Review

Soft Tissue Substitutes in Periodontal and Peri-Implant Soft Tissue Augmentation. A Systematic Review.

Roberto Rotundo *, Vanessa Bonafede, Gian Luca Pancrazi, Alessia Grassi, Lara Ceresoli, Giovanna Laura Di Domenico

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Review

Soft Tissue Substitutes in Periodontal and Peri-Implant Soft Tissue Augmentation. A Systematic Review

Rotundo Roberto [1,*], Bonafede Vanessa [2], Pancrazi Gian Luca [2], Grassi Alessia [2], Cerasoli Lara [2] and Di Domenico Giovanna Laura [2]

[1] Professor, Periodontology Unit, University Vita-Salute and IRCCS San Raffaele, Milan, Italy
[2] Trainee Specialist in Oral Surgery, University Vita-Salute and IRCCS San Raffaele, Milan, Italy
* Correspondence: rotundo.roberto@unisr.it

Abstract: The present review compared the efficacy of soft tissue substitutes (STS) and autogenous free gingival graft (FGG) or connective tissue graft (CTG) in mucogingival procedures to increase keratinized tissue (KT) width around teeth and implants. Two independent examiners performed the electronic search on Medline and Cochrane Library based on the following PICO's format: (P) adult patients; (I) soft tissue substitutes and FGG/CTG; (C) STS vs CTG; STS vs FGG; STS vs CTR; (O) KT width gain; (S) Systematic Reviews, Randomized Controlled Trials. Results showed that around teeth, all biomaterials showed superior performance compared to CAF alone for treating gingival recessions. However, when compared to CTG, ADM yields the most similar outcomes to the gold standard (CTG), even though in multiple recessions CTG still continue to be considered the most favorable approach. Use of STSs (acellular matrix or tissue engineered) in combination with an apically positioned flap resulted in a significantly less gain of KTW compared to what achieved with FGG and APF. Around dental implants, free gingival grafts were deemed more effective than soft tissue substitutes in enhancing keratinized mucosa width.

Keywords: gingiva; dental implants; gingival recessions; soft tissue substitute; surgery; review; keratinized tissue

1. Introduction

Since 1963, the Autogenous Free Gingival Graft (FGG) has been used in periodontal surgery to enhance the width of attached gingiva around teeth [1,2]. The same technique was also used to cover exposed dental roots [3]. Later on, in order to achieve better esthetic results, complete root coverage, increased keratinized tissue width (KTW), and long-term treatment stability, the autogenous Subepithelial Connective Tissue Graft (SCTG) combined with the Coronally Advanced Flap (CAF) have been largely used and, nowadays, recognized as the surgical technique with the highest performance [4]. This approach is, therefore, acknowledged as the "gold standard" for treating both single and multiple gingival recession defects (GRD) around teeth and dental implants [5].

Despite its high success rate, SCTG shows some drawbacks, including the necessity for two surgical sites (recipient and donor), pain and discomfort during donor site healing, and limited availability of donor tissue.

Meanwhile, several studies have started to test the use of soft tissue substitutes (STS) in mucogingival surgery revealing interesting results mainly based on their easier and less invasive approach, eliminating the need to harvest tissue from the palate [4,6,7]. Since the 1980s, STS have been introduced as alternative materials to autogenous grafts for increasing gingival width, showing their advantages over autogenous grafts, such as their widespread availability, avoidance of a secondary surgical site, reduced surgical time, and patient preference. It should be considered that the risk of moderate/severe postoperative swelling and pain increases by 3% and 4%, respectively, for each minute of the surgical procedure. Therefore, the reduction of the surgical time represents one of the most determinant factors for the patient morbidity.

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Scaffolds, based on their origin, have been categorized as allogenic, xenogeneic, alloplastic, and living constructs (including cells). The most commonly used biomaterials include acellular dermal matrix grafts, single/bilayer collagen matrix, volume-stable collagen matrix, porcine-derived acellular dermal matrix, and polymeric matrices human amniotic membrane [8].

This review is aimed to report the characteristics, clinical applications, and limitations of Extracellular Matrix (ECM)-based technologies in periodontal and peri-implant soft tissue augmentation.

1.1. Soft Tissue Substitutes

Biomaterials used as connective tissue substitutes should ideally show certain properties, such as ease of adaptation and positioning at the level of the affected site, stabilization of the blood clot, integration with host tissues, reduction of time and pain related to the removal of an autologous graft. The most common used STS are described as follows.

1.2. Acellular dermal matrix

It is a soft tissue graft that undergoes a decellularization process obtained from human skin. In fact, it is used not only in dentistry but also in aesthetic medicine and surgery. In dentistry, the purpose of its use is to avoid a second surgical site due to a graft harvest, and it is applied in root coverage procedures, as well as in augmentation of periodontal and peri-implant soft tissues [4,9].

1.3. Human Amniotic Membrane

This biomaterial is obtained from healthy donors during cesarean section, and is composed of the membrane that covers the amniotic cavity, which undergoes a process of preparation and consequent elimination of the cellular component, maintaining a single epithelial layer, the basement membrane and collagen. It also contains growth factors that contribute to the properties of this biomaterial in terms of healing and angiogenesis [10].

1.4. Porcine-derived acellular dermal matrix

Collagen matrix of porcine origin is a dense and smooth material used with the aim of promoting adhesion to the recipient site, angiogenesis and tissue integration. Like any scaffold, it supports clot stabilization and provides stability. It is widely used in dentistry, particularly in periodontal surgery, soft tissue augmentation and the treatment of gingival recessions. Within the porcine-derived matrices, it is possible to identify a bilayer collagen matrix or a volume-stable collagen matrix. The latter shows as a main characteristic to maintain good stability, elasticity and volume. It stimulates angiogenesis, fibroblast growth, tissue integration. Unlike the bilayer collagen matrix, which can also be used in an open environment, the volume-stable matrix requires submerged healing [4].

