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Meta-analysis

Effectiveness of soft tissue augmentation using subepithelial connective tissue graft in comparison with free gingival graft and no graft for increasing the width of keratinized mucosa around dental implants: a meta-analysis

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ABSTRACT

The soft tissues around dental implants are important to prevent inflammatory peri-implant diseases and ensure the long-term survival of a dental implant. Periodontal plastic surgery has evolved from traditional mucogingival surgery, according to Zuhr et al as a result of the development of subepithelial connective tissue grafts/free gingival grafts. So, the aim of this review was to compare the effectiveness of soft tissue augmentation using subepithelial connective tissue graft in comparison with free gingival graft and no graft for increasing the width of keratinized mucosa around dental implants. The review was according to PRISMA protocol. A comprehensive search of the specialized databases was performed to include the studies. Quality assessment and meta-analysis were carried out. 10 articles included. Two articles evaluated KTW with FGG and SCTG; FGG and no graft (3); SCTG and no graft (5). All the included studies assessed either primary or secondary outcome measures. In the end, it was concluded that for soft tissue volume augmentation, SCTG is a treatment choice for an increase in KTW at implant sites.

Keywords: Dental implants, Soft tissue augmentation, Free gingival graft, Subepithelial connective tissue graft, Keratinized mucosa

INTRODUCTION

Dental implants have structures and surfaces that are distinct from those of natural teeth and are frequently placed in patients who have a history of poor oral hygiene and edentulism. As a consequence, they are more likely to experience inflammation and bone loss due to plaque accumulations or microbial invasion. Maintaining a suitable amount of gingiva firmly linked to the surrounding periosteum and bone has been cited as a goal in implant maintenance. [1] The number of dental implants implanted every year in developed countries is estimated to be around 300,000 and 428,000 and about 100,000-250,000 in developing countries.[2] Prerequisite for dental implants is to maintain peri-implant tissues and implants in a healthy, aesthetically appealing condition in order to achieve long-term survival.[2]

The idea that periodontal health can be preserved with ideal plaque control in regions with little to no attached gingiva is supported by several experimental studies. Early studies have found clinical inflammation in all regions with less than 2 mm of keratinized gingiva. But a newer concept states the presence of even 1 mm of attached gingiva is sufficient to prevent gingivitis and stabilize the gingival margin and also for maintaining periodontal health. [3]

When the structure and function of the mucosa surrounding the implants were investigated, it was found

that both natural teeth and dental implants exhibit a similar soft tissue reaction to plaque, hence ag adjacent to dental implants is equally important as in natural teeth.[1]

Patients with a weak periodontium continue to face significant difficulties with aesthetic implant-supported rehabilitation. The stability of the facial and interproximal peri-implant soft tissue surrounding single implants in the aesthetic zone is crucial to achieving the best cosmetic results since implant prostheses must replicate not only the lost teeth but also the associated soft tissue architecture.[4]

The existence of keratinized gingiva around implants may improve patient comfort in all individuals. In order to increase WKM surrounding implants, several surgical methods have been documented. These include the apically positioned flap/vestibulopathy (APF/VP) (Basegmez, 2012), pedicle graft (PG) (Wood, 1972; Grupe and Warren, 1956), free gingival graft (FGG) (Sullivan and Atkins, 1968) (Bjorn, 1963), Acellular dermal matrix (ADM) (Aichelmann-reidy, 2001; Batista, 2001; Harris, 2003; Wei, 2000), Xenogenic bilayer collagen matrix (CM) (Mcguire, 2014; sSanz 2009), and newer cell-engineered grafts (mMcGuire 2005; mMcGuire 2008).[6]

Despite the different approaches, most research supports the use of autogenous grafts, such as FGG and SCTG, taken from the palate, which continue to be the gold standard for soft tissue augmentation techniques (Schreyer et al). To obtain a thicker graft without compromising the greater palatine neurovascular bundle, FGGS and SCTGS are harvested from the palate between the first molar and canine teeth.[6]

The free gingival graft is the oldest surgical procedure performed in periodontal surgery. The graft is obtained from the palate or the maxillary tuberosity and is composed of connective tissue with an overlying epithelium, leaving a significant section of the lesion open for primary healing. Although it provides the optimum keratinized tissue width, it differs from subepithelial connective tissue grafting in which we only harvest the connective tissue from the palate and suture back the epithelium to the palate. Hence a secondary form of healing and far less donor site morbidity.[7]

