Efficacy of Xenogenic collagen matrix as an alternative option to different soft tissue augmentation methods for the treatment of multiple adjacent gingival recessions: a systematic review

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ABSTRACT:

BACKGROUND: Gingival recession occurs when there is a loss of marginal gingival tissues, leading to the displacement of the gingival border below the cemento-enamel junction (CEJ) and exposing the root surface. This exposure of the root surface can lead to unaesthetic appearance, dentinal hypersensitivity, and an increased risk of root caries, cervical wear, and difficulties in achieving proper plaque control. Therefore, it is necessary to cover the exposed root surfaces with soft tissue, wherever feasible, to provide adequate protection. It has been demonstrated that a recently developed xenogeneic collagen matrix can facilitate the regeneration of keratinized gingival tissue around teeth. The aim of this review is determine

the efficacy of xenogenic collagen matrix as an alternative option to different soft tissue augmentation methods for the treatment of multiple adjacent gingival recessions.

METHODOLOGY: An electronic search of the following databases MEDLINE (NCBI PubMed and PMC), Cochrane Central Register of Controlled Trials (CCRCT), Science Direct, Google Scholar, EMBASE, EBSCO, K Hub was done along with a hand search of peer reviewed journals for relevant articles. The following combinations of title, abstract, Medical Subject Heading Terms (MeSH) and keywords were used to search through the above-mentioned databases. (Multiple adjacent gingival recessions) AND (Root Coverage) AND (Periodontal plastic surgeries) AND (Xenogenic Collagen Matrix) AND (Porcine derived collagen matrix) AND (Xenogenic collagen membrane). Risk of Bias assessment was also performed for randomized controlled trials included.

RESULTS:

A total of 22 articles were included in this systematic review. Xenogenic collagen matrix was carried out in the included studies as an alternative option to different soft tissue augmentation methods for the treatment of multiple adjacent gingival recessions.

CONCLUSION:

The use of a xenogeneic collagen matrix is a viable alternative to various soft tissue augmentation techniques for treating multiple adjacent gingival recessions.

INTRODUCTION

Gingival recession refers to the displacement of the gingival margin below the cementoenamel junction (CEJ) of a natural tooth or the platform of a dental implant. Gingival recession is a prevalent issue affecting a substantial proportion of the population, with causes including

periodontal disease, thin biotype, eruption pattern, and mechanical trauma. It can be localized (one tooth) or multiple (more than one or two teeth). Patients often seek corrective treatment due to root hypersensitivity and esthetic concerns. The goals of recession treatment are to achieve full root coverage, enhance the overall aesthetic appearance, and ensure long-term stability.[1]

There are various treatment options available for gingival recession, which are chosen based on the patient's primary concern. Treatment may include non-surgical or surgical procedures. Over time, several surgical techniques have been suggested for gingival recession treatment. These techniques include pedicle flaps such as rotational flaps (such as laterally positioned flaps and double papilla flap) and advancement flaps (such as coronally positioned graft and semilunar flap). Recent techniques include the tunneling technique and modifed coronally advanced tunnel (MCAT) technique.[2]

In accordance with the techniques, various soft tissue augmentation methods and periodontal plastic procedures have been introduced for root coverage. The primary objective of periodontal plastic surgery is to achieve a stable and complete root coverage with a tissue margin attached at the cementoenamel junction (CEJ), increase the dimensions of keratinized gingiva, such as thickness and width, and maintain a healthy gingival sulcus. In recent decades, various surgical approaches have been evaluated to achieve root coverage for multiple adjacent gingival recessions with predictability and consistency.[3]

A newly developed alternative is a porcine-derived collagen matrix (PDCM). PDCM offers several advantages, including early vascularization and good soft-tissue ingrowth, excellent wound healing, and easy handling. It can also serve as scaffold for cells to enhance blood clot stability and conduce thin growth of blood vessels. [4]

In the last decade, two types of xenogenic collagen membranes have been extensively studied. The first is a porcine-derived, bilayered type I and III 3D collagen membrane called (Mucograft, Geistlich, Wolhusen, Switzerland) while the second is a porcine-derived acellular dermal collagen matrix (PADM) known as (Mucoderm, Botiss Dental). Porcine derived acellular dermal matrix (PADM) is a type of collagen matrix that is derived from the dermis of pigs. The process involves several steps to remove antigenic components and prepare the matrix for clinical use. PADM acts as a scaffold for the proliferation of fibroblasts and endothelial cells, which allows for the vascularization of its structure. PADM has been used as a substitute for connective tissue grafts in the treatment of gingival recession and has shown promising results in terms of clinical outcomes and patient satisfaction. The xenogenic collagen matrix is a smooth, white to off-white, resorbable collagen dressing derived from cross-linked, purified collagen obtained from bovine hide. This 3D -matrix has outer layer compact, intends to hold sutures and protect the defect in open healing situations while the inner layer is porous. The thickness and porous structure of the membrane enable it to collect fluids and blood at the defect site, thereby promoting cell development, wound healing, and stimulating neo angiogenesis. These properties help to increase root attachment to the gingiva and promote gingival thickness. [2,3,4]

The use of xenogenic collagen membranes may be viewed as a viable alternative treatment option to the standard free grafting method, as it aims to minimize patient morbidity and enhance safety. The aim of this review is to determine the efficacy of xenogenic collagen matrix as an alternative option to different soft tissue augmentation methods for the treatment of multiple adjacent gingival recessions.

AIM AND OBJECTIVES

AIM: To answer the following PI(E)COS question.

In patients with periodontitis, what is the efficacy of xenogenic collagen matrix (XCM) as an alternative option to different soft tissue augmentation methods for the treatment of multiple adjacent gingival recessions?

Where,

PARTICIPANTS/POPULATION(P) - Patients having multiple adjacent gingival recessions

INTERVENTION(S), EXPOSURE(S) - Xenogenic collagen matrix (XCM)

COMPARATOR(S)/CONTROL(C) - Surgical treatment for multiple adjacent gingival recessions

STUDY DESIGN- In-vivo human randomized and/or controlled clinical trials.

PRIMARY OUTCOME- recession height (RH), recession width (RW), and keratinized tissue width (KTW), mean root coverage (MRC)

MEASURES OF EFFECT OF PRIMARY OUTCOME- The parameters evaluated in each of the eligible randomized and/or controlled clinical trial, should have been evaluated at baseline and at the subsequent follow- up visit/s as per the criteria specified in each trial.

SECONDARY OUTCOME(S)-Probing pocket depth (PPD), clinical attachment level (CAL)

MEASURES OF EFFECT OF SECONDARY OUTCOME(S). - The effects of the additional outcome of each of the eligible clinical trials, should have been evaluated at baseline and at the subsequent follow-up visit/s as per the criteria specified in each trial.