1.5. Polymeric matrices

There are also polymeric matrices on the market derived from proteins, polysaccharides, polynucleotides. One of the main advantages of natural polymers is biocompatibility. They stimulate healing and act as scaffolds for tissue regeneration. The main derivative protein is collagen, although one of the main disadvantages of collagen derivatives seems to be tissue contraction. Depending on the characteristics required, biomedical engineering with the combination of molecules is able to obtain various types of synthetic scaffolds, which compared to natural derivatives have the advantage of a longer shelf life, as well as showing greater elasticity and tensile strength, compensated, however, by lower biodegradability, so they are often used in combination with natural polymers [11].

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2. Materials and Methods

This systematic review was conducted on the basis of the following question, "What is the efficacy of soft tissue substitutes in mucogingival surgery around teeth or around dental implants in terms of soft tissue augmentation and root coverage?" This question was created according to the format of the following PICOS strategy [12]:

- Population (P): adults (≥ 18 years) presenting reduced keratinized tissue around teeth and implants
- Intervention (I): root coverage procedures, soft tissue augmentations
- Comparisons (C): soft tissue substitutes vs no treatment or connective tissue graft/free gingival graft
- Outcomes (O): keratinized tissue width, root coverage with at least 6 months of follow-up
- Study design (S): systematic reviews, randomized clinical trials

2.1. Inclusion criteria.

Studies published before November 2023 written in English were included. Systematic Reviews and Randomized Controlled Studies dealing with the use of collagen-based Soft Tissue Substitutes in periodontal plastic surgery around teeth and implants were selected.

2.2. Exclusion criteria

In vitro or in vivo animal studies, retrospective clinical trials, clinical trials without control, case reports, narrative review articles, editorials, opinion pieces, surveys, conferences, commentary articles. Studies on bio-modulators or non collagen-based matrices were excluded, as well as studies without full text available and non-English language studies.

2.2. Outcomes

Primary outcomes: Root Coverage; Gingival / Peri-implant Soft Tissue Augmentation.

2.3. Strategy search

The search process was performed by two different reviewers using different electronic databases: MEDLINE (via PubMed), Scopus, and Web of Science. The search strategy was outlined based on the MeSH terms in PubMed and adapted to each database. The following search query were adopted: ((“collagen matrix” [All Fields] OR “soft tissues substitute” [All Fields] OR "Biocompatible Materials/therapeutic use” [Mesh terms] OR “Collagen Type I/therapeutic use” [Mesh terms] OR “Collagen Type III/therapeutic use” [Mesh terms] OR “human fibroblast-derived dermal substitute” [All Fields] OR "acellular dermal matrix" [All fields] OR “dermal matrix allograft” [All Fields] OR “soft tissue allograft” [All Fields] OR “xenogeneic collagen matrix” [All Fields] OR “Mucograft” [Supplementary Concept] OR “Alloderm” [Supplementary Concept] OR “Fibro gides” [All Fields] OR “Mucoderm” [Supplementary Concept] OR “Novomatrix” [All Fields] OR “Derma” [All Fields] OR “connective tissue graft” [All fields] OR “connective tissue” [Mesh Terms] OR “subepithelial connective tissue” [All fields] OR “periodontal and plastic surgery” [All fields] OR “soft tissue graft” [Mesh Terms] OR “coronally advanced flap” [All fields] OR “Bilaminar technique” [All fields] OR “Free Gengival Graft” [All fields] OR “Dental Implants” [Mesh Terms] OR “Tooth Root/surgery” [Mesh terms] OR “Gingivoplasty/methods” [Mesh terms]) AND (“gingival recession" [All fields] OR “reduced keratinized tissue" [All fields] OR “gingival recessions" [Mesh Terms] OR "gingival recession treatment” [All fields] OR "gingival recession coverage" [Mesh Terms] OR "recession near gingiva" [All fields] OR "recession defect" [Mesh Terms] OR "exposure near root" [All fields] OR "exposed near root" [Mesh Terms] OR "gingiva near defect" [All fields]) AND (“root coverage” [All fields] OR "keratinized tissue width" [All fields])) NOT (Comment [Publication Type] OR Selezionati Congress [Publication Type] OR Editorial [Publication Type] OR Case Reports [Publication Type] OR Clinical Conference [Publication Type] OR Comment [Publication Type] OR Consensus Development Conference [Publication Type]).

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2.4. Selection of studies, data extraction and synthesis.

After removing duplicate records, titles and abstracts (when available) of all reports identified through the electronic and manual searches, they were independently screened by two review authors (GLP and VB). When studies met the inclusion criteria or when insufficient data from abstracts for evaluating inclusion criteria were gained, the full article was obtained. The full text of all eligible studies was independently assessed by the two review authors (GLP and VB). All studies matching the inclusion criteria then underwent data extraction. Any disagreements were resolved through discussion or consultation with other authors (RR, GLDD and ME).

3. Results

3.1. Comparison [Soft Tissue Substitutes vs no Treatment]. See Tables 1–4. Figure 1.

3.1.1. Allogeneic dermal matrix (ADM)

Root coverage procedures

A meta-analysis by Chambrone et al. [4] indicated no statistically significant difference between the coronally advanced flap (CAF) plus ADM graft and CAF alone concerning CRC, recession reduction (RecRed), and keratinized tissue width (KTW) gain. It is crucial to note that these findings originated from two studies focusing on single recession defects with 6 months of follow-up [13,14].

These data are in disagreement with the only RCT study at 12-months follow-up, comparing ADM in the treatment of multiple gingival defects [15]. Inter-group differences were found to be statistically significant for RecRed, attachment gain, KTW and GT increase and mean defect coverage in favour of test group ($p < 0.05$).

