. Please check/approve the changes..
- From a systemic (health) point of view, there is a lack of clear evidence regarding the effect of periodontal surgery on peripheral blood markers of inflammation. However, the paucity of evidence suggests that surgery might determine an inferior systemic perturbation in terms of the acute-phase response if compared with nonsurgical treatment. This might be because of the smaller extension of the treated area and the fact that surgery is usually performed when plaque is under control, causing, most probably, an inferior bacteremia.
- Several factors have been suggested to affect the degree of pocket elimination/closure/reduction after periodontal surgery. Patient-related factors (such as plaque control or smoking), defect-related factors (such as morphology, width or localization of the residual pocket requiring treatment AUTHOR: ‘to treat’ replaced

with ‘requiring treatment’. Do you agree?) and therapist-related factors concerning therapist experience (therapist surgical hand- AUTHOR: Is the phrase ‘therapist surgical hand-’ correct? Would it be possible to clarify what ‘hand-’ means?and surgical technique choice) may influence the surgical outcome.

Conclusion

Residual pockets are associated with progression of periodontal disease and tooth loss. Nonsurgical retreatment of these sites rarely proved to be effective in closing the pockets. Thus, surgical treatment of residual pockets is a treatment option that should not be underestimated by the clinician. However, differences in terms of patient, site or technique selection, may greatly affect the final outcome.

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Fig. 1 Residual periodontal pocket of 5 mm (A), at the surgical opening (B) and the pocket closed 6 months postoperatively (C).

Fig. 2 Classification of access flaps used in randomized
AUTHOR: Figure 2, the year of publication in each reference has been replaced with the reference number. Please check that the reference numbers added are correct, and please provide the references for Trombelli et al. 2007 and Cortellini et al. 2009 as they are missing from the list. clinical trials.

Fig. 3 Suprabony defect before surgical intervention (A), radiographic appearance (B) and intraoperative view (C). Healing after 6 months is illustrated (D).