

Efficacy of maxillary tuberosity connective tissue grafts in periodontal and peri-implant soft tissue procedures: a systematic review

Katie Chung, DDS¹

Anastasia Kelekis-Cholakis, DMD, Dip. Perio²

Adnan Shah, BDS, MDS^{3,4}

Charlene Solomon, BChD, MSc, MChD⁵

Chrysi Stavropoulou, DDS, MDent¹

¹Division of Periodontology, Dr. Gerald Niznick College of Dentistry, University of Manitoba, Winnipeg, Manitoba, Canada

²Dr. Gerald Niznick College of Dentistry, University of Manitoba, Winnipeg, Manitoba, Canada

³Division of Oral & Maxillofacial Surgery, Dr. Gerald Niznick College of Dentistry, University of Manitoba, Winnipeg, Manitoba, Canada

⁴University of Health Sciences Lahore, Lahore, Punjab, Pakistan

⁵Division of Prosthodontics, Dr. Gerald Niznick College of Dentistry, University of Manitoba, Winnipeg, Manitoba, Canada

Correspondence to: Dr Chrysi Stavropoulou, D344 - 790 Bannatyne Avenue, Dr. Gerald Niznick College of Dentistry, University of Manitoba, Winnipeg, MB, Canada, R3E 0W2. Phone: +1-204-272-3075 Fax: +1-204-272-3077. Email: Chrysi.Stavropoulou@umanitoba.ca

Abstract

The objective of this systematic review was to assess the efficacy of maxillary tuberosity connective tissue grafts (MT-CTGs) in periodontal plastic surgeries at tooth and implant sites. An electronic search of literature in OVID, Embase, Cochrane and Scopus databases and a manual search up to August 2022 were performed to identify clinical studies at all levels of evidence with a minimum 3 month follow-up. Out of 880 potential publications, 10 studies were included, which included randomized controlled trials (RCTs), cohort studies and case reports. Due to study heterogeneity, a meta-analysis was not performed. Risk of bias was assessed with the Cochrane Risk of Bias 2 tool, the Newcastle-Ottawa Scale and the JBI Critical Appraisal checklist. MT-CTGs were more commonly utilized for peri-implant soft tissue augmentation, with keratinized mucosa thickness gain of 3-4 mm. Favourable gingival recession and mucosal dehiscence coverage outcomes, and satisfactory aesthetic ratings were reported though untoward hyperplastic tissue reactions at treated sites have also been documented. The limited evidence suggests MT-CTGs to be a sound soft tissue graft choice which may perform as well as lateral palate CTGs in periodontal soft tissue surgeries. Their true effect is yet to be determined with more well-designed long-term RCTs.

Introduction

The use of autogenous soft tissue grafts to treat mucogingival deformities was first introduced with the free gingival graft (FGG) in the 1960s. The subepithelial connective tissue graft (CTG) was later introduced in 1974¹, which soon gained popularity for its use in root coverage procedures following Langer and Langer's bilaminar technique². Currently, CTG plus coronally advanced flap (CAF) is the gold standard for root coverage.³ Greater complete root coverage (CRC) and mean root coverage (RC), and less relapse are achieved with CTG+CAF compared to CAF alone.^{3,4} The bilaminar approach with CTG is also beneficial for soft tissue augmentation (STA) around dental implants. In a recent systematic review, Tavelli et al.⁵ reported that the bilaminar technique with CTG obtained the most keratinized mucosa (KM) thickness gain and was positively associated with marginal bone level stability. Thicker KM has been associated with higher implant survival rates, and lower levels of marginal bone loss, plaque accumulation and brushing discomfort.⁶ Soft tissue deficiencies are common after tooth extractions and should be appropriately addressed for implant and pontic site development with STA. STA can also correct aesthetic problems such as vertical and horizontal facial soft tissue deficiencies which may also present with exposure or show-through of the implant fixture or abutment.

The most cited CTG donor site is the lateral hard palate (LP). The palatal mucosa is comprised of squamous cell epithelium, lamina propria and periosteum, with the lamina propria being the layer of interest for CTG harvest.⁷ In the posterior regions, there is a submucosal layer subjacent to the lamina propria containing adipose and glandular tissue.⁷ Though the LP is an effective graft source, its main disadvantage is donor site morbidity, which may interfere with daily oral function and affect patient satisfaction.⁸⁻¹⁰ Numerous palatal harvesting and wound dressing techniques have been developed to mitigate postoperative sequelae and complications.⁸⁻
¹⁰ The LP also presents with anatomical challenges, including the greater palatine neurovascular

bundle and the potential presence of palatal exostoses and root prominences, which may complicate CTG harvest and postoperative healing.

An alternative CTG donor site is the maxillary tuberosity (MT), which has less overall graft availability but offers advantages over the LP. Use of MT soft tissue was first proposed for ridge augmentation by Studer et al.¹¹ This group reported significantly thicker soft tissue in the MT measuring 3.7-5.8 mm, whereas LP thickness varied between 1.6-4.5 mm.¹¹ Sanz-Martin et al.¹² found MT-CTGs to be composed of a higher percentage of lamina propria and a smaller proportion of submucosa than LP-CTGs. Though the MT can be more difficult to surgically access especially in dentate patients, it may result in less postoperative discomfort as its location is less involved with mastication and speech. The anatomic and biological benefits offered by the MT appear desirable for clinical augmentation and patient-centered outcomes. Therefore, this systematic review aimed to assess the efficacy of MT-CTGs in periodontal and peri-implant soft tissue surgeries.