Peri-implant soft tissue augmentation procedures

Currently, there is no available evidence regarding the outcomes using ADM for peri-implant soft-tissue augmentation procedures in comparison to no graft.

3.1.2. Xenogeneic acellular dermal matrix (XDM)

Currently, there is no available evidence regarding the outcomes using XDM in comparison to no graft, for both root coverage and peri-implant soft-tissue augmentation procedures.

3.1.3. Bilayered collagen matrix (CMX)

Root coverage procedures

A recent systematic review and network meta-analysis aimed to rank different biomaterials used in adjunct to CAF, based on their performance in root coverage for gingival recessions [16]. Authors concluded that all biomaterials (CTG, ADM, platelet concentrates, and CMX) had superior performance compared to CAF alone, for probing depth, keratinized tissue width, clinical attached level, and recession depth parameters. When considering studies aimed to test the adjunctive effect of CMX to CAF alone, the review included only 4 studies: two on multiple gingival recession defects with 12 months of follow-up [17,18] and two on single defects with 36 months of follow-up [19,20].

These results are similar to those found by a SR aiming to evaluate the effectiveness of connective tissue graft substitutes for the treatment of gingival recessions compared with CAF alone [21].

Different data were reported by a 12-months randomized controlled trial comparing CMX+CAF to CAF in the treatment of single recessions defects [22]. The CAF + CMX showed a higher KTT gain (CAF, 0.1 ± 0.3 mm; CAF + CM, 0.6 ± 0.2 mm; P = 0.0001) and KTW gain (CAF, 0.3 ± 0.6 mm; CAF + CM, 0.9 ± 0.8 mm; P = 0.002) when compared with the CAF group. On the contrary, the estimated %RC did not present a significant difference between the groups (CAF, 70.3 ± 22%; CAF + CM, 69 ± 21.6%; – P = 0.7).

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Peri-implant soft tissue augmentation procedures

Limited evidence is currently available comparing the effect of applying a CMX with no soft tissue graft during implant placement.

A recent 12-months RCT was conducted to assess whether grafting the buccal peri-implant mucosa using either a CTG or CMX at implant placement in preserved alveolar ridges resulted in less mid-buccal mucosa recession compared to no grafting (NG) [23]. 90%, 75%, and 70% of the patients in the NG, CTG, and CMX groups, respectively, displayed more than 2 mm of keratinized mucosa. A 1- to 2-mm-wide zone of keratinized mucosa was seen in 5%, 15%, and 10% of patients in the NG, CTG, and CMX groups, respectively. In the CMX group, 5% of the patients had a keratinized mucosa of up to 1 mm. In the NG, CTG, and CMX groups, 5%, 10%, and 15%, respectively of the patients showed no keratinized mucosa.

3.1.4. Volume-stable collagen matrix (VCMX)

Currently, there is no available evidence regarding the outcomes using this newly introduced collagen matrix in comparison to no graft, for both root coverage and peri-implant soft-tissue augmentation procedures alone.

3.2. Comparison [soft tissue substitutes vs. CTG/FGG]. See Tables 1-4. Figure 1.

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Table 1. Soft Tissue Substitutes *vs* No Treatment around Teeth.

STUDY TYPE	AUTHORS	YEAR	SURGICAL PROCEDURE	TEST GROUP	CONTROL GROUP	N. of patients/ N. of teeth or implants	FOLLOW UP (months)	CRC	mRC	KTW	STT	CONCLUSION
RCT	Ahmedbeyli et al	2014	CAF for multiple recessions	CAF + ADM	CAF	T: 12/24 C: 12/24	12	T: 91,7% C: 50%	T: NA C: NA	T: from 2.48 ± 0.50mm to 3.69 ± 0.54mm C: from 2.58 ± 0.71mm to 3.19 ± 0.92mm	T: from 0.75 ± 0.06mm to 1.41 ± 0.11mm C: from 0.71 ± 0.08mm to 0.77 ± 0.09mm	CAF+ADM is a valid approach for multiple recessions with thin phenotype
RCT	Stefanini et al	2016	CAF for single recessions	CAF + CMX	CAF	SPLIT-MOUTH 45/90	12	T: 42% C: 38%	T: 76.28% C: 75.05%	T: from 1.97mm to 3.02mm C: from 2.00mm to 2.64mm	T: baseline-to 12mo 0,52 mm C: baseline-to 12mo 0,27 mm	PROMs, RES and RC did not significantly differ between groups. Thickness and KTW were enhanced following CAF+CMX
RCT	Cardaropoli et al	2014	CAF for multiple recessions	CAF + CMX	CAF	32/112	12	T: 72% C: 58%	T: NA C: NA	T: from 1.89±0.9mm to 2.96±0.76mm	T: from 0.84±0.37 mm to 1.810±0.48 mm	Test group showed significantly

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										C: from 1.91±1.01mm to 2.61±1.08 mm	C: from 0.81±0.36 mm to 0.94±0.36 mm	greater results than the control group
RCT	Rotundo et al	2019	CAF for multiple recessions	CAF + CMX	CAF	24/61	12	T: 63% C: 52%	T: 2.0 ± 0.8 mm C: 2.0 ± 1.1 mm	T: from 3.3±1.5mm to 2.7±1.2 mm C: from 3.5±1.8mm to 2.5±1.1mm	T: from 1. 4±0. 7mm to 1.7±0.7mm C: from 1. 5±0. 6mm to 1.2 ±0.5mm	CAF+ XCM provide a similar root coverage to CAF alone, but a significant increase in gingival thickness
SR	Chambrone et al.	2019	1.CAF for multiple recessions 2. CAF for single recession	1.CAF + ADMG 2.CAF + ADMG	1. CAF 2. CAF	48 studies in total, 2 studies evaluated	> 6	from 0% to 91.6% for ADMG from 7.7% to 81.8% for CAF	from 50% to 96% for ADMG from 55.9% to 95.4% for CAF	NA	NA	ADMG appear as the soft tissue substitute that may provide the most similar outcomes to those achieved by SCTG

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Table 2. Soft Tissue Substitutes *vs* Free Gingival Graft /Connective Tissue Graft around Teeth.