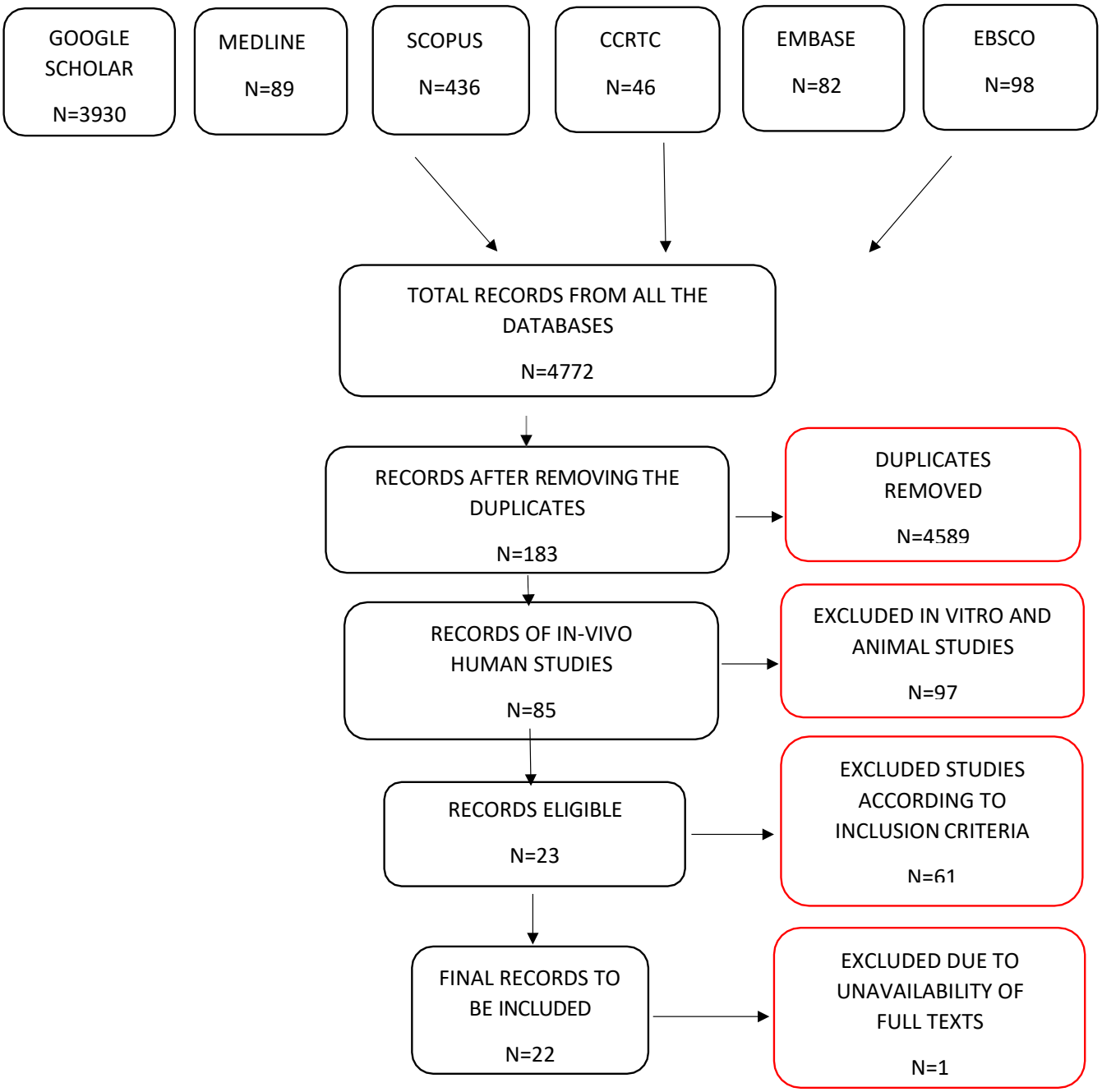
OBJECTIVES:

1. To systematically review the literature in order to produce a database of outcome variables that have been utilized for Clinical parameters.

2. Critical appraisal of the primary and secondary outcome variables assessed in the literaturewith respect to xenogenic collagen matrix (XCM).

3. To analyze the efficacy xenogenic collagen matrix (XCM) as an alternative option to different soft tissue augmentation methods in the treatment of multiple adjacent gingival recessions over primary and secondary outcome(s).

ANNEXURE I:
PRISMA
FLOWCHART



RESULTS

STUDY SELECTION

A full search from multiple databases resulted in 4772 articles. Relevant articles were identified by two independent reviewers, 4590 duplicates were removed. 182 articles were selected for full text evaluation after screening the title and abstracts. For publications in which only

abstracts were available, full texts were requested and obtained. For publications in languages other than English, the corresponding authors were contacted and requested for translated version of the manuscript. 98 articles of in vitro and animal studies were excluded. Only In-vivo human studies were included. 84 articles of in vivo human studies were found. By applying the inclusion criteria, 62 articles were excluded. Total articles fulfilling the inclusion criteria were 22. Therefore 22 articles fulfilled the criteria to be included in the current systematic review. Data was extracted from these publications and was critically analysed for efficacy of Xenogenic collagen matrix as an alternative option to different soft tissue augmentation methods for the treatment of multiple adjacent gingival recessions.

CHARACTERISTICS OF INCLUDED STUDIES

All the included studies were in-vivo trials conducted on human subjects. Randomized clinical trials were included. Out of 22 included studies, 15 were conducted in accordance with the guidelines by the World Medical Association Declaration of Helsinki. All authors of the included studies sought approval of the protocol from

Ethical Committee except 3. Amongst the included randomized clinical trials, 11 were split mouth design. (TABLE 1)

Out of 22 studies, 4 studies were conducted in Sao Paulo, Brazil and 1 in Gujarat India; rest of them were conducted in Italy, Syria, Egypt, Switzerland, Germany, etc. Average sample size of the included studies was 12-45 participants. Mean age of the participants was 18-70 years. The participants in each trial were selected as per the inclusion criteria of individual trial based upon age and periodontal status. Written informed consent was obtained by participant population as reported in 22 of the included studies. (TABLE 2)

TABLE 1 : STUDY CHARACTERISTICS

Sr no	**Author name (year of study)**	**Journal name**	**Study design**	**Approval of protocol**	**Conducted in accordance with**
1	Michael K. McGuire et al 2010	Journal of Periodontology	single-masked, randomized controlled split-mouth study	Essex Institutional Review Board, Lebanon, NJ	NS