Materials and Methods

Study Protocol and Registration

The review protocol was registered under identification number CRD42021260885 with the International Prospective Register of Systematic Reviews (PROSPERO).

PICO Question

Population (P): adult patients (≥ 18 years old) undergoing periodontal and peri-implant soft tissue surgery; Intervention (I): MT-CTG; Comparison (C): no treatment, LP-CTG, xenogeneic graft, allogeneic graft; Outcome (O): primary outcomes of recession reduction (RecRed), RC, CRC, keratinized tissue (KT) or mucosa (KM) thickness gain, keratinized tissue width (KTW) gain, keratinized mucosa width (KMW) gain, probing depth (PD) reduction and/or clinical attachment

level (CAL) gain reported in mm or %; and if available, secondary patient-related outcomes such as morbidity and aesthetic satisfaction were assessed

Eligibility Criteria and Search Strategy

Comprehensive search strategies were established to identify studies for this systematic review. Electronic and manual literature searches were conducted by two independent reviewers (KC and CS) based on the inclusion and exclusion criteria and search strategy shown in Table 1.

The OVID, Embase, Cochrane and Scopus electronic databases were searched for studies published up to August 2022. All reference lists of the selected studies were checked for cross-references. A manual search was performed in the following journals from 1985 to 2022: *International Journal of Periodontics & Restorative Dentistry*, *Journal of Periodontology*, *Journal of Clinical Periodontology* and *International Journal of Oral & Maxillofacial Implants*.

Data Extraction

Two independent reviewers (KC and CS) screened the titles, abstracts and full text of the included articles. At each stage, any disagreements were resolved by a third independent reviewer (AC). A meta-analysis could not be performed due to high study heterogeneity.

Quality and Risk of Bias Assessment

The assessment of methodological quality and risk of bias were performed using the Cochrane Risk of Bias (RoB) 2 for randomized studies (low, some concerns, high)¹³, the Newcastle-Ottawa Scale (NOS) for cohort studies (maximum 9 stars)¹⁴ and the JBI Critical Appraisal for case reports (inclusion, exclusion, further information should be sought)¹⁵.

Results

Included Studies

The search process identified 880 potential studies. After duplicate removal, title and abstract screening and full text review (Table 2), 10 publications met the inclusion criteria, consisting of three randomized controlled trials (RCTs)¹⁶⁻¹⁸, five cohort studies¹⁹⁻²³ and two case reports^{24,25} (Figure 1). Inter-rater reliability was near perfect at the title and abstract level ($\kappa = 0.898$), and substantial at the full text level ($\kappa = 0.728$).

Risk of Bias

The RCTs¹⁶⁻¹⁸ expressed some concerns largely due to selection of the reported results (Figure 2). With the NOS quality assessment, one cohort study²¹ received 8 out of 9 stars, one study²⁰ received 7 stars and the remaining three studies^{19,22,23} received 6 stars (Table 3). The two case reports^{24,25} were included for qualitative analysis upon completion of the JBI Critical Appraisal.

Effects of Interventions

The general characteristics and main findings of the included studies are displayed in Table 4.

Tooth sites

RecRed was observed in three root coverage studies: 1.5 mm²⁵, 3 mm²⁴, and 3.14 ± 0.15 mm¹⁹. CRC for Miller class I and II recession defects was attained at 4 sites in 2 patients in a case report²⁴, while CRC was achieved at $95.0 \pm 1.84\%$ of sites and $94.7 \pm 1.9\%$ of patients in another study¹⁹. Hirsch et al.¹⁹ also observed mean RC of $98.9 \pm 0.39\%$ and mean KTW gain of 2.45 mm. Park²⁵ reported KTW gain of 1-2 mm at a Miller Class III recession site in one patient.

Baseline and final PDs were ≤ 3 mm at the recipient site.²⁴ Mean PD reduction of 4.08 ± 0.24 mm and mean CAL gain of 3.76 ± 0.27 mm occurred at the donor site after a mean of 32.68 months.¹⁹

For patient-related outcomes, no objective aesthetic analyses were used. A decrease in tooth hypersensitivity from 15 patients to 1 patient was reported.¹⁹

Implant sites

For STA prior to implant placement, Dellavia et al.²⁰ found the MT-CTG group to continually increase in mean KM thickness over time, from 2.1 ± 0.2 mm at baseline to 5.8 ± 0.2 mm at 1 month to 6.8 ± 1.1 mm at 1 year, whereas the LP-CTG group demonstrated a slight decrease from 1 month (5.5 ± 0.5 mm) to 1 year (4.9 ± 0.6 mm) and did not exhibit further changes up to 21 months.