Establishing long-term peri-implant health based on stable peri-implant soft tissue dimensions, minimum bleeding indices, and stable marginal bone levels is the major goal of implant therapy.[8]

Particularly, the use of a variety of techniques and materials has been studied to augment the keratinized tissue surrounding dental implants. Width of keratinized tissue could be successfully increased in every investigation. Due to significant study heterogeneity, which includes the absence of control groups in some studies and the use of soft tissue grafting at different times (simultaneously with implant placement, during the implant healing process, and then after the insertion of the final reconstruction), it is difficult to recommend a specific technique.[5]

In order to establish peri-implant health and to reduce the occurrence of peri-implant illness, surgical operations to enhance the width of keratinized tissue soft tissue augmentation should be performed.

In addition, there are no clinical recommendations for any specific soft tissue transplant that would use a free gingival graft, a subepithelial connective tissue graft, or nothing at all to accomplish better outcomes. This question can only be answered by (randomized) controlled clinical trials comparing implant sites with and without soft tissue augmentation, studies comparing distinct soft tissue augmentation and management techniques, and reported outcome measures determining peri-implant health.[5]

METHODS

Protocol and registration

The preferred reporting items for the systematic review and meta-analysis (PRISMA 2020) statement were followed in conducting the current systematic review, and the protocol was registered in the PROSPERO international prospective register of systematic reviews (ref no: crd42021254731), which is maintained by the centre of reviews and dissemination at the university of York in York, UK. (https://www.crd.york.ac.uk/prospero/#recorddetails).[32]

Study design and eligibility criteria

The inclusion and exclusion criteria were established using the population, exposure, comparison, outcome, and study design (PECOS) technique. The following questions were the focus of this study: What is the effect of soft tissue augmentation procedures to increase the width of keratinized tissue or the thickness of the mucosa at dental implant sites using subepithelial connective tissue graft in comparison to implant sites without soft tissue grafting procedures or with free gingival graft on the peri-implant health in systemically healthy patients with dental implants? All human prospective and retrospective follow-up studies, randomized controlled trials (RCTs), or controlled clinical trials (CCTs) studies using free gingival graft for soft tissue augmentation for increasing the width of keratinized mucosa around dental implants and studies using sub-epithelial connective tissue graft for soft tissue augmentation for increasing the width of keratinized mucosa around dental implants.

Studies' findings are determined after surgery to widen keratinized tissue or thicken the mucosa around dental implants, including any peri-implant bleeding index or parameter. Studies done with any implant system.

Articles released between January 1, 2010, and December 31, 2021, in English.

Search and information sources

A comprehensive search of the scientific literature was conducted without any restrictions on the study setting and period until December 31, 2021, in the following databases and repositories: PubMed, Google Scholar, Scopus, Rajiv Gandhi university of health sciences repository, and KLE Academy of higher education and research repository. At each stage of the study screening, 4 independent researchers namely VK, RV, ANZ, and NS independently screened the titles and abstracts obtained by search strategy and included them if they met the inclusion criteria. Full text of relevant articles that met the inclusion criteria was then reviewed and any uncertainty or disagreements were resolved by discussion with the fifth author (AK). All references obtained from the above-mentioned databases were imported into the Mendeley desktop application version 1.19.8. Duplicates were removed using the merge option under the duplicate items section. None of the authors was blinded to the journal titles, study authors, or institutions where the studies were conducted.

Study selection and data collection

Data collection was independently performed by four reviewers (VK, RV, ANZ, and NS) at three different stages. First, titles were carefully read to exclude articles outside the scope of this research and articles that were not retrievable. Subsequently, the abstracts of articles that met the inclusion criteria were reviewed, and articles with in-vitro, animal studies, case series, case reports, and descriptive and analytical studies were excluded. Studies treating recession defects, enhancing only the keratinized tissue around teeth, enhancing soft tissue in patients who are completely edentulous, and studies in which the impact of soft tissue augmentation surgery was not considered in the analysis (for example, combining guided bone regeneration and soft tissue augmentation). Four reviewers (VK, RV, ANZ, and NS) then read the full texts of pertinent papers that satisfied the inclusion criteria, and any questions or discrepancies were then discussed with the fifth author (AK). Lists of the study characteristics of the studies that were included. Finally, the search yielded 10 articles for inclusion in systematic review and meta-analysis. All the excluded studies were recorded with the reason for exclusion. None of the authors were blinded to the journal titles, study authors, or the institution where the study was conducted.