2	Sofia Aroca et al 2013	Journal of clinical periodontology	randomized, controlled, split-mouth clinical study	Ethical committee of the Semmelweis University Budapest, Hungary (protocol: 5242-0/2010-101SEKU; 365/ PI/10)	NS
3	Karin Jepsen et al 2013	Journal of clinical periodontology	multicentre single-blinded, randomized, controlled, split-mouth trial	Ethical committee of human subject trials Germany, Italy, Sweden and Spain	Helsinki Declaration of 1975 as revised in 2000
4	Daniele Cardaropoli et al 2014	The International Journal of Periodontics and Restorative Dentistry	Prospective randomized controlled study	NS	Helsinki Declaration of 1975 as revised in 2000
5	Yuri Castro et al 2014	Journal of Oral Research	A parallel randomized clinical trial	The Ethics Committee of the Faculty of Dentistry of the Universidad Nacional Mayor de San Marcos	Helsinki Declaration of 1975 as revised in 2000

6	Danilo Maeda Reino et al 2015	Brazilian Dental Journal	A randomized controlled clinical trial using a split-mouth	The Human Research Committee of the Institution (2010.1.1217.58.7)	The Declaration of Helsinki on experimentation involving human subjects and received the identifier NCT02129504
7	Marta Cieslik-Wegemund et al 2016	Journal of Periodontology	A randomized controlled clinical trial	the Local Ethical Committee (Institutional Review Board associated with the Medical University of Silesia, Katowice, Poland; protocol resolution no. KNW/0022/KB1/108/12)	NS
8	Maurizio S. Tonetti et al 2017	Journal of clinical periodontology	A randomized controlled trial	The Freiburg Ethic Committee International (FEKI code 011/1546)	Helsinki Declaration of 1975 as revised in 2000
9	Haydar Barakat et al 2018	World Journal of Dentistry	A Comparative Clinical Study	The Internal Ethical Committee of Damascus University, Damascus, Syria	NS
10	Onder Gurlek et al 2019	Journal of Esthetic and Restorative Dentistry	single-centered, split-mouth, randomized,	The Local Ethics Committee (Ege University, School of Medicine No. 17-11.1/9.).	The Declaration of Helsinki, as revised in 2002

			controlled clinical trial		
11	Rotundo Roberto et al 2019	Journal of clinical periodontology	a single-centre, superiority, assessor-blind clinical trial	The Local authority (Azienda USL 3 Pistoia, prot. 24/CESM 19.11.2012)	The Declaration of Helsinki on experimentation involving human subjects.
12	Rodrigo NAHAS et al 2019	Brazilian Oral Research Journal	a single-blind, randomized clinical trial with a split-mouth design	NS	The Helsinki Declaration of 1975, revised in 2000 0 (IRB approval no. 401.807).
13	Haydar Barakat et al 2020	Indian Journal of Dental Research	A Randomized Clinical Split-mouth Trail	The Internal Ethical Committee of Damascus University, Damascus, Syria	Helsinki Declaration of 1975 as revised in 2000
14	Séverine Vincent-Bugnas et al 2020	Journal of Periodontal & Implant Science	single-center split-mouth randomized study	The CCP Sud Mediterranee II Institutional Review Board (No. 16.085) and French National Agency for	Helsinki Declaration of 1975 as revised in 2000

				Medicines and Health Products Safety	
15	Kleber Tanaka Suzuki et al 2020	Journal of Clinical Oral Investigations	a randomized controlled clinical trial	The Research Ethics Committee of University of Sao Paulo (protocol CAAE 58534216.5.0000.5419)	The Declaration of Helsinki from the World Medical Association (2008)
16	Dragana L. Rakasevic et al 2020	Journal of Esthetic and Restorative Dentistry	a split-mouth, single-center, prospective randomized controlled clinical trial	The Ethics Committee (approval No #36/24)	The Helsinki Declaration of 1975, as revised in 2000.
17	Jonathan Meza-Mauricio et al 2021	Journal of Clinical Oral Investigations	a parallel, randomized, single center controlled clinical trial	Guarulhos University Board (approval 2.290.510)	The Declaration of Helsinki on experimentation involving human subjects, as revised in 2013.
18	Alireza Fathiazar et al 2021	Journal of Dentistry, Shiraz University of Medical Sciences	a double blind, split-mouth randomized clinical trial	The institute review committee for human subjects with code number (IR.IAU.DENTAL. REC.1397.023) and the human subjects ethics board	The Helsinki Declaration of 1975, as revised in 2013.

				of the Iranian registry of clinical trials (IRCT code: IRCT20140318017053N10)	
19	Rajya Lakshmi Mikkili et al 2022	Journal of Clinical Oral Investigations	prospective randomized controlled clinical study	The institutional Ethical Committee (IEC with IEC number IECVDC/19/PG01/PI/IVV/48 and registered under clinical trial (CTRI) no. CTRI/2020/03/024238	NS
20	B. Molnar et al 2022	Journal of Clinical Oral Investigations	a split-mouth randomized clinical trial	The ethical committee of the Semmelweis University (protocol: 5242–0/2010-101SEKU; 365/PI/10).	The Helsinki Declaration of 1975, as revised in 2013.
21	Yesha Haresh Raval et al 2022	Journal of Indian Society of Periodontology	A randomized, parallel-arm comparative study	NS	NS
22	Mohamed Mousatafa et al 2022	Egyptian Dental Journal	A Randomized controlled clinical trial	The Research Ethics committee at faculty of Dentistry Ain Shams University (FDASU-Rec IM 111803)	NS

TABLE 2 : PARTICIPANT CHARACTERISTICS

Sr no.	Author name	Geographic area	Mean age (in years)	Gender	Consent	Sample size	Type of recession
1	Michael K. McGuire et al 2010	Lebanon, NJ	43.7 – 12.2	8 males, 17 females	Obtained	25	
2	Sofia Aroca et al 2013	Budapest, Hungary	≥18	NS	Obtained	22	Miller's Class I and II
3	Karin Jepsen et al 2013	Germany, Italy, Sweden and Spain	18	NS	Obtained	45	Miller's Class I and II
4	Daniele Cardaropoli et al 2014	Torino, Italy	38.4± 11.1	17 males, 15 females	Obtained	32	Miller's Class I and II
5	Yuri Castro et al 2014	Peru	30 to 60	NS	Obtained	12	Miller's Class I and II
6	Danilo Maeda Reino et al 2015	Sao Paulo, Brazil	26 to 46	NS	Obtained	20	Miller's Class I and II