Similarly, simultaneous MT-CTG STA with delayed implant placement resulted in mean KM thickness increasing from 2.4-2.5 mm to 5.4-5.8 mm ($p < 0.001$) after 3 years in a split-mouth study.²¹ Split thickness recipient sites demonstrated mean KMW increase from 0.6 ± 0.6 mm to 5.1 ± 0.72 mm, significantly greater to the lack of KMW change with a full thickness tunnel ($p < 0.001$).²¹ Mean midbuccal dehiscences of 1.4 ± 0.6 mm and 2.6 ± 0.7 mm developed in the split and full thickness groups, respectively ($p < 0.001$).²¹ A 12-month RCT investigating immediate implant placement (IIP) observed MT-CTG to provide greater stability of the midbuccal mucosal level (MBML) (0.1 ± 0.8 mm) than at non-grafted sites (-0.5 ± 1.1 mm, $p = 0.03$).¹⁸

Four studies from two research groups performed staged STA post-implant placement. In two RCTs, Rojo et al.^{16,17} treated peri-implant buccal horizontal deficiencies. After 3 months, MT-CTG and LP-CTG groups achieved similar mean KM thickness gain of 0.79 ± 0.10 mm and 0.69 ± 0.23 mm, respectively ($p = 0.64$).¹⁶ At 4 and 12 months, there was no difference in mean KM thickness between groups or timepoints.¹⁷ Similar mean KMW was gained with MT-CTG (1.28 ± 0.67 mm) and LP-CTG (0.87 ± 0.99 mm, $p = 0.29$) at 3 months¹⁶, with minimal changes between 4 and 12 months (MT-CTG 0.18 ± 0.53 mm; LP-CTG -0.42 ± 0.9 mm, $p = 0.03$)¹⁷. Rocuzzo et

al.^{22,23} treated peri-implant buccal vertical deficiencies with MT-CTG. Mean dehiscence reduction was 1.7 ± 0.3 mm after 1 year ($p = 0.0004$). Mean dehiscence coverage was $89.6 \pm 13.1\%$ and $86 \pm 19\%$, and complete dehiscence coverage was 56.3% and 62% at 1 and 5 years, respectively.^{22,23}

Mean PDs at MT-CTG sites did not change significantly from baseline at 1 or 5 years^{22,23}, nor did they differ with clinical significance from LP-CTG sites at 3, 4 and 12 months^{16,17}.

MT-CTG was associated with acceptable aesthetic satisfaction. Mean final visual analogue scale (VAS) scores were 8.5 ± 0.3 and 8.1 ± 0.9 at 1 and 5 years, respectively.^{22,23} There was no difference in mean modified Pink Esthetic Score (PES)²⁶ between MT-CTG and LP-CTG groups, respectively reported to be 9.15 ± 2.34 and 10.07 ± 2.19 after 3 months¹⁶, and 8.54 ± 2.43 and 8.37 ± 2.46 after 1 year ($p = 0.59$)¹⁷. When comparing mean PES to the non-grafted group (6.4 ± 1.5), the MT-CTG group fared similarly (6.8 ± 1.5 , $p = 0.21$).¹⁸

Adverse Effects

No complications were reported in most studies.^{18,19,21-23,25} Hyperplastic tissue reactions at MT-CTG-treated sites were observed in two studies at 3 months and 12 months, which were subsequently corrected by surgery to reduce bulk.^{20,24} However the hyperplastic response recurred with approximately 70% tissue rebound in the subsequent 9 months in one study.²⁰

Discussion

The present systematic review shows MT-CTGs to be a safe and valid graft choice for periodontal plastic surgery. The majority of the included studies provide proof of principle with high or some concern for bias. Studies were heterogenous in design with many lacking blinding, patient randomization, control group(s), adjustment of confounding variables and statistical analyses.

Several implant studies suggest that MT-CTGs can perform similarly to LP-CTGs in KM thickness gain and KMW gain at 1 year.^{16,17,20} A KM thickness gain of approximately 3-4 mm was reported^{11,20}, whereas LP-CTG and xenogeneic collagen matrix resulted in mean KM thickness gain of 1.2 ± 0.3 mm and 0.9 ± 0.2 mm in another study²⁷. Puisys et al.²¹ observed significant KTW gain from 0.6 ± 0.6 mm to 5.1 ± 0.72 mm when MT-CTG was utilized with a split thickness tunnel; however split thickness flap use in two RCTs^{16,17} resulted in mean KMW gain of <1 mm in both MT-CTG and LP-CTG groups. All studies herein described use of split thickness flaps, and the impact of flap periosteum and thickness on MT-CTG clinical outcomes is yet to be determined.

CTG promotes midbuccal marginal stability at IIP sites and a meta-analysis by Seyssens et al.²⁸ concluded the risk for ≥ 1 mm asymmetry in MBML was 12-fold lower following IIP+CTG. Zuiderveld et al.¹⁸ were in agreement and reported a tendency for the MT-CTG group to exhibit less change than the non-grafted control group at 12 months ($p = 0.18$).

None of the included tooth studies compared MT-CTG directly with another treatment modality. MT-CTG+CAF achieved 95% CRC and 98.9% mean RC at mean 32.7 months in a cohort study¹⁹, which were greater than the previously published outcomes of LP-CTG+CAF at similar Miller Class I and II defects. CRC at 58.3-86% and 66.7% of sites were observed in RCTs at 1 and 9 years, respectively.^{29,30} A 8-week split-mouth study observed no difference in mean RC between MT-CTG ($67 \pm 12\%$) and LP-CTG sites ($62 \pm 13\%$, $p = 0.102$).³¹

While the true effect of MT-CTG remains unknown, its application may be most beneficial for KM thickness gain. Histologically MT-CTGs contain a higher composition of denser and less vascularized lamina propria than LP-CTGs, which is favourable for volume gain and less shrinkage.^{11,20} Molecular analyses did not identify differences in Type I and III collagen content in MT- and LP-CTGs, however there were greater levels of lysyl hydroxylase 2 (LH2) in MT-