STUDY TYPE	AUTHORS	YEAR	SURGICAL PROCEDURE	TEST GROUP	CONTROL GROUP	N. of patients/ N. of teeth or implants	FOLLOW UP (months)	CRC	mRC	KTW	STT	CONCLUSION
RCT	Barros et al	2015	STA for single recessions	STA + ADM	STA + CTG	SPLIT MOUTH 15/30	12	T: from 3.47 ± 0.42mm to 0.93 ± 0.60mm C: from 3.15 ± 0.33mm to 0.67 ± 0.61mm	T: NA C: NA	T: from 1.90 ± 0.54mm 3.20 ± 0.77mm C: from 2.05 ± 0.78mm to 3.20 ± 1.01mm	T: NA C: NA	The extended flap technique can improve the root coverage results
RCT	Elmahdi et al	2022	TUN for multiple recessions	MCAT + ADM	MCAT + CTG	12/69	9	T: from 2.87 ± 0.31mm to 0.76 ± 0.65mm C: from 2.76 ± 0.89mm to	T: NA C: NA	T: from 3.03 ± 0.72mm to 3.12 ± 0.69mm C: from 2.65 ± 0.92mm to 3.82 ± 1.3mm	T: from 1.10 ± 0.20mm to 1.65 ± 0.39mm C: from 1.33 ± 0.54mm to 2.26 ± 0.63mm	The use of ADM may represent a valid alternative to SCTG when used in conjunction with MCAT

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								0.53 ± 0.48mm				
RCT	Meza-Mauricio et al	2021	CAF for multiple recessions	CAF + XDM	CAF + CTG	42/130	12	T: 70.3% C: 83.3%	T: 80.19% C:91.79%	T: from 2.43 ± 1.12mm to 3.06 ± 0.92mm C: from 2.42 ± 1.29mm to 3.34 ± 1.11mm	T: from 0.81 ± 0.23mm to 1.26 ± 0.22mm C: from 0.85 ± 0.25mm to 1.53 ± 0.38mm	CAF+CTG was superior to CAF+XDM in CRC and STT. CAF+XDM was superior in patient morbidity and surgical time
RCT	Vincent-Bugnas et al	2021	TUN for multiple recessions	MCAT + PADM	MCAT + CTG	12/74	12	T: 24.3% ± 8.2% C: 48.7% ± 6.8%	T: 68.8% ± 23.4% C: 80.6% ± 23.7%	T: from 2.1 ± 1.6mm to 2.5 ± 1.2mm C: from 2.2 ± 1.3mm to 3.0 ± 1.0mm	T: from 0.8 ± 0.2mm to 1.2 ± 0.2mm C: from 0.8 ± 0.3mm to 1.9 ± 0.3mm	CTG gave better results, however, PADM reduced morbidity
RCT	Gürlek et al	2020	CAF for multiple recessions	CAF + XADM	CAF + CTG	SPLIT MOUTH 12/82	18	T: 87.8% C: 87.8%	T:NA C:NA	T: from 3.40 ± 1.20mm to 3.70 ± 0.93mm C: from 3.70 ± 1.10mm to 4.20 ± 0.98mm	T:NA C:NA	Soft tissue shrinkage and increase in PD can be observed with XADM. CTG gives

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												stable clinical outcomes
RCT	Rakasevic et al	2020	TUN for multiple recessions	MCAT + XDM	MCAT + CTG	12/114	12	T: 46.8% C: 51.9%	T: 85.25 ± 14.9% C: 87.6 ± 15.1%	T: from 2.44 ± 1.3mm to 3.28 ± 0.9mm C: from 2.43 ± 1.4mm to 3.27 ± 1.03mm	T: from 0.61 ± 0.2mm to 1.39 ± 0.44mm T: from 0.69 ± 0.26mm to 1.3 ± 0.38mm	The use of porcine-derived dermal collagen matrix could be considered a CTG substitute
RCT	Cardaropoli et al	2012	CAF for multiple recessions	CAF + CMX	CAF + CTG	18/22	12	T: 72% C: 81%	T:NA C:NA	T: from 2.23 ± 0.56mm to 3.45 ± 0.85mm C: from 2.05 ± 0.82mm to 3.32 ± 0.70mm	T: from 0.82 ± 0.34mm to 1.82 ± 0.51mm C: from 0.86 ± 0.39mm to 2.09 ± 0.44mm	The collagen matrix represents a possible alternative to CTG
RCT	McGuire et al	2010	CAF for single recessions	CAF + CMX	CAF + CTG	25/NA	12	T: 88.5% C:99.3%	T:NA C:NA	T: from 2.44 to 3.59mm C: from 2.78 to 3.98±mm	T:NA C:NA	CM+CAF presents a viable alternative to CTG+CAF, without the morbidity of soft tissue graft harvest