7	Marta Cieslik-Wegemund et al 2016	Katowice, Poland	20 to 50	Female-19, Male-9	Obtained	28	Miller's Class I and II
8	Maurizio S. Tonetti et al 2017	Italy, Hong Kong, France, Switzerland, Germany	NS	NS	Obtained	187	
9	Haydar Barakat et al 2018	Damascus, Syria	25 to 45	4 male and 6 female	Obtained	10	Miller's Class I and II
10	Onder Gurlek et al 2019	Izmir, Turkey	Above 18	NS	Obtained	12	Miller's Class I and II
11	Rotundo Roberto et al 2019	London, UK	18 years or older	NS	Obtained	24	
12	Rodrigo NAHAS et al 2019	Sao Paulo, Brazil	≥ 18	NS	Obtained	15	Miller's Class I
13	Haydar Barakat et al 2020	Damascus, Syria	20 to 45	11 male and 11 female	Obtained	22	Miller's Class I and II

14	Séverine Vincent-Bugnas et al 2020		23 to 55	8 women and 4 men	Obtained	12	Cairo's RT1
15	Kleber Tanaka Suzuki et al 2020	Sao Paulo	24 to 50	9 males and 9 females	Obtained	18	Cairo's RT1
16	Dragana L. Rakocevic et al 2020	Serbia	≥ 18	NS	Obtained	27	Type I
17	Jonathan Meza-Mauricio et al 2021	Sao Paulo, Brazil	≥18	NS	Obtained	42	Cairo's RT1
18	Alireza Fathiazar et al 2021	Tehran, Iran		NS	Obtained	7	Miller's Class I and II
19	Rajya Lakshmi Mikkili et al 2022		18 to 60	NS	Obtained	28	Miller's Class I and II
20	B. Molnar et al 2022	Budapest, Hungary	≥18	NS	Obtained	16	Miller's Class I and II (RT I)

21	Yesha Haresh Raval et al 2022	Vadodara, Gujarat	30–70	NS	Obtained	34	Cairo's RT1 and RT2
22	Mohamed Mousatafa et al 2022	Cairo, Egypt	20 - 40	NS	Obtained	16	Miller's Class I and II

TABLE 3 : METHODOLOGICAL CHARACTERISTICS

Sr.no.	**Author nae**	**No of patients in Test /Control**	**Total no of sites or recessions**	**Intervention group (XENOGENIC COLLAGEN MATRIX)**	**Control group**	**Follow up**
1	Michael K. McGuire et al 2010	10/10	NS	CM+CAF	CTG+CAF	6 months and 1 year
2	Sofia Aroca et al 2013	11/11	156	MCAT + CM	MCAT + CTG	28 days, 3, 6 and 12 months

3	Karin Jepsen et al 2013	NS	90	CAF + CM	CAF	3-month and 6-month
4	Daniele Cardaropoli et al 2014	16/16	113	CAF + CM	CAF	4 weeks and 3, 6 and 12 months
5	Yuri Castro et al 2014	6/6	NS	PTF + CMP	PTF + SCG	
6	Danilo Maeda Reino et al 2015	10/10	NS	EFT+PCM	CAF+PCM	3 and 6 months
7	Marta Cieslik-Wegemund et al 2016	14/14	106 (T - 49/ C- 47)	collagen matrix using the tunnel technique	connective tissue graft combined with the tunnel technique	3 and 6 months
8	Maurizio S. Tonetti et al 2017	92/95	186	Xenogenic collagen matrix + coronally advanced flap	autologous connective tissue graft + coronally advanced flap	6-month

9	Haydar Barakat et al 2018	5/5	48	(PCM + CAF)	(CTG + CAF)	6-month
10	Onder Gurlek et al 2019	41/41	82	XADM + M-CAF	CTG + M-CAF	6 and 18-months
11	Rotundo Roberto et al 2019	12(/12	NS	CAF+CMX	CAF	3, 6, and 12 months
12	Rodrigo NAHAS et al 2019	9/7	82	CM + mCAF	CTG + mCAF	3, 6, and 12 months
13	Haydar Barakat et al 2020	10/10	NS	PCM + CAF	CTG + CAF	12 months
14	Séverine Vincent-Bugnas et al 2020	6/6	74 (T – 37/ C – 37)	MCAT + PADM	MCAT + CTG	12 months
15	Kleber Tanaka Suzuki et al 2020	6/8	NS	eCAF+ MD	eCAF + SCTG	3 and 6 months

16	Dragana L. Rakocevic et al 2020	10/10	NS	MCAT + XDM	MCAT + CTG	6 and 12 months
17	Jonathan Meza-Mauricio et al 2021	18/18	130	CAF+XDM	CAF+CTG	6 and 12 months
18	Alireza Fathiazar et al 2021	NS	24	Coronally advanced flap + Mucoderm®	Coronally advanced flap + connective tissue graft (CTG)	1, 3 and 6 months
19	Rajya Lakshmi Mikkili et al 2022	14/14	64 (T – 31/ C – 33)	MCAT+ PDCM	MCAT+SCTG	3 and 6 months
20	B. Molnar et al 2022	11/11	114	MCAT+CM	MCAT+CTG	1 month, 3 months, 6 months, 12 months and 9 years
21	Yesha Haresh	17/17	34 (T – 17/ C – 17)	CAF+XCM	CAF+PRF	6 months

	Raval et al 2022					
22	Mohamed Mousatafa et al 2022	8/8	NS	xenogeneic acellular dermal matrix + tunneling technique	connective tissue graft + tunneling technique	3 and 6 months

TABLE 4 : SUMMARY OF PRIMARY AND ADDITIONAL OUTCOMES

SR NO	**AUTHOR NAME**	**CLINICAL PARAMETERS**					
		RECESSION HEIGHT (RH) (BASELINE/ FOLLOW UP)	**RECESSION WIDTH (RW) (BASELINE/ FOLLOW UP)**	**KERATINIZED TISSUE WIDTH (KTW) (BASELINE/ FOLLOW UP)**	**MEAN ROOT COVERAGE (MRC) (PERCENTAGE %)**	**PROBING DEPTH (PD) (BASELINE/ FOLLOW UP)**	**CLINICAL ATTACHMENT LEVEL (CAL) (BASELINE/ FOLLOW UP)**