CTG.^{11,20} Furthermore Dellavia et al.²⁰ identified a 4-fold increase of *LH2b/COL-1* mRNA levels in MT fibroblasts compared to LP fibroblasts. Elevated *LH2b/COL-1* mRNA levels were significantly and positively associated with presence of a hyperplastic tissue response. This group speculated that a higher proportion of LH2b promotes Type 1 collagen hydroxylation, resulting in more crosslinking events, less degradation, and finally excess collagen accumulation.²⁰ Hyperplastic tissue reactions associated with MT-CTGs have been previously described with unsatisfactory aesthetics, unpredictable surgical resolution and a propensity for continual enlargement.^{20,32} Their prevalence and exacerbating factors have not been identified. Histologic analyses of hyperplastic tissue specimens removed during corrective gingivectomy procedures revealed normal KM tissue morphology with hyperkeratosis and dense connective tissue, with no to few inflammatory cells.^{24,32} Surgeons should inform patients of this potential side effect and be wary of MT-CTG application in aesthetically demanding cases.

In most cases, MT-CTGs provided an aesthetic outcome as satisfactorily as LP-CTGs. No differences in modified PES were reported up to 1 year.^{16,17} For mucosal dehiscence coverage, the clinician-reported VAS scores in Rojo et al.'s studies^{22,23} were respectively 8.1 ± 0.3 and 8.5 ± 0.9 at 1 and 5 years, which were similar to the periodontist-rated VAS scores of 8.75 ± 1.02 at 1 year and 8.95 ± 0.91 at 5 years in Zucchelli's LP-CTG study³³.

Conclusions

Due to the limited evidence available, the efficacy of MT-CTGs remains inconclusive. The maxillary tuberosity as a CTG donor site can be used successfully for root coverage and peri-implant STA, and may provide similar clinical outcomes as the lateral palate. Satisfactory aesthetic outcomes can be achieved, however the grafted site may experience a hyperplastic response after several months. More well-designed and controlled clinical trials with larger sample sizes and long-term follow-up are needed to elucidate the role of MT-CTG in periodontal plastic surgeries.

Acknowledgments

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References

1. Edel A. Clinical evaluation of free connective tissue grafts used to increase the width of keratinised gingiva. *J Clin Periodontol* 1974;1:185-196.
2. Langer B, Langer L. Subepithelial connective tissue graft technique for root coverage. *J Periodontol* 1985 Dec;56:715-720.
3. Cairo F, Nieri M, Pagliaro U. Efficacy of periodontal plastic surgery procedures in the treatment of localized facial gingival recessions. A systematic review. *J Clin Periodontol* 2014;41:S44-62.
4. Barootchi S, Tavelli L, Di Gianfilippo R, Byun HY, Oh TJ, Barbato L, Cairo F, Wang HL. Long term assessment of root coverage stability using connective tissue graft with or without an epithelial collar for gingival recession treatment. A 12-year follow-up from a randomized clinical trial. *J Clin Periodontol* 2019;46:1124-1133.
5. Tavelli L, Barootchi S, Avila-Ortiz G, Urban IA, Giannobile WV, Wang HL. Peri-implant soft tissue phenotype modification and its impact on peri-implant health: A systematic review and network meta-analysis. *J Periodontol* 2021;92:21-44.
6. Sanz M, Schwarz F, Herrera D, McClain P, Figuero E, Molina A, Monje A, Montero E, Pascual A, Ramanauskaite A, Renouard F, Sader R, Schiegnitz E, Urban I, Heitz-Mayfield L. Importance of keratinized mucosa around dental implants: Consensus report of group 1 of the DGI/SEPA/Osteology Workshop. *Clin Oral Implants Res* 2022;333:S47-55.
7. Harris RJ. Histologic evaluation of connective tissue grafts in humans. *Int J Periodontics Restorative Dent* 2003;23:575-583.
8. Stavropoulou C, Atout RN, Brownlee M, Schroth RJ, Kelekis-Cholakias A. A randomized clinical trial of cyanoacrylate tissue adhesives in donor site of connective tissue grafts. *J Periodontol* 2019;90:608-615.

9. Basma HS, Saleh MHA, Abou-Arraj RV, Imbrogno M, Ravida A, Wang HL, Li P, Geurs N. Patient-reported outcomes of palatal donor site healing using four different wound dressing modalities following free epithelialized mucosal grafts: A four-arm randomized controlled clinical trial. *J Periodontol* 2023;94:88-97.
10. Puri K, Kumar A, Khatri M, Bansal M, Rehan M, Siddeshappa ST. 44-year journey of palatal connective tissue graft harvest: A narrative review. *J Indian Soc Periodontol* 2019;23:395-408.
11. Studer SP, Allen EP, Rees TC, Kouba A. The thickness of masticatory mucosa in the human hard palate and tuberosity as potential donor sites for ridge augmentation procedures. *J Periodontol* 1997;68:145-151.
12. Sanz-Martín I, Rojo E, Maldonado E, Stroppa G, Nart J, Sanz M. Structural and histological differences between connective tissue grafts harvested from the lateral palatal mucosa or from the tuberosity area. *Clin Oral Investig* 2019;23:957-964.
13. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898.
14. Wells GA, Wells G, Shea B, Shea B, O'Connell D, Peterson J, Welch, Losos M, Tugwell P, Ga SW, Zello GA, & Petersen JA. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses. 2014: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
15. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, Qureshi R, Mattis P, Lisy K, Mu P-F. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris

E, Munn Z (eds). JBI Manual for Evidence Synthesis. JBI, 2020:
<https://synthesismanual.jbi.global>

16. Rojo E, Stroppa G, Sanz-Martin I, Gonzalez-Martín O, Alemany AS, Nart J. Soft tissue volume gain around dental implants using autogenous subepithelial connective tissue grafts harvested from the lateral palate or tuberosity area. A randomized controlled clinical study. *J Clin Periodontol* 2018;45:495-503.
17. Rojo E, Stroppa G, Sanz-Martin I, Gonzalez-Martín O, Nart J. Soft tissue stability around dental implants after soft tissue grafting from the lateral palate or the tuberosity area - A randomized controlled clinical study. *J Clin Periodontol* 2020;47:892-899.
18. Zuiderveld EG, Meijer HJA, den Hartog L, Vissink A, Raghoobar GM. Effect of connective tissue grafting on peri-implant tissue in single immediate implant sites: A RCT. *J Clin Periodontol* 2018;45:253-264.
19. Hirsch A, Attal U, Chai E, Goultchin J, Boyan BD, Schwartz Z. Root coverage and pocket reduction as combined surgical procedures. *J Periodontol* 2001;72:1572-1579.
20. Dellavia C, Ricci G, Pettinari L, Allievi C, Grizzi F, Gagliano N. Human palatal and tuberosity mucosa as donor sites for ridge augmentation. *Int J Periodontics Restorative Dent* 2014;34:179-186.
21. Puisys A, Auzbikaviciute V, Vindasiute-Narbutė E, Zukauskas S, Razukevicius D, Dard MM. Full versus partial thickness flap to determine differentiation and over keratinization of non-keratinized mucosa. A 3-year split mouth randomized pilot study. *Clin Exp Dent Res* 2021;7:1061-1068.
22. Rocuzzo M, Gaudio L, Bunino M, Dalmaso P. Surgical treatment of buccal soft tissue recessions around single implants: 1-year results from a prospective pilot study. *Clin Oral Implants Res* 2014;25:641-646.

23. Rocuzzo M, Dalmaso P, Pittoni D, Rocuzzo A. Treatment of buccal soft tissue dehiscence around single implant: 5-year results from a prospective study. *Clin Oral Investig* 2019;23:1977-1983.
24. Jung UW, Um YJ, Choi SH. Histologic observation of soft tissue acquired from maxillary tuberosity area for root coverage. *J Periodontol* 2008;79:934-940.
25. Park JB. Clinical showcase. Treatment of gingival recession with subepithelial connective tissue harvested from the maxillary tuberosity by distal wedge procedure. *J Can Dent Assoc* 2009;75:643-646.
26. Fürhauser, R., Florescu, D., Benesch, T., Haas, R., Mailath, G., Watzek, G. Evaluation of soft tissue around single-tooth implant crowns: The pink esthetic score. *Clin Oral Implants Res* 2005; 16:639-644.
27. Cairo F, Barbato L, Tonelli P, Batalocco G, Pagavino G, Nieri M. Xenogeneic collagen matrix versus connective tissue graft for buccal soft tissue augmentation at implant site. A randomized, controlled clinical trial. *J Clin Periodontol* 2017;44:769-776.
28. Seyssens L, De Lat L, Cosyn J. Immediate implant placement with or without connective tissue graft: A systematic review and meta-analysis. *J Clin Periodontol* 2021;48:284-301.
29. Zucchelli G, Mounssif I, Mazzotti C, Stefanini M, Marzadori M, Petracci E, Montebugnoli L. Coronally advanced flap with and without connective tissue graft for the treatment of multiple gingival recessions: a comparative short- and long-term controlled randomized clinical trial. *J Clin Periodontol* 2014;41:396-403.
30. Rasperini G, Acunzo R, Pellegrini G, Pagni G, Tonetti M, Pini Prato GP, Cortellini P. Predictor factors for long-term outcomes stability of coronally advanced flap with or without connective tissue graft in the treatment of single maxillary gingival recessions: 9 years results of a randomized controlled clinical trial. *J Clin Periodontol* 2018;45:1107-1117.

31. Amin PN, Bissada NF, Ricchetti PA, Silva APB, Demko CA. Tuberosity versus palatal donor sites for soft tissue grafting: A split-mouth clinical study. *Quintessence Int* 2018;49:589-598.
32. Gluckman H, Du Toit J, Pontes CC, Hille J. Hyperplastic Response Following Soft Tissue Augmentation in the Esthetic Zone. *Clin Adv Periodontics* 2019;9:50-54.
33. Zucchelli G, Felice P, Mazzotti C, Marzadori M, Mounssif I, Monaco C, Stefanini M. 5-year outcomes after coverage of soft tissue dehiscence around single implants: A prospective cohort study. *Eur J Oral Implantol* 2018;11:215-224

Figure legends

		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Rojo et al. ¹⁶						
	Rojo et al. ¹⁷						
	Zuiderveld et al. ¹⁸						