All the potentially qualified studies were plotted in a standardized data extraction sheet in Microsoft excel with the help of an expert and discussion was done in case of any disagreement. The following criteria were predetermined for extracting data: The major interest was to check the increase in the width of keratinized mucosa as a primary outcome. Studies mentioning peri-implant health such as bleeding index, probing depth value, plaque index, and time-point intervention as secondary outcomes.

The individual data collected by the four reviewers (VK, RV, ANZ, and NS) were combined at the last and any disagreement was resolved by discussion with the fifth reviewer (AK).

Risk of bias in individual studies

The major aim of the quality assessment was to determine the potential for selection bias [eligibility criteria, sampling strategy, sample size, primary outcome, and secondary outcomes]. The risk of bias in individual studies was assessed under the headings according to the Cochrane handbook book.

Objectives of the study mentioned the population under the study, the setting in which the study was conducted, eligibility criteria for including or excluding the participants, sampling strategy used, mention of calculating sample size for the study based on a previous study, primary and secondary outcome measures for KTW treatment success.

A total of 8 domains were assessed. A score of one was given for fulfilling conditions in each domain and zero when unclear or otherwise. The maximum possible score was 8 and a study scoring 5-7 was classified as a high-quality study, 3-4 as a moderate-quality study, and less than or equal to two as a low-quality study. The judgment for assessing the quality of the study was made independently by four review authors based on the criteria mentioned below. It was later cross-checked by the other review author. Any disagreements if present were resolved by discussion. Only high-quality studies were selected in our systematic review.

Effect measures and synthesis method

A comprehensive meta-analysis was carried out using statistics and data software (RevMan 5.4.1 software). The primary outcome measured was the keratinized tissue width of the gingiva (KTW) and the secondary outcomes were GI, PI, and PPD. The pooled weighted mean (WM) and the 95% confidence interval (CI) of each variable were estimated and a random-effects model was applied for the meta-analysis.

Forest plots were produced to graphically represent WM and 95% ci for the primary outcome. Heterogeneity was assessed with the tau^2 test, which ranges between 0% and 100%, (0-40%: minimal heterogeneity, 30-60%: moderate heterogeneity, 50-90%: representing substantial heterogeneity, and 75-100%: considerable heterogeneity). To evaluate the potential influences of different treatment modalities, WM, and 95% CI were calculated separately for the primary outcome. In addition, funnel plots were used to assess the presence of publication biases.

In the end, 10 studies remained that underwent qualitative synthesis. After quality synthesis, all 10 articles were included for systematic review and meta-analysis. The reference numbers allotted to the included articles in the figures will be used throughout the rest of the review.

RESULTS

Study selection

The electronic and manual searches identified 115 articles, 19 articles in PubMed, 65 in Google Scholar, and 31 in Scopus, and title screening was done. Of the 19 articles selected after title screening, 4 articles were duplicates and were excluded.

Further, abstract screening was done for 19 articles and 9 articles were excluded for reasons mentioned. 19 articles selected, only 10 articles met the inclusion criteria and could answer the main focused question which compared the effect of soft tissue augmentation using subepithelial connective tissue graft in comparison with free gingival graft and no graft for increasing the width of keratinized mucosa around dental implants (Figure 1).