1	Michael K. McGuire et al 2010	Test (3.14/0.52) Control (3.20/0.10)	Test (4.06/1.34) Control (4.30/0.26)	Test (2.44/3.78) Control (2.78/4.04)	Test (83.5) Control (97.0)	Test (1.26/1.60) Control (1.38/1.70)	Test (4.40/2.12) Control (4.50/1.80)
2	Sofia Aroca et al 2013	Test (1.9/0.6) Control (1.8/0.2)	Test (3.8/1.4) Control (3.8/0.5)	Test (2.1/2.4) Control (2.0/2.7)	Test (71 ± 21%) Control (90 ± 18%)	Test (1.4/1.4) Control (1.3/1.3)	Test (3.2/1.9) Control (3.1/1.4)
3	Karin Jepsen et al 2013	Test (3.46/0.84) Control (3.34/0.89)	Test (4.08/1.89) Control (4.10/2.01)	Test (1.97/2.59) Control (2.00/2.40)	Test (76.11) Control (76.44)	Test (1.33/1.30) Control (1.48/1.33)	Test (4.79/2.14) Control (4.82/2.22)
4	Daniele Cardaropoli et al 2014	Test (2.48/0.20) Control (2.43/0.58)	Test (0.84/0.81) Control (0.81/0.94)	Test (1.89/2.96) Control (1.91/2.61)	Test (93.25 ± 10.01%) Control (81.49 ± 23.45%)	Test (1.09/1.15) Control (1.06/1.03)	Test (3.57/1.34) Control (3.49/1.61)
5	Yuri Castro et al 2014	CMP (2.67 ± 1.03/ 2.17 ± 0.98) SCG (4.33 ± 1.03/ 3.17 ± 0.4)	NS	CMP (2.5 ± 0.083/ 4.5 ± 0.83) SCG (3.33 ± 2.16/ 4.33 ± 2.06)	CMP (16.67 ± 25.82%) SCG (24.72 ± 13.55%)	CMP (1.67 ± 0.51/ 1) SCG (1.5 ± 0.54/ 1)	CMP (4.33 ± 1.46/ 3.17 ± 0.98) SCG (5.83 ± 1.16/ 4.17 ± 0.4)
6	Danilo Maeda	CAF + PCM (3.49 ± 0.61/ 1.34 ± 0.60)	CAF + PCM (3.58 ± 0.52/ 2.61 ± 1.16)	CAF + PCM (1.66 ± 0.73/ 1.95 ± 0.73)	CAF + PCM (60.78 ± 14.95%) EF+ PCM	CAF + PCM (1.82 ± 0.48/ 2.29 ± 0.66)	CAF + PCM (5.31 ± 0.89/ 3.63 ± 1.02)

	Reino et al 2015	EF+ PCM (3.47 ± 0.60/ 0.64 ± 0.60)	EF+ PCM (3.68 ± 0.55/ 2.05 ± 1.69)	EF+ PCM (1.74 ± 0.76/ 1.79 ± 0.56)	(82.33 ± 16.64%)	EF + PCM (1.82±0.48/ 2.24±0.66)	EF + PCM (5.29 ± 0.91 2.88 ± 1.30)
7	Marta Cieslik-Wegemund et al 2016	TUN +CTG (2.7 ± 0.9 / 0.2 ± 0.4) TUN + CM (3.0 ± 0.8/ 0.4 ± 0.3)	TUN +CTG (3.1 ± 0.6/ 0.5 ± 0.9) TUN + CM (3.6 ± 0.9/ 0.7 ± 0.6)	TUN +CTG (2.3 ± 1.5/ 3.3 ± 1.7) TUN + CM (2.6 ± 1.8/ 3.4 ± 1.5)	TUN +CTG (95 ± 11%) TUN + CM (91 ± 13%)	NS	TUN +CTG (3.8 ± 0.8/ 1.2 ± 0.4) TUN + CM (4.0 ± 0.8/ 1.4 ± 0.3)
8	Maurizio S. Tonetti et al 2017	CAF + CMX (2.5/1.7) CAF + CTG (2.5/2.1)	NS	CAF + CMX (3.0/-0.1) CAF + CTG (2.9/0.5)	CAF + CMX (48%) CAF + CTG (70%)	CAF + CMX (1.5/-0.1) CAF + CTG (1.5/-0.3)	NS
9	Haydar Barakat et al 2018	PCM + CAF (3.23 ± 0.49/ 0.17 ± 0.28) CTG + CAF (3.25 ± 0.53/ 0.08 ± 0.19)	NS	PCM + CAF (1.83 ± 0.32/ 3.41 ± 0.50) CTG + CAF (1.75 ± 0.33/ 3.17 ± 0.43)	PCM + CAF (95.23 ± 7.89%) CTG + CAF (97.84 ± 4.94%)	PCM + CAF (0.85 ± 0.27/ 0.71 ± 0.25) CTG + CAF (0.85 ± 0.31/ 0.69 ± 0.29)	PCM + CAF (4.08 ± 0.52/ 0.87 ± 0.34) CTG + CAF (4.10 ± 0.69/ 0.77 ± 0.36)
10	Onder Gurlek et al 2019	XADM + M-CAF (2.70 ± 1.00/ 0.22 ± 0.42)	XADM + M-CAF (3.10 ± 0.71/ 0.68 ± 1.30)	XADM + M-CAF (3.40 ± 1.20/ 3.70 ± 0.98)	XADM + M-CAF (78%) CTG + M-CAT (87.8%)	XADM + M-CAF (1.70 ± 0.66/ 1.90 ± 0.52)	XADM + M-CAF (4.40 ± 1.10/ 0.56 ± 1.20)

		CTG + M-CAT (2.60 ± 0.77/ 0.17 ± 0.50)	CTG + M-CAT (3.10 ± 0.88/ 0.24 ± 0.66)	CTG + M-CAT (3.70 ± 1.10/ 4.20 ± 1.00)		CTG + M-CAT (1.80 ± 0.62/ 1.70 ± 0.56)	CTG + M-CAT (4.40 ± 1.00/ 0.39 ± 0.83)
11	Rotundo Roberto et al 2019	CAF+CMX (2.3/0.2) CAF (2.6/0.5)	CAF+CMX (3.2/0.7) CAF (3.6/1.0)	CAF+CMX (3.3/3.5) CAF (3.5/2.8)	CAF+CMX (73%) CAF (71%)	CAF+CMX (1.5/1.5) CAF (1.5/1.1)	CAF+CMX (3.8/1.8) CAF (4.4/1.6)
12	Rodrigo NAHAS et al 2019	mCAF + CM (2.7 ± 1.1/ 0.9 ± 1.0) mCAF + CTG (2.8 ± 1.1/ 0.4 ± 0.6)	NS	mCAF + CM (2.2 ± 1.0/2.6 ± 0.9) mCAF + CTG (2.1 ± 1.0/3.2 ± 1.5)	mCAF + CM (77.7%) mCAF + CTG (82.14%)	mCAF + CM (1.1 ± 0.4/1.2 ± 0.4) mCAF + CTG (1.3 ± 0.4/1.7 ± 0.5)	mCAF + CM (3.8 ± 1.1/ 2.1 ± 1.2 mCAF + CTG (4.0 ± 1.2/ 2.1 ± 0.9)
13	Haydar Barakat et al 2020	PCM + CAF (2.67±0.65/ 0.20±0.37) CTG + CAF (2.55±0.69/ 0.12±0.27)	NS	PCM + CAF (2.17±0.65/ 3.53±0.82) CTG + CAF (2.20±0.61/ 3.50±0.65)	PCM + CAF (93.07%) CTG + CAF (94.05%)	PCM + CAF (1.22±0.34/ 1.65±0.40) CTG + CAF (1.02±0.44/ 1.42±0.41)	PCM + CAF (3.90±0.87/ 1.85±0.65) CTG + CAF (3.62±1.02/ 1.55±0.60)