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RCT	Tonetti et al	2021	CAF for multiple recessions	CAF + CMX	CAF + CTG	125/307	36	T: 3% C: 3%	T:NA C:NA	C: from 2.8 ± 1.3mm to 0.5 ± 1.0mm T: from 2.6 ± 1.2mm to 0.0 ± 1.2mm	T:NA C:NA	CMX reported shorter time to recovery, lower morbidity and more natural appearance of tissue texture and contour
RCT	Aroca et al	2013	TUN for multiple recessions	MCAT + CMX	MCAT + CTG	22/156	12	T: 42% C: 85%	T: 71 ± 21% C: 90 ± 18%	T: from 2.1 ± 0.9mm to 2.4 ± 0.7 mm C: from 2.0 ± 0.7mm to 2.7 ± 0.8mm	T: from 0.8 ± 0.2mm to 1.0 ± 0.3mm C: from 0.8 ± 0.3mm to 1.3 ± 0.4mm	CM reduce surgical time and patient morbidity, but gives lower CRC when used in conjunction with MCAT
RCT	Molnár et al	2022	TUN for multiple recessions	MCAT + PXCM	MCAT + CTG	22/114	9 years	T: 1% C: 1%	T: 23.07 ± 44.5% C: 39.7 ± 35.17%	T: from 2.00 ± 0.9mm to 2.97 ± 0.95mm C: from 2.03 ± 0.65mm to 3.28 ± 1.14mm	T: from 0.83 ± 0.26mm to 1.49 ± 0.32mm C: from 0.86 ± 0.29mm to 1.57 ± 0.35mm	MCAT in conjunction with either CM or CTG for MAGR is likely to show a relapse over a period of 9 years

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RCT	McGuire et al	2022	CAF for single recessions	CAF + VCMX	CAF+CTG	SPLIT MOUTH 30/60	12	T: 63.2% C: 70.7%	T: NA C: NA	T: from 2.5 ± 1.25mm to 3.3 ± 1.3mm C: from 2.3 ± 0.88mm to 3.6 ± 1.31mm	T: from 158.37 ± 72.89 to 72.35 ± 38.40mm2 C: from 189.40 ± 73.87 to 39.23 ± 30.92mm2	VCMX+CAF root coverage was inferior to CTG+CAF but produced less morbidity
SR	Chambrone et al	2019	1.CAF for single recession 2.CAF for multiple recessions 3.CAF for single recession	1.CAF + ADMG 2.CAF + CMX 3.CAF + ADMG	1.CAF + CTG 2.CAF + CTG 3.CAF + CTG	48 studies in total, 2 studies evaluated	> 6	from 0% to 91.6% for ADMG 18.1% to 95.6% for SCTG	from 50% to 96% for ADMG from 64.7% to 99.3% for SCTG	NA	NA	There was insufficient evidence of a difference in GR reduction and KTW gain between ADMG + CAF and SCTG + CAF
SR	de Carvalho Formiga et al	2020	CAF	1.ADM 2.ADM 3.PCM 4.CMX	1.CTG 2.CTG 3.CTG 4.CTG	14 studies in total, 4 studies evaluated (conducted after 2010)	> 6	No statistically significant differences	The CTG increased the MRC (+ 7.6 percentage points)	On 2 mm recessions, CTG showed superiority above other biomaterials, but on 3 mm	NA	CTG, acellular dermal matrix allograft and xenogenic collagen matrix provided similar results

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										recessions, it seemed to have the same results		for root coverage
SR	Halim, et al	2023	CAF	1.CMX 2.CMX 3.CMX 4.CMX 5. ADM	1.CTG 2.CTG 3.CTG 4.CTG 5.CTG	5 studies in total, 5 studies evaluated	> 6	T: 70.3 C: 83.3 T: 24.3±8.2 C:48.7± 6.8 T: 70.7 C: 87.7 T: 51.9 C: 46.8 T: NA C: NA	T:91.79±10.1 C:89.19±16.3 T:80.6±23.7 C:68.8± 23.4 T: NA C: NA T:87.6±15.1 C:85.25±14.9 T: NA C: NA	T: 0.85±0.25 C: 0.81±0.23 T: 0.8±0.3 C: 0.8± 0.2 T: NA C: NA T: 0.69±0.26 C: 0.61±0.2 T:NA C:NA	T:2.42±1.29 C:2.43±1.12 T: 2.2±1.3 C: 2.1± 1.6 T: 3.7±1.10 C: 3.40±1.2 T: 2.43±1.4 C: 2.44±1.3 T:2.05±0.78 C:1.90±0.54	CTG is considered superior for gingival recession therapy. If it is contraindicated, the AADM and XDM might be considered as alternatives

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Table 3. Soft Tissue Substitutes *vs* No Treatment around Dental implants.

STUDY TYPE	AUTHORS	YEAR	SURGICAL PROCEDURE	TEST GROUP	CONTROL GROUP	N. of patients/ N. of teeth or implants	FOLLOW UP (months)	CRC	mRC	KTW	STT	CONCLUSION
RCT	Frizzera et al	2018	STA (Immediate implant placement and provisionalization)	STA + CMX	No soft tissue augumentation	16/16	12	T: NA C: NA	T: NA C: NA	T: NA T: NA C: NA	T: from 0,98 to 2.1mm C: from 1 to 2.11mm	CMX reduced MPR, provided better contour of the alveolar ridge, and increased STT
RCT	Zuiderveld et al	2018	STA (in conjuction with implant placement)	STA + CMX	No soft tissue augumentation	40/40	12	T: NA C: NA	T: loss of 0.17±1.3mm C: loss of 0.48±1.5mm	T: NA C: NA	T: NA C: NA	CMX does not result in a more favorable esthetic outcome than when no soft tissue graft was applied
RCT	Lee et al	2023	STA in conjuction with implant placement	STA + ADM	No soft tissue augumentation	31/31	12	ADM maintained buccal soft-tissue contours 3–5 mm	T: NA C: NA	Changes in were not significantly different between the groups	T: from 1.34 ± 0.25mm to 2.57 ± 0.30 mm C: from 1.18 ± 0.31mm to 1.18 ± 0.31mm	STA enhanced STT and maintained soft-tissue contours but did not prevent peri-implant

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								below the initial soft-tissue margin				mucosal recession
RCT	Frizzera et al	2018	STA with BT (Immediate implant placement and provisionalization)	STA + CMX	No soft tissue augumentation	16/16	12	T: NA C: NA	T: NA C: NA	T: NA C: NA	T: from 0,98 to 2.1mm C: from 1 to 2.11mm	STT improvements are seen in the CTR and CMX gr, but it produced a ridge depression and soft tissue color alterations
RCT	Zuiderveld et al	2018	STA (in conjuction with implant placement)	STA + CMX	No soft tissue augumentation	40/40	12	T: NA C: NA	T: loss of 0.17±1.3mm C: loss of 0.48±1.5mm	T: NA C: NA	T: NA C: NA	STS does not result in a more favorable esthetic outcome than when no STS was applied during implant placement

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Table 4. Soft Tissue Substitutes *vs* Free Gingival Graft /Connective Tissue Graft around Dental Implants.