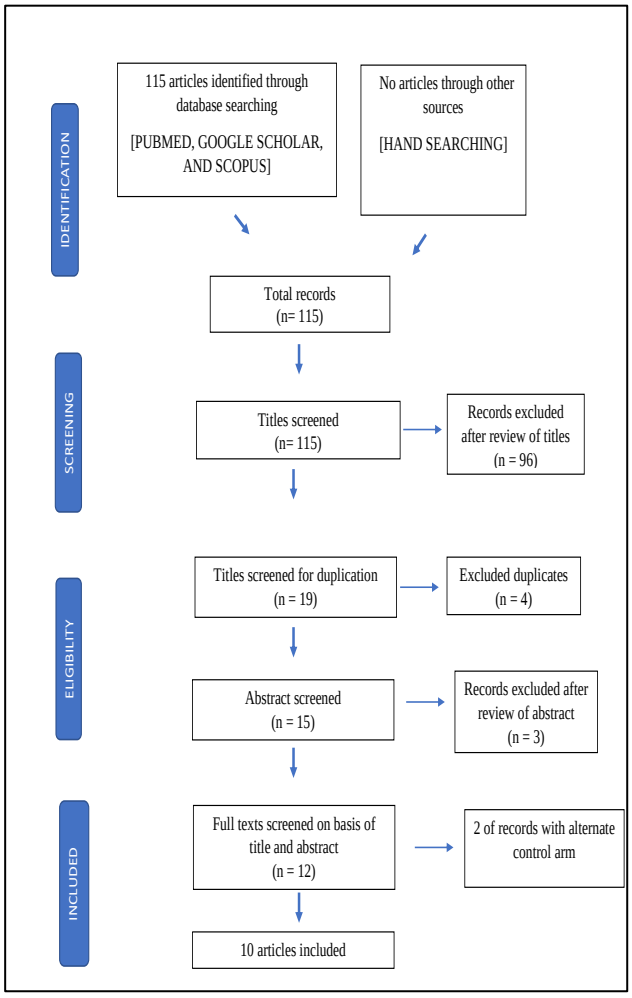

Figure 1: Flow diagram depicting the process of selection and exclusion of articles at each step.

Study design and subject features

Seven randomized controlled trials (Study no. 2, 3 and 6-10), two prospective clinical studies (Study no. 1 and 4), and a retrospective study (Study no. 5) were included. Of the 7 RCTs, only one study by Raoffi et al (Study no. 10) evaluated the effectiveness of the use of both FGG and SCTG for soft tissue augmentation in dental implants. Two RCTs, done by Se-lim oh et al (study no 2) and Zheng et al (Study no 3) compared the effectiveness of FGG in dental implants with no graft. The remaining RCTs, (study no 6-9) compared the effectiveness of SCTG in dental implants with no graft presented by Yoshino et al, Abdelsamie et al, Rungcharassaeng et al, and Saad et al. One prospective study clinical study was done by Roccuzzo et al (study no. 1) evaluated the effectiveness of FGG with no graft in dental implants. Other one prospective study clinical study was done by Roccuzzo et al (Study no. 4) evaluated the effectiveness of SCTG with no graft in dental implants. The one retrospective study done by Speroni et al (Study no. 5) evaluated the effectiveness of SCTG with no graft in dental implants. The study characteristics of the included studies is mentioned.

Study characteristics

Quantitative analysis of the studies selected for the systematic review

A total of 10 eligible articles were included in this review, of which 8 studies evaluated primary outcome i.e., KTW, of which 3 studies had both primary (KTW) and secondary (PPD, GI, GI) outcomes; 2 articles had only secondary outcomes (PPD, GI, and PI). Out of 10 studies, 7 studies were RCT, studies were prospective studies and the remaining 1 study was a retrospective study.

Out of 10 studies, 3 studies showed soft tissue augmentation procedures done by FGG in comparison with no graft. 5 studies showed soft tissue augmentation procedures done by SCTG in comparison with no graft. 2 studies have compared both FGG and SCTG soft tissue augmentation procedures. The time period of intervention in each study had a different follow-up period. 1 study which is a prospective comparative study had a longer followed up period of 10 years. 4 studies have followed up period of 1 year out of which one is a retrospective study and the remaining is and 1 study has 2 years follow-up period 1 study has a follow-up period of 3 years. The minimum follow-up period is 3 months which is included in 1 study and six months of follow-up is done in 3 studies.

Studies included in this review were published from the year 2010 to 2021. The age group of individuals incorporated in the studies that were included in this review was in the range of 20-70 years. The maximum sample size set in this review to be included was set in the range of 130 samples more or less including males and

females. The minimum sample size was set in the range of 14 samples more or less including males and females.

Risk of bias across studies

Independent evaluations of the included studies' quality were carried out by VK, RV, ANZ, and NS. When there was a disagreement, AK served as a mediator to reach an accord. Evaluation of the randomized controlled trials' quality. All 10 of the selected studies (study nos. 2, 3, 6-10) were randomized clinical trials. RevMan software (version 5.4.1) was used to carry out Cochrane's tool for randomized controlled trials. It comprises the following six domains.