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
 Some concerns
 Low

Fig 1 PRISMA flow diagram of the search strategy and selection process

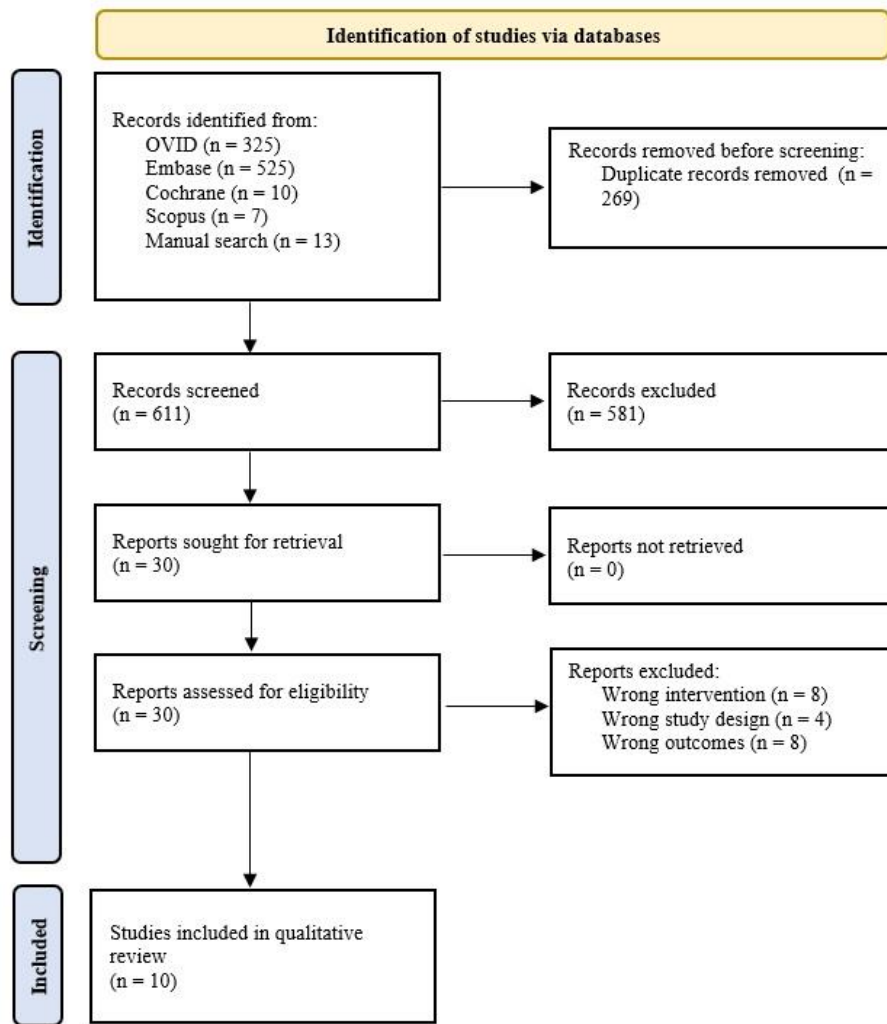


Fig 2 Cochrane Risk of Bias 2 results for RCTs

Table 1 Electronic Search Strategy

Inclusion criteria	English language publications of human studies, root coverage or soft tissue augmentation procedures with maxillary tuberosity soft tissue graft at tooth or implant sites, minimum follow-up period of 3 months
Exclusion criteria	Animal studies, <i>in vitro</i> studies, subjects with uncontrolled systemic disease, subjects with uncontrolled periodontitis
Search strategy	<ol style="list-style-type: none">1. Tuberosity.mp2. (connective OR soft) AND tissue3. mouth membrane OR mouth mucosa4. 2 OR 35. 1 AND 46. “soft tissue” OR “connective tissue” OR “keratinized tissue” OR “keratinized mucosa” OR “mucogingival” OR “root coverage” OR “gingiva*” OR “recession” OR “peri-implant mucosa” OR “peri-implant tissue” OR “peri-implant area” OR periodont* OR “tooth root” OR “dental implant” OR “tissue transplantation” OR graft OR autograft7. Augment* OR surgery OR therapy OR treatment OR manage* OR enhanc* OR graft* OR thicken*8. 6 AND 79. “Distal wedge”10. 8 OR 911. 5 AND 10

Table 2 Full Text Review – Study Exclusion

Exclusion reason	Study	DOI or PMID if indicated	Details
Wrong intervention	Muthukumar et al. (2016)	10.4103/0972-124X.193164	CTG harvested from LP
	Franceschi et al. (2018)	10.1155/2018/1672170	
	Azzi et al. (2001)	PMID: 11829388	
	Stipetic et al. (2005)	PMID: 16117330	No surgical intervention with MT-CTG
	Raghoebar et al. (2017)	10.1016/j.joms.2017.09.005	MT-FGG harvested with MT hard tissue as one piece
	Houmani et al. (2021)	PMID: 34210931	
	Zufia et al. (2019)	10.1111/jerd.12480	
	Younes & Khairallah (2020)	10.1155/2020/3945076	
Wrong study design	Zuhr et al. (2014)	10.1111/jcpe.12185	Narrative review
	Zucchelli et al. (2020)	10.1002/JPER.19-0350	
	Tavelli et al. (2019)	10.1002/JPER.18-0615	
	da Rosa et al. (2014)	10.1016/j.prosdent.2014.03.020	Technique introduction with no clinical results
Wrong outcomes	Gomborena et al. (2021)	10.1111/jerd.12716	Did not report primary/secondary outcomes
	Sanz-Martin et al. (2019)	10.1007/s00784-018-2516-9	
	Godat et al. (2018)	PMID: 30188146	Did not objectively report primary/secondary outcomes
	Kina et al. (2018)	10.21767/2471-3082.100038	
	De Molon et al. (2015)	10.1111/jerd.12154	
	Gluckman et al. (2019)	10.1002/cap.10047	
	Meltzer 1979	10.1902/jop.1979.50.6.320	
	Nizam & Akcali (2019)	10.11607/prd.2736	