14	Séverine Vincent-Bugnas et al 2020	MCAT + PADM (2.8±1.0/ 1.0±0.8) MCAT + CTG (2.9±0.9/ 0.6±0.74)	MCAT + PADM (2.6±0.7/ 0.9±0.8) MCAT + CTG (2.4±0.7/ 0.7±0.8)	MCAT + PADM (2.1±1.6/ 2.5±1.2) MCAT + CTG (2.2±1.3/ 3.0±1.0)	MCAT + PADM (68.8±23.4%) MCAT + CTG (80.6±23.7%)	MCAT + PADM (1.8±0.5/ 1.6±0.4) MCAT + CTG (1.9±0.6/ 1.7±0.5)	MCAT + PADM (4.6±1.2/ 2.6±0.9) MCAT + CTG (4.8±1.0 2.3±0.8)
15	Kleber Tanaka Suzuki et al 2020	eCAF + MD (3.33 ± 0.89/ 1.61 ± 1.19) eCAF + SCTG (3.21 ± 0.80/ 1.00 ± 0.94)	eCAF + MD (3.89 ± 0.60/ 3.28 ± 1.33) eCAF + SCTG (4.10 ± 0.63/ 2.62 ± 1.82)	eCAF + MD (0.82 ± 0.27/ 1.01 ± 0.36) eCAF + SCTG (0.86 ± 0.39/ 1.27 ± 0.30)	eCAF + MD (60.86 ± 26.18%) eCAF + SCTG (71.74 ± 25.36%)	NS	NS
16	Dragana L. Rakocevic et al 2020	MCAT + PADM (2.9 ± 1.35/ 0.5 ± 0.75) MCAT + CTG (2.6 ± 1.23/ 0.47 ± 0.7)	MCAT + PADM (2.6 ± 1.1/ 0.57 ± 0.8) MCAT + CTG (2.44 ± 0.9/ 0.53 ± 0.7)	MCAT + PADM (2.44 ± 1.3/ 2.92 ± 0.9) MCAT + CTG (2.43 ± 1.4/ 2.7 ± 0.9)	MCAT + PADM (88.78 ± 14.04%) MCAT + CTG (84.10 ± 17.77%)	MCAT + PADM (1.27 ± 0.45/ 1.09 ± 0.45) MCAT + CTG (1.29 ± 0.46/ 1.12 ± 0.33)	MCAT + PADM (4.09 ± 1.4/ 1.09 ± 1.22) MCAT + CTG (3.86 ± 1.32/ 1.09 ± 1.34)
17	Jonathan Meza-	CAF+XDM	CAF+XDM	CAF+XDM	CAF+XDM (80.19%)	CAF+XDM	CAF+XDM

	Mauricio et al 2021	(2.81 ± 0.77/ 0.53 ± 0.63) CAF+ CTG (3.00 ± 0.78/ 0.50 ± 0.78)	(4.45 ± 1.53/ 2.78 ± 2.34) CAF+ CTG (4.36 ± 1.42/ 1.81 ± 2.27)	(2.43 ± 1.12/ 3.15 ± 1.00) CAF+ CTG (2.42 ± 1.29/ 3.16 ± 1.22)	CAF+ CTG (91.79%)	(1.76 ± 0.55/ 2.73 ± 0.59) CAF+ CTG (1.74 ± 0.47/ 2.71 ± 0.60)	(4.14 ± 0.99/ 2.72 ± 1.08) CAF+ CTG (4.56 ± 1.27/ 2.68 ± 1.19)
18	Alireza Fathiazar et al 2021	CAF+MUCODERM (3.83±1.11/ 2.75±1.65) CAF + SCTG (3.92±1.08/ 1.25±0.96)	NS	CAF+MUCODERM (1.58±1.8/3 2.42±2.23) CAF + SCTG (1.33±1.43/ 4.25±2.73)	CAF+MUCODERM (31±26%) CAF + SCTG (64±26%)	CAF+MUCODERM (1.17±0.38/ 1.75±0.62) CAF + SCTG (1.25±0.45/ 2.17±0.93)	CAF+MUCODERM (4.92±1.37/ 4.42±1.67) CAF + SCTG (5.25±1.05/ 3.5±1)
19	Rajya Lakshmi Mikkili et al 2022	MCAT+PDCM (2.55 ± 0.50/ 0.87 ± 0.49) MCAT+SCTG (2.55 ± 0.75/ 0.91 ± 0.52)	MCAT+PDCM (3.42 ± 0.84/ 1.84 ± 0.93) MCAT+SCTG (3.42 ± 0.66/ 1.97 ± 1.21)	MCAT+PDCM (1.32 ± 0.47/ 2.52 ± 0.57) MCAT+SCTG (1.33 ± 0.47/ 2.24 ± 0.70)	MCAT+PDCM (65 ± 22.09%) MCAT+SCTG (63.3 ± 22.3%)	MCAT+PDCM (2.72 ± 0.27/ 2.39 ± 0.29) MCAT+SCTG (2.76 ± 0.25/ 2.42 ± 0.30)	MCAT+PDCM (5.68 ± 0.73/ 3.26 ± 0.62) MCAT+SCTG (5.87 ± 0.65/ 3.47 ± 0.82)
20	B. Molnar et al 2022	MCAT+CM (1.81±0.63/ 0.50±0.40)	NS	MCAT+CM (2.00±0.90/ 2.32±0.95) MCAT+CTG	MCAT+CM (73.25±21.05%) MCAT+CTG (88.07±20.90%)	NS	NS