Selection bias

The method of randomization was found to be adequately generated in 10 studies, whereas the randomization method was described adequately in a study thereby imparting low risk. Methods of allocation concealment were sealed envelope, open-labeled method, and code system, whereas allocation concealment was not clearly mentioned in 6 studies.[11-18,20]

Performance bias

Blinding of both participants and personnel was done in 6 studies, whereas blinding only participants was carried out in a study, thereby revealing a low risk of bias in 9 out of 10 included studies. In a study, blinding was not performed leading to a high risk of bias.[11-13,15-17,19]

Detection bias

Except for one article where the blinding of outcome assessment was carried out, we judge that the outcome measurement was not likely to be influenced by the lack of blinding of outcome assessment in 7 other studies thereby adjudged to have a low risk of bias. A high risk of bias was reported in three study.[11-15,20]

Attrition bias

Because the recruited participants in each study completed the clinical trial, all the included studies were deemed to have a low risk of bias.[11-20]

Reporting bias

All included studies reported all intended outcomes, including both primary and secondary outcomes, and as a result, the risk of bias was deemed to be low.[11-20]

Other bias

All the included studies appeared to be free of other sources of bias and hence low risk of the bias was reported.[11-20]

The overall risk of bias

Two studies had an overall low risk of bias, six studies, two studies, and two studies had an overall unknown risk of bias.[11,13-16,18] The risk of bias graph is shown in Figure 2, and it shows the review authors' assessments of each risk of bias item across all included studies as percentages. The risk of bias summary is depicted in Figure 3 and includes the review authors' assessments of each risk of bias item for each included study. Results of individual studies and meta-analyses.

For meta-analysis 7 articles were selected as data from them could be ambiguously extracted regarding the changes in the clinical parameters in primary outcomes. The forest plot for KTW was recorded in 8 articles (Study no 1, 2, 3, 5, 6, 7, 8 and 10). They are demonstrated in figures (Figure 4). A random-effect model was applied as significant heterogeneity was found in the studies and is shown with the help of forest plots. The funnel plot shows publication bias of primary outcome (KTW) represented in Figure 4.

However, a high heterogeneity (I^2) value ranging from 78% to 94% was observed with respect to an intervention group and attributed to varying sample size, different study designs, and various soft tissue augmentation procedures for evaluating the increased keratinized tissue width (KTW) around dental implant.

Figure 2: A summary of the risk of bias: review authors' judgments about each risk of bias item for each included study.

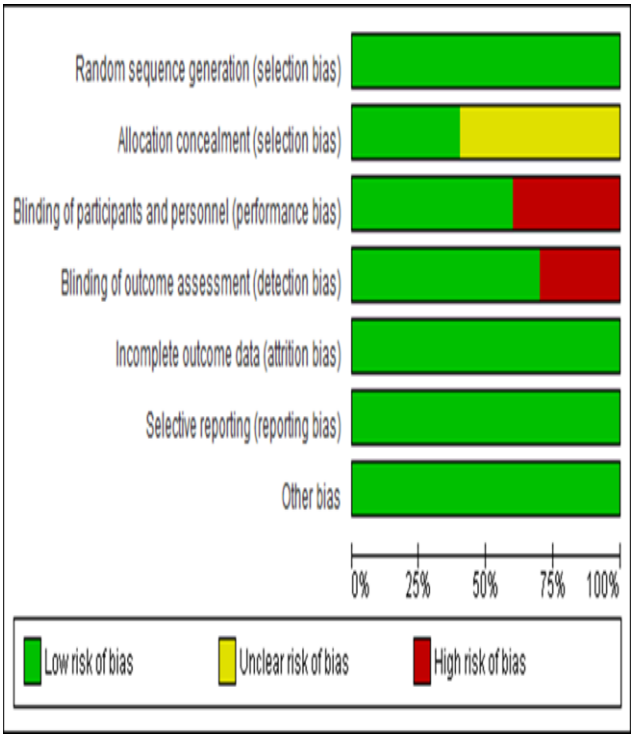

Figure 3: Risk of bias: review authors' judgements about each other risk of bias item present as percentages across all included studies.