CTG = connective tissue graft; DOI = digital object identifier; FGG = free gingival graft; LP = lateral palate; MT = maxillary tuberosity; PMID = PubMed identifier

Table 3 Newcastle-Ottawa Quality Assessment Scale for Cohort Studies

Study	Selection				Comparability (2)	Outcome			Total (9)
	Representativeness of exposed cohort (1)	Selection of non- exposed cohort (1)	Ascertainment of exposure (1)	Demonstration that outcome was absent at start of study (1)		Assessment of outcome (1)	Length of follow-up (1)	Adequacy of follow-up (1)	
Puisys et al. ²¹	*	*	*	*	*	*	*	*	8
Dellavia et al. ²⁰		*	*	*	*	*	*	*	7
Hirsch et al. ¹⁹	*		*	*		*	*	*	6
Roccuzzo et al. ²²	*		*	*		*	*	*	6
Roccuzzo et al. ²³	*		*	*		*	*	*	6

Table 4 Characteristics of the Included Studies

Tooth studies

Study	Study Setting, Country	Study Design, Follow-up	Patients/ teeth (n)	Drop-outs/ Lost to follow-up	Periodontal status and smoking habits	Goal of surgery	Flap design	Jaw	Main results
Hirsch et al. ¹⁹	University, Israel	Prospective cohort, Mean 32.68 months	25 patients 44 teeth	0	Unknown periodontal status, PD >5 mm at donor site, non-smokers and smokers ≤20 cigarettes/day	Root coverage for Miller Class I and II recession at recipient site, pocket reduction at donor site	Split thickness coronally advanced flap	Maxilla	<p><u>Site level</u> CRC (%): 95 ± 1.84 RC (%): 98.9 ± 0.39 RecRed (mm): 3.14 ± 0.15 KTW gain (mm): 2.45</p> <p><u>Patient-level</u> CRC (%): 94.7 ± 1.9 CAL gain (mm) at donor site: 3.76 ± 0.27 PD reduction (mm) at donor site: 4.08 ± 0.24</p> <p>Tooth sensitivity: decreased from 15 patients to 1 patient</p>
Jung et al. ²⁴	Hospital, Korea	Case reports, 31 and 35 months	2 patients 4 teeth	0	Unknown periodontal status, non-smokers	Root coverage for Miller Class I and II recession	Case 1: split thickness pouch Case 2: tunnel and semilunar technique	Maxilla	<p>RC (%): 100 RecRed (mm) in 1 patient: 3 KTW gain (mm): 4</p> <p>Hyperplastic response observed in 1 patient</p>
Park ²⁵	Hospital, Korea	Case report, 13 months	1 patient 1 tooth	0	Unknown periodontal status, unknown smoking status	Root coverage for Miller Class III recession at recipient site, pocket reduction at donor site	Split thickness coronally advanced flap	Mandible	RecRed (mm): 1.5 KTW change (mm): from 2 mm to 3-4 mm

Implant studies

Study	Study Setting, Country	Study Design, Follow-up	Patients/implants (n)	Drop-outs/ Lost to follow-up	Periodontal status and smoking habits	Goal of surgery	Flap design at recipient site	Jaw	Main results
Rojo et al. ¹⁶	University, Spain	RCT – parallel design, 3 months Test group: MT-CTG Control: LP-CTG	32 patients 36 implants	3 patients 3 implants	Healthy, FMPS and FMBS <20%, non-smokers and smokers ≤10 cigarettes/day	Peri-implant soft tissue augmentation of buccal deficiencies	Split thickness flap	24 maxilla 12 mandible	<p>KM thickness gain (mm, p = 0.64) · MT-CTG 0.79 ± 0.10 · LP-CTG: 0.69 ± 0.23 KMW gain (mm, p = 0.29): · MT-CTG 1.28 ± 0.67 · LP-CTG: 0.87 ± 0.99 PD reduction (mm, p = 0.68) · MP-CTG: 0.13 ± 0.47 · LP-CTG: 0.02 ± 0.63</p> <p>Modified PES: · MT-CTG: 9.15 ± 2.34 · LP-CTG: 10.07 ± 2.19</p>
Rojo et al. ¹⁷	University, Spain	RCT – parallel design, 12 months	32 patients 36 implants	5 patients 5 implants	Healthy, FMPS and FMBS <20%, non-	Peri-implant soft tissue augmentation of buccal	Split thickness flap	24 maxilla	Outcomes between 4 and 12 months

		Test group: MT-CTG Control: LP-CTG			smokers and smokers ≤10 cigarettes/day	deficiencies		12 mandible	<p>KM thickness gain (mm, p = 0.87):</p> <ul style="list-style-type: none"> · MT-CTG 0.04 ± 0.23 · LP-CTG: 0.03 ± 0.22 <p>KMW difference (mm, p = 0.03)</p> <ul style="list-style-type: none"> · MT-CTG: 0.18 ± 0.53 · LP-CTG: -0.42 ± 0.9 <p>PD reduction (mm, p = 0.6)</p> <ul style="list-style-type: none"> · MP-CTG: 0 ± 0.33 · LP-CTG: 0.04 ± 0.34 <p>Modified PES:</p> <ul style="list-style-type: none"> · MT-CTG 8.54 ± 2.43 · LP-CTG 8.37 ± 2.46
Zuiderveld et al. ¹⁸	University, the Netherlands	RCT – parallel design, 12 months Test group: MT-CTG Control: no soft tissue graft	60 patients 60 implants	2 patients 2 implants	Healthy, FMPS and FMBS <20%, non-smokers and smokers ≤10 cigarettes/day	Peri-implant soft tissue augmentation with immediate implant placement for aesthetics	Split thickness tunnel	Maxilla	<p>MBML change (mm , p = 0.03):</p> <ul style="list-style-type: none"> · MT-CTG: 0.1 ± 0.8 · Control: -0.5 ± 1.1 <p>PES (p = 0.21):</p> <ul style="list-style-type: none"> · MT-CTG: 6.8 ± 1.5 · Control: 6.4 ± 1.5
Dellavia et al. ²⁰	University, Italy	Prospective cohort, 21 months Test group: MT-CTG Control: LP-CTG	14 patients	0	Healthy, unknown smoking status	Soft tissue augmentation of Class I ridge defects, pre-implant placement	Split thickness envelope flap	Maxilla	<p>KM thickness gain (mm):</p> <ul style="list-style-type: none"> · MT-CTG: from 2.1 ± 0.2 to 6.8 ± 1.1 · LP-CTG: from 2.0 ± 0.2 to 4.9 ± 0.6 <p>MT-CTG associated with hyperplastic response</p>
Puisys et al. ²¹	Private practice, Lithuania	Prospective cohort - split mouth design, 3 years Test group 1: split thickness tunnel Test group 2: full thickness tunnel	10 patients 40 implants	0	Unknown periodontal status, non-smokers and smokers ≤10 cigarettes/day	Augmentation of keratinized mucosa at implant sites with <1.0 mm KMW	Split or full thickness tunnel	Mandible	<p>KM thickness gain (mm, p <0.001):</p> <ul style="list-style-type: none"> · Split: from 2.5 ± 0.51 to 5.8 ± 0.41 (p = 0.028) · Full: from 2.4 ± 0.88 to 5.4 ± 0.68 (p = 0.028) <p>KMW change (mm, p<0.001):</p> <ul style="list-style-type: none"> · Split: from 0.6 ± 0.6 to 5.1 ± 0.72 (p <0.001) · Full: from 0.5 ± 0.51 to 1 ± 0.57 (p <0.001) <p>Final vertical REC (mm, p<0.001):</p> <ul style="list-style-type: none"> · Split: 1.4 ± 0.6 · Full: 2.6 ± 0.7
Rocuzzo et al. ²²	Private practice, Italy	Prospective cohort, 12 months	16 patients 16 implants	0	Absence of PD ≥5 mm at adjacent interproximal sites, FMPS and FMBS <15%, non-smokers and smokers ≤15 cigarettes/day	Peri-implant soft tissue dehiscence coverage with no interproximal bone loss or adjacent papillae recession	Split thickness envelope flap	Maxilla	<p>RecRed (mm, p = 0.0004): 1.7 ± 0.3</p> <p>CRC (%): 56.3</p> <p>RC (%): 89.6 ± 13.1</p> <p>PD gain (mm, p = 0.0004): 1.4 ± 0.2</p>

									VAS difference (p <0.0001): 4.9 ± 0.4 Final VAS:8.5 ± 0.3
Roccuzzo et al. ²³	Private practice, Italy	Prospective cohort, 5 years	16 patients 16 implants	3 patients 3 implants	Absence of PD ≥5 mm at adjacent interproximal sites, FMPS and FMBS <15%, non-smokers and smokers ≤15 cigarettes/day	Peri-implant soft tissue dehiscence coverage with no interproximal bone loss or adjacent papillae recession	Split thickness envelope flap	Maxilla	REC change (mm): from 1.9 ± 0.7 to 0.2 ± 0.3 CRC (%): 62% RC (%): 86 ± 19 PD change (mm, p = 0.88): from 2.7 ± 0.4 to 2.9 ± 0.6 VAS change: from 3.6 ± 0.6 to 8.1 ± 0.9

When available, the main results are reported as mean ± standard deviation.

CAL = clinical attachment level; CRC = complete root coverage; CTG = connective tissue graft; FMBS = full mouth bleeding score; FMPS = full mouth plaque score; KM = keratinized mucosa; KMW = keratinized mucosa width; KT = keratinized tissue; KTW = keratinized tissue width; LP = lateral palate; MBML = midbuccal mucosal level; MT = maxillary tuberosity; PD = probing depth; PES = Pink Esthetic Score; RC = root/dehiscence coverage; RCT = randomized controlled trial; REC = recession; RecRed = recession reduction; SD = standard deviation; VAS = visual analogue scale; WES = White Esthetic Score