STUDY TYPE	AUTHORS	YEAR	SURGICAL PROCEDURE	TEST GROUP	CONTROL GROUP	N. of patients/ N. of teeth or implants	FOLLOW UP (months)	CRC	mRC	KTW	STT	CONCLUSION
RCT	Frizzera et al	2018	STA (Immediate implant placement and provisionalization)	STA + CMX	STA+CTG	16/16	12	T: NA C: NA	T: NA C: NA	T: NA C: NA	T: from 0.98 to 3.04mm C: from 1 to 2.11mm	CTG avoided marginal peri-implant recession and provided greater thickness of the soft tissue at the implant facial aspect
RCT	Zuiderveld et al	2018	STA (in conjuction with implant placement)	STA + CMX	STA+CTG	40/40	12	T: NA C: NA	T: loss of 0.17±1.3mm C: loss of 0.04±1.1mm	T: NA C: NA	T: NA C: NA	CTG gr displayed more keratinized mucosa width than CMX gr
RCT	Lee et al	2023	STA in conjuction with implant placement	STA + ADM	STA + CTG	30/30	12	ADM gr showed soft-	T: NA C: NA	Changes between the groups were not significantly different	T: from 1.34 ± 0.25mm to 2.57 ± 0.3mm	STA enhanced soft-tissue thickness and maintained

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								tissue margin 3–5 mm below the initial level			C: from 1.24 ± 0.25mm to 2.38 ± 0.32mm	soft-tissue contours but did not prevent peri-implant mucosal recession
RCT	Happe et al	2022	STA in conjuction with immediate implant placement	STA + ADM	STA + CTG	20/20	12	T: NA C: NA	T: NA C: NA	T: NA C: NA	T: NA C: NA	ADM showed no difference regarding color match and Pink Esthetic Score in comparison CTG
RCT	Schmitt et al	2016	VP after implant placement	VP + CMX	VP + CTG	48/48	5 years	T: NA C: NA	T: NA C: NA	T: 12.96 ± 2.86mm C: 13.06 ± 2.26mm	T: NA C: NA	CMX consent minor surgery time, less morbidity, and more esthetic appearance
RCT	Thoma et al	2023	STA after implant placement	STA + VCMX	STA + CTG	20/20	5 years	T: NA C: NA	T: NA C: NA	T: NA C: NA	T: from 3.0 to 3.0mm C: from 3.0 to 3.3mm	Both groups resulted in stable peri-implant tissues, favorable

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												esthetics, and clinically negligible contour changes
RCT	Thoma et al	2020	STA before implant placement	STA + VCMX	STA + CTG	20/20	3 years	T: NA C: NA	T: NA C: NA	T: NA C: NA	T: from 3.0 to 3.5mm C: from 3.0 to 3.3mm	Both gr demonstrated negligible differences, stable buccal tissue contour, esthetics and STT slightly increased
RCT	Solonko et al	2022	APF	APF + CMX	APF + FGG	49/49	12	T: from 1.1 to 1.0mm C: from 0.9 to 0.7mm	T: NA C: NA	T: from 0.4 to 0.0mm C: from 0.7 to 1.0mm	T: NA C: NA	KM gain was higher with the FGG. CM was better appreciated by the patients
SR	Moraschini et al	2020	CAF	1. CAF + CMX	1.CAF+CTG 2.CAF+CTG	11 studies in total, 5	> 6	T: NA C: NA	T: NA C: NA	1.XCM: 2.1±1.2mm CTG: 3.2±0.8mm	1.XCM: 2.8±0.7mm CTG:3.1±1.3mm	CTG demonstrated the best

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				2. CAF+CMX 3. CAF+CMX 4. CAF+CMX 5. CAF+CMX	3.CAF+CTG 4.CAF+CTG 5.CAF+CTG	studies evaluated				2.T: NA C: NA 3.XCM:1.7±1.3mm CTG:4.0±1.1mm 4.T: NA C: NA 5.XCM:6.51±1.98mm FGG:7.76±1.99mm	2.XCM: 2.5±1.3mm CTG: 3.28 ±1.7mm 3. T: NA C: NA 4. XCM: 1.66±0.01mm CTG: 2.86±0.01mm 5. T: NA C: NA	treatment ranking of probability results, followed CMX
SR	Montero et al	2022	CAF	1.CMX 2.CMX 3.CMX	1.FGG 2.APF 3.APF/FGG	4 studies in total, 3 studies evaluated	> 6	T: NA C: NA	T: NA C: NA	For all studies, there was a statistically significant increase in KM	T: NA C: NA	FGG are more effective in KM augmentation than soft tissue substitutes. CMX may be an alternative

ADM: allogeneic dermal matrix; APF: apically positioned flap; BT: bilaminar technique; C: control group; CAF: coronally advanced flap; CRC: complete root coverage; CTG: connective tissue graft; FGG: free gingival graft; mRC: mean root coverage; NA: not applicable; NR: not reported; STA: soft tissues augmentation procedure; STT: soft tissues thickness; T: test group; TUN: tunnel technique; XDM: xenogeneic dermal matrix; XCM: xenogeneic collagen matrix; VXCM: volume-stable collagen matrix.