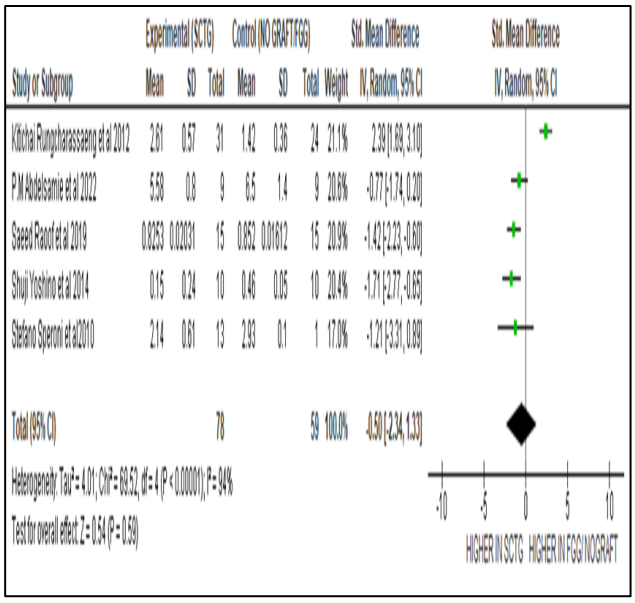

Figure 4: Meta-analysis for the amount of reduction in Keratinized tissue width of gingiva KTW among included studies. Forest plot of comparison: 1 SCTG vs FGG/ NO GRAFT, outcome: 1.1 increase in width of keratinized gingiva.

Results of meta-analysis

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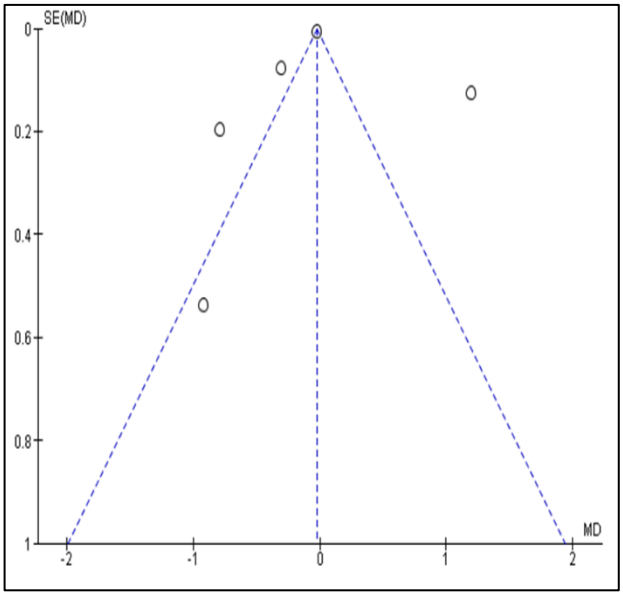

Figure 5: Funnel plot showing publication bias for keratinized tissue width of gingiva KTW.

DISCUSSION

In order to compare the efficacy of soft tissue augmentation using subepithelial connective tissue graft with free gingival graft and no graft for increasing the width of keratinized mucosa around dental implants, the current systematic review concentrated on RCTs, CCTs, prospective comparative study, and retrospective study. In an effort to find an explanation, 10 randomised controlled studies (Studies no. 1-10) were found. In this systematic review, gingiva's keratinized tissue width (KTW) was the main outcome assessed. PI, GI, and PPD were the secondary outcomes that were examined.

The overall improvement in the clinical parameters i.e., gain in keratinized tissue width of gingiva in FGG and SCTG groups. On comparison with FGG and SCTG, there is an increase in KTW in the SCTG group when compared to FGG group (study no. 5 and 10).

A total of 330 volunteers between the age of 20-65 years was recruited who required soft tissue augmentations.

The volunteers were then divided into two groups; the intervention group-SCTG and FGG and control group-no graft and FGG. The clinical parameters in the group received are described. Comparison of keratinized tissue width of gingiva in all included studies (Study no. 1, 2, 3, 5, 6, 7, 8 and 10) showed an overall increase in keratinized tissue width of gingiva in the intervention group when compared to the control group ($p<0.05$).

Increase in width of keratinized tissue

Gain of keratinized tissue

Regarding different methods and materials to supplement keratinized tissue around dental implants, seven studies, in particular, have been published. Every study showed that it was possible to successfully increase the width of keratinized tissue. Due to the studies' significant heterogeneity, some studies lacked control groups and applied the soft tissue transplantation at various time points. The choice of the papers that were chosen to be included also reveals developments and trends in clinical research. The choice of the papers that were chosen to be included also reveals developments and trends in clinical research.