		MCAT+CTG (1.78±0.54/ 0.21±0.30)		(2.03±0.65/ 2.78±0.82)			
21	Yesha Haresh Raval et al 2022	CAF + XCM (2.12±0.92/ 0.88±0.85 CAF + PRF (2.06±0.827/ 0.82±0.809)	CAF + XCM (2.85±1.34/ 1.47±1.73) CAF + PRF (2.41±1.064/ 1.29±1.105)	CAF + XCM (2.41±0.79/ 3.18±0.88) CAF + PRF (1.76±0.752/ 2.59±0.870)	NS	NS	CAF + XCM (3.24±1.2/ 1.88±0.99) CAF + PRF (3.18±1.074/ 2.06±0.899)
22	Mohamed Mousatafa et al 2022	XADM + TUN (1.75±0.46/ 0.50±0.76) CTG + TUN (2.38±1.30/ 0.88±1.13)	XADM + TUN (2.38±0.52/ 0.75±1.16) CTG + TUN (2.12±0.83/ 1.25±1.49)	XADM + TUN (4.00±1.41/ 5.20±1.30) CTG + TUN (2.88±0.64/ 3.62±0.52)	XADM + TUN (62.50±44.32 %) CTG + TUN (73.75±38.89 %)	XADM + TUN (1.38±0.52/ 1.32±0.36) CTG + TUN (1.25±0.46/ 1.20±0.46)	XADM + TUN (3.12±0.64/1 .62±1.51) CTG + TUN (3.62±1.60/2 .00±1.60)

TABLE 5 : RISK OF BIAS ASSESSMENT FOR INCLUDED STUDIES

Sr.no.	**Author name**	**Risk of bias assessments**					**Overall assessment**
		DOMAIN 1	***DOMAIN 2***	***DOMAIN 3***	***DOMAIN 4***	***DOMAIN 5***	
1.	Michael K. McGuire et al 2010	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias
2.	Sofia Aroca et al 2013	Low risk	Low risk	Low risk	Low risk	Some concern	Some concern
3.	Karin Jepsen et al 2013	High risk	Low risk	Low risk	Low risk	Low risk	High risk of bias
4.	Daniele Cardaropoli et al 2014	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias
5.	Yuri Castro et al 2014	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias

6.	Danilo Maeda Reino et al 2015	Some concerns	Low risk	Low risk	Some concern	Low risk	Some concern
7.	Marta Cieslik-Wegemund et al 2016	Low risk	Some concerns	Low risk	Low risk	Low risk	Low risk of bias
8.	Maurizio S. Tonetti et al 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Some concerns
9.	Haydar Barakat et al 2018	Some concerns	Low risk	Low risk	High risk	Low risk	Low risk of bias
10.	Onder Gurlek et al 2019	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias
11.	Rotundo Roberto et al 2019	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias
12.	Rodrigo NAHAS et al 2019	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns

13.	Haydar Barakat et al 2020	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias
14	Séverine Vincent-Bugnas et al 2020	Low risk	High risk	Low risk	Low risk	Low risk	High risk of bias
15	Kleber Tanaka Suzuki et al 2020	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias
16	Dragana L. Rakasevic et al 2020	High risk	Low risk	Some concerns	Low risk	Low risk	High risk of bias
17	Jonathan Meza-Mauricio et al 2021	Low risk	Some concerns	Low risk	Some concern	Low risk	Some concern
18	Alireza Fathiazar et al 2021	High risk	Low risk	Low risk	Low risk	Low risk	High risk of bias
19	Rajya Lakshmi	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concern

	Mikkili et al 2022						
20	B. Molnar et al 2022	High risk	Low risk	Low risk	Low risk	Low risk	High risk of bias
21	Yesha Haresh Raval et al 2022	Low risk	Low risk	Some concerns	Some concern	Low risk	Some concern
22	Mohamed Mousatafa et al 2022	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk of bias

DISCUSSION

In present systematic review, 22 studies compared recession height and keratinized tissue width, 16 studies compared recession width, 21studies compared mean root coverage (MRC) in the test (xenogenic collagen matrix) and control group. Probing depth and Clinical attachment level showed nearly non-significant results between the test and control group in the included studies.

In the present systematic review **Michael K. McGuire et al 2010** carried out a study on xenogenic collagen matrix, this was the first clinical trial to investigate the efficacy of a xenogeneic collagen matrix as a potential alternative to the gold standard treatment of subepithelial connective tissue graft (CTG) with coronally advanced flap (CAF) for

recession defect coverage. The study assessed both traditional clinical measurement parameters, such as root coverage, probing pocket depth (PPD), and clinical attachment level (CAL), as well as subjective criteria, including color and texture match, pain or discomfort, and esthetics reported by the subjects. The results indicated that at 6 months, CM+CAF achieved an average root coverage of 83.5%, compared to 97% for CTG+CAF, and at 1 year, 88.5% versus 99.3%, respectively. While statistically significant differences were observed, when considering the subjective outcomes reported by the subjects, the use of CM+CAF presented a compelling alternative to the traditional CTG gold standard. The study suggest that using CM+CAF can be a viable and attractive option to using CTG+CAF, particularly when taking into account patient-reported outcomes. CM serves as a suitable substitute for CTG, eliminating the need for harvesting from the palate and providing an easily accessible supply. They found that CM had favorable handling properties, and its thickness was unique compared to other membranes. The study's authors also recommended exploring the effectiveness of using CM to treat multiple teeth, in addition to the single-tooth approach examined in the study.

Aroca et al 2013 carried out a study on xenogenic collagen matrix, in this randomized controlled trial (RCT), the effectiveness of treating Miller Class I and II multiple adjacent gingival recessions (MAGR) using a modified coronally advanced tunnel (MCAT) technique with either a xenogeneic collagen matrix (CM) or connective tissue graft (CTG) found that both treatments resulted in statistically significant root coverage compared to baseline, but the CM treatment had lower complete root coverage (CRC) compared to CTG. In this study, the MRC amounted to 71 ± 21% in the test and 90

±18% in the control group, respectively. In terms of KTW both treatments yielded comparable improvements.

Jepsen K et al 2013 in his study as the primary outcome for efficacy, measured the percentage of root coverage at 6 months, resulting in the test group (CAF + CM) in a higher % RC of 75.29% versus 72.66% in the control group (CAF). The study did not find a significant difference in the percentage of root coverage achieved with the use of CM compared to the control group, it did find a significant increase in gingival thickness and width of keratinized tissue with the use of CM.

Castro Y et al 2014 in his study stated that both techniques were effective in improving clinical treatment of gingival recessions. Differences were not significant for several clinical parameters. Improvement in probing depth, keratinized gingiva and clinical attachment level were similar for both groups. Root coverage percentage seem to be better with the connective graft (24%) than the collagen matrix (16 %). The results of the study also suggested that the use of the matrix is similar to connective grafts when the goal is to increase the gingival biotype with the advantage of avoiding a second intervention site for removal of donor tissue.