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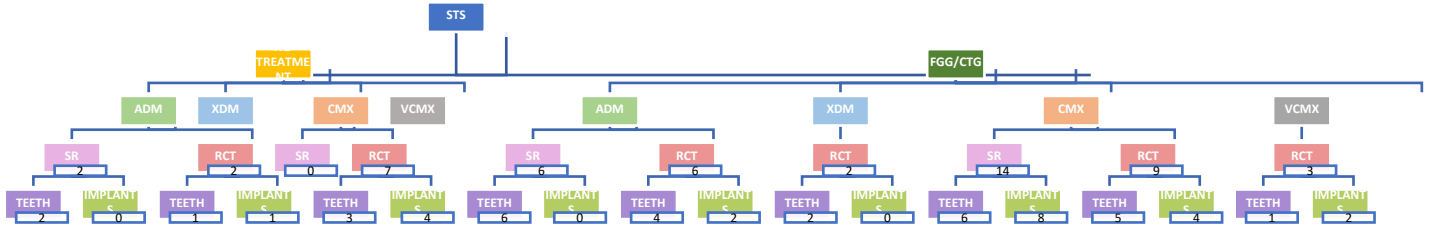

Figure 1. Flow-chart diagram of selected studies.

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3.2.1. Allogeneic dermal matrix (ADM) (AlloDerm®, SureDerm™, Puros Dermis®).

Root coverage/Gingival augmentation procedures

Extensive literature examines the effectiveness of ADM (acellular dermal matrix) in root coverage procedures, showing a range of complete root coverage (CRC) from 0% to 91%. Chambrone et al. [4] in their systematic review concluded that ADM yielded the most similar outcomes to the gold standard "connective tissue graft" (CTG). Meta-analysis findings did not reveal significant differences in CRC, recession reduction (RecRed), and keratinized tissue width (KTW) gain between the coronally advanced flap (CAF) plus ADM graft versus CAF plus CTG. However, it is important to note that these observations stem from studies focused on single recession defects [24–27].

A more recent systematic review by de Carvalho Formiga et al. [28] comparing CTG with ADM in localized gingival recession defects reported similar CRC outcomes. Interestingly, when considering different thresholds of recession depth, CTG demonstrated superiority in 2 mm recessions, whereas it yielded comparable results in 3 mm recessions.

In contrast, a randomized controlled trial (RCT) addressing multiple gingival recessions treated with the tunnel technique in combination with ADM or CTG revealed significant RecRed, increased gingival thickness (GT), and gains in clinical attachment level (CAL) in both groups nine months post-treatment [29]. The control group displayed more significant gains in KTW (CTG: 1.15 ± 1.16 mm vs. ADM: 0.21 ± 0.84 mm, p= 0.0003), increased GT (CTG: 0.94 ± 0.52 mm vs. ADM: 0.53 ± 0.41 mm, p= 0.002), and a higher percentage of mean root coverage (mRC) (CTG: 82.62 ± 16.30% vs. ADM: 72.72 ± 23.36%; p= 0.046), while RecRed and CAL gain did not significantly differ between the groups.

Bertl et al. [30] (2017) in their SR compared the effectiveness of soft tissue substitutes and autogenous free gingival grafts in non-root-coverage procedures to increase KTW around teeth. From this review, only 1 study, comparing ADM vs FGG, satisfied the inclusion criteria of the present SR [31]. Results showed was no statistically significant difference in changes of PI, GI, PD, and GR (P>0.05) with the exception of PD in the FGG group (1.01 +/- 0.03 versus 1.27 +/- 0.20 mm, P= 0.042). Although the ADM group received wider grafts than the FGG group (8.81 +/- 0.46 versus 6.70 +/- 0.89 mm), the attached gingiva gain was significantly smaller (2.59 +/- 0.92 versus 5.57 +/- 0.44 mm) and the graft shrinkage significantly greater (71 +/- 10% versus 16 +/- 12%) in the ADM group than in the FGG group.

Peri-implant soft tissue augmentation procedures

In a recent systematic review comparing soft tissue substitutes and autogenous gingival grafts, free gingival grafts (FGG) were deemed more effective than soft tissue substitutes in enhancing keratinized mucosa width (KMW) around dental implants [32].

It is worth noting that among the six RCT/CCT studies evaluated for overall KMW augmentation, only one specifically examined an ADM, namely AlloDerm® [33]. The results from this study favored FGG, demonstrating superior final KMW (3.58 mm ± 0.40 vs. 2.47 mm ± 0.32; p < 0.001) and KMW gain (2.57 mm ± 0.50 vs. 1.58 mm ± 0.37; p < 0.001) at a six-month follow-up.

Similarly, a recent 6-month RCT investigating peri-implant soft-tissue changes after immediate implant placement along with soft-tissue augmentation using ADM or CTG corroborated these findings [34].

In contrast, a 12-month RCT assessing tissue alterations in immediate implant sites with SCTG or ADM compared to sites without soft tissue augmentation showed a slight decrease in mean KMWs across all three groups compared to baseline. However, the changes in KMW were not significantly different among these groups [35].

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3.2.2. Xenogeneic acellular dermal matrix (XDM) (Mucoderm®)

Root coverage procedures

A recent systematic review aimed to compare long-term (≥1 year) root coverage outcomes between allogeneic and xenogeneic dermal matrices and the established gold standard CTG [36]. Despite a limited number of qualifying studies over the past decade (2014 to March 2023)—only five meeting the inclusion criteria, with four specifically comparing XDM to CTG [37–40] — findings were primarily reported at 12-month follow-up, except for Gurlek et al. [39], which extended to 18 months. The overall analysis of KTW across these studies indicated a mean difference of 0.26 mm (95% CI: –0.5 to 0.02). Additionally, a meta-analysis of mean root coverage (mRC) derived from three studies revealed a mean difference of 9.19% (95% CI: –13.95 to –4.43) [37,38,40]. Notably, both parameters favored CTG over dermal matrices.