Four investigations (investigations 6, 7, 8, and 9) compared the mean increased keratinized width of gingiva in the SCTG group with the control group and found that there was an increase in keratinized width of gingiva in the SCTG group. Within these three articles, Shuji Yoshino et al have explained briefly about time intervals from baseline to 12 months; i.e.; 0-3 months, 0-6 months, 0-12 months, 3-6 months, 3-12 months, 6-12 months. During this time interval, there was no statistically significant result within 3-6 months and 0-3 months. But the statistically significant result was seen between the time interval of 0-12 months; 0-6 months; 6-12 months and 3-12 months. ($p<0.001$) and implant used in this study was a conical “platform-switched” interface, which could be beneficial in maintaining peri-implant MBL biologically and mechanically. These studies are in line with several studies done by Chung, Tsuda and Maeda reported that MBL changes for IIPP procedure using platform-switched implants changes from +1.30 to -0.85 mm and this is less negative compared to non-platform-switched implants (-0.22 to -1.02 mm).[30-32]

In comparison with FGG with no graft; there is an increased keratinized width of gingiva in the FGG group when compared to the control group. It is theorized that FGG provides adequate width of keratinized tissue, higher survival rates of dental implants, the health of the peri-implant mucosa, and an improved aesthetic outcome. According to Roccuzzo et al and Oh et al the outcome was as expected. Although there was no statistically significant difference between the two groups ($p>0.05$), the peri-implant soft tissue collapsed in the Zheng et al study, and the changes (mucosal margin and soft tissue thickness) were significantly greater in the control group than the FGG group.

The research by Raoffi et al which examined both FGG and SCTG, revealed that there was a rise in the breadth of keratinized tissue in the SCTG group, which was 3.097, 0.002 wider than that of the FGG group. In their study, Roccuzzo et al found that the mean MTH was 2.89 mm after 12 months postoperatively, with a mean extra rise of 1.75 mm compared to baseline ($p=0.0001$). Between the 12- and 36-month observations, there were no MTH differences that were statistically significant ($p=0.09$). By contrasting these two papers, it can be shown that the SCTG group's gingiva has wider keratinized tissue than the FGG group.

Pocket probing depth

According to Becker et al increased periodontal PD (PPD) is a key sign that there is a significant chance that an infection would spread to the implant mucosa.[9] Four investigations (investigations 1, 2, 3, and 4) measured PPD. In comparison to the control group, the intervention group's periodontal probing depth increased in all three studies (Studies 1, 2, and 4). In contrast, one study (Study no. 3) found no statistically significant difference in improvement between the control and intervention groups.

Gingival and plaque index

Implant success is allegedly influenced by both mechanical component strength (implant components and superstructure) and biological tissue reactivity (soft tissues and bone). Both the soft tissue's sensitivity to bacterial invasion and the bone's susceptibility to stress has been linked to bone loss surrounding implants.[10] Patient compliance is one of the most important factors in ensuring the longevity and efficacy of dental implants. Four studies (Study no 1, 3, 4 and 9) reported the gingival and plaque index and it states that there is a reduction in indices when compared to the baseline in both the control and interventional group. But there was a statistically significant result seen in the intervention group compared to the control group.

Limitation

Dental implants can be used to undertake soft tissue augmentation treatments employing a variety of different modalities, including autogenous graft, xenograft, allogenic, and alloplastic materials. There is enough research using autogenous grafts for soft tissue augmentation treatments in dental implants that have been described in the literature. But few RCTs were yielded while comparing FGG and SCTG. This systematic review yielded 10 RCTs that addressed the focused question. All these studies presented variations in sample size, and inconsistencies in the follow-up period. In addition, all

the included studies did not entirely report the primary and secondary outcomes.

Therefore, there is a weighty need for more RCTs to be conducted with a focus on appropriate outcomes and consistency in the follow-up period. This would provide considerable evidence for the possible benefits of using SCTG over FGG in soft tissue augmentation procedures in dental implants.

CONCLUSION

The present systematic review revealed that the gain of KM at implant sites, based on combination with SCTG rendered a gain in keratinized tissue for an observation period of more than 2 years to 10 years. In contrast to gingival augmentation, only one study reported the contrary results. However, some shrinkage may occur with all applied grafting materials and may result in a decrease in the width of keratinized tissue. Again, some shrinkage of the augmented sites has to be considered. From an aesthetic point of view, soft tissue volume grafting concomitant with immediate implant placement may result in superior outcomes with respect to papilla height and the level of the marginal mucosa. Based on the results obtained from the current systematic review and meta-analysis, for soft tissue volume augmentation, autogenous tissue (SCTG) has to be considered the treatment of choice resulting in an increase in soft tissue thickness at implant sites and in partially edentulous sites have overall improvement in clinical parameters. (i.e.; primary and secondary outcome)

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