D.M.Reino et al 2015 conducted a study which compared PCM with SCTG, it stated that the root coverage obtained after 3 months was superior for the test group (82.33%) compared with the control group (60.78%) Moreover, the test group showed a greater reduction in height and width of the gingival recessions when compared to the control group at 3 and 6 months.

Haydar Barakat et al 2018 carried out a comparative clinical study, it stated that at 6-month follow-up, the results showed no statistical differences in GR reduction in both groups with a mean of 0.17 in the PCM + CAF group and 0.08 in the CTG + CAF group. Regarding RC, the PCM + CAF group experienced a mean of 95.23% at 6 months with a 71% CRC, compared with a mean of 97.84% in the CTG + CAF group with 83% CRC. For PD and CAL parameters, there were no statistical differences between test and control sites and both treatments were statistically significant at 6-month follow-up. Later on **Haydar Barakat et al 2020** conducted A Randomized Clinical Split-Mouth Trial (A 1-Year Follow-Up) and found no statistically significant differences in PD or CAL parameters between the two groups and he stated that CTG + CAF provided better outcomes than PCM + CAF in treating GR type I and II by Miller. However, the difference in WKT gain between the two groups was non-statistically significant. Overall, the study suggested that both techniques can be effective in treating gingival recessions, but CTG + CAF may yield slightly better outcomes in some cases.

GULEK et al 2019 The results of the study indicated that both CTG and XADM are effective treatments for multiple gingival recessions, as evidenced by the Root Coverage data collected at 6 and 18-month intervals in both groups. However, there are notable differences between the control and test groups. Specifically, the control group showed significantly lower RD and stable soft tissue margins at 18-month, whereas the test group experienced soft tissue recession between 6 and 18-month, with positive mean RD changes. These observations suggested that CTG may have an additive effect over XADM in root coverage of multiple defects. The study showed an unexpected outcome, there was an significant increase in PD values observed only in the test group.

Rakasevic et al et al 2020 conducted a study with an objective to assess the clinical outcomes and stability of MAGR treatment at 6 and 12 months post-surgery, by comparing the use of XDM and CTG in conjunction with the MCAT. The study showed a statistically significant enhancement in all assessed clinical parameters for both treatment modalities, when compared to baseline. When comparing the outcomes at 6 and 12 months, MRC slightly decreased at the test sites (MRC). On the other hand, at the control sites, MRC slightly increased from 6 to 12 months. The observed change in MRC (12m − 6 m) was statistically significant between the groups, favoring CTG.

Mauricio et al 2021 study reported that there were no notable differences in mRC, GR, RW, and KTW measurements between the groups at the 6- and 12-month follow-up in this study. CAF + CTG treatment resulted in a slightly higher mRC percentage compared to the CAF + XDM group (91.79% vs. 80.19% at 12 months). The study also showed that the mean increase of KTW obtained did not differ significantly between XDM (0.63 mm) and CTG (0.9 mm). The xenogeneic collagen matrix used in the study was found to modify the gingival phenotype to some degree, albeit to a lesser extent than CTG. However, it has the advantage of not requiring a second surgical site and a shorter operative time.

B. Molnár et al 2022 study aimed to assess the long-term outcomes of MCAT treatment in conjunction with either CM or CTG, for class 1 MAGR. The findings indicated that both graft materials can lead to positive aesthetic outcomes that are sustained over a period of 9 years. However, a noteworthy observation was the statistically significant lower MRC recorded in the lower jaw, as compared to the upper

jaw in the CM-treated group. MRC amounted 23% in the test and 40% in the control group, respectively. Moreover KTW showed only a minor difference that favored the CTG group. **Raval et al 2022** compared the use of XCM and PRF in conjunction with CAF in treating Cairo's RT1 and RT2 gingival recession. The study showed that in the test group (XCM), statistical significance reduction of CAL, RW and RH was observed after 6 months but from Intergroup analysis it was found that at the end of 6 months, there was no difference seen statistically in the test and the control groups for any clinical criteria. The use of PRF or XCM has been found to be as effective as CTG, with no significant difference between the two. **Mohamed Mousatafa et al 2022** study reported that xenogeneic acellular dermal matrix and connective tissue graft showed improvement in all clinical parameters when compared with baseline conditions. Study also reported marked improvement for both the GRD and GRW with values measured at baseline being significantly higher.The study's findings on mean root coverage (MRC) indicated that there was no statistically significant difference between both groups at different intervals. The control group achieved a higher value of MRC at 6 months, but this difference was not statistically significant.

The present systematic review included an evaluation of the risk of bias of the various studies selected for inclusion, in accordance to the Revised Cochrane Risk Bias Tool for Randomized Trials edited by "Julian PT Higgins and their co-authors in 2019" which is more modified and highly considered as RoB2 tool. The majority of studies were rated as "Low risk of bias" i.e. 10 of the included studies. There was lack of information regarding blinding of participants, personnel, outcome assessment, data of missing patients, size and placement of xenogenic collagen matrix, sample size calculation was observed in the studies.

There are certain limitations observed in the included studies:

1. Immunogenicity: Xenogeneic collagen matrix products are derived from animal sources, which may lead to immunological reactions in some patients. This may result in complications, such as inflammation and rejection of the graft.
2. Disease transmission: Although the risk is minimal, xenogeneic collagen matrix products carry a risk of disease transmission from the animal source to humans.
3. Variable quality: The quality of xenogeneic collagen matrix products may vary depending on the animal source and processing methods used. This may affect the clinical outcomes of the treatment.
4. Cost: Xenogeneic collagen matrix products may be more expensive than other grafting materials, such as autogenous grafts or allogeneic grafts.
5. Handling: Xenogeneic collagen matrix products may require special handling and storage conditions to maintain their structural integrity and biological activity.

So, it is imperative that further researchers or dentists should discuss these limitations and evaluate the potential risks and benefits before deciding on the use of xenogeneic collagen matrix products in the treatment of multiple gingival recession cases.

CONCLUSION

Xenogenic collagen matrix in the treatment of multiple adjacent recession can influence several clinical parameters such as RH, RW, KTW, MRC, CAL and PD compared to different soft tissue augmentation methods.

Methodological limitations of the included studies preclude any conclusions regarding efficacy of xenogenic collagen matrix as an primary or secondary mode of option to

different soft tissue augmentation methods for the treatment of multiple adjacent gingival recessions. But this do not specify that xenogenic collagen matrix is not efficacious. Rather it states that there is insufficient data to confirm our conclusion. More number of fine randomised controlled trials are required before recommendations for use of xenogenic collagen matrix can be made. Within the limitations of these studies, present systematic review concludes that xenogeneic collagen matrix is a viable alternative to various soft tissue augmentation techniques for treating multiple adjacent gingival recessions.

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