In a similar vein, Santamaria et al. [41] conducted a study comparing clinical outcomes between XDM and CTG in conjunction with MCAF and cervical partial restoration for multiple gingival recessions. Their findings at 1-year follow-up demonstrated a CRC of 50.7% for XDM and 72.9% for CTG, indicating a statistically significant disparity between the two groups ($p < 0.001$). Moreover, CTG exhibited more substantial increases in both KTW (CTG: 0.96 mm vs. XDM: 0.3 mm, $p = 0.04$) and gingival thickness (CTG: 0.9 mm vs. XDM: 0.3 mm, $p < 0.001$).

Peri-implant soft tissue augmentation procedures

The only comparative study on peri-implant soft tissue augmentation, comparing XDM to CTG, assessed the clinical aesthetic outcome of peri-implant mucosa after extraction and immediate implant placement. At the 12-month post-surgery visit, XDM demonstrated no discernible difference in the overall aesthetic appearance concerning color match and Pink Esthetic Score (PES) when compared to autogenous soft tissue grafts [42].

3.2.3. Bilayered collagen matrix (CMX) (First generation – not cross-linked – commercial name: Mucograft®)

Root coverage procedures

A recent meta-analysis, combining two randomized controlled trials [43,44] focusing on single recession defects, calculated a weighted mean of −7.63 ± 5.43% for mean root coverage (mRC). This suggested a leaning toward CTG being more effective than CMX, though this trend lacked statistical significance [28].

This trend aligns with Tonetti et al.'s [45]findings for multiple recessions, yet contrasts with Aroca et al.'s study [46], which favored CTG (CMX: 73.2 ± 21.0% vs. CTG: 88.0 ± 20.9%; $p= 0.021$).

In a recent study presenting the 9-year outcomes of a prior RCT by Aroca et al. [46], among the 16 participants from the 9-year follow-up, mRC decreased from 73.2% to 23.0% in the CMX group and from 88.0% to 39.7% in the CTG group [47]. Interestingly, there were no significant differences between the groups after 9 years ($p= 0.179$). Notably, both CMX and CTG groups showed increases in keratinized tissue width (KTW) and mucosal thickness (MTT), with no significant differences between them ($p = 0.7197$ for KTW; $p = 0.8403$ for MTT).

However, Lakshmi et al.'s study [48] presented contrasting findings, indicating the superior performance of CMX over CTG concerning both complete root coverage (CRC) and KTW when utilized with MCAT for treating multiple gingival recessions.

Peri-implant soft tissue augmentation procedures

In a recent meta-analysis comparing the augmentation of KMW between soft tissue substitutes and autogenous grafts, the findings indicated no statistically significant difference [32]. Specifically, the use of a porcine collagen matrix (Mucograft®) demonstrated similar KMW gain at the 6-month follow-up compared to both types of autogenous grafts (FGG or CTG). This analysis, involving five

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studies, reported a weighted mean difference (WMD) of −0.8 mm (95% CI [−1.6; 0.0]; p = 0.062) [49–53].

3.2.4. Volume-stable collagen matrix (VCMX)

(Second generation – cross linked - commercial name: Fibrogide®)

Root coverage procedures

Currently, there is limited available evidence regarding the root coverage outcomes using this newly introduced collagen matrix in comparison to those achieved with CTG.

Findings from a randomized controlled trial investigating single gingival recessions revealed that at the 1-year follow-up, the mean root coverage was 63.2 ± 31.56% for the VXCM group and 84.49 ± 19.98% for the CTG group. There was a statistically significant difference between the two groups ($p<0.0001$). In terms of changes in keratinized tissue width (KTW) at the 1-year follow-up, the CTG group exhibited a shift from 2.3 ± 0.88 mm to 3.6 ± 1.31 mm, while the VXCM group shifted from 2.5 ± 1.25 mm to 3.3 ± 1.3 mm [54].

Peri-implant soft tissue augmentation procedures

Likewise, there is limited evidence available when comparing outcomes following soft tissue augmentation procedures using VCMX and CTG. Only two randomized controlled trials, encompassing one patient cohort, reported results of this comparison at 3- and 5-years [55,56]. At the 5-year follow-up, implant sites augmented with VXCM displayed a slight, though not statistically significant, increase in KMW from 3 years (2.5 mm) to 5 years (3.1 mm). In contrast, implants treated with CTG exhibited a mean KMW of 3.2 mm at the 3-year follow-up and 3.3 mm at the 5-year visit. However, the authors did not observe any significant differences in KMW between VXCM and CTG. Regarding volumetric changes, both groups showed clinically negligible alterations from baseline to 5 years (VXCM: from 2.7 mm to 3.2 mm; CTG: from 3.2 mm to 3.4 mm) [56].

3.3. Comparison [soft tissue substitutes vs. soft tissue substitutes]

The only randomized clinical trial aimed to compare directly the use of two different matrices (XDM vs. CMX) for the treatment of single gingival recessions was Santamaria et al. [22], reporting results at 6 months of follow-up.

4. Conclusions

Based on the available evidence, the alternative use of soft tissue substitutes at the conventional grafting procedures by means of free gingival graft or connective tissue graft resulted still questionable.

In particular, around ***teeth***, all biomaterials show superior performance compared to CAF alone for treating gingival recessions. However, when compared to CTG, ADM yields the most similar outcomes to the gold standard (CTG), even though in multiple recessions CTG still continue to be considered the most favorable approach. Use of STSs (acellular matrix or tissue engineered) in combination with an apically positioned flap resulted in a significantly less gain of KTW compared to what achieved with FGG and APF.

Around ***dental implants***, free gingival grafts were deemed more effective than soft tissue substitutes in enhancing keratinized mucosa width